## Modern day scourge helped ancient Earth escape a deathly deep freeze

***The planet's present day greenhouse scourge, carbon dioxide, may have played a vital role in helping ancient Earth to escape from complete glaciation, say scientists in a paper published online today***

The planet's present day greenhouse scourge, carbon dioxide, may have played a vital role in helping ancient Earth to escape from complete glaciation, say scientists in a paper published online today. In their review for Nature Geoscience, UK scientists claim that the Earth never froze over completely during the Cryogenian Period, about 840 to 635 million years ago.

This is contrary to the Snowball Earth hypothesis, which envisages a fully frozen Earth that was locked in ice for many millions of years as a result of a runaway chain reaction that caused the planet to cool.

What enabled the Earth to escape from a complete freeze is not certain, but the UK scientists in their review point to recent research carried out at the University of Toronto. This speculates that the advancing ice was stalled by the interaction of the physical climate system and the carbon cycle of the ocean, with carbon dioxide playing a key role in insulating the planet.

The Toronto scientists say that as Earth's temperatures cooled, oxygen was drawn into the ocean, where it oxidized organic matter, releasing the greenhouse gas carbon dioxide into the atmosphere.

The review's lead author, Professor Phillip Allen, from Imperial College London's Department of Earth Science and Engineering, says that something must have kept the planet's equatorial oceans from freezing over. He adds: "In the climate change game, carbon dioxide can be both saint and sinner. These days we are so concerned about global warming and the harm that carbon dioxide is doing to our planet. However, approximately 600 million years ago, this greenhouse gas probably saved ancient Earth and its basic life forms from an icy extinction."

Professor Allen, whose previous research has found evidence demonstrating hot and cold cycles in the Cryogenian period, says a plethora of papers has been published and much debate has been devoted to the Snowball Earth theory since it was originally proposed. He says: "Sedimentary rocks deposited during these cold intervals indicate that dynamic glaciers and ice streams continued to deliver large amounts of sediment to open oceans. This evidence contradicts the Snowball Earth theory, which suggests the oceans were frozen over. Yet, many scientists still believe Snowball Earth to be correct."

Professor Allen hopes his review in Nature will prompt climate modellers to realign their thinking about the Cryogenian period and review their models to reflect a warmer Earth during this time. He adds: "There is so much about Earth's ancient past that we don't know enough about. So it is really important that climate modellers get their targets right. They need to build into their calculations a warmer planet, with open oceans, despite lower levels of solar radiation at this time. Otherwise, climate models about the Earth's distant past are aiming for a target that never existed."

*Notes to editors:*

*1. "Sedimentary challenge to Snowball Earth", review article, Nature Geoscience, Sunday 30 November 2008*

*Philip A. Allen1 and James L. Etienne2*

*(1) Department of Earth Science & Engineering, Imperial College London, South Kensington Campus, London SW7 2AZ, UK.*

*(2) Neftex Petroleum Consultants Ltd, 97 Milton Park, Abingdon, Oxfordshire OX14 4RY, UK. Out of hours duty press officer: +44 (0)7803 886 248*

## Claudin 11 stops the leaks in neuronal myelin sheaths

Devaux and Gow demonstrate how a tight junction protein called claudin 11 makes the neuronal myelin sheath a snug fit. The study will be published in the December 1, 2008 issue of the Journal of Cell Biology (www.jcb.org).

Like the rubber coating on a copper wire, the myelin sheath—a membrane extension of glial cells that spirals around the axons of neurons—creates an insulation layer that prevents current leakage from axons and aids electrical conduction along the length of the axon.

Claudin 11 forms tight junctions between successive spiral layers of the myelin sheath, but it was unknown whether it was required for myelin to act as a good insulator. To examine this question, Devaux and Gow compared electrical recordings from the optic nerve of wild-type and claudin 11 knockout mice. They found that although claudin 11 deficiency caused no gross defects in the appearance of the myelin sheath, it slowed electrical signals—at least in neurons with small-diameter axons.

Using a computer model that incorporates the resistive and capacitive properties of axons (and their myelin sheaths), the authors showed that claudin 11 adds to the electrical resistance of myelin by preventing leakage of charged ions (and electrical current) through the spiral space between myelin layers. The reduced resistance in the absence of claudin 11 affects small-diameter axons most severely because such axons have thinner myelin

sheaths and thus less insulation to begin with. Because neurons with small-diameter axons are mostly found in the CNS, the authors speculate that defects in claudin 11 could be associated with deficits in cognition and perception, like those found in schizophrenia or neurodegenerative diseases.
*Devaux, J., and A. Gow. 2008. J. Cell Biol. doi:10.1083/jcb.200808034.*

## Prostate cancer spurs new nerves

Prostate cancer – and perhaps other cancers – promotes the growth of new nerves and the branching axons that carry their messages, a finding associated with more aggressive tumors, said researchers from Baylor College of Medicine in the first report of the phenomenon that appears today in the journal Clinical Cancer Research.

Previous research showed that prostate cancer follows the growth of nerves, but this is the first time that scientists have demonstrated that the tumors actually promote nerve growth.

"This is the first report of this phenomenon," said Dr. Gustavo Ayala, professor of pathology and urology at BCM and first author of the article. "It represents an important new target in prostate cancer treatment, as prostate cancers are more aggressive when neurogenesis is present."

Ayala noted that this finding is comparable to the discovery of angiogenesis or the growth of new blood vessels. Both are part of the wound repair process. "We also believe that axongenesis and neurogenesis is found not only in prostate cancer, but is potentially a more global phenomenon, particularly relating to those cancers that grow along nerve paths," said Ayala, also a researcher in the Dan L. Duncan Cancer Center at BCM.

Ayala and his colleagues studied the neurogenesis in tissue culture, in human tissues of patients who had had prostate cancer and compared to prostate tissues from patients who had died of other ailments. They calculated the density of nerves in human prostate tissues, including those with prostate cancer. They found that nerve density was considerably higher in patients with prostate cancer and in precancerous lesions. As part of the study, he used an entire prostate gland to reconstruct the prostate and enable scientists to see the growth of nerves and axons in three-dimensions, a computerized process that took substantial continuous computer processing.

He and his colleagues have even identified a possible method of regulating the growth of new nerves and axons through a protein called semaphorin 4F. Semaphorins are embryologically active molecules that regulate nerve growth and direction. Most disappear in adults, but semaphoring 4F is active in wound repair. When prostate cancer cells overproduce semaphorin 4F, new nerves result. Blocking semaphoring 4F prevents the growth of new nerves.

*Others who took part in this research include: Hong Dai, Michael Powell, Rile Li, Yi Ding, Thomas M. Wheeler, David Shine, Timothy Thompson, Dov Kadmon, BrianJ. Miles, Michael M. Ittmann and David Rowley, all of BCM. Thompson is now with The University of Texas M.D. Anderson Cancer Center.*
*Funding for this research came from the National Institutes of Health and the Tumor Microenvironment Network of the National Cancer Institute. When the embargo lifts, the full article will be available at http://clincancerres.aacrjournals.org/.*

## Brain waves show sound processing abnormalities in autistic children

CHICAGO – Abnormalities in auditory and language processing may be evaluated in children with autism spectrum disorder by using magnetoencephalography (MEG), according to a study presented today at the annual meeting of the Radiological Society of North America (RSNA).

"Using MEG, we can record the tiny magnetic fields associated with electrical brain activity," said Timothy Roberts, Ph.D., vice chair of research in the Department of Radiology at Children's Hospital of Philadelphia. "Recorded brain waves change with every sensation, thought and activity. It's like watching a movie of the brain in real time."

Typically used for epilepsy evaluation, MEG can also be used to identify timing abnormalities in the brains of patients with autism. "We found that signatures of autism are revealed in the timing of brain activity," Dr. Roberts said. "We see a fraction of a second delay in autistic patients."

Autism is a complex developmental disability that affects approximately one in every 150 American children, mostly boys, according to the Autism Society of America. Autism inhibits the brain functions that govern the development of social and communication skills.

For a MEG exam, a helmet that houses magnetic detectors and looks similar to an old-fashioned hair dryer is lowered over the patient's head while the patient remains in a seated position. The helmet analyzes electrical currents from the brain.

For the study, 64 patients, age six to 15, with a diagnosis of autism spectrum disorder were evaluated with MEG. Audio stimulation was introduced to the children in the form of beeps, tones in pairs, vowels or sentences. Sounds were presented at different frequencies and tone pairs in rapid succession, including unusual streams of incongruous tones and vowels. The results were analyzed and compared with the results from a control group of age-matched non-autistic children.

The findings showed that in the children with autism there was a fraction of a second delay in the brain's response while processing the rapid succession sounds and the unusual streams, giving researchers an insight into the dysfunction of the auditory processing system in autistic children. "This delay in processing certain types and streams of sound may underpin the subsequent language processing and communication impairment seen in autistic children," Dr. Roberts said.

Dr. Roberts predicts that the signatures of autism found in brain activity will become biomarkers to improve classification of the disorder and aid in treatment and therapy planning. "We hope that in the future these signatures will also be revealed in the infant brain to help diagnose autism and allow earlier intervention," he said.

*Co-authors are J. Christopher Edgar, Ph.D., Deborah M. Zarnow, M.D., and Susan E. Levy, M.D.*
*Disclosure: This study was funded by the National Institutes of Health and by the Nancy Lurie Marks Family Foundation.*
*Note: Copies of RSNA 2008 news releases and electronic images will be available online at RSNA.org/press08 beginning Monday, Dec. 1.*

## Antibiotics: Single largest class of drugs causing liver injury

### *Study finds CNS agents also commonly associated with drug-induced liver injury*

Bethesda, MD (Dec. 1, 2008) – Antibiotics are the single largest class of agents that cause idiosyncratic drug-induced liver injury (DILI), reports a new study in Gastroenterology, an official journal of the American Gastroenterological Association (AGA) Institute. DILI is the most common cause of death from acute liver failure and accounts for approximately 13 percent of cases of acute liver failure in the U.S. It is caused by a wide variety of prescription and nonprescription medications, nutritional supplements and herbals.

"DILI is a serious health problem that impacts patients, physicians, government regulators and the pharmaceutical industry," said Naga P. Chalasani, MD, of the Indiana University School of Medicine and lead author of the study. "Further efforts are needed in defining its pathogenesis and developing means for the early detection, accurate diagnosis, prevention and treatment of DILI."

In this prospective, ongoing, multi-center observational study — the largest of its kind — patients with suspected DILI were enrolled based upon predefined criteria and followed for at least six months. Those with acetaminophen liver injury were excluded.

Researchers found that DILI was caused by a single prescription medication in 73 percent of the cases, by dietary supplements in 9 percent and by multiple agents in 18 percent. More than 100 different agents were associated with DILI; antimicrobials (45.5 percent) and central nervous system agents (15 percent) were the most common. Of the dietary supplements causing DILI, compounds that claim to promote weight loss and muscle building accounted for nearly 60 percent of the cases. The study found that at least 20 percent of patients with DILI ingest more than one potentially hepatotoxic agent.

DILI remains a diagnosis of exclusion and thus detailed testing should be performed to exclude competing causes of liver disease; importantly, acute hepatitis C virus (HCV) infection should be carefully excluded in patients with suspected DILI by HCV RNA testing. Researchers found no relationship between gender and severity of DILI, but individuals with diabetes experienced more severe DILI.

*This study is an initial analysis of an ongoing prospective study of DILI. Its primary aim is to develop well-characterized cases of medication-related liver injury on which to conduct hypothesis-driven research targeted at developing means to diagnose, prevent and treat DILI. DILI is the most frequent adverse drug-related event leading to abandonment of potentially promising new drug candidates during pre-clinical or clinical development, failure to achieve drug approval, and withdrawal or restriction of prescription drug use after approval.*
*The Drug-Induced Liver Injury Network is funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and was established in 2003 and will operate through 2013. It consists of eight clinical centers, one data coordinating center and NIDDK investigators. Visit http://dilin.dcri.duke.edu/ to learn more.*

## Fractional dose of scarce meningitis vaccine may be effective in outbreak control

A partial dose of a commonly used vaccine against meningitis may be as effective as a full dose, according to new research published December 2 in the open-access journal PLoS Neglected Tropical Diseases. Fractional dosing would enable large-scale vaccination campaigns during epidemics, especially at a time of global vaccine shortages.

In the study, immune responses in patients receiving smaller doses of a meningitis vaccine were comparable to a full dose. The study's findings contributed to a 2007 WHO recommendation that a fractional dosing strategy be utilized in the context of severe vaccine shortages during a meningitis epidemic.

Meningitis epidemics occur nearly every year across a wide swath of sub-Saharan Africa, dubbed the "Meningitis Belt". Outbreaks are caused by specific bacterial strains (primarily Neisseria meningitidis serogroups A and W135), which current vaccines target. Because of global shortages of meningococcal vaccines, the researchers investigated the use of lower doses.

In a 2004 randomized clinical trial of 750 healthy volunteers (2-19 years old) in Uganda, immune response, assessed by serum bactericidal activity (SBA), was measured for 1/5 and 1/10 doses against a full dose. SBA response and safety/tolerability using 1/5 dose were comparable to full dose for three serogroups (A, Y, W135), though not a fourth (C).

Although another measure of immune response, IgG level, was lower for fractional doses, the aim of mass vaccination during epidemics is short-term protection, which is best measured by SBA.

Because of the lack of vaccine producers and publicly financed vaccine stock, current supplies will likely be insufficient in the case of a large-scale epidemic. Efforts are under way to increase production, but this will not be soon enough if a massive epidemic occurs in the coming months as meningitis season nears. If a large-scale outbreak occurs, WHO will need to quickly advise countries on the fractionate strategy before vaccine supplies run out, the authors say.

"In view of the current shortage of meningococcal vaccines for Africa, the use of 1/5 fractional doses should be considered as an alternative in mass vaccination campaigns," the authors say.

*http://dx.plos.org/10.1371/journal.pntd.0000342 (link will go live on Tuesday, December 2)*

***CITATION**: Guerin PJ, Næss LM, Fogg C, Rosenqvist E, Pinoges L, et al. (2008) Immunogenicity of Fractional Doses of Tetravalent A/C/Y/W135 Meningococcal Polysaccharide Vaccine: Results from a Randomized Non-Inferiority Controlled Trial in Uganda. PLoS Negl Trop Dis 2(12): e342. doi:10.1371/journal.pntd.0000342*

## Lack of vitamin D could spell heart trouble

### *Researchers issue recommendations to screen for and treat vitamin D deficiency*

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

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

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

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

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

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

**Vitamin D Basics**

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

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

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

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

**Treating Vitamin D Deficiency**

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

1. 50,000 IU vitamin D2 or D3every 2 weeks;
2. 1,000 to 2,000 IU vitamin D3 daily;
3. Sunlight exposure for 10 minutes for Caucasian patients (longer for people with increased skin pigmentation) between the hours of 10 a.m. to 3 p.m.

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

## Stanford scientists' discovery of virus in lemur could shed light on AIDS

STANFORD, Calif. — The genome of a squirrel-sized, saucer-eyed lemur from Madagascar may help scientists understand how HIV-like viruses coevolved with primates, according to new research from the Stanford University School of Medicine. The discovery, to be published online on Dec. 1 in the Proceedings of the National Academy of Sciences, could provide insight into why non-human primates don't get AIDS and lead to treatments for humans.

Scientists have long believed that lentiviruses — the family of viruses that includes HIV — started infecting primates within the past million years. In fact, said Rob Gifford, PhD, former postdoctoral researcher in infectious diseases and geographical medicine and lead author of the new study, lentiviruses may have been present in ancestral primates as long as 85 million years ago.

A type of retrovirus, lentiviruses replicate by inserting their RNA into a cell's DNA. Some retroviruses have been known to infect cells that mature into sperm or eggs, incorporating viral DNA into the genome of the host. Until last year, when Gifford discovered Rabbit Endogenous Lentivirus type K among the DNA of the European rabbit, no one knew lentiviruses could be inherited in this way.

"It allows us to put a timeline on the evolution of primate lentiviruses," said Robert Shafer, MD, associate professor (research) of infectious diseases and geographical medicine and senior author of the paper.

Gifford began computer-based screening of the DNA of 21 primates for which at least partial genome sequencing was available. He searched each species for strings of nucleotides that matched the modern lentivirus genome and found one lurking in the DNA of the tiny gray mouse lemur.

Ancestors of the modern lemur colonized Madagascar about 75 million years ago, and since then, lemurs and their lentivirus-carrying African cousins have been evolving separately. Four hundred kilometers of ocean divide the two branches, giving mainland primates limited opportunities to swap germs with lemurs. And the last of the occasional land bridges between the two disappeared beneath the sea 14 million years ago, suggesting that lentiviruses are likely at least that old, say the researchers.

High-end estimates of the age of this lentivirus, called pSIVgml, could range back 85 million years, when the primate family that includes lemurs split from the evolutionary branch that would eventually give rise to monkeys, apes and humans. "Lentiviruses could be very ancient indeed," Gifford said.

Gifford remains cautious about overestimating the virus's age, warning that the virus could have been spread within the last 14 million years by something that could cross the ocean, such as a bat. But Shafer says that sort of cross-species transmission is unlikely, because bats and primates are very distant relatives. The leap from primate to bat and back would be difficult for a lentivirus to make.

Gifford's find suggests lentiviruses could be discovered in other places they've never been seen, like Asian and New World monkeys. "As far as we're aware, nobody's really looked that hard," said Gifford. He is one of few researchers using genome databases to search for retroviruses.

Finding widespread lentivirus-primate interaction might open doors for HIV/AIDS research. Primates infected with the simian version of HIV are protected from developing AIDS by several genes which code for proteins in the immune system that slow or block retroviral reproduction. Previous research suggests these genes evolved in response to millions of years of retrovirus infection.

Until now, scientists thought lentiviruses were too young to have participated in this evolutionary back-and-forth. But if Gifford and his colleagues find more evidence that lentiviruses and primates have been in each other's genetic business for many millions of years, they could turn that assumption on its head. In the process, they might lead the way to a deeper understanding of the evolution of ancient innate immune defenses against retroviruses, which could have implications for HIV treatments or vaccines.

The research "raises a bunch of interesting questions about how mammals have dealt with these types of viruses over a minimum of 14 million years, what kind of defenses they have developed, and why some

mammal species have lost these type of viruses," said Beatrice Hahn, PhD, a professor in the department of medicine at the University of Alabama at Birmingham who studies human retroviruses. She hopes to see more research into the presence of lentiviruses in mammal genomes. "This is molecular archaeology," she said. "There may be a lot of gold in these sequences that hasn't been mined yet."

*Gifford and Shafer collaborated on this study with researchers from the Imperial College of London and the Institute for Emergent Infections at the James Martin 21st Century School at Oxford. The research was supported by the National Institute of Allergy and Infectious Diseases and the James Martin 21st Century School.*

## Test-tube babies profitable business for the state

Increased financial support for IVF fertilization would be downright profitable for the state. Test-tube babies are an investment for the future, not an expense. This is shown by Anders Svensson, who studied this issue in a bachelor's thesis in economics at Lund University School of Economics and Management in Sweden. His article on the subject was recently published in Scandinavian Journal of Public Health (SJPH).

In many countries in Europe, too few children are being born for the population to replace itself. In the future this can entail major problems when it comes to financing health care and pensions, for example. In Greece, Italy, and Spain roughly 1.3 children are born per woman, and in Sweden the figure is 1.88. At the same time, in Sweden, for instance, some 10 percent of all couples are unable to have children for various reasons, even though they wish to.

"Subsidized in vitro fertilization is not a total solution for aging populations, but it is part of a strategy. And it's important to have plan to make Sweden and other countries better able to deal with the future," says Anders Svensson, today a medical student, who is the lead author of the article and who was prompted by a suggestion from the American think tank Rand to look at state-subsidized IVF treatment.

The author of the article points out that there are great regional differences in Sweden today when it comes to how easy it is to get access to county-subsidized in vitro fertilization. Certain county councils will not pay if the couple already has children; some pay for two attempts only, and others for three attempts.

"Actually roughly half of all test-tube fertilizations are paid for out of pocket, which means that only those who can afford it can undergo IVF treatment."

In the longer term the state benefits from subsidizing the costs of test-tube children for couples that are involuntarily childless.

"This is a group that could potentially help boost population growth. Our calculations show that in a long-term perspective in vitro fertilization doesn't cost the state anything at all since the state actually sees a return on its investment in the form of the tax monies the individual will pay during his or her lifetime."

Anders Svensson uses a scenario where every test-tube baby is an average person in terms of longevity and income, for example. The study is based on a net present value calculation, which factors in inflation and other parameters. If the state invests in a test-tube baby today, that investment today is worth SEK 254,000, calculated only on what the individual will pay in income tax and value-added tax – other taxes have not been counted, which means that the state's profit per individual is likely underestimated.

"The effect on the Swedish population curve is comparable to raising state child allowances by 25 percent, but at a lower cost."

In other countries, IVF children are probably even more profitable, since Sweden has a relatively costly welfare system. In a similar calculation based on British conditions, two co-authors of the article in SJPH, Federico Callo, Rand, and Mark Connolly, Global Market Access Solutions, have found that every IVF child yields a profit of GBP 160,069.

"The difference can largely be explained by the fact that schooling, elderly care, and health care are relatively higher costs for the Swedish state than for the UK state. In other words, the Swedish welfare system is more expensive, which reduces the profits," says Anders Svensson.

One third of all inhabitants in Europe will be older than 65 years old in 2050, compared with every sixth person today.

"If we want to maintain our various welfare systems as they look today, we need to reverse the downward population trend, since in the future fewer and fewer working people will be supporting more and more old people."

Increased subsidization would moreover reduce some of the personal suffering that comes from wanting to have children, but not being able to.

"Test-tube fertilization differs from all other medical treatment. It creates life instead of extending life. This is unique," says Anders Svensson.

## New Research Projects Shortage Of General Surgeons By 2010

COLUMBUS, Ohio – In less than two years, there may not be enough surgeons in U.S. hospitals to treat the critically injured or chronically ill.

A new study suggests that the number of available general surgeons, who often perform life-saving operations on patients in emergency rooms, will not keep up with public demand. As the population continues to grow, there will be a shortage of 1,300 general surgeons in 2010. That shortage will worsen each decade, reaching a deficit of 6,000 by 2050.

That means people will have to wait longer for emergency treatment and for elective general surgery, said Thomas E. Williams, co-author of the study and clinical associate professor of surgery at Ohio State University.

The overwhelming costs of obtaining a medical degree are a large deterrent for many young students, despite scholarships and financial aid. The cost of obtaining a medical degree leaves many students with $125,000 to $150,000 in debt after completing medical school.

"People may wait hours in an emergency room if there is a shortage of surgeons. But the problem is that if you're not operated on within a few hours, your disease progresses and that can create more serious problems in other areas of the body. These are problems that you would not have had with prompt surgical attention," said Williams, who is also a retired thoracic and cardiac surgeon.

In emergency rooms, general surgeons are called upon to determine whether or not to operate on a patient. But an increasing number of medical professionals choose to specialize in other fields such as cardiac or orthopedic surgery. So the shortage of general surgeons will directly impact emergency rooms around the country, which rely on general surgeons.

The projections were made based on data from the U.S. Census Bureau and The American Board of Surgery. The data included population statistics and projections, medical school graduation rates, and information on the number of surgeons currently practicing.

The study was published in a recent issue of the journal Surgery. Williams conducted the study with E. Christopher Ellison, professor and chair for the department of surgery at Ohio State. The pair has co-authored a book with fellow Ohio State professor Bhagwan Satiani, entitled "The Coming Surgeon Shortage: Who will fix our hearts, your hip, and deliver our grandchildren?" The book is expected to be released late next year.

The shortage was calculated by taking the difference between the number of retiring surgeons and those entering the workforce. This number is then compared to the expected need for general surgeons. Previous research has shown that 7.53 general surgeons are needed for every 100,000 people to keep the current level of care. The current study shows this number will not be met as early as 2010.

There are about 21,500 general surgeons practicing in the United States today. Each surgeon practices for an estimated 30 years and about 705 surgeons die or leave the workforce every year for personal reasons or retirement. Meanwhile, nearly 1,000 new surgeons enter the workforce each year. But of that number, only 850 will practice general surgery. After accounting for retiring surgeons, that means only 145 new general surgeons will enter the workforce annually, far less than is needed given the continuous rise in the population.

But some authorities have suggested that as many as 600 of these 1000 surgeons are entering other surgical specialties each year, creating an even larger shortage of general surgeons than the current study projects.

"Many doctors today want to specialize in areas such as vascular, colon, or thoracic surgery. They'll train for one or two more years beyond general surgical residency so they have more professional expertise, and probably won't take the general surgery calls in emergency rooms," Williams said. "But if even more surgeons are getting these specialized certificates, the problem will just get worse. We'll see fewer available doctors for patients in the emergency rooms who depend on these general surgical procedures for their care."

Williams estimates that it will cost $62.5 million per year ($750 million total) to train the additional 1,875 general surgeons needed by 2020. Because training is 5 years in duration, each year of training costs approximately $80,000, including salary, benefits, and other direct and indirect costs.

Despite recent attempts to increase the number of medical students and establish new medical schools, there are several barriers standing in the way.

Attracting students to the medical field is a growing problem, Williams said. The overwhelming costs of obtaining a medical degree are a large deterrent for many young students, despite scholarships and financial aid. The cost of obtaining a medical degree leaves many students with $125,000 to $150,000 in debt after completing medical school.

In addition, students required to train as residents are often underpaid for their work, Williams said. The average resident earns between $40,000 and $45,000 per year for three to seven years before they are board-

certified. Compare that to the average salary of a first-year associate at a New York law firm, who will earn $150,000 to $200,000 per year.

The lawyer will typically work on weekdays, with some evening and weekend work when needed. The resident, on the other hand, will work nights, weekends, and uneven hours for up to seven years for lesser pay.

"This lifestyle can serve as a deterrent for many who might otherwise choose surgery. When you are married and have children you need a more predictable schedule. Someone has to take the kids to music lessons or football practice. One of the problems in surgery is that it's often unpredictable and that makes it hard to lead a scheduled lifestyle," he said. "What we need to do is make this profession more attractive through programs to help reduce costs and arranging the 80 hour work weeks to more manageable schedules. Without these changes, we simply won't keep up with the increasing demand."

## Eating eggs when pregnant affects breast cancer in offspring

***New article in the FASEB Journal shows that the 'genetic impact' of a pregnant woman's diet has a profound effect on her child***

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

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

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

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

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

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

## Antarctic islands surpass Galapagos for biodiversity

* 16:05 01 December 2008 **by Tamsin Osborne**

A group of isolated Antarctic islands have proved to be unexpectedly rich in life. The first comprehensive biodiversity survey of the South Orkney Islands, near the tip of the Antarctic Peninsula, has revealed that they are home to more species of sea and land animals than the Galapagos. The findings raise the issue of what sort of impact climate change - already hitting the Antarctic hard - will have on this rich biodiversity.

Researchers from the British Antarctic Survey and the University of Hamburg, Germany, carried out the survey using a combination of trawl nets, sampling as deep as 1500m, and scuba divers. The team found over 1200 species, a third of which were not thought to live in the region. They also identified five new species.

The majority of animals were found in the sea, with most living on the seabed.

These findings go against the traditional view that biodiversity declines away from the tropics and towards the polar regions, says lead researcher David Barnes of the British Antarctic Survey.

"Our paper makes the point that if you go right the way across different animal groups rather than taking one specific animal group, which is what most biodiversity studies do, then you get a much better perspective of

real biodiversity," he says. "This is the first place in either polar region, not just the Antarctic, where we've actually got a biodiversity across all groups."

Previous research has shown that Antarctic waters harbour a surprising diversity of plankton and larvae and that deep-sea life in the Southern Ocean is similarly rich. But the new study is the first to look at all animals on land as well as in the seas. "As the sea gets warmer, then temperate species will move into Antarctica and Antarctic species will shift further south or into colder regions," says Barnes. "The South Orkney Islands is the one place where we have a real possibility of detecting new things arriving and things leaving."

Jon Copley, a marine ecologist at the University of Southampton, UK, agrees. "The starting point for any conservation strategy has got to be knowing what you've got to conserve," he says, "and this study provides a very valuable baseline in that regard."

While biodiversity in this region may not decrease as a result of the warming, says Barnes, it is likely that the changes in species composition will result in an overall loss in the Earth's biodiversity.

"All that it will take is for a few things to alter," says Barnes. "It is only a matter of time."

*Journal reference: Journal of Biogeography, DOI: 10.1111/j.1365-2699.2008.02030.x*

## Delays in Radiation Therapy Lead to Increased Breast Cancer Recurrence

### *One in Five Older Women With Early Breast Cancer Experience Delayed or Incomplete Radiation Treatment*

NEW YORK (Dec. 1, 2008) — A new analysis of the National Cancer Institute's cancer registry has found that as many as one in five older women experience delayed or incomplete radiation treatment following breast-conserving surgery, and that this suboptimal care can lead to worse outcomes.

Dr. Heather Taffet Gold of Weill Cornell Medical College and colleagues found that among a nationally representative sample of nearly 8,000 breast cancer registry patients aged 65 and older, almost 1,300 women experienced delayed radiotherapy and approximately 270 had incomplete radiotherapy. Of these women, those with Stage 1 breast cancer had worse health outcomes associated with this less-than-ideal therapy, while those with a precancerous lesion called ductal carcinoma in situ (DCIS) were not as affected.

"Timeliness of post-surgical radiotherapy is important in reducing the risk of subsequent recurrence or new breast malignancies in patients with early breast cancer. Delaying treatment by eight weeks or more significantly increased the odds for recurrence," says Dr. Gold, the study's lead author and an assistant professor of public health in the Division of Health Policy in the Department of Public Health at Weill Cornell Medical College. "One possible reason for the delays is that the coordination of care can be a challenge as treatment is usually delivered by multiple providers from different specialties, including surgeons, radiation oncologists and medical oncologists."

Stage 1 breast cancer patients with radiation treatment delayed by eight weeks were 1.4 times more likely to have a recurrence or subsequent new primary breast tumor compared with those receiving timely treatment; they also had reduced survival. Patients whose radiotherapy was delayed by 12 weeks or longer were four times more likely to have a recurrence or subsequent new breast tumor. And women who had incomplete radiation treatment for Stage 1 breast cancer — those who underwent fewer than three weeks of the typical five-to-seven-week regimen — had a higher rate of overall mortality, with a 32 percent higher likelihood of death.

The researchers also found treatment disparities in subgroups of older women. "Older black women were more likely to delay radiation treatment, whereas women living in areas with a high concentration of radiation oncologists were less likely to delay. Additionally, older women living in high-poverty areas were less likely to complete radiation treatment," says Dr. Gold.

The work appears in the latest online issue of the journal Cancer and the Dec. 1, 2008, print issue. Research collaborators include Huong T. Do, M.A., and Andrew W. Dick, Ph.D., senior economist at the RAND Corporation in Pittsburgh, Pa.

The study is based on an evaluation of women aged 65 and older diagnosed with either DCIS or Stage 1 breast cancer from 1991 to 1999 and followed through 2002 in registries of the Surveillance, Epidemiology, and End Results (SEER) Program sponsored by the National Cancer Institute.

This nationally representative, population-based study of older women provided a unique opportunity to study the effects of suboptimal treatment in the community setting. "Our findings indicate that radiation treatment should be made easier for all patients to ensure completion and that delays should be minimized. To improve health outcomes following treatment for breast cancer, health care facilities and providers should implement supportive services, such as transportation, and provide educational materials to encourage and ease access to optimal radiation treatment, thereby improving disease-free and overall survival," said Dr. Andrew Dick, senior author on the study.

*The study was supported by a Mentored Research Scholar Grant awarded to Dr. Gold by the American Cancer Society.*

## New medication brings hope of jet lag cure

A team of researchers from Monash University, The Brigham and Women's Hospital (Boston), Harvard Medical School and Vanda Pharmaceuticals has found a new drug with the potential to alleviate jet lag and sleep disorders caused by shift work. Dr Shantha Rajaratnam from Monash University's School of Psychology, Psychiatry and Psychological Medicine said tasimelteon, a drug which acts on melatonin receptors in the brain, could be a highly effective treatment for circadian rhythm sleep disorders. The research was released today in respected publication, The Lancet.

"Our studies show that tasimelteon is able to effectively shift the rhythm of melatonin levels in the body, which are a well-established marker of the human biological clock," Dr Rajaratnam said.

"This drug has the potential to improve the quality and quantity of sleep for patients with transient insomnia caused by jet lag. "Tasimelteon improved a patient's ability to fall asleep and then stay asleep when bedtime was shifted earlier by five hours. "This is the equivalent of travelling eastwards and putting your clock back five hours, such as returning from India to Melbourne, or Dubai to Perth. "About two thirds of all international travellers who cross time zones experience jet lag symptoms, which include disruption of sleep, difficulty getting to and staying asleep, sleepiness during waking hours and gastrointestinal symptoms."

He said the drug could also help those who work at night or early in the morning. "An estimated one in five work outside the regular nine-to-five pattern. In the United states alone it is estimated 19.7 million people start work between 2.30 and 7 am," Dr Rajaratnam said.

"Our work has shown the drug to be highly potent, having the strongest effect when first taken; a single dose treatment was found to be effective for this type of sleep disturbance." The drug is in the later stages of trials and must undergo rigorous testing before being made available to consumers.

## Patient photos spur radiologist empathy and eye for detail

CHICAGO – Including a patient's photo with imaging exam results may enable a more meticulous reading from the radiologist interpreting the images, as well as a more personal and empathetic approach, according to a study presented today at the annual meeting of the Radiological Society of North America (RSNA).

"Our study emphasizes approaching the patient as a human being and not as an anonymous case study," said lead author Yehonatan N. Turner, M.D., radiology resident at Shaare Zedek Medical Center in Jerusalem, Israel.

Many radiologists have limited contact with patients. A referring physician will order imaging exams, such as MRI or computed tomography (CT), and the radiologist interprets the results, never having met the patient. Technological advances have further distanced the radiologist from interaction with the patient. With the advent of teleradiology, radiologists are now able to view images from remote locations via the Internet or satellite.

"We feel it is important to counteract the anonymity that is common in radiologic exams, especially with the growth of teleradiology," Dr. Turner said.

The researchers set out to determine if the addition of a patient's photograph to the file would affect how radiologists interpreted the results.

For the study, 318 patients referred for CT agreed to be photographed prior to the exam. The images of the patients were added to their files in the hospital's picture archiving and communication system (PACS), a network for storage and retrieval of medical images. The photograph appeared automatically when a patient's file was opened.

After interpreting the results of the exams, 15 radiologists were given questionnaires to gather data about their experience. All 15 radiologists admitted feeling more empathy towards the patients after viewing their photos. In addition, the photographs revealed medical information such as suffering or physical signs of disease.

More importantly, the results showed that radiologists provided a more meticulous reading of medical image results when a photo of the patient accompanied the file.

Incidental findings are unexpected abnormalities found on an image that may have health implications beyond the scope of the original exam. In order to assess the effect of the photographs on interpretation, 81 examinations with incidental findings were shown in a blinded fashion to the same radiologists three months later but without the photos. Approximately 80 percent of the radiologic incidental findings reported originally were not reported when the photograph was omitted from the file.

The radiologists involved in the study commented that while the addition of the photo did not lengthen the time spent reading, it was a factor in how meticulously they interpreted the images. All 15 radiologists agreed that the inclusion of a photograph in a patient's file should be adopted into routine practice. The photos can also be included in long-distance teleradiology practices.

"The photos were very helpful both in terms of improving diagnosis and the physicians' own feelings as caregivers," Dr. Turner said. "Down the road, we would like to see photos added to all radiology case files."

*Co-authors are Irith Hadas-Halpern, M.D., and David Raveh, M.D.*
***Note:** Copies of RSNA 2008 news releases and electronic images will be available online at RSNA.org/press08 beginning Monday, Dec. 1.*

## Swapping your body becomes a virtual reality

* 16:09 02 December 2008 **by Helen Thomson**

Ever wanted Arnie's abs or the legs of Julia Roberts? Maybe you'll get the chance to make believe they are your own in future, now that the illusion of "body-swapping" has been successfully created in the lab.

Spooky as it sounds, neuroscientists at the Karolinska Institute in Stockholm, Sweden, were able to use simple camera trickery to fool volunteers into perceiving the bodies of both mannequins and other people as their own.

To create the illusion, scientists fitted two CCTV cameras onto the head of a male mannequin, and sent the output from the cameras to two small screens in front of the subject's eyes. When both the dummy's and subject's heads were tilted downwards, the subject saw the dummy's body where they would normally have seen their own.

When the stomachs of both volunteer and mannequin were stroked simultaneously, the volunteer saw the mannequin's stomach being touched while feeling the corresponding sensation on their own midriff. After two minutes of this, the subject developed a strong sense that the mannequin's body was their own.

"It feels like I'm the mannequin," one volunteer reported. "Wow, this is cool," said another.

***Wearing goggles hooked up to cameras on a mannequin gave the illusion that the mannequin's body was the subject's own* (Credit: Staffan Larsson)**

**Out-of-body experience**

"This shows how easy it is to change the brain's perception of the physical self," says Henrik Ehrsson, research leader in the department of clinical neuroscience, who headed the project. "By manipulating sensory impressions, it's possible to fool the self not only out of its body but into other bodies, too."

The scientists also mounted the camera onto a second person's head in order to test whether subjects could perceive someone else's body as their own. When the two turned to shake each other's hand, the subject perceived the camera-wearer's body as their own, giving the sensory impression of shaking hands with themselves.

The strength of the illusion was further demonstrated when the researchers held a knife to the camera-wearer's arm. By measuring the electrical resistance of the subject's skin, they could detect that the subject's emotions were aroused, showing that the subject experienced the knife as a threat to their own body.

**Man, woman or table?**

Although the illusion was maintained even when the subject was of a different sex to the camera-wearer, it was not possible to fool the subject into identifying with objects such as a box or table.

Nevertheless Kynan Eng, a researcher in neuroinformatics at the University of Zurich, Switzerland, says he suspects that after a stimulus of an appropriate kind and duration, people could "produce measurable ownership responses to any virtual or real object, such as an often-used tool".

"The potential applications of this research and related work include dealing with psychological body-image disturbances such as anorexia, and stroke rehabilitation," says Eng, who recently discovered that it is possible to induce someone's brain to temporarily incorporate a virtual limb into their own body image.

*Journal reference: PLoS ONE, DOI: 10.1371/journal.pone.0003832*

## Mini heart attacks lessen damage from major ones

### *New class of lipids suggests new treatment approach for heart attacks*

Researchers have discovered one potential mechanism by which briefly cutting off, then restoring, blood flow to arteries prior to a heart attack lessens the damage caused, according to a study published today in the journal Cardiovascular Research. The new mechanism points to how future drugs could provide protection ahead of heart attacks and strokes for those at highest risk. In the nearer term, the work may help to prevent damage caused as U.S. heart surgeons temporarily cut off blood flow 450,000 times each year to perform coronary artery bypass graft surgeries. Lastly, the discoveries hold clues to the value of the Mediterranean diet beyond red wine.

In severely diseased coronary arteries, fatty deposits in blood vessel walls become more likely to rupture, which releases proteins into the blood that cause blood clots and cut off blood flow. When a vessel becomes completely blocked (ischemia) the downstream tissue begins to die for lack of oxygen and nutrients. Worse yet, when blood flow is restored (reperfusion), the returning blood throws off cellular chemistry, creating as a side-product a burst of highly reactive "free radicals" that tear apart cell components and cause cells to self-destruct. Later in the process, the immune system attacks the cardiac tissue damaged by ischemia and reperfusion, causing inflammation which can lead to heart failure.

In 1986 then medical student Chuck Murry at Duke University first described a technique called ischemic preconditioning (IPC), which quickly cuts off then restores blood flow to the heart. He found that IPC somehow protected heart tissue against the damage caused by subsequent, prolonged blood vessel blockages. An emerging theory holds that this natural early warning system of IPC has evolved to protect against heart attack. Labs worldwide are seeking to re-create or strengthen this natural protection against ischemia/reperfusion (IR) injury. In the current study, researchers for the first time determined that IPC caused more of a key molecule, nitro-linoleic acid (LNO2), to be made in ischemic cells.

"LNO2 appears to be important in the mechanism by which IPC triggers the body's natural defense mechanisms against heart attack before the major attack comes," said Paul S. Brookes, Ph.D., associate professor of Anesthesiology and of Pharmacology and Physiology at the University of Rochester Medical Center. "Obviously, this natural response, when it follows a major heart attack, is often too little too late. Our hope is that boosting the effect in patients at high risk, perhaps by administering LNO2 beforehand, will reduce heart attack damage in the future. Even sooner, we may be able dramatically reduce reperfusion injury suffered in surgical settings."

**Study Details**

Going into the study, the mechanisms underlying IPC protection were controversial, but a consensus had emerged recently that mitochondria were involved. The cell's powerhouse, mitochondria use oxygen to convert nutrients into cellular energy supply.

As they do so, they create a gradient of protons across their membranes. When the gradient becomes too large, it triggers the mitochondria to use oxygen to generate free radicals. The problem gets much worse when blood returns to a vessel after a blockage, bringing with it a surge of oxygen and nutrients.

It has long been thought that a group of proteins in the mitochondrial membrane act as a "safety valve" by dissipating too large proton gradients when necessary, which slows free radical generation. The current study identified a novel mechanism involving LNO2, by which IPC turns on this safety valve.

Given their results, the authors propose the following protective mechanism: temporary ischemia causes the generation of nitrated lipids inside the mitochondria via currently unknown mechanisms involving metabolites of the gas nitric oxide (NO). These lipids, including LNO2, then become attached to two proteins – adenine nucleotide translocase and uncoupling protein 2 – changing their shape such that they allow a proton leak across the mitochondrial membrane. The leak lowers the proton gradient just enough to lessen free radical production.

While the current study only looked at the immediate effects of LNO2 treatment, the literature suggests that LNO2 also limits the misplaced immune response seen after reperfusion, suggesting a dual treatment effect. Past studies found that LNO2 inhibits Nfkappa B, a protein known to switch on genes that drive inflammation. LNO2 also activates peroxisome proliferator activated receptor gamma and heme oxygenase 1, both of which block inflammation.

The major finding of the study is that LNO2 is formed naturally in mitochondria during IPC in an isolated rat heart, and that adding extra LNO2 protects heart muscle cells from IR injury. The team measured the ability of isolated rat heart cells to survive ischemia using a dye that the live cells keep out, but that dead cells take in. That enabled researchers to count how many cells survived with and without LNO2 added.

In normal cells following ischemia 70 percent died, but for those receiving extra LNO2 (0.5 micromolar), only 30 percent died. The amount of the LNO2 added was not much more than naturally occurs, suggesting its effect is "extremely potent," researchers said. The LNO2-related proton leak also occurs at the protein level within seconds, a vital quality of any future therapy, considering that IR injury greatly increases with each second it is allowed to proceed.

Brookes is part of the Mitochondrial Research & Innovation Group (MRIG) at the Medical Center, which last year reported in the Journal of Molecular and Cellular Cardiology on the design and testing of a series of patented nitric oxide donors that break down and release NO only within the mitochondria, and protect the heart from ischemia. The team believes these NO donors may work in part by increasing LNO2 supply. In the acute setting, such drugs may offer an advantage over standard nitric oxide donors like nitroglycerin, which increase

blood flow in diseased arteries by causing them to dilate throughout the body. Standard NO donors also depress cardiac function by decreasing the pressure of blood returning from the body back into the heart. Early tests in a mouse model have confirmed that the new MRIG NO donor drugs are cardioprotective in-vivo, and do not cause system-wide vessel dilation side effects.

Bruce Freeman, Ph.D., chair of the Department of Pharmacology & Chemical Biology at the University of Pittsburgh School of Medicine, also led the study. Other contributors included postdoctoral fellow Sergiy Nadtochiy, Ph.D. in Rochester, and Paul Baker, Ph.D. research assistant professor in Pittsburgh.

"Our interest in this area stems from the fact that many different stimuli appear to funnel down into the mitochondria where they may trigger LNO2 production, any of which may suggest a new way to prevent damage," Freeman said. "Along with IPC, olive oil has been shown to produce LNO2 in the stomach, offering an explanation for the value of the Mediterranean diet."

## New test for depression

A new universal test to predict the risk of someone succumbing to major depression has been developed by UCL (University College London) researchers. The online tool, predictD, could eventually be used by family doctors and local clinics to identify those at risk of depression for whom prevention might be most useful.

The risk algorithm, developed by a team led by UCL Professors Michael King and Irwin Nazareth, was tested in 6,000 people visiting their family doctor in six countries in Europe (UK, Spain, Portugal, the Netherlands, Slovenia and Estonia). Its accuracy was also tested in nearly 3,000 GP attendees in a further country, Chile, in South America. The study, published in the Archives of General Psychiatry, followed-up the participants at six and 12 months. The team modelled their approach on risk indices for heart disease, which provide a percentage risk estimate over a given time period. The algorithm was as accurate at predicting future episodes of depression as similar instruments developed in Europe to predict future risk of heart problems.

A website has been set up for the risk algorithm, at **http://www.ucl.ac.uk/predict-depression/**

Further testing of the tool as an early detector of depression is planned in randomised trials of prevention in Europe. The team are also exploring the feasibility of using the instrument in China, with plans to set up a study on the prediction of depression in a Chinese community setting. This would be the first ever research initiative of its kind within Asia.

Professor Michael King, UCL Department of Mental Health Sciences, says: “Depression is a common problem throughout the world, but although we know how to treat it, we know very little about how to prevent its onset. We have ways of predicting the onset of heart disease or stroke, but none for predicting people’s risk of major depression. Our study is one of the first to develop a risk algorithm for just this purpose.”

“Risk tools such as ours are needed to focus more effort on preventing depression. For example, people identified as at risk by an online tool could be flagged on a GP’s computer. Recognition of those at risk could help with watchful waiting or active support, such as restarting treatment in patients with a history of depression. Patients could also be advised on the nature of depression or on cognitive behaviour therapies to help reduce their risk of developing major depression.”

“Major depression is now a leading cause of illness and disability world-wide and reducing its prevalence is one of the greatest public health challenges of the twenty-first century. Depression will rank second to cardiovascular disease as a global cause of disability by 2020. Up to a quarter of people who visit their doctor experience major depression, with relapses frequently occurring for up to 10 years.”

“The next stage of our research will be to establish how GPs could use our tool to help prevent the onset of depression. We are hoping to run a large-scale trial to explore the tool’s use in prevention.”

***Notes for Editors***

*1. For more information, please contact Professor Michael King on tel: +44 (0)20 7830 2397, email m.king@medsch.ucl.ac.uk.*
*2. Alternatively, please contact Jenny Gimpel in the UCL Media Relations Office on tel: +44 (0)20 7679 9726, mobile: +44 (0)7747 565 056, out of hours +44 (0)7917 271 364, e-mail: j.gimpel@ucl.ac.uk.*
*3. ‘Development and validation of an international risk prediction algorithm for episodes of major depression in general practice attendees’, by Michael King et al., is published in the December issue of the Archives of General Psychiatry at http://archpsyc.ama-assn.org/. Copies of the paper can also be obtained from the UCL Media Relations Office.*
*4. This study was funded by the European Commission.*

## Memories may be stored on your DNA

* 02 December 2008 **by Devin Powell**, Washington DC

REMEMBER your first kiss? Experiments in mice suggest that patterns of chemical "caps" on our DNA may be responsible for preserving such memories.

To remember a particular event, a specific sequence of neurons must fire at just the right time. For this to happen, neurons must be connected in a certain way by chemical junctions called synapses. But how they last over decades, given that proteins in the brain, including those that form synapses, are destroyed and replaced constantly, is a mystery.

Now Courtney Miller and David Sweatt of the University of Alabama in Birmingham say that long-term memories may be preserved by a process called DNA methylation - the addition of chemical caps called methyl groups onto our DNA.

Many genes are already coated with methyl groups. When a cell divides, this "cellular memory" is passed on and tells the new cell what type it is - a kidney cell, for example. Miller and Sweatt argue that in neurons, methyl groups also help to control the exact pattern of protein expression needed to maintain the synapses that make up memories.

***Could memories be stored by making modifications to your DNA?*** **(Image: flaivoloka, stock.xchng)**

They started by looking at short-term memories. When caged mice are given a small electric shock, they normally freeze in fear when returned to the cage. However, then injecting them with a drug to inhibit methylation seemed to erase any memory of the shock. The researchers also showed that in untreated mice, gene methylation changed rapidly in the hippocampus region of the brain for an hour following the shock. But a day later, it had returned to normal, suggesting that methylation was involved in creating short-term memories in the hippocampus (Neuron, DOI: 10.1016/j.neuron.2007.02.022).

To see whether methylation plays a part in the formation of long-term memories, Miller and Sweatt repeated the experiment, this time looking at the uppermost layers of the brain, called the cortex.

They found that a day after the shock, methyl groups were being removed from a gene called calcineurin and added to another gene. Because the exact pattern of methylation eventually stabilised and then stayed constant for seven days, when the experiment ended, the researchers say the methyl changes may be anchoring the memory of the shock into long-term memory, not just controlling a process involved in memory formation.

"We think we're seeing short-term memories forming in the hippocampus and slowly turning into long-term memories in the cortex," says Miller, who presented the results last week at the Society for Neuroscience meeting in Washington DC.

"The cool idea here is that the brain could be borrowing a form of cellular memory from developmental biology to use for what we think of as memory," says Marcelo Wood, who researches long-term memory at the University of California, Irvine.

## Is Empty Nest Best? Changes in Marital Satisfaction in Late Middle Age

The phrase “empty nest” can conjure up images of sad and lonely parents sitting at home, twiddling their thumbs, waiting for their children to call or visit. However, a new study, reported in Psychological Science, a journal of the Association for Psychological Science, suggests that an empty nest may have beneficial effects on the parents’ marriage.

University of California, Berkeley psychologists Sara M. Gorchoff, Oliver P. John and Ravenna Helson tracked the marital satisfaction of a group of women over 18 years, from the time they were in their 40s to when they were in their early 60s.

The results of this study revealed that marital satisfaction increased as the women got older. Marital satisfaction increased for women who stayed with the same partners and for women who remarried.

What was most striking about the results was that women who had made the transition to an empty nest increased more in marital satisfaction than women who still had children at home. Even more interesting, it was shown that an empty nest does not increase levels of marital satisfaction simply because the parents have more time to spend with each other. Instead the results suggest that women whose children had left home enjoyed their time with their partners more compared to women whose children were still at home. In other words, it was an increase in the quality, and not the quantity, of time spent together once children moved out, that led to increases in marital satisfaction.

Gorchoff is quick to point out that the results do not suggest that all children should be sent away to boarding school for the sake of their parents’ marriage. Rather, she notes that “this research does suggest that women should not wait until their children leave home to schedule enjoyable time with their partners.”

*For more information about this study, please contact: Sara M. Gorchoff (gorchoff@berkeley.edu)*
*Psychological Science is ranked among the top 10 general psychology journals for impact by the Institute for Scientific Information. For a copy of the article "Contextualizing Change in Marital Satisfaction During Middle Age: An 18 Year*

*Longitudinal Study" and access to other Psychological Science research findings, please contact Barbara Isanski at 202-293-9300 or bisanski@psychologicalscience.org.*

## Old as you want to be: Study finds most seniors feel younger

ANN ARBOR, Mich.---Older people tend to feel about 13 years younger than their chronological age.

That is one of the findings of a study forthcoming in the Journals of Gerontology: Psychological Science. The researchers analyzed the responses of 516 men and women age 70 and older who participated in the Berlin Aging Study, tracking how their perceptions about age and their satisfaction with aging changed over a six-year period.

"People generally felt quite a bit younger than they actually were, and they also showed relatively high levels of satisfaction with aging over the time period studied," said Jacqui Smith, a psychologist at the University of Michigan Institute for Social Research (ISR). Smith conducted the study with colleagues Anna Kleinspehn-Ammerlahn and Dana Kotter-Gruehn at the Max Planck Institute for Human Development in Berlin.

"We examined individual changes over time, and expected the gap to increase. But we were surprised to find that it was maintained, on average. Perhaps feeling about 13 years younger is an optimal illusion in old age," Smith said.

Smith and colleagues found that some of the oldest participants did feel even younger over time. But poor health reduced the gap between felt age and actual age.

The researchers also assessed how old people thought they looked, asking them: "How old do you feel when you look at yourself in a mirror?" They responded by selecting an age on a scale that ranged from 0 to 120 years. In general, at the start of the study people said they looked about 10 years younger than they were. By the end of the study, this gap had narrowed; people felt they looked only about seven years younger than their chronological age.

In general, women perceived their appearance as being closer to their actual age, Smith said. "Women saw themselves as about four years older than their male peers," she said. "There are several likely reasons for this gender gap in subjective physical age. One is that women may be more aware of their appearance than men, especially given the negative stereotypes of older bodies."

To assess satisfaction with aging, researchers asked participants to what extent they agreed with these five statements: "Things keep getting worse as I get older;" "I have as much pep as I had last year;" "As I get older, I am less useful;" "As I get older, things are better than I thought they would be;" and "I am as happy now as I was when I was younger."

Initially, men were more satisfied than women with their own aging. But over the six-year period studied, men's satisfaction decreased more than women's. Poor health magnified these patterns, Smith said.

According to Smith, examining changes in how people feel about the aging process in old age can provide important indicators about the resilience and vitality of the older self. In unpublished research based on the Berlin Aging Study, she and colleagues have found that people who feel younger are less likely to die than those who don't, given the same level of chronological age and equivalent physical health.

"Feeling positive about getting older may well be associated with remaining active and experiencing better health in old age," she said. "Thus, studies on self-perceptions of aging can contribute to our understanding of potential indicators of resilience in older adults and the aging self."

*Related Links: Jacqui Smith: http://www.rcgd.isr.umich.edu/people/smith.html*
*Institute for Social Research (ISR): www.isr.umich.edu*
*ISR Psychosocial Aging Group: http://sites.isr.umich.edu/psychosocial-aging*
*Berlin Aging Study: http://www.base-berlin.mpg.de/*

## Vaccine and drug research aimed at ticks and mosquitoes to prevent disease transmission

### *Research to be presented in December at the ASTMH annual meeting*

Most successful vaccines and drugs rely on protecting humans or animals by blocking certain bacteria from growing in their systems. But, a new theory actually hopes to take stopping infectious diseases such as West Nile virus and Malaria to the next level by disabling insects from transmitting these viruses. Research to be presented at the 57th American Society of Tropical Medicine and Hygiene (ASTMH) annual meeting in New Orleans, explains how vaccines and drugs may not only be able to stop disease transmission, but also prematurely kill the vectors carrying these diseases; such vectors include ticks, sand flies and mosquitoes – the insects responsible for most deaths world wide.

"In order to successfully slow the transmission rate of these potentially fatal diseases, we need to reduce the lifespan of the vector, or block them from becoming infected in the first place," explains Brian Foy, Ph.D., at Colorado State University. "One of our goals is to curtail the spread of mosquito-borne diseases through

strategic use of compounds, known as endectocides, to target hosts. This new strategy will make blood meals from humans lethal to mosquitoes so they die before they can transmit a disease." Endectocides are currently mass administered to human populations to control the worm parasites that cause river blindness and are widely used in animals for worm control.

Professor Foy says that thanks to new technologies using genomics, scientists can now sift through vector genomes to more quickly and accurately find protein targets, which can then aid in the development of more specified drugs and vaccines.

A vaccine developed using functional genomics is already in early stages for cattle, whose production is greatly affected by tick-borne diseases. Katherine Kocan, Ph.D., at Oklahoma State University, concentrates her research on tick vaccines and anaplasmosis, a tick-transmitted disease of cattle that infects the red blood cells, causing mild to severe anemia and often death. "Even if the cow doesn't die," explains Professor Kocan, "the bacteria serve as a continued source of infection for cows and ticks. We are working on a vaccine to target tick-protective genes, so when ticks feed on immunized cattle, the vaccine antibodies interfere directly with the biology of the tick and its feeding pattern which results in reduced tick populations." The vaccine model being developed for cattle, which we call a dual target vaccine approach because both ticks and tick-borne pathogens are targeted, will likely be applicable to other ticks and the bacteria that they transmit.

According to Professor Foy, this theory of vaccine and drug development would offer many advantages over currently-used mosquito and tick-borne disease control measures: it would be more targeted than environmental spraying of insecticides; proper application would kill older frequently-biting insects and interrupt disease transmission; resistance would be slower to develop; and there may be little cross-resistance from agricultural applications.

## 'Test and treat everyone' to vanquish HIV

TO CRUSH the virus, test everyone for HIV and treat those who have it immediately.
That's the conclusion of Charles Gilks of the World Health Organization, and his colleagues, who calculated the impact that such action would have in South Africa, which has a very high prevalence of HIV. They worked out that treating everyone with the virus with antiretroviral drugs would reduce incidence from 20 per 1000 people to just 1 per 1000 within 10 years (The Lancet, DOI: 10.1016/S0140-6736(08)61697-9). That's because the drugs keep levels of the virus in the blood down, making people less infectious - even if they have unsafe sex.

Although giving these drugs to vastly more people would initially be very expensive, Gilks calculates that within 20 years, the costs would be less than continuing with the existing strategy of only treating people who already have symptoms, as many more people would have HIV by that time.

The strategy would have the most impact in the developing world, where prevention is geared towards safe sex and circumcisions, rather than expensive drugs.

## Deep-voiced men not guaranteed to impress

* 00:01 03 December 2008 **by Ewen Callaway**

Women might swoon over Barry White's deep bass, yet when looking for a provider, they find Justin Timberlake's falsetto sounds sexier.

A new study among African hunter-gatherers found that women who were nursing a child prefer higher-pitched male voices than fertile women who had not recently given birth.

The Hadza - hunter-gatherers native to northern Tanzania - have limited exposure to the mass media. Cut off from the daily bombardment of advertisements, pop songs and newscasts that's typical in much of the world, they were an ideal population in which to study innate sexual preferences, says Coren Apicella, an anthropologist at Harvard University and leader of the study.

"They're also an evolutionarily relevant population - they live like we lived 200,000 years ago," she says. "Most of our psychological preferences probably evolved when we were hunter-gatherers."

For her dissertation, Apicella spent six months studying vocal preferences among Hadza men and women. In a previous study, she and colleagues found that deep-voiced men sire more children than tenors.

**Can he hunt with that voice?**

In the new study, she tested the vocal preferences of 88 Hadza men and women. They heard a member of the opposite sex saying the Swahili word "hujambo" - loosely translated as hello - in a computer-altered high and low register. Women were asked whether the voice belonged to someone likely to make a good hunter and husband, while men rated the voices in terms of skill as a forager and suitability as a wife.

Hadza men judged deeper-voiced women to be better foragers, but they fancied the highest-pitched women, Apicella found. Women judged Barry Whites to be better hunters, but offered no clear preference for what a husband should sound like.

When she started analysing the data, Apicella realized that about half the women she tested had been nursing children. When she divided women by this characteristic, a trend emerged. Nursing women favoured higher-pitched tones, while fertile women showed a slight preference for the deeper voices.

When Hadza women start breast-feeding, their foraging falls off. "They rely on men a lot more to bring in food and resources," says Apicella. "Maybe a higher-pitched voice is signalling pro-social behaviour."

Explaining why men develop deep voices after puberty is a long-standing evolutionary puzzle, says David Puts, an anthropologist at Pennsylvania State University in University Park, who commends Apicella for reaching beyond the typical study group of university students.

"It's really important to do this sort of research on foraging cultures [and] non-Western cultures," he says. However, Puts thinks that deeper voices might be more important for asserting dominance than wooing females. Experimental alterations in male voice pitch affect male perceptions far more than those of females, he has found. "It makes a guy look like he could win fights, and it makes him a little bit more attractive to women."

*Journal reference: Proceedings of the Royal Society B (DOI: 10.1098/rspb.2008.1542)*

## A New Picture of the Early Earth

**By KENNETH CHANG**

The first 700 million years of Earth's 4.5-billion-year existence are known as the Hadean period, after Hades, or, to shed the ancient Greek name, Hell.

That name seemed to fit with the common perception that the young Earth was a hot, dry, desolate landscape interspersed with seas of magma and inhospitable for life. Even if some organism had somehow popped into existence, the old story went, surely it would soon have been extinguished in the firestorm of one of the giant meteorites that slammed into the Earth when the young solar system was still crowded with debris.

***AGES AGO** Analyses of crystals in rocks in Australia, left, have formed a new picture of the early Earth, depicted with young oceans in the painting at right.* **Left, Bruce Watson; right, Don Dixon**

Scars on the surface of the Moon record a hail of impacts during what is called the Late Heavy Bombardment. The Earth would have received an even more intense bombardment, and the common thinking until recently was that life could not have emerged on Earth until the bombardment eased about 3.85 billion years ago.

Norman H. Sleep, a professor of geophysics at Stanford, recalled that in 1986 he submitted a paper that calculated the probability of life surviving one of the giant, early impacts. It was summarily rejected because a reviewer said that obviously nothing could have lived then.

That is no longer thought to be true.

"We thought we knew something we didn't," said T. Mark Harrison, a professor of geochemistry at the University of California, Los Angeles. In hindsight the evidence was just not there. And new evidence has suggested a new view of the early Earth.

Over the last decade, the mineralogical analysis of small hardy crystals known as zircons embedded in old Australian rocks has painted a picture of the Hadean period "completely inconsistent with this myth we made up," Dr. Harrison said.

Geologists now almost universally agree that by 4.2 billion years ago, the Earth was a pretty placid place, with both land and oceans. Instead of hellishly hot, it may have frozen over. Because the young Sun put out 30 percent less energy than it does today, temperatures on Earth might have been cold enough for parts of the surface to have been covered by expanses of ice.

In a new analysis, published in the current issue of the journal Nature, the zircons, the only bits of earth older than 4 billion years definitively known to have survived, provide another tantalizing hint about the Hadean period. Dr. Harrison and two U.C.L.A. colleagues, Michelle Hopkins, a graduate student, and Craig Manning, a professor of geology and geochemistry, report that minerals trapped inside zircons offer evidence that the processes of plate tectonics — the forces that push around the planet's outer crust, forming and shaping the continents and oceans — had already begun.

"The picture that's emerging is a watery world with normal rock recycling processes," said Stephen J. Mojzsis, a professor of geology at the University of Colorado who was not involved with the U.C.L.A. research. "And that's a comforting thought for the origin of life."

With the old views of the Hadean period, the origin of life on Earth posed a huge problem. The earliest, and still debated, evidence for life lies within rocks in Greenland dated at 3.83 billion years. The rocks show a shift in the relative amounts of carbon-12, the usual form of carbon, and carbon-13, a less common but stable form of carbon. That shift was attributed to the presence of microorganisms, which would tend to concentrate the lighter carbon.

What was surprising, perhaps unbelievable, in the old views was that life started immediately at the end of the Late Heavy Bombardment, seemingly showing up the instant that it was possible.

In the new view of the early Earth, life could have emerged hundreds of millions of years earlier. "This means the door is open for a long, slow chemical evolution," Dr. Mojzsis said. "The stage was set for life probably 4.4 billion years ago, but I don't know if the actors were present."

The revolution in early Earth studies comes largely from rocks in western Australia. The rocks are three billion years old, but they contain zircons that are older. Zircons, made primarily of the elements zirconium, oxygen and silicon, are extremely hard and durable and can survive conditions that erode, melt or otherwise transform the rock around them.

The zircons also contain enough uranium that they can be precisely dated by the decay of that uranium. In 2001, two groups, one led by Dr. Harrison and the other by John W. Valley of the University of Wisconsin, reported that the Australian zircons formed during the Hadean period as long ago as 4.4 billion years and were later embedded in the younger, 3-billion-year-old rocks.

The relative amounts of oxygen isotopes in the zircons points to the presence of water. Minerals like clays and carbonates that form in water prefer to incorporate oxygen-18 into their crystal structure, and the zircons contain relatively high levels of oxygen-18 compared to the more common oxygen-16.

In the U.C.L.A. study, the researchers studied tiny mineral grains trapped inside the zircons between 4 billion and 4.2 billion years ago as they were being formed. From the mix of elements they identified in the minerals, the scientists could calculate the depth and temperature at which the zircons crystallized — 1,300 degrees Fahrenheit at a depth of 15 miles — and the calculations showed a flow of heat coming out of that part of the Earth of 75 milliwatts per square meter.

That is too cool. The Earth during the Hadean period may not have been hellish, but it was hotter than today, and the heat flow should have been about three times the amount that was calculated.

That meant the zircons formed in a cool part of the crust. On Earth today, one such place is a subduction zone, where an ocean plate slides under a continental plate and is pushed into the mantle. The waterlogged ocean plate then melts at relatively low temperatures. The U.C.L.A. scientists believe that the high water content and the low temperatures inferred from the zircons thus point to the existence of such a subduction zone. And a subduction zone could not have existed unless some type of plate tectonics was already at work.

"It's not a smoking gun," Dr. Harrison said. "But we're left without any other plausible explanation."

Many geologists believe that the crust was too thin or the interior too hot for plate tectonics to occur back then. Neither Venus nor Mars shows obvious signs of plate tectonics, past or present, suggesting that only a limited range of planetary temperature and structure give rise to the phenomenon.

Dr. Sleep of Stanford said of the U.C.L.A. findings: "It may well be a subduction zone. It looks like a subduction zone."

Dr. Valley has also concluded the Earth became cool and watery early in its history, but remains skeptical about the inferences about plate tectonics.

"To me, it's not ruled out by anything," he said, "but it's far from proven with the certainty that Mark states it." Dr. Valley said it was possible that some of the elements measured by the U.C.L.A. researchers might have infiltrated the zircons through tiny cracks.

If plate tectonics were overturning the Earth's crust during the Hadean period, it would have shaped not just the land forms, but also the air and the climate.

In the 1980s, a climate model proposed a thick atmosphere of heat-trapping carbon dioxide, raising the average surface temperature to 185 degrees Fahrenheit, not quite boiling.

But if plate tectonics had already begun, much of the carbon dioxide would be trapped in carbonate rocks and then pushed into Earth's interior. In 2001, a climate model by Dr. Sleep and Kevin Zahnle of the NASA Ames Research Center found that the late Hadean Earth then would have been somewhat chilly.

Neither near-boiling temperatures nor the chilly conditions make life impossible, but these factors could change ideas about how and when life started.

Earth, like the other planets, coalesced more than 4.5 billion years ago. It is commonly hypothesized that almost immediately, a Mars-size object about 4,000 miles wide hit it — a true cataclysm that vaporized much of the object and Earth. Some of the debris ejected into orbit became the Moon. The molten Earth cooled quickly, probably within a few million years, and nothing that large ever struck again.

Dr. Sleep said his calculations suggested that during the 700 million years of the Hadean period about 15 objects 100 miles wide or wider hit the Earth. About four of the objects were wider than 200 miles, and those collisions would have been violent enough to boil off most of the oceans. (By contrast, the more recent object that hit the Earth 65 million years ago and helped kill off the dinosaurs was about 6 miles wide.)

But in numerical simulations that will be presented this month at a meeting of the American Geophysical Union in San Francisco, Dr. Mojzsis and Oleg Abramov, a postdoctoral researcher at the University of Colorado, show that the Late Heavy Bombardment impacts were not quite as lethal as had been thought.

"Things are hurt really bad," Dr. Mojzsis said. But the computer calculations indicated that even rocks up to 300 miles wide would not kill everything, that pockets would exist where organisms that thrive in high-temperature environments like hydrothermal vents could survive.

Genetic studies of current life support that notion, pointing to an organism that lived in a high-temperature environment as the last common ancestor. That does not mean that life started there, but that is almost certainly where survivors of the giant impacts would have huddled.

For the question of whether life existed during the Hadean period, researchers would like to find carbon and then perform an isotope analysis similar to what was done with the Greenland rocks. Despite analyzing 160,000 grain-size zircons, the U.C.L.A. researchers have not found carbon. (Another group has reported the presence of small diamonds, but that has not been confirmed.)

The search for more substantial amounts of Hadean rock also continues. Three months ago, researchers reported that a swath of bedrock in northern Quebec might be 4.28 billion years old, which would provide a mother lode of material to study. That bedrock includes intriguing structures known as banded iron formations, which are believed to occur only with the help of living organisms. But other scientists have questioned the age of the rocks, suggesting that they may really be 3.8 billion years old.

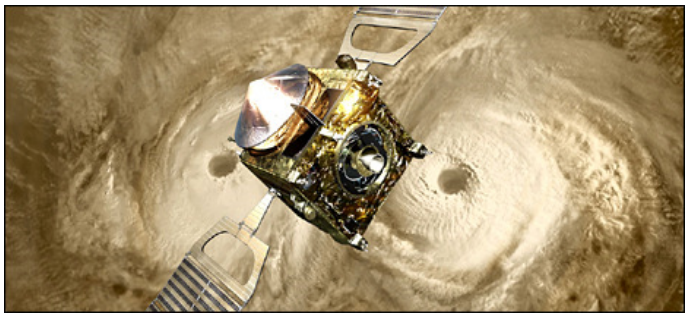
Dr. Mojzsis said "Hadean" might not be a misleading name for the earliest eon of Earth's history, after all. The ancient Greek concept of hell was not one of fire and brimstone. "In Greek mythology, Hades was a dark, cold, mysterious place," he said. "It seems to me the Hadean is living up to that moniker."

## Venus ultraviolet puzzle 'solved'

**By Paul Rincon** Science Reporter, BBC News

One of the many mysteries of Earth's nearest planetary neighbour Venus has been cracked, Nature journal reports.

Scientists have long puzzled over conspicuous patches in the Venusian clouds that appear dark at ultraviolet (UV) light wavelengths. They now think these are solid particles or liquid droplets that get transported from deep in the atmosphere up to the planet's cloud tops. But a riddle remains: scientists still don't know what they are made up of.



***Venus Express has been studying our near neighbour since 2006***

The features are distributed within the thick clouds of sulphuric acid and sulphur dioxide that shroud the hothouse planet. "These (UV features) have been observed since 1929. We see them in images from the Pioneer Venus probe and in ground-based observations," said Dr Dmitri Titov, from the Max Planck Institute for Solar System Research in Germany.

It had previously been unclear whether these were caused by differences in the height of the cloud tops, temperature differences or variation in composition of the clouds.

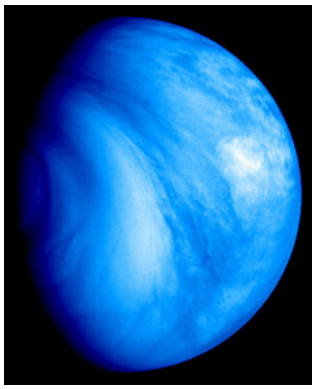
**Darkness and light**

Data from the European Space Agency (Esa) spacecraft show that areas near Venus' equator which appear dark in ultraviolet light are regions of relatively high temperature. The scientists think this is where intense convection brings up the mysterious dark material from below.

Bright regions at Venus' mid-latitudes are areas where the temperature in the atmosphere decreases with depth, which prevents air from rising. The effect is most extreme in a wide belt around the poles, which has

been dubbed the "cold collar". At low and mid-latitudes, the cloud top is located at a constant altitude of about 72km in both the dark and light regions, which suggests the light and dark patches do not result from changes in elevation.

Instead, the most likely cause is the uneven distribution of a mysterious chemical in the atmosphere that absorbs ultraviolet light, creating bright and dark zones.



*Venus' clouds have markings that are light and dark in the ultraviolet range*

Although the exact chemical species that creates the high-contrast zones remains elusive, a complex compound of sulphur is now a favourite. But a full answer may have to wait for a subsequent Venus mission.

"It seems that Venus Express will not completely solve this," Dr Titov told BBC News. "This species is very strange because it doesn't have particular features - just very broad ones. So we can't say exactly what it is made of. It's probably some kind of chemical hidden inside cloud droplets."

He added: "We need to send balloons (to Venus). The balloons will be ideal because they will be flying in this region. And if we have a chemical laboratory... on board the balloon we will really understand what this is."

**Sun block**

Balloons were deployed in the Venusian atmosphere during the Soviet-French Vega 1 mission in 1985. And both the US and Europe have carried out technical studies on a next-generation Venus mission which could feature a balloon or lander.

Some researchers have even speculated whether Venusian microbes could survive high in the planet's atmosphere, where the temperature and pressure are quite Earth-like. Here, they say, the ultraviolet-absorbing chemical could act as an "umbrella" to shield life forms from the destructive UV rays coming from the Sun.

Further down, conditions are quite different. The planet's surface is heated to an average temperature of 467C (872F) - hot enough to melt lead. And the dense atmosphere generates a surface pressure 90 times greater than that on Earth.

Another key question for the mission is whether Venus is still volcanically active. Venus Express has found a highly variable quantity of the volcanic gas sulphur dioxide in the atmosphere.

Some observers think this could be to do with recent volcanic activity on the surface.

But others say the lack of rain on Venus to scrub the atmosphere clean of sulphur dioxide means Venus Express could be detecting events that happened millions of years ago.

"We're not ready to say definitively one way or another on the basis of this evidence before we analyse all the data," said Fred Taylor, Venus Express interdisciplinary scientist at the University of Oxford.

He told the Oxford Science Blog: "However, there's plenty of indirect evidence for volcanic activity on Venus so, in my opinion, it's about how much activity is going on and the role it plays in the planet's climate. I think it's probably just a matter of time before we 'see' a volcano erupting."

## Gulf war costs US consumers 3 to 15 cents a gallon

How much does the US military spend on guaranteeing a supply of oil-based fuels from the Persian Gulf to road vehicles in the states? Between 3 and 15 cents for every gallon, in 2004 terms. So say Mark Delucchi at University California David Institute of Transportation Studies and his colleague economist James Murphy at the University of Alaska Anchorage.

Using 2004 figures (the most recent available) they calculate that the amount the military spend on both war and peacetime operations would be cut by up to $73 billion a year if the Gulf had no oil. And up to $25 billion of those savings would come from not having to keep supplying the drivers of America with fuel derived from Gulf oil. When broken down, this sum equates to between 3 and 15 cents added to every gallon of fuel at the US pumps. So how did the team come up with these numbers?

The pair used five steps to get their final figure:

1. Estimate of the amount spent annually to defend all US interests in the Persian Gulf.
2. Deduct the cost of defending non-oil interests in the Persian Gulf, such as promoting political stability in the region. They estimate that 50 to 75% of military expenditure in the Gulf is purely oil-related.
3. Deduct the cost of defending against the risk of a worldwide oil-price shock related to the use of Persian Gulf oil by other countries.
4. Deduct the cost of protecting US oil company interests in the Gulf that are separate from protecting oil supplies.
5. Deduct the cost of protecting oil supplies not used for transport fuel - for example, those used for heating and power plants.

The authors say the figures should be part of any future discussions of the true cost of road transport. I look forward to them appearing in arguments being made by everyone from advocates of increased drilling in US waters, to those lobbying to promote electric cars. ***Read their full paper in the journal Energy Policy*.**

## First 'placebo gene' discovered

* 03 December 2008 **by Andy Coghlan**

FOR the first time, a gene is being linked to increased susceptibility to the placebo effect, the mysterious capacity some people have to benefit from sham treatments.

The gene might not play a role in our response to treatment for all conditions, and the experiment involved only a small number of people. Nonetheless, the discovery is a milestone in the quest to understand this phenomenon, which often blurs the results of clinical trials "To our knowledge, it's the first time anyone has linked a gene to the placebo effect," says Tomas Furmark of Uppsala University in Sweden.

He and his colleagues recruited 25 people with an exaggerated fear of public humiliation, otherwise known as social anxiety disorder. Participants had to give a speech at the start and end of an eight-week treatment - which unbeknownst to them and their doctors, was actually a placebo.

Ten volunteers responded to the placebo much better than the rest. By the end of the experiment, their anxiety scores had halved, whereas the others' stayed the same. Brain scans also showed that activity in the amygdala, the brain's "fear" centre, had dropped by 3 per cent.

To see if there were genetic differences between responders and non-responders, Furmark screened them for a variant of the gene for tryptophan hydroxylase-2, which makes the brain chemical, serotonin. Previous studies suggested that people with two copies of a particular "G" variant are less anxious in standard "fear" tests. Sure enough 8 of the 10 responders had two copies, while none of the non-responders did (Journal of Neuroscience (DOI: 10.1523/JNEUROSCI.2534-08.2008).

Furmark believes the effect of the gene may extend to other conditions where the amygdala is involved, such as phobias, pain disorders and even depression. However, he cautions that only further studies will reveal whether the gene influences the placebo effect more generally.

Echoing Furmark's caution is Fabrizio Benedetti of the University of Turin, Italy. "We know that there's not a single placebo effect but many." Some may work through genetics, he adds, others through the expectation of a reward.

Edzard Ernst of the Complementary Medicine Peninsula Medical School in Exeter, UK, agrees the results need to be replicated and tested in several clinical settings.

## Treatment for advanced hepatitis C doesn't work, researchers find

***NIH study shows decline in health of those with advanced liver disease due to hepatitis C***

ST. LOUIS –An NIH funded multi-center clinical trial found no benefit from "maintenance therapy," low-dose peginterferon used for hepatitis C patients who have not responded to an initial round of treatment. In addition, the study showed a surprising health decline in patients with liver disease over the course of four years.

A Saint Louis University researcher was lead author and chairman of the study, which will be published in the Dec. 4 issue of the New England Journal of Medicine. The study ruled out low-dose peginterferon maintenance therapy as a treatment for patients with advanced chronic hepatitis.

"This course of treatment had been adopted by a number of doctors in the U.S. and in other countries, though it had yet to be proven to work. That practice should be stopped based on the results of this trial. There is no rationale for using maintenance therapy," said Adrian Di Bisceglie, M.D., professor of internal medicine, chief of hepatology and co-director of the Liver Center at Saint Louis University. "The treatment is clearly ineffective."

About 4 million people in the U.S. have been infected with hepatitis C; an estimated 10,000 to 12,000 people die from complications each year in this country. Hepatitis C is caused by a virus, transmitted by contact with blood, and may initially be asymptomatic. For patients who develop a chronic hepatitis C infection, inflammation of the liver may develop, leading to fibrosis and cirrhosis (scarring of the liver), as well as other complications including liver cancer and death.

For patients with chronic hepatitis C, the prognosis varies. About half fully recover after an initial course of peginterferon and ribavirin anti-viral therapy that may last from six months to a year.

The remaining patients, known as non-responders, may improve but the virus is not eliminated. Researchers studied these patients, looking at those with advanced liver disease as identified by liver biopsies that showed advanced scarring. These patients were at greatest risk for worsening.

The study looked at 1050 patients at 10 different clinical sites. Researchers gave patients peginterferon for three and a half years, but in lower doses to try to suppress but not eliminate the virus, with the hope of slowing

the dire consequences of liver disease. Half of the patients were treated with a low dose of peginterferon and half were put into a control group for a total of four years.

The results were clear; maintenance therapy did not stop liver disease from progressing.

In addition, researchers were startled by the rate of progression of liver disease. After four years, 30 percent of the patients in both the treatment and control groups had developed liver failure, liver cancer, or had died. Among those with milder cirrhosis, 10 to 12 percent developed severe liver disease, also unexpected.

"Hepatitis patients in these circumstances got very ill over the course of four years, surprisingly so," said Di Bisceglie. "The lesson we learned is that once chronic hepatitis C gets to the stage of advanced fibrosis, patients can decline rapidly."

As doctors look to the future, their hope rests on new drugs that are currently in clinical trials.

*The clinical trial, Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis (HALT-C), was funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), a component of the National Institutes of Health (NIH).*

## Researchers identify cell group key to Lyme disease arthritis

### *La Jolla Institute and Albany Med researchers show important role of NK T cells in fighting Lyme disease*

SAN DIEGO – (December 3, 2008) A research team led by the La Jolla Institute for Allergy & Immunology and Albany Medical College has illuminated the important role of natural killer (NK) T cells in Lyme disease, demonstrating that the once little understood white blood cells are central to clearing the bacterial infection and reducing the intensity and duration of arthritis associated with Lyme disease.

"Our findings are that the NK T cells are critical to preventing the chronic inflammatory infection that causes Lyme arthritis and they participate in clearing the bacteria which cause it," said Mitchell Kronenberg, Ph.D., the La Jolla Institute's president & scientific director and co-senior author on the study, which used a mouse model of Lyme disease. Lyme disease is caused by Borrelia burgdorferi, a bacterium transmitted to humans by the bite of infected deer ticks. Typical symptoms include fever, headache, fatigue, and sometimes skin rashes. If left untreated, it can spread to the joints, the heart and the nervous system, and it can lead to serious health problems. Lyme disease currently is the most common vector (insect)-borne disease in the United States.

"What this study demonstrates is that NK T cells are an important part of our defense against Lyme disease," said Timothy J. Sellati, Ph.D., an associate professor at Albany Medical College and co-senior author on the study. "This offers the possibility that we can exploit that knowledge therapeutically and potentially develop immunological agents that can trigger more NK T cells to aide in fighting this disease." Sellati added that "NK T cells alone cannot clear Lyme disease, but are a key part of a collective immune defense."

The study's findings are outlined in a paper, "NKT cells prevent chronic joint inflammation after infection with Borrelia burgdorferi," published this week in the online version of the journal Proceedings of the National Academy of Sciences.

In an earlier study published in Nature Immunology, Kronenberg, Sellati and co-workers had shown that a glycolipid, a type of fat, found in the membrane of Borrelia burgdorferi triggered an immune response from the NK T cells. "We had found that if you gave that lipid to mice or humans, it would activate NK T cells," Kronenberg said. While this suggested the cells might play a significant role in Lyme disease, "we were missing in vivo (in the body) evidence showing that the NK T cells were activated following infection and were important for killing and clearing the Lyme disease bacteria," he said, noting that the latest study demonstrates this in an animal model.

Sellati said the finding is particularly important because it opens new lines of investigation as to the causes of chronic Lyme disease. "That's what's so exciting when you identify a new cell type as playing a central role in preventing the disease process," he said. "So in those individuals who have a more severe form of the disease, you can study their NK T cells and see if there's some deficiency that prevents those NK T cells from killing and clearing the bacteria."

In their studies, the researchers worked to model the natural route of Lyme disease infection as closely as possible. "The way people typically get Lyme disease is that they're out hiking and they get bitten by a deer tick," said Kronenberg. "So what we did in the lab was to get ticks infected with Borrelia burgdorferi from collaborators at the University of Connecticut Health Science Center and then used those ticks to infect mice in a confined and controlled environment."

The researchers used one group of mice genetically engineered not to have NK T cells, while the control group had the cells. "The mice that didn't have NK T cells were not as capable of clearing the (Lyme disease) bacteria," Kronenberg said. "And they developed a chronic arthritis, while the control mice did not." He said the results were quite marked. "You could see under the microscope more numerous inflammatory cells in the joints of the mice that lacked the NK T cells weeks after infection."

Discovered in the 1990s, NK T cells are disease-fighting white blood cells of the immune system whose inner workings are still being defined. While most T cells respond to foreign proteins to protect the body, NK T cells are unique in that they respond to glycolipids, which are natural biochemicals made of linked fat and sugar. Prized for initiating a fast and vigorous immune response, NK T cells are emerging as a subject of significant scientific interest because of their potential for fighting bacterial infections and cancer. Kronenberg and Sellati have been among the nation's leaders in studying these cells.

Kronenberg's laboratory was among the first to identify bacteria which naturally induce an immune response from the NK T cells. Thus far, he has identified two such bacteria— Borrelia burgdorferi and Sphingomonas species, a fairly benign bacteria found throughout the environment. However, he believes many other types of bacteria may also trigger the NK T cells. "This is an exciting possibility that needs to be further explored as it could lead to the development of treatments for many bacterial diseases."

## Researchers Discover New Enzyme in Cancer Growth

***Protein may explain why cancer grows; spreads*** OU Public Affairs

Oklahoma City, OK -- While studying the mechanics of blood clots, researchers at the University of Oklahoma Health Sciences Center discovered a new enzyme that not only affects the blood, but seems to play a primary role in how cancer tumors expand and spread throughout the body. The research appeared in recent issues of the journal Blood and the Journal of Thrombosis and Haemostasis.

A research group at OU led by Patrick McKee first discovered the enzyme called sFAP in plasma. After studying the biochemical makeup of the protein and identifying the gene that controlled its function, they began to search gene sequencing databases worldwide to find what it was. They didn't find the enzyme listed for blood, but got a match with a virtually identical protein known to cause cell growth in tissue, including in cancer. With McKee's discovery that the protein also exists in blood, scientists have a new avenue to study the spread of cancer.

"One thing all cancer cells need as they grow is something that acts as scaffolding. They have to attach to the scaffolding to divide and migrate. This enzyme excavates space around a malignancy and helps create the scaffolding," said McKee, M.D., principle investigator on the project.

The main function of the original FAP protein that was known to exist in tissue is to accelerate tissue growth and expand cells during fetal development, the healing of severe wounds and during growth of selected cancers such as breast, lung, pancreatic and colon.

Other than in these situations, the original form of FAP is not normally expressed in tissues at all. When it does appear, the protein helps activated fibroblasts, which growing cancer cells are able to recruit and stimulate to multiply within the malignancy itself. This creates space and the framework on which cancer cells attach, divide and eventually spread.

If FAP could be inhibited, then cancer growth could be slowed or halted, which in combination with chemotherapy or radiation might offer the potential to actually cure the malignancy, the OU team believes.

McKee and his group of investigators hold one patent on the enzyme and three more are under review for the development of an inhibitor. Based on the discovery and numerous publications of their work, the OU Health Sciences Center recently received a $365,000 federal grant from the U.S. Department of Defense to work on an inhibitor with cancer investigators at the University of Arkansas for Medical Sciences.

## Mayo Clinic identifies best treatments for long-term survival in brain tumor patients

***Patients who had aggressive surgeries were free of tumor recurrence an average of 15 years after diagnosis***

ROCHESTER, Minn. - A new Mayo Clinic study found that patients with low-grade gliomas survived longest when they underwent aggressive surgeries to successfully remove the entire tumor. If safely removing the entire tumor was not possible, patients survived significantly longer when surgery was followed by radiation therapy. This study is available online as an advance publication in Neuro-Oncology (http://neuro-oncology.dukejournals.org/cgi/content/abstract/15228517-2008-102v1).

Gliomas are a type of brain tumor that form in the brain or spinal cord tissue and can spread within the nervous system. Low-grade gliomas are malignant and slow growing; overall, patients' average survival is five to seven years after diagnosis, even with treatment. Annually, about 17,000 Americans are diagnosed with a glioma. Of that total, 3,000 to 4,000 are categorized as low-grade. Mayo Clinic physicians treat more than 4,000 adults and children who have gliomas and other brain and nervous system tumors each year.

"Mayo Clinic has a long history of expertise in treating patients with brain tumors," says Nadia Laack, M.D., a Mayo Clinic radiation oncologist and lead author of this study. "This makes our study unique in terms of the large volumes of patients seen here and the extensive length of follow-up."

Dr. Laack and a team of Mayo Clinic researchers studied the records of 314 adult patients with low-grade gliomas who were diagnosed between 1960 and 1992 and had an average of 13 years of follow-up. Nearly half of the patients who underwent aggressive surgeries (gross total resection or radical subtotal resection) were free of tumor recurrence 15 years after diagnosis.

When performing aggressive surgery was not a safe option, postoperative radiation therapy nearly doubled average survival. The average survival time was three years in patients who did not receive radiation therapy, while those who had radiation therapy survived an average of six years.

"This study is exciting because it shows how well glioma patients can do after surgery," says Dr. Laack. "An average of 15 years tumor-free is better than any previously published results. It is also exciting to discover that patients can benefit from radiation therapy. It not only lengthens the time before the tumor comes back, it actually improves the length of time people live. This builds on previous Mayo Clinic data that suggested similar results from a small study published nearly 20 years ago."

According to Dr. Laack, these findings may be controversial due to common concerns about possible long-term side effects of radiation therapy. At Mayo Clinic, these potential side effects are minimized by tightly focusing radiation therapy on the tumor, she says.

*Other members of the Mayo Clinic research team included David Schomas, M.D.; Ravi Rao, M.D.; Fredric Meyer, M.D.; Brian O'Neill, M.D.; Caterina Giannini, M.D., Ph.D.; and Paul Brown, M.D. Edward Shaw, M.D. of Wake Forest University Baptist Medical Center also was a collaborator in this study.*

## Happiness is a collective -- not just individual – phenomenon

**Written by David Cameron**

BOSTON, Mass. (Dec. 4, 2008) —If you're happy and you know it, thank your friends—and their friends. And while you're at it, their friends' friends. But if you're sad, hold the blame. Researchers from Harvard Medical School and the University of California, San Diego have found that "happiness" is not the result solely of a cloistered journey filled with individually tailored self-help techniques. Happiness is also a collective phenomenon that spreads through social networks like an emotional contagion.

In a study that looked at the happiness of nearly 5000 individuals over a period of twenty years, researchers found that when an individual becomes happy, the network effect can be measured up to three degrees. One person's happiness triggers a chain reaction that benefits not only their friends, but their friends' friends, and their friends' friends' friends. The effect lasts for up to one year.

The flip side, interestingly, is not the case: Sadness does not spread through social networks as robustly as happiness. Happiness appears to love company more so than misery.

"We've found that your emotional state may depend on the emotional experiences of people you don't even know, who are two to three degrees removed from you," says Harvard Medical School professor Nicholas Christakis, who, along with James Fowler from the University of California, San Diego co-authored this study. "And the effect isn't just fleeting." These findings will be published online Dec. 4 in the BMJ.

For over two years now, Christakis and Fowler have been mining data from the Framingham Heart Study (an ongoing cardiovascular study begun in 1948), reconstructing the social fabric in which individuals are enmeshed and analyzing the relationship between social networks and health. The researchers uncovered a treasure trove of data from archived, handwritten administrative tracking sheets dating back to 1971. All family changes for each study participant, such as birth, marriage, death, and divorce, were recorded. In addition, participants had also listed contact information for their closest friends, coworkers, and neighbors. Coincidentally, many of these friends were also study participants. Focusing on 4,739 individuals, Christakis and Fowler observed over 50,000 social and family ties and analyzed the spread of happiness throughout this group.

Using the Center for Epidemiological Studies Depression Index (a standard metric) that study participants completed, the researchers found that when an individual becomes happy, a friend living within a mile experiences a 25 percent increased chance of becoming happy. A co-resident spouse experiences an 8 percent increased chance, siblings living within one mile have a 14 percent increased chance, and for next door neighbors, 34 percent.

But the real surprise came with indirect relationships. Again, while an individual becoming happy increases his friend's chances, a friend of that friend experiences a nearly 10 percent chance of increased happiness, and a friend of *that* friend has a 5.6 percent increased chance—a three-degree cascade.

"We've found that while all people are roughly six degrees separated from each other, our ability to influence others appears to stretch to only three degrees," says Christakis. "It's the difference between the structure and function of social networks."

These effects are limited by both time and space. The closer a friend lives to you, the stronger the emotional contagion. But as distance increases, the effect dissipates. This explains why next door neighbors have an effect, but not neighbors who live around the block. In addition, the happiness effect appears to wear off after roughly one year. "So the spread of happiness is constrained by time and geography," observes Christakis, who is also a professor of sociology in the Harvard Faculty of Arts and Sciences. "It can't just happen at any time, any place."

They also found that, contrary to what your parents taught you, popularity *does* lead to happiness. People in the center of their network clusters are the most likely people to become happy, odds that increase to the extent that the people surrounding them also have lots of friends. However, becoming happy does not help migrate a person from the network fringe to the center. Happiness spreads through the network without altering its structure.

"Imagine an aerial view of a backyard party," Fowler explains. "You'll see people in clusters at the center, and others on the outskirts. The happiest people tend to be the ones in the center. But someone on the fringe who suddenly becomes happy, say through a particular exchange, doesn't suddenly move into the center of the group. He simply stays where he is—only now he has a far more satisfying sense of well-being. Happiness works not by changing where you're located in the network; it simply spreads through the network."

Fowler also points out that these findings give us an interesting perspective for this holiday season, which arrives smack in the middle of some pretty gloomy economic times. Examination of this dataset shows that having $5,000 extra increased a person's chances of becoming happier by about 2 percent. But that the same data also show, as Fowler notes, that "Someone you don't know and have never met—the friend of a friend of a friend—can have a greater influence than hundreds of bills in your pocket."

This is the third major network analysis by Christakis and Fowler that shows how our health is affected by our social context. The two previous studies, both published in the New England Journal of Medicine, described the social network effects in obesity and smoking cessation.

The research was funded by the National Institutes of Health/National Institute on Aging, a Pioneer Grant from the Robert Wood Johnson Foundation, and a contract from the National Heart, Lung, and Blood Institute to the Framingham Heart Study.

*Full citation: BMJ, early online publication, December 4, 2008 Dynamic spread of happiness in a large social network: longitudinal analysis over 20 years in the Framingham Heart Study*

*James H Fowler(1), Nicholas A Christakis(2) 1-University of California, San Diego, San Diego CA 2-Harvard Medical School, Boston, MA*

## Spanish Inquisition couldn't quash Moorish, Jewish genes

### *Finding suggests modern history, not just prehistory, can leave a strong mark on a region's genetic signature*

**By Tina Hesman Saey**

Hold the history book presses. The Moorish invasion of Spain was never completely repelled, a new genetic analysis reveals. As many as one in 10 men from Spain and Portugal still carry genetic evidence of North African ancestry, and nearly twice that number had Sephardic Jewish ancestors, reveals a study in the Dec. 12 American Journal of Human Genetics. Those results don't fit with expectations from the historical record.

Sephardic Jews, who were likely in the Iberian Peninsula since Roman times, were supposed to all have fled the region in the wake of pogroms and persecutions between the early eighth and 14th centuries. In the late 15th century, 160,000 Spanish Jews (Sepharadh is the Hebrew word for Spain) were expelled and then settled in other parts of the Mediterranean.

Moors from northern Africa swept into Spain in 711, colonizing the peninsula and spreading Islam. But during the Spanish Inquisition, Spanish Muslims were driven out or forced to convert in a wave of religious intolerance. But the new study, which analyzed Y chromosomes from 1,140 men from the Iberian Peninsula, shows that, even though large numbers of Sephardic Jews and Spanish Muslims left the peninsula, these groups also left behind descendents and a strong genetic presence.

Genetic studies of populations are often used to track movements of people from prehistoric times. But these results indicate that more modern events - religious persecution and conversion, modern migration and intermarriage - can shape human genetic landscapes more than previously suspected.

Certain groups have minor genetic variations that are characteristic. The researchers in this study used genetic markers found in North African populations, specifically Morocco and Algeria, to trace the North African contribution in the Iberian Peninsula. Sephardic Jewish genetic markers came from populations in Israel and Turkey.

Studies such as the new one "tell the true history of everyone's ancestors and not just the history book lessons of kings and queens," says James Wilson, a population geneticist at the University of Edinburgh in

Scotland who was not involved in the study. Wilson said he would have expected to find small but significant evidence of North African ancestry in southern Spain, where the Moorish reign lasted longest, but “to find it in the west defies my expectations,” he said. The researchers expected to find a gradient, with stronger ancestry in the south that would lessen farther north. In fact, they found a weaker North African presence in southern Spain.

Sephardic Jewish roots run deep in the peninsula, the researchers found. Nearly 20 percent of men in the study showed evidence of Sephardic Jewish ancestry. “We think it might be an over estimate,” says Francesc Calafell, a human population geneticist at the Institute of Evolutionary Biology and Pompeu Fabra University in Barcelona, Spain. Calafell and Mark Jobling at the University of Leicester in England led the study.

The genetic makeup of Sephardic Jews is probably common to other Middle Eastern populations, such as the Phoenicians, that also settled the Iberian Peninsula, Calafell says. “In our study, that would have all fallen under the Jewish label.” Still, the findings reflect how religious intolerance on the peninsula led to conversion of non-Christian groups and then integration into the larger Christian community, he says.

## Universe's dark matter mix is 'just right' for life

* 04 December 2008 **by Anil Ananthaswamy**

IT'S not just the nature of dark matter that's a mystery - even its abundance is inexplicable. But if our universe is just one of many possible universes, at least this conundrum can be explained.

The total amount of dark matter - the unseen stuff thought to make up most of the mass of the universe - is five to six times that of normal matter. This difference sounds pretty significant, but it could have been much greater, because the two types of matter probably formed via radically different processes shortly after the big bang. The fact that the ratio is so conducive to a life-bearing universe "looks like a tremendous coincidence", says Raphael Bousso at the University of California, Berkeley.

Ben Freivogel, also at UCB, wondered if the ratio can be explained using the anthropic principle which, loosely stated, says that the properties of the universe must be suitable for the emergence of life, otherwise we wouldn't be here asking questions about it. In order to avoid questions about how these properties became so finely tuned, the anthropic principle is combined with the idea that our universe is part of a multiverse, in which each universe has randomly determined properties.

Freivogel focused on one of the favoured candidate-particles for dark matter, the axion. Axions have the right characteristics to be dark matter, but for one problem: a certain property called its "misalignment angle", which would have affected the amount of dark matter produced in the early universe. If this property is randomly determined, in most cases it would result in a severe overabundance of dark matter, leading to a universe without the large-scale structure of clusters of galaxies. To result in our universe, it has to be just the right value.

In a multiverse, each universe will have a random value for the axion's misalignment angle, giving some universes the right amount of dark matter needed to give rise to galaxies, stars, planets and life as we know it.

Freivogel combined the cosmological models of large-scale structure formation with the physics of axions to predict the most likely value for the ratio of dark matter to normal matter that would allow observers like us to emerge. He assumed that the number of observers in a universe is proportional to the number of galaxies within it.

In Freivogel's model, changing the ratio of matter type impacts the formation of galaxies, and hence observers; for example, too little dark matter would prevent the formation of galaxies and stars. His calculations show that of all the observers that might exist across the many universes, most would live in a universe with the dark matter abundance found in ours. In other words, we would be less likely to be here if our abundance of dark matter were different (www.arxiv.org/abs/0810.0703).

Of all the observers across many universes, most would live in a universe with the dark matter abundance found in ours  Bousso is impressed by the analysis. "It is another piece that fits nicely into the puzzle, and it didn't have to fit nicely," he says. Leonard Susskind of Stanford University adds: "It is not the first anthropic explanation [for dark matter], but it is more compelling than the others" because it explains the axion's overabundance problem.

## Caltech researchers find ancient climate cycles recorded in Mars rocks

PASADENA, Calif.-- Researchers at the California Institute of Technology (Caltech) and their colleagues have found evidence of ancient climate change on Mars caused by regular variation in the planet's tilt, or obliquity. On Earth, similar "astronomical forcing" of climate drives ice-age cycles.

Using stereo topographic maps obtained by processing data from the high-resolution camera onboard NASA's Mars Reconnaissance Orbiter, the Caltech scientists, led by graduate student Kevin Lewis and Oded Aharonson, associate professor of planetary science, along with John Grotzinger, the Fletcher Jones Professor of Geology, identified and measured layered rock outcrops within four craters in the planet's Arabia Terra

region. The layering in different outcrops occurs at scales ranging from a few meters to tens of meters, but at each location the layers all have similar thicknesses and exhibit similar features.

Based on a pattern of layers within layers measured at one location, known as Becquerel crater, the scientists propose that each layer was formed over a period of about 100,000 years and that these layers were produced by the same cyclical climate changes.

In addition, every 10 layers were bundled together into larger units, which were laid down over an approximately one-million-year period; in the Becquerel crater, the 10-layer pattern is repeated at least 10 times. This one-million-year cycle corresponds to a known pattern of change in Mars's obliquity caused by the dynamics of the solar system.

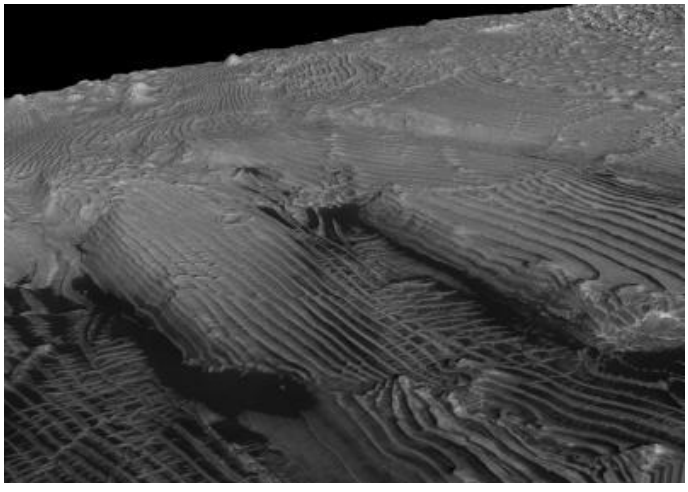
"Due to the scale of the layers, small variations in Mars's orbit are the best candidate for the implied climate changes. These are the very same changes that have been shown to set the pacing of ice ages on the Earth and can also lead to cyclic layering of sediments," says Lewis, the first author of a paper about the work published in this week's issue of Science.

***Sequences of cyclic sedimentary rock layers exposed in an unnamed crater (located at 8N, 353E) in Arabia Terra, Mars. These images were created by draping HiRISE image PSP_002733_1880 over HiRISE stereo topography (1m/pixel). Vertical exaggeration is 2X.*** **Topography: Caltech; HiRISE Images: NASA/JPL/Univ. of Arizona**

The tilt of Earth on its axis varies between 22.1 and 24.5 degrees over a 41,000-year period. The tilt itself is responsible for seasonal variation in climate, because the portion of the Earth that is tipped toward the sun--and that receives more sunlight hours during a day--gradually changes throughout the year. During phases of lower obliquity, polar regions are less subject to seasonal variations, leading to periods of glaciation.

Mars's tilt varies by tens of degrees over a 100,000-year cycle, producing even more dramatic variation. When the obliquity is low, the poles are the coldest places on the planet, while the sun is located near the equator all the time. This could cause volatiles in the atmosphere, like water and carbon dioxide, to migrate poleward, where they'd be locked up as ice.

When the obliquity is higher, the poles get relatively more sunlight, and those materials would migrate away. "That affects the volatiles budget. If you move carbon dioxide away from the poles, the atmospheric pressure would increase, which may cause a difference in the ability of winds to transport and deposit sand," Aharonson says. This is one effect that could change the rate of deposition of layers such as those seen by the researchers in the four craters.



Another effect of the changing tilt would be a change in the stability of surface water, which alters the ability of sand grains to stick together and cement in order to form the rock layers.

"The whole climate system would be different," Aharonson says.

However, such large changes in climate would influence a variety of geologic processes on the surface. While the researchers cannot tie the formation of the rhythmic bedding on Mars to any particular geologic process, "a strength of the paper is that we can draw conclusions without having to specify the precise depositional process," Aharonson says.

***Sequences of cyclic sedimentary rock layers exposed in an unnamed crater (located at 8N, 353E) in Arabia Terra, Mars. These images were created by draping HiRISE image PSP_002733_1880 over HiRISE stereo topography (1m/pixel). Vertical exaggeration is 2X.*** **Topography: Caltech; HiRISE Images: NASA/JPL/Univ. of Arizona**

"This study gives us a hint of how the ancient climate of Mars operated, and shows a much more predictable and regular environment than you would guess from other geologic features that indicate catastrophic floods, volcanic eruptions, and impact events," Lewis adds. "More work will be required to understand the full extent of the information contained within these natural geologic archives," he says.

"One of the fun things about this project for me is that we were able to use techniques on Mars that are the bread and butter of studies of stratigraphy on Earth," says Aharonson. "We substituted a high-resolution camera

in orbit around Mars and stereo processing for a geologist's Brunton Compass and mapboard, and were able to derive the same quantitative information on the same scale. This enabled conclusions that have qualitative meaning similar to those we chase on Earth."

*The paper, "Quasi-Periodic Bedding in the Sedimentary Rock Record of Mars," will be published in the December 5 issue of Science. The work was supported by NASA's Mars Data Analysis Program and the NASA Earth and Space Science Fellowship program.*

## Well-armed immune cells help long-term nonprogressors contain HIV

To help develop an effective HIV vaccine, researchers are trying to better understand how the immune systems of a small minority of HIV-infected people known as long-term non-progressors (LTNPs) contain the virus naturally. CD8+ T cells, which kill cells infected with HIV, enable LTNPs to control HIV, but it has been unclear how CD8+ T cells mediate that control so effectively. A new report shows that the ability to stockpile two molecular weapons makes the HIV-specific CD8+ T cells of LTNPs superior cellular killers.

Lead author Stephen Migueles, M.D., senior author Mark Connors, M.D., and colleagues at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, used cutting-edge technology to examine individual CD8+ T cells for their killing prowess. The study included new techniques to measure how many HIV-infected cells each CD8+ T cell destroys, and how rapidly. In laboratory experiments, the scientists found that CD8+ T cells taken from LTNPs efficiently killed HIV-infected cells in less than 1 hour. In contrast, the CD8+ T cells of progressors, or individuals who do not contain the virus without antiretroviral therapy, killed HIV-infected cells inefficiently, even when the CD8+ T cells were present in high numbers or came from progressors being successfully treated with antiretroviral therapy.

When CD8+ T cells kill HIV-infected cells, a protein, perforin, made by the CD8+ T cells punches holes in the infected cells. Then a second protein, granzyme B, penetrates those holes and causes the cells to die. Previously, the researchers found that HIV-specific CD8+ T cells of progressors, unlike those of LTNPs, make little perforin when they encounter an HIV-infected cell. It remained unclear, however, whether this deficiency explained why HIV-specific CD8+ T cells of progressors are poor killers. The current study demonstrates a direct relationship between the quantity of both perforin and granzyme B that CD8+ T cells accumulate over time and the ability of CD8+ T cells to eliminate HIV-infected cells. This discovery significantly advances the understanding of the cellular mechanisms unique to LTNPs that explain why their immune systems, unlike those of the majority of HIV-infected people, can control HIV without antiretroviral therapy.

According to the NIAID scientists, their results also suggest that an HIV vaccine might control virus replication if it could stimulate HIV-specific CD8+ T cells to robustly stock and rapidly deliver perforin and granzyme B to HIV-infected cells.

*ARTICLE: SA Migueles et al. Lytic granule loading of CD8+ T cells is required for HIV-infected cell elimination associated with immune control. Immunity DOI 10.1016/j.immuni.2008.10.010 (2008).*

*WHO: Mark Connors, M.D., chief of the HIV-Specific Immunity Section, Laboratory of Immunoregulation, NIAID.*

## Dormant stem cells for emergencies

Many specialized cells, such as in the skin, intestinal mucosa or blood, have a lifespan of only a few days. For these tissues to function, a steady replenishment of specialized cells is indispensable. This is the task of so-called "adult" stem cells also known as tissue stem cells.

Stem cells have two main characteristics: First, they are able to differentiate into all the different cell types that make up their respective tissue – a property called pluripotency. Second, they need to renew themselves in order to be able to supply new specialized tissue cells throughout life. These processes have best been studied in mouse bone marrow.

Up to now, scientists have assumed that adult stem cells have a low division rate. According to theory, they thus protect their DNA from mutations, which happen particularly during cell division and can lead to transformation into tumor stem cells. However, the actual number of divisions of a blood stem cell throughout an organism's lifespan has remained unknown.

Professor Dr. Andreas Trumpp and Dr. Anne Wilson have now discovered a group of stem cells in mouse bone marrow that remain in a kind of dormancy almost throughout life. Trumpp, who has been head of the Cell Biology Division at DKFZ since summer 2008, had carried out these studies at the Ecole Polytechnique Fédérale in Lausanne, Switzerland, jointly with colleagues at the Ludwig Institute for Cancer Research located in the same city.

The scientists labeled the genetic material of all mouse blood cells and subsequently investigated how long this label is retained. With each division, the genetic material is apportioned to the daughter cells and, thus, the labeling dilutes. During these studies, the investigators discovered the dormant stem cells which divide only about five times throughout the life of a mouse. Translated to humans, this would correspond to only one cell

division in 18 years. Most of the time, these cells, which constitute no more than about 15 percent of the whole stem cell population, remain in a kind of dormancy with very low metabolism. In contrast, stem cells of the larger group, the "active" stem cells, divide continuously about once a month.

However, in an emergency such as an injury of the bone marrow or if the messenger substance G-CSF is released, the dormant cell population awakes. Once awakened, it shows the highest potential for self-renewal ever to be observed in stem cells. If transplanted into irradiated mice, these cells replace the destroyed bone marrow and restore the whole hematopoietic system. It is possible to isolate new dormant stem cells from the transplanted animals and these cells are able to replace bone marrow again – this can be done several times in a row. The situation is different with "active" stem cells, where bone marrow replacement can successfully be carried out only once.

"We believe that the sleeping stem cells play almost no role in a healthy organism," Trumpp explains. "The body keeps its most potent stem cells as a secret reserve for emergencies and hides them in caves in the bone marrow, also called niches. If the bone marrow is damaged, they immediately start dividing daily, because new blood cells are needed quickly." Once the original cell count is restored and the bone marrow is repaired, these stem cells go back to deep sleep. The larger population of "active" stem cells, however, keeps up the physiological balance of blood cells in the normal healthy state.

Andreas Trumpp expects that these results may give valuable impetus to our understanding of cancer stem cells: "Cancer stem cells, too, probably remain in a dormant state most of the time – we think that this is one of the reasons why they are resistant to many kinds of chemotherapy that target rapidly growing cells. If we were able to wake up these sleepers before a patient receives treatment, it might be possible to also eliminate cancer stem cells for the first time and, thus, to treat the disease much more effectively by destroying the supply basis."

In a second article*, Dr. Elisa Laurenti from Trumpp's team shows that the two cancer genes c-Myc and N-Myc play a vital role in the functioning of stem cells. The two genes provide the blueprints for what are called transcription factors, which in turn regulate the activity of other genes and are overactive particularly in cancer cells. If both c-Myc and N-Myc are switched off at the same time in mice, the animals quickly start suffering from a general lack of blood cells and quickly die.

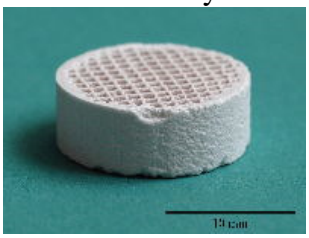
The two genes are not only responsible for survival of nearly all blood cells, but they also jointly control the two prime characteristics of stem cells - the capability of self-renewal and the potential to produce differentiated blood cells. This result is not only relevant for our understanding of stem cells, but it also explains the damage that can be caused by overactive Myc genes. Trumpp explains: "In tumors, too, c-Myc and N-Myc are presumably responsible for the self-renewal of cancer stem cells and, thus, for uncontrolled growth."

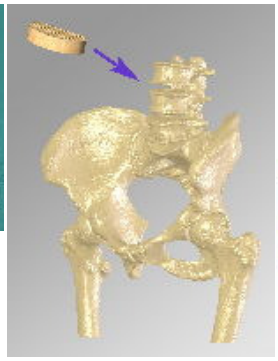
*Anne Wilson; Gabriela Oser; Richard van der Wath; William Blanco; Elisa Laurenti; Maike Jaworski; Cyrille Durant; Leonid Eshkind; Ernesto Bockamp; Pietro Lio; Robson MacDonald, and Andreas Trumpp: Hematopoietic stem cells reversibly switch from dormancy to self-renewal during homeostasis and repair. CELL 2008, DOI 10.1016/j.cell.2008.10.048*

**Elisa Laurenti, Barbara Varnum-Finney, Anne Wilson, Isabel Ferrero, William E. Blanco-Bose, Armin Ehninger, Paul S. Knoepfler, Pei-Feng Cheng, H. Robson MacDonald, Robert N. Eisenman, Irwin D. Bernstein, and Andreas Trumpp: Hematopoietic Stem Cell Function and Survival Depend on c-Myc and N-Myc Activity. CELL Stem Cell 2008, DOI 10.1016/j.stem.2008.09.005*

## Warwick drives forward new bone implant technology for tissue engineering

A method of producing synthetic bone, using techniques normally used to make catalytic converters for cars, is being developed by researchers at WMG at the University of Warwick.





The team is now working closely with Warwick Ventures, the University's technology transfer office, to find a suitable partner to help commercialise the technology, and will be presenting their work on 9 December at the national university technology showcase event, Bioversity.

WMG's Dr Kajal Mallick is developing the technique along with his postgraduate researcher James Meredith. They strongly believe it could offer substantial clinical benefits to patients undergoing bone implant surgery.

The technique involves state-of-the-art extrusion of the implant material through a mould, to produce a 3-dimensional honeycomb texture, with uniform pores throughout. The material can then be sculpted by the

surgeon to precisely match the defect. After implantation bone cells will be transported into the implant and begin to form new bone.

"We worked with a Japanese company which manufactures catalytic converters and used their facility to produce samples which we could then test in the laboratory," explains Dr Mallick.
"We found that we were able to use calcium phosphates – a family of bioceramics that are routinely used in bone implant operations, but by using this technique we were able to improve significantly both the strength and porosity of the implant."

Dr Mallick added: "At the present time, there is no product available in the market place that satisfies both these key properties simultaneously. It is nearly an ideal scaffold structure for efficient blood flow and formation of new bone cells."

The increased strength of the material means it could be used in spinal surgery, or in revision hip and knee operations, where currently non-degradable materials such as titanium or steel may be used. The advantage of increased and interconnected porosity is that the implant can quickly be filled with blood vessels, resulting in a more rapid healing process.

James Meredith is working to complete an Engineering Doctorate in this research area. He says: "The synthetic bone we are developing is as strong as normal healthy bone yet porous enough to allow bone cells to inhabit it and generate new bone. Over a period of time, we expect the synthetic bone will resorb, leaving only natural bone. I hope that if we can find an industrial partner to take this to market, we will enable treatment of conditions which up to this point have only been possible using metal replacement parts or low strength foam-like bone substitutes"

The team's research is being presented on 9 December at Bioversity 2008, a national university technology showcase event. Bioversity is part of the biotechnology conference, Genesis 2008, organised by The London Biotechnology Network.

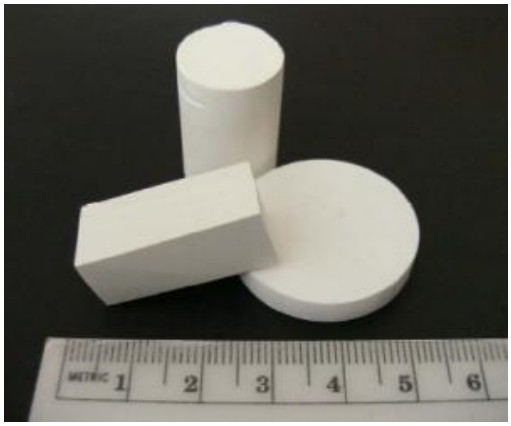
*For media enquiries, please contact: Peter Dunn, Press and Media Relations Manager,*
*University of Warwick, Tel: 024 76 523708 or 07767 655860 email: p.j.dunn@warwick.ac.uk*

## Mother of pearl mimic is toughest ever ceramic

* 14:32 05 December 2008 **by Colin Barras**

A new synthetic material similar in structure to nacre - mother of pearl - is likely the toughest ceramic-based material ever made, according to US researchers. The low-density, high-strength material could find use in aerospace construction, they say. When it comes to high performance materials, nature still has the upper hand over human engineers.

Bone, wood and mother of pearl have properties far exceeding the values expected from a simple mix of their constituent elements. These are both hard to deform and tricky to facture. The secret lies in their structure: lubricating layers are included between brittle strong ones to redistribute strain.



***Samples of the new strong and tough ceramic*** **(Image: Science)**

Copying natural laminated materials has proved difficult, despite the best efforts of many researchers, says Robert Ritchie at the Lawrence Berkeley National Laboratory in California. Those best efforts have resulted in only very thin films, not bulk specimens with real-world practicality. "We have done this here," Ritchie told New Scientist, "a ceramic/polymer composite that simulates mother of pearl." The new samples are several centimetres across (see image, top right).

To create the new material, Ritchie's research team take a mixture of aluminium oxide and water and carefully freeze it to encourage ice to form in sheets. The ice acts as a mould, sandwiching the aluminium oxide in flat layers between the sheets. Freeze-drying then removes the ice, leaving layers of aluminium oxide that can be baked to lock the stack in place.

**Nacre faker**

The final structure is similar to that of the aragonite layers that make up 95% of the volume of mother of pearl. Aragonite is a form of calcium carbonate that many molluscs produce to line their shells.

In nature, these layers are interleaved with a lubricant that helps redistribute any strain, making mother of pearl extremely tough. Ritchie's team found that it could improve the toughness of the synthetic material in the same way, by adding a slippery polymer into the pore space left by the ice. The polymer takes up the strain when the brittle ceramic is flexed or pulled. The resulting material is extremely tough and strong - two properties that tend to be mutually exclusive in synthetic materials.

To describe how resistant a material is to breaking even when it is already cracked, engineers use a measure called "fracture toughness". The new material has a fracture toughness almost double that of a simple mixture of aluminium oxide and polymer - a value of 30 megapascals per square root metre.

**Mysteries of scale**

That figure is probably the highest on record for a ceramic material, says Ritchie.

François Barthelat at McGill University in Montreal, Canada, calls the ice-template fabrication method "an innovative and ingenious approach" to duplicating microstructures. Of all the attempts to match mother of pearl's properties this is "the closest to natural nacre in terms of composition, structure and mechanical performance," he says.

Andre Studart at Harvard University is also impressed with these first large pieces of artificial nacre. He adds, however, that there are still many secrets of natural materials that remain a mystery. One of the largest is how such structures manage to spread stresses across multiple scales, sharing it out across metres and nanometres simultaneously. *Journal reference: Science (DOI: 10.1126/science.1164865)*

## Apple or pear shape is not main culprit to heart woes — it's liver fat

**By Jim Dryden**

For years, pear-shaped people who carry weight in the thighs and backside have been told they are at lower risk for high blood pressure and heart disease than apple-shaped people who carry fat in the abdomen. But new findings from nutrition researchers at Washington University School of Medicine in St. Louis suggest body-shape comparisons don't completely explain risk.

In two studies, they report excess liver fat appears to be the real key to insulin resistance, cholesterol abnormalities and other problems that contribute to diabetes and cardiovascular disease. Having too much fat stored in the liver is known as nonalcoholic fatty liver disease.

"Since obesity is so much more common now, both in adults and in children, we are seeing a corresponding increase in the incidence of nonalcoholic fatty liver disease," says senior investigator Samuel Klein, M.D., the Danforth Professor of Medicine and Nutritional Science. "That can lead to serious liver disorders such as cirrhosis in extreme cases, but more often it tends to have metabolic consequences."

Klein, who heads the Division of Geriatrics and Nutritional Science and runs Washington University's Center for Human Nutrition, studied obese adolescents. They were divided into two groups: obese with excessive liver fat and those with no evidence of fatty liver disease. The groups were matched by age, sex, body mass index, body fat percentage and degree of obesity.

The researchers determined that children with fatty liver disease also had abnormalities in glucose and fat metabolism, including lower levels of HDL cholesterol, the so-called good cholesterol. Those without a fatty liver did not have markers of metabolic problems. Whether shaped like pears or apples, it was fat in the liver that influenced metabolic risk.

"Abdominal fat is not the best marker for risk," says Klein, who also directs the Nutrition Support Service at Barnes-Jewish Hospital. "It appears liver fat is the real marker. Abdominal fat probably has been cited in the past because it tends to track so closely with liver fat. But if you look at people where the two don't correspond - with excess fat in the liver but not in the abdomen and vice versa - the only thing that consistently predicts metabolic derangements is fat in the liver."

In a second study, Klein's team found nonalcoholic fatty liver disease was related to the release of larger amounts of fatty acids into the bloodstream that were, in turn, linked to elevated triglycerides and to insulin resistance, a key precursor to type 2 diabetes.

"Multiple organ systems become resistant to insulin in these adolescent children with fatty liver disease," he says. "The liver becomes resistant to insulin and muscle tissue does, too. This tells us fat in the liver is a marker for metabolic problems throughout the entire system."

The findings indicate that children and adults with fatty liver disease should be targeted for intensive interventions, according to Klein. Those who are obese but don't have fatty liver disease still should be encouraged to lose weight, but those with evidence of fatty liver are at particularly high risk for heart disease and diabetes. They need to be treated aggressively with therapies to help them lose weight because weight loss can make a big difference.

"Fatty liver disease is completely reversible," he says. "If you lose weight, you quickly eliminate fat in your liver. As little as two days of calorie restriction can improve the situation dramatically, and as fat in the liver is reduced, insulin sensitivity and metabolic problems improve."

*Fabbrini E, deHaseth D, Deivanayagam S, Mohammed BS, Vitola BE, Klein S. Alterations in fatty acid kinetics in obese adolescents with increased intrahepatic triglyceride content. Obesity (2008), published online Oct. 2008. doi:10.1038/oby.2008.494*

*Deivanayagam S, Mohammed BS, Vitola BE, Naguib GH, Keshen TH, Kirk EP, Klein S. Nonalcoholic fatty liver disease is associated with hepatic and skeletal muscle insulin resistance in overweight adolescents. American Journal of Clinical Nutrition, 88(2) pp. 257-262, Aug. 2008.*

*This research was supported by grants from the National Institute of Diabetes and Digestive and Kidney Diseases and the National Center for Research Resources of the National Institutes of Health.*

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

### *Results from the European study IMMIDIET show that moderate wine intake is associated with higher levels of omega-3 fatty acids considered as protective against coronary heart disease*

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

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

Omega-3 fatty acids, mainly derived from fish, are considered as protective against coronary heart disease and sudden cardiac death, thus their high blood concentration is definitely good for our health. Now European researchers found that moderate alcohol drinking acts like a 'trigger', boosting the amount of omega-3 fatty acids in our body.

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

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

"From our previous studies we know that association between wine drinking and increased concentration of omega-3 fatty acids have been observed – says Michel de Lorgeril, from the University of Grenoble, partner of the IMMIDIET project and co-leader of the study - Nevertheless, it was not possible to separate the effects of wine from those of beer or spirits. Our study of 3 populations with different dietary habits and different consumption of alcoholic beverages types allowed us to explore this aspect.".

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

Polyphenols are naturally occurring compounds contained in a different variety of food and beverages, such as wine. Due to their strong antioxidant activity, they are able to reduce oxidation processes caused by free radicals. "We consider these data to be a major finding - de Lorgeril concludes - opening a new window in the field of cardiovascular prevention. Beyond the alcohol issue, our results raise crucial questions regarding the effects of polyphenols on lipids (both in blood and cell membranes) and possibly of lipids on polyphenols".

**The IMMIDIET study**

Funded by the European Union under Key Action 1: Food, Nutrition and Health QLK1-CT-2000-00100, IMMIDIET aims to acquire fundamental knowledge in the field of cardiovascular disease, especially regarding the interaction between genetics and lifestyle.

At the core of the study there is an important episode of Italian migration: Belgium, a country that became the new home for thousands of Italians, mostly from the Abruzzo region, who came to work in the mines. Many of those emigrants didn't come back to Italy but remained in their new country. Some of them married a Belgian partner. Their

genes remained the same, of course, but how much "Italy" is still there in their diet? And how much did they transmit it to their spouses? Moreover, how many Italian emigrants assimilate dietary habits of the country in which they were guests? In this framework, the role of genetic factors and lifestyle can be assessed to explore new ways in prevention of cardiovascular diseases.
To carry on the research, married couples have been recruited in three European areas: South-East London in England, Limburg in Belgium and Abruzzo in Italy. In the first phase of the study the couples involved were formed by people from the same area, Italians married with Italians (in the Abruzzo region), Belgians married with Belgians (in the Limburg area) and English married with English (in the South-East part of London)".
The second phase of IMMIDIET recruited mixed Italian–Belgian couples to understand if, acquiring dietary habits from Abruzzo, the Belgian partner changed his own risk regarding heart diseases.

## UCLA expert blames American values for health-care crisis

### *Reforming the system will require strong medicine, tough choices*

To heal our ailing health care system, we need to stop thinking like Americans. That's the message of two articles by UCLA's Dr. Marc Nuwer, a leading expert on national health care reform, published this week in Neurology, the journal of the American Academy of Neurology.

"Americans prize individual choice and resist limiting care," says Nuwer, a professor of clinical neurology at the David Geffen School of Medicine at UCLA. "We believe that if doctors can treat very ill patients aggressively and keep every moment of people in the last stages of life under medical care, then they should. We choose to hold these values. Consequently, we choose to have a more expensive system than Europe or Canada."

**Consider these statistics:**

* The United States boasts the world's most expensive health care system, yet only one-sixth of Americans are insured. Medical expenditures exceed $2 trillion annually, making health care the economy's largest sector, four times bigger than national defense.

* By 2015, the U.S. government is projected to spend $4 trillion on health care, or 20 percent of the nation's gross domestic product.

* An aging population will boost spending. Half of Medicare costs support very sick people in their last stages of life, and experts estimate that Medicare funds will be exhausted by 2018.

* 31 percent of U.S. health care funds go toward administration. "We push a lot of paper," Nuwer says. "We spend twice as much as Canada, which has a more streamlined health care system that demands doctors complete less paperwork."

* 10 percent of U.S. expenses are spent on "defensive medicine" - pricey tests ordered by doctors afraid of missing anything, however unlikely. "Doctors don't want to be accused in court of a delayed diagnosis, so they bend over backwards to find something - even if it's a rare possibility - in order to cover themselves," Nuwer says.

Reforming the U.S. health care system with the goal of providing universal, affordable, high-quality care will require rethinking our overall values and paying greater attention to care-related expenditures, according to Nuwer.

Part of the current problem, he says, is that doctors are oblivious to the price tags of options they're prescribing for patients. He recommends educating physicians about the costs of care, including imaging, blood tests and specific drugs. "Does a fancy electric wheelchair cost $500 or $50,000?" Nuwer asks. "Most doctors have no clue. We need to give physicians feedback about the dollar signs behind their orders."

*Nuwer's co-authors on both articles include Dr. G.L. Barkley (Henry Ford Hospital, Detroit); Dr. G.J. Esper (Emory University School of Medicine, Atlanta); Dr. P.D. Donofrio (Vanderbilt University School of Medicine, Nashville); Dr. J.P. Szaflarski (University of Cincinnati Academic Health Center); and Dr. T.R. Swift (Medical College of Georgia, Augusta).*

## 'Zinc Zipper' Plays Key Role In Hospital-Acquired Infections

CINCINNATI—Hospital-acquired infections that are resistant to traditional antibiotic treatment have become increasingly common in recent years, confounding health care professionals and killing thousands of Americans.

Now, in studies that could lead to new ways to prevent this growing public health danger, a team of University of Cincinnati (UC) researchers is exploring a “zinc zipper” that holds bacterial cells together and plays a key role in such infections.

Hospital-acquired infections affect about 1.7 million people per year in the United States and result in an estimated 99,000 deaths annually, according to the Centers for Disease Control. About two-thirds of all hospital-acquired infections can be traced to two staphylococcal species, Staphylococcus aureus - including methicillin-resistant strains (MRSA) that are particularly difficult to treat - and Staphylococcus epidermidis.

In an article appearing in the Dec. 1 online edition of Proceedings of the National Academy of Sciences, researchers in UC's department of molecular genetics, biochemistry and microbiology detailed findings that the presence of zinc is crucial to the formation of infection-causing biofilms.

Staphylococci can grow as biofilms, which are specialized communities of bacteria that are highly resistant to antibiotics and immune responses. They are remarkably adhesive and can grow on many surfaces, including implanted medical devices such as pacemakers, heart valve replacements and artificial joints. Preventing or inhibiting the growth of such biofilms would dramatically reduce the incidence of staph infections.

UC researchers in the lab of Andrew Herr, PhD, an assistant professor and Ohio Eminent Scholar in structural biology, found that zinc causes a protein on the bacterial surface to act like molecular Velcro, allowing the bacterial cells in the biofilm to stick to one another. Zinc chelation, or removal, prevented biofilm formation by Staphylococcus epidermidis and Staphylococcus aureus. The researchers used a chelation agent called DTPA (diethylenetriamine pentaacetic acid) to remove the zinc from a sample biofilm.

"We've shown that if you remove the zinc, you prevent the biofilm from forming, and if you add zinc back, the biofilm can grow," says Herr. "So we're hopeful that we can use this sort of approach to prevent these biofilms from ever taking hold in the first place."

The most practical applications, Herr says, might involve coatings for implanted medical devices, or rinses that a surgeon could use to clear the area around the implant.

Systemic removal of zinc, such as through an intravenous injection, is impractical for now because DTPA is approved by the U.S. Food and Drug Administration only for people with radio isotope poisoning. In addition, zinc is known to activate immune cells and play many other important roles in the body, so a proper balance would need to be developed.

*Herr had access to funds from the Ohio Eminent Scholars Program and also received a pilot grant from the Cincinnati Microbial Pathogenesis Center for the study. He intends to apply for a National Institutes of Health grant in 2009 to continue his research.*

*The research team, in addition to Herr, consisted of graduate student Deborah Conrady; postdoctoral fellows Cristin Brescia, PhD, and Katsunori Horii, PhD; and UC molecular genetics, biochemistry and microbiology professors Alison Weiss, PhD, and Daniel Hassett, PhD.*

## Mix of taiji, cognitive therapy and support groups benefits those with dementia

Those diagnosed with early stage dementia can slow their physical, mental and psychological decline by taking part in therapeutic programs that combine counseling, support groups, Taiji and qigong, researchers report. Some of the benefits of this approach are comparable to those achieved with anti-dementia medications.

The findings are detailed in the American Journal of Alzheimer's Disease and Other Dementias.

"Most of the research on dementia and most of the dollars up until this point have gone into pharmacological interventions," said Sandy Burgener, a professor of nursing at the University of Illinois and lead author on the study. "But we have evidence now from studies like mine that show that other approaches can make a difference in the way people live and can possibly also impact their cognitive function."

In the study, 24 people with early stage dementia participated in an intensive 40-week program. The intervention included biweekly sessions of cognitive behavioral therapy and support groups, along with three sessions per week of traditional Chinese martial arts exercises and meditation, called qigong (chee-gong) and Taiji (tye-jee). A comparison group of people with early stage dementia did not participate in these programs for the first 20 weeks of the intervention.

Researchers are discovering that multi-disciplinary approaches – those that address patients' physical, mental and psychological dimensions – show the most promise in treating people with dementia, Burgener said.

"There's a lot of support for multi-modal therapies for persons with dementia, especially those with early stage dementia," she said. "Not only can we help people have a higher quality of life, but these treatments support neuronal function and have the potential for neuronal regeneration."

Earlier studies have shown that such programs can work as well as anti-dementia drugs, Burgener said.

Qigong and Taiji combine simple physical movements and meditation. Qigong is a series of integrated exercises believed to positively affect the mind, body and spirit. Taiji is a type of qigong that melds Chinese philosophy with martial and healing arts, said Yang Yang, a professor of kinesiology and community health and a co-author of the study. He is a master Taiji and qigong instructor whose research focuses on the efficacy of Taiji and qigong for older adults.

Cognitive behavioral therapy is a form of psychotherapy that seeks positive alternatives to the beliefs and behaviors that can undermine a person's health and happiness. Research has shown that cognitive behavioral therapy and support groups aid those who struggle with depression and other physical or mental health problems.

Participants in the program benefited in a variety of ways. After 20 weeks, those in the treatment group improved in several measures of physical function, including balance and lower leg strength, while those in the comparison group did not. There were also positive cognitive and psychological effects, Burgener said.

"We saw gains in self-esteem in the treatment group and pretty severe declines in self-esteem in the comparison group," she said. "Those in the treatment group also had sustained and slightly improved mental status scores, which meant we were impacting cognitive function."

Both groups saw increases in depression, Burgener said, but the increase for those in the treatment group was a fraction of that seen in the comparison group. No additional benefits were seen after 40 weeks, but participants were able to maintain their initial gains.

The intervention was quite popular with the study subjects and their caregivers. Although designed (and funded) to include only 10 participants and 10 people in the comparison group, Burgener and her colleagues enrolled 46 people in the program, with those in the comparison group starting the intervention after 20 weeks.

"People drove from all over to be in this study because there's nothing like this available for them anywhere else," Burgener said. The program was so popular that she and her colleagues have kept it going for more than three years, with many of the first participants and their caregivers still engaged.

"The clinical findings, from my perspective, go far beyond the statistical findings," Burgener said. "People were happier when they were in the treatment group. Two men came in with walkers and left without them. One is in our Taiji group three years later and is still not using a walker."

Another participant began the program with a score of 26 on a 30-point test of mental status. A score of 24 or below is suggestive of dementia, Burgener said. This man stayed with the group and was recently re-tested. His score was still 26. "That's never going to show up as a statistical finding but that case example is pretty profound," she said.

Burgener is an advocate for further research into non-pharmacological interventions for people with dementia, which she sees as co-therapies to the drugs that are given to many people when they are first diagnosed. "Funders and insurance companies are willing to put money into drugs, but it's been a hard sell to get money for these kinds of programs," she said.

## Gene packaging tells story of cancer development

To decipher how cancer develops, Johns Hopkins Kimmel Cancer Center investigators say researchers must take a closer look at the packaging.

Specifically, their findings in the December 2, 2008, issue of PLoS Biology point to the three dimensional chromatin packaging around genes formed by tight, rosette-like loops of Polycomb group proteins (PcG). The chromatin packaging, a complex combination of DNA and proteins that compress DNA to fit inside cells, provides a repressive hub that keeps genes in a low expression state. "We think the polycomb proteins combine with abnormal DNA methylation of genes to deactivate tumor suppressor genes and lock cancer cells in a primitive state," says Stephen B. Baylin, M.D., Virginia and D.K. Ludwig Professor of Oncology and senior author.

Prior to this discovery, investigators studying cancer genes, looked at gene silencing as a linear process across the DNA, as if genes were flat, one dimensional objects. Research did not take into account the way genes are packaged.

To better understand the role of the PcG packaging, the team compared embryonic cells to adult colon cancer cells. The gene studied in the embryonic cells was packaged by PcG proteins, in a low expression state, and had no DNA methylation. When the gene received signals for cells to mature, the PcG loops were disrupted and the gene was highly expressed. However, when the same gene was abnormally DNA methylated, as is the case in adult, mature colon cancer cells, the PcG packaging loops were tighter and there was no gene expression. "These tight loops touch and interact with many gene sites folding it into a structure that shuts off tumor suppressor genes," says Baylin. However, when the researchers removed DNA methylation from the cancer cells, the loops loosened somewhat, back to the state of an embryonic cell, and some gene expression was restored.

DNA methylation is a normal cellular process, but when it goes awry and genes are improperly methylated, it can shut down important tumor suppressing cell functions. Demethylating agents, drugs that target and remove abnormal DNA methylation from genes, have been introduced as potential new cancer therapies. For these therapies to be fully effective, Baylin says, researchers may also need to look for agents that disrupt PcG loops.

*Working with Baylin on this research were Vijay K. Tiwari, Kelly M. McGarvey, Julien D. F. Licchesi, Joyce E. Ohm, James G. Herman, and Dirk Schübeler.*

*The research was funded by the National Institutes of Environmental Health Sciences, the National Institutes of Health, and the Novartis Research Foundation.*

## New Target Discovered to Treat Epileptic Seizures Following Brain Trauma or Stroke

New therapies for some forms of epilepsy may soon be possible, thanks to a discovery made by a team of University of British Columbia and Vancouver Coastal Health Research Institute neuroscience researchers.

The researchers found that hemichannels – the same channels the researchers previously found to that cause cell death following a stroke – may also cause epileptic seizures that occur following head trauma or a stroke. The findings, published tomorrow in Science, will allow researchers to focus on new treatments that block these channels. A hemichannel is a channel that can form in nerve cells which allows chemical ions to pass through. "The glutamate receptor that is linked to cell death following a stroke also triggers opening of hemichannels," says UBC Psychiatry Prof. Brian MacVicar, who is a member of the Brain Research Centre at UBC and VCH Research Institute. "Therefore both stroke itself or the glutamate released by a stroke can open hemichannels and cause cell death or epileptic seizures."

The researchers tested the effect of glutamate at levels less than those reached during stroke and found that more moderate activation of glutamate receptors opens hemichannels and causes seizure but does not produce cell death associated with stroke. Glutamate is one of the brain's most abundant chemical messengers. Gap junctions are connections that allow molecules and ions, to flow between cells. Junctions are composed of two hemichannels that bridge intercellular space.

When epileptic seizures occur, hemichannels unexpectedly open near the synapses, which disrupt the normal electrical activity of the brain leading to seizures. "We found that blocking hemichannels reduced the epilepsy-like discharges," says Roger Thompson, a former UBC Psychiatry post-doctoral Fellow who is now an Assistant Professor of Cell Biology, Anatomy and Clinical Neurosciences at the University of Calgary.

"With these results we are confident that the discovery of safe blockers of hemichannels will provide a new therapy in the treatment to reduce cell loss and seizures that are caused by stroke," says MacVicar, who also holds the Canada Research Chair in Neuroscience at UBC. "The next step will be to develop a compound to block brain cell hemichannels from opening," says MacVicar. "Therapies for epilepsy patients who have suffered a stroke or head trauma may be available within five to 10 years."

According to the BC Epilepsy Society it is estimated that one out of 12 people will have a seizure in their lifetime, and close to one in 100 Canadians have epilepsy. An epileptic seizure is an abnormal burst of electrical activity within the brain.

## Humans 80,000 Years Older Than Previously Thought?

**Kate Ravilious** for National Geographic News

Modern humans may have evolved more than 80,000 years earlier than previously thought, according to a new study of sophisticated stone tools found in Ethiopia. The tools were uncovered in the 1970s at the archaeological site of Gademotta, in the Ethiopian Rift Valley. But it was not until this year that new dating techniques revealed the tools to be far older than the oldest known Homo sapiens bones, which are around 195,000 years old.

Using argon-argon dating - a technique that compares different isotopes of the element argon - researchers determined that the volcanic ash layers entombing the tools at Gademotta date back at least 276,000 years.

Many of the tools found are small blades, made using a technique that is thought to require complex cognitive abilities and nimble fingers, according to study co-author and Berkeley Geochronology Center director Paul Renne.

Some archaeologists believe that these tools and similar ones found elsewhere are associated with the emergence of the modern human species, Homo sapiens. "It seems that we were technologically more advanced at an earlier time that we had previously thought," said study co-author Leah Morgan, from the University of California, Berkeley. The findings are published in the December issue of the journal Geology.

**Desirable Location**

Gademotta was an attractive place for people to settle, due to its close proximity to fresh water in Lake Ziway and access to a source of hard, black volcanic glass, known as obsidian. "Due to its lack of crystalline structure, obsidian glass is one of the best raw materials to use for making tools," Morgan explained.

In many parts of the world, archaeologists see a leap around 300,000 years ago in Stone Age technology from the large and crude hand-axes and picks of the so-called Acheulean period to the more delicate and diverse points and blades of the Middle Stone Age.

At other sites in Ethiopia, such as Herto in the Afar region northeast of Gademotta, the transition does not occur until much later, around 160,000 years ago, according to argon dating. This variety in dates supports the idea of a gradual transition in technology. "A modern analogy might be the transition from ox-carts to automobiles, which is virtually complete in North America and northern Europe, but is still underway in the developing world," said study co-author Renne, who received funding for the Gadmotta analysis from the

National Geographic Society's Committee for Research and Exploration. (The National Geographic Society owns National Geographic News.)

Morgan, of UC Berkeley, speculates that the readily available obsidian at Gademotta may explain why the technological revolution occurred so early there.

**Complicated family tree**

The lack of bones at Gademotta makes it difficult to determine who made these specialist tools. Some archaeologists believe it had to be Homo sapiens, while other experts think that other human species may have had the required mental capability and manual dexterity.

Regardless of who made the tools, the dates help to fill a key gap in the archaeological record, according to some experts. "The new dates from Gademotta help us to understand the timing of an important behavioral change in human evolution," said Christian Tryon, a professor of anthropology from New York University, who wasn't involved in the study.

If anything, the story has now become more complex, added Laura Basell, an archaeologist at the University of Oxford in the U.K. "The new date for Gademotta changes how we think about human evolution, because it shows how much more complicated the situation is than we previously thought," Basell said. "It is not possible to simply associate specific species with particular technologies and plot them in a line from archaic to modern."

## Company tries to get gun classed as medical device

* Updated 19:01 05 December 2008 **by Ewen Callaway**

A US company claims to have received federal approval to market a 9-mm handgun as a medical device and hopes the US government will reimburse seniors who buy the $300 firearm. But the US Food and Drug Administration says there are currently no formal designations of the gun as a medical device.

Called the Palm Pistol, the weapon is designed for people who have trouble firing a normal handgun due to arthritis and other debilitating conditions. "It's something that they need to assist them in daily living," says Matthew Carmel, president of Constitution Arms in Maplewood, New Jersey, which hopes to manufacture the Palm Pistol - now just a patent and specifications. "The justification for this would be no more or less for a [walking aid] or wheelchair, or any number of things that are medical devices," he says.

The sales information reads: "It is also ideal for seniors, disabled or others who may have limited strength or manual dexterity. Using the thumb instead of the index finger for firing, it significantly reduces muzzle drift, one of the principal causes of inaccurate targeting. Point and shoot couldn't be easier."

Constitutional Arms informed a medical technology blog that the FDA had approved the Palm Pistol as a medical device, classifying it as a "Daily Activity Assist Device".

The company reportedly said that they are now seeking a Durable Medical Equipment coding for the gun, which if awarded would allow it to be prescribed and reimbursement paid through Medicare or private health insurance.

***Currently at the design stage, the Palm Pistol is intended for people such as the elderly or disabled who have trouble handling a normal weapon*** **(Illustrations: Constitution Arms)**

**Health benefits?**

But FDA spokeswoman Siobhan DeLancey denies that the agency has formally labelled the gun a medical device: "At this time, there have been no formal designations of the Palm Pistol by the FDA as a medical device." "The FDA doesn't make a determination about a weapon, they make a determination about medical products that are designed to help people and improve their health," says Bill Maisel, Director of the Medical Device Safety Institute at Beth Israel Deaconess Medical Center in Boston.

Carmel contends that he submitted documentation to the FDA to get Palm Pistol listed as a Class I medical device - a classification reserved for devices that pose little risk to a patient's health, such as stethoscopes and walking aids.

**Registration doubts**

As evidence of the government's stamp of approval, Carmel points to a notice (pdf format) he received from FDA. Dated 2 December 2008, it reads: "You have successfully entered your facility registration and device listing information," then goes onto list an address in Maplewood, New Jersey, for Constitution Arms.

"I see that a facility has been registered. That does not register a device or a pistol," Maisel says.

Even if the FDA were to approve the Palm Pistol as a medical device, securing Medicare reimbursement is another issue entirely, says Kevin Schulman, an expert on medical device regulation at Duke University Medical Center in Durham, North Carolina. "Medicare does not cover everything that FDA approves."

**'Nice gimmick'**

To reimburse a drug, treatment or device, Medicare must determine that it is reasonable and necessary in the course of medical treatment, he says. "The first question for Medicare is whether this would be potentially beneficial, and the answer seems to be obviously no."

Constitution Arms is taking pre-orders for the Palm Pistol, while Carmel determines whether the market is large enough to go into production. "I've been getting a lot of calls," he says.

For $25, customers can be one of the first to own the weapon, which Carmel expects to deliver by 2010. The refundable deposit will sit in an escrow account and serve as proof to investors that the Palm Pistol has a sizeable market, he says.

The potential for Medicare reimbursement, and perhaps even payment from private insurers will also encourage investors. "It's not implanted in the body, but the obvious result of this thing [a bullet] could be," says Schulman. "It's a nice gimmick for this manufacturer, but I can't imagine that Medicare would pay for this, since it doesn't meet their criteria," he says. "They're trying to game the system, clearly, but hopefully they won't get much further."

## Brain quirk makes eyewitnesses less reliable

* 16:14 05 December 2008 **by Ewen Callaway**

Eyewitness accounts of crimes could be more untrustworthy than we thought.

Describing an event straight after it occurs makes witnesses more susceptible to providing false information in subsequent retellings, a new study finds.

"In a real-life situation, if you're an eyewitness, the first thing you're going to do after you witness an event is call 911," says Jason Chan, a psychologist at Iowa State University in Ames, who led the new study.

This initial recollection could prime a witness' brain to accept a mistaken account, he says, be it from television, lawyers, the police, or another witness.

Rather than crimes, Chan's team tested the memories of 36 university students and 60 retirees who watched an episode of the television drama 24. Immediately after seeing the episode - in which terrorists hijack a jet - half of the subjects took a quiz on what they had just seen.

About 30 minutes later, everyone listened to a short description of the episode, which included details that were either lies or truths. For instance: "The terrorist knocks the flight attendant unconscious with a hypodermic needle" (true); or "The terrorist knocks the flight attendant unconscious with a chloroform rag" (false).

**Recall test**

Next, everyone took the same recall test, earlier administered to just half the participants. "What we found was completely surprising," Chan says.

Students and retirees who earlier recalled the TV episode got fewer questions right and more wrong - subjects could leave questions unanswered - than people who hadn't been previously quizzed.

"If you recall the event earlier, you increase susceptibility to misinformation," Chan says.

He offers two possible explanations for his team's results. Firstly, testing is well established as a memory aid in teaching, but not everything we learn is correct. Recalling the episode of 24 may have reinforced people's prior misconceptions, Chan says. "Taking a test, recalling something, actually enhances your ability to learn misinformation."

A second possibility, not exclusive to the first, is that the act of remembering makes a memory malleable, and therefore susceptible to misinformation.

**Malleable mind?**

In experiments not unlike the film Eternal Sunshine of the Spotless Mind, researchers erased long-term memories in rodents by jogging the same memory while tweaking chemical signals involved in forming and maintaining memories.

Misinformation could work via the same mechanism - called reconsolidation. However, Chan calls these results preliminary. "Our study shows that reconsolidation of episodic memory may exist."

"This is a really surprising result," says Elizabeth Loftus, a psychologist at the University of California, Irvine, who first showed the potential for false information to seep into memory in the 1970s.

Scores of studies have shown that testing benefits learning, rather than hinders it. "Here is a way in which testing seems to have harmed people rather the usual finding that it's helping people," she says.

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## Maintaining the brain's wiring in aging and disease

Researchers at the Babraham Institute near Cambridge, supported by the Alzheimer's Research Trust and the Biotechnology and Biological Sciences Research Council (BBSRC), have discovered that the brain's circuitry survives longer than previously thought in diseases of ageing such as Alzheimer's disease. The findings were published today in the journal Brain.

Alzheimer's disease causes nerve cells in the brain to die, resulting in problems with memory, speech and understanding. Little is known about how the nerve cells die, but this new research has revealed how they first lose the ability to communicate with each other, before deteriorating further.

"We've all experienced how useless a computer is without broadband. The same is true for a nerve cell (neuron) in the brain whose wiring (axons and dendrites) has been lost or damaged," explained Dr Michael Coleman the project's lead researcher. "Once the routes of communication are permanently down, the neuron will never again contribute to learning and memory, because these 'wires' do not re-grow in the human brain."

But axons and dendrites are much more than inert fibre-optic wires. They are homes to the world's smallest transport tracks. Every one of our hundred billion nerve cells continuously shuttles hundreds of proteins and intracellular packages out along its axons and dendrites, and back again, during every minute of every day. Without this process, the wires cannot be maintained and the nervous system will cease to function within a few hours.

During healthy ageing this miniature transport system undergoes a steady decline, but the challenges are immense. Axons up a metre long have to survive and function for at least eight or nine decades. Over this period, our homes will need rewiring several times, but in our brains the wires are all original, surviving from childhood. In Alzheimer's disease, axons swell dramatically, ballooning to 10 or 20 times their normal diameter. These swellings disrupt transport but not, it seems, completely. Enough material gets through the swellings to keep more distant parts of the axon alive for at least several months, and probably for a year or more. This is important because it suggests a successful therapy applied during this early period may not only halt the symptoms, but allow a degree of functional recovery.

"We've been able to look at whole nerve cells affected by Alzheimer's", said Dr Michael Coleman. "For the first time we have shown that supporting parts of nerve cells are alive, and we can now learn how to intervene to recover connections. This is very important for treatment because in normal adult life, nerve cell connections constantly disappear and reform, but can only do so if the supporting parts of the cell remain. Our results suggest a time window in which damaged connections between brain cells could recover under the right conditions."

This basic research gives hope over the longer term to the 700,000 people in the UK who live with dementia. Understanding how the brain responds to disease also tells us a lot about how it functions in all of us.

## Spider love: Little guys get lots more

Big males outperform smaller ones in head-to-head mating contests but diminutive males make ten times better lovers because they're quicker to mature and faster on their feet, a new study of redback spiders reveals.

Published in the current online issue of Journal of Evolutionary Biology, the study shows the importance of maturation in defining mating and paternity success. In field enclosures, researchers simulated two competitive contexts favouring the development of differently sized male redbacks (Latrodectus hasselti). The larger males were more successful at mating with and impregnating females when they competed directly with smaller males. However, when faster maturing smaller males were given a one-day head start, reflecting their earlier maturation in nature, they had a ten-times higher paternity rate than larger males.

Courtship between redbacks lasts an average of 50 minutes when males are competing and 4.5 hours for single, non-competing males. Copulation lasts from 6 to 31 minutes, and males are usually injured or killed during the process.

"The results reveal that big males don't get it all their own way," says lead author, UNSW postdoctoral fellow, Dr Michael Kasumovic, who co-authored the paper with Maydianne Andrade of the University of Toronto. "Nature favours larger and smaller males under different circumstances. Larger males experienced a longer maturation process so they are unable to search for and mate with females and produce offspring at the same rate as smaller redback spiders.

"Large size and weaponry are strong predictors of a male's competitive strengths because those traits help them dominate smaller males when they compete for food and mating rights. However, evidence from studies of midges, dung flies and seed beetles reveals that smaller males develop sooner than larger males and often mate before larger competing males arrive on the scene. Size isn't the only ruler by which we can measure a male's quality. Many other factors, including maturation time, are critical in that definition."