

Infections may lead to faster memory loss in Alzheimer's disease

ST. PAUL, Minn. – Getting a cold, stomach bug or other infection may lead to increased memory loss in people with Alzheimer's disease, according to research published in the September 8, 2009, print issue of *Neurology*®, the medical journal of the American Academy of Neurology.

The study found that people who had respiratory, gastrointestinal or other infections or even bumps and bruises from a fall were more likely to have high blood levels of tumor necrosis factor- α , a protein involved in the inflammatory process, and were also more likely to experience memory loss or other types of cognitive decline than people who did not have infections and who had low levels of the protein.

The blood levels and cognitive abilities of 222 people with Alzheimer's disease with an average age of 83 were measured at the beginning of the study and three more times over six months. Caregivers were interviewed to determine whether the participants had experienced any infections or accidental injury that could lead to inflammation.

A total of 110 people experienced an infection or injury that led to inflammation during the study. Those people experienced memory loss that was at twice the rate of those who did not have infections or injuries.

People who had high levels of the protein in their blood at the beginning of the study, which may indicate chronic inflammation, had memory loss at four times the rate of those with low levels of the protein at the start of the study. Those who had high levels of the protein at the start of the study who also experienced acute infections during the study had memory loss at 10 times the rate of those who started with low levels and had no infections over the six-month period.

"One might guess that people with a more rapid rate of cognitive decline are more susceptible to infections or injury, but we found no evidence to suggest that people with more severe dementia were more likely to have infections or injuries at the beginning of the study," said study author Clive Holmes, MRCPsych, PhD, of the University of Southampton in the United Kingdom. "More research needs to be done to understand the role of tumor necrosis factor-alpha in the brain, but it's possible that finding a way to reduce those levels could be beneficial for people with Alzheimer's disease." *The study was supported by the Alzheimer's Society in London, UK.*

Researchers find first evidence of virus in malignant prostate cells

XMRV retrovirus is associated with more aggressive tumors

(SALT LAKE CITY) – In a finding with potentially major implications for identifying a viral cause of prostate cancer, researchers at the University of Utah and Columbia University medical schools have reported that a type of virus known to cause leukemia and sarcomas in animals has been found for the first time in malignant human prostate cancer cells.

If further investigation proves the virus, XMRV (Xenotropic murine leukemia virus-related virus), causes prostate cancer in people, it would open opportunities for developing diagnostic tests, vaccines, and therapies for treating the cancer, according to the study published Sept. 7 online in the *Proceedings of the National Academy of Sciences*. Prostate cancer is expected to strike nearly 200,000 U.S. males this year, making it the second most common form of cancer, outside of skin cancers, among men.

"We found that XMRV was present in 27 percent of prostate cancers we examined and that it was associated with more aggressive tumors," said Ila R. Singh, M.D., Ph.D., associate professor of pathology at University of Utah and the study's senior author. "We still don't know that this virus causes cancer in people, but that is an important question we're going to investigate."

Singh, also a member of the U of U's Huntsman Cancer Institute and associate medical director at ARUP Laboratories, moved to Utah from Columbia University Medical Center in 2008, where she began this research. She remains an adjunct faculty member at Columbia.

Along with providing the first proof that XMRV is present in malignant cells, the study also confirmed that XMRV is a gammaretrovirus, a simple retrovirus first isolated from prostate cancers in 2006 by researchers at the University of California, San Francisco (UCSF), and the Cleveland Clinic. Gammaretroviruses are known to cause cancer in animals, but have not been shown to do so in humans. The UCSF study did not examine benign (non-malignant) prostate tissues, so could not link XMRV to prostate cancer. They also did not find the virus in malignant cells.

Singh and her fellow researchers examined more than 200 human prostate cancers, and compared them to more than 100 non-cancerous prostate tissues. They found 27 percent of the cancers contained XMRV, compared to only 6 percent of the benign tissues. The viral proteins were found almost exclusively in malignant prostatic cells, suggesting that XMRV infection may be directly linked to the formation of tumors.

Retroviruses insert a DNA copy of their genome into the chromosomes of the cells they infect. Such an insertion sometimes occurs adjacent to a gene that regulates cell growth, disrupting normal cell growth, resulting in more rapid proliferation of such a cell, which eventually develops into a cancer. This mechanism of

carcinogenesis is followed by gammaretroviruses in general. Singh is currently examining if a similar mechanism might be involved with XMRV and prostate cancer.

In another important finding of the study, Singh and her colleagues also showed that susceptibility to XMRV infection is not enhanced by a genetic mutation, as was previously reported. If XMRV were caused by the mutation, only the 10 percent of the population who carry the mutated gene would be at risk for infection with virus. But Singh found no connection between XMRV and the mutation, meaning the risk for infection may extend to the population at large.

While the study answers important questions about XMRV, it also raises a number of other questions, such as whether the virus infects women, is sexually transmitted, how prevalent it is in the general population, and whether it causes cancers in tissues other than the prostate.

"We have many questions right now," Singh said, "and we believe this merits further investigation."

Viruses have been shown to cause cancer of the cervix, connective tissues (sarcomas), immune system (lymphoma), and other organs. If the retrovirus is shown to cause prostate cancer, this could have important implications for preventing viral transmission and for developing vaccines to prevent XMRV infection in people.

Using insects to test for drug safety

Insects, such as some moths and fruit flies, react to microbial infection in the same way as mammals and so can be used to test the efficiency of new drugs, thereby reducing the need for animal testing. Dr Kevin Kavanagh from the National University of Ireland – Maynooth, presented his research findings at the Society for General Microbiology's meeting at Heriot Watt University, Edinburgh, today (8 September).

Neutrophils, which are a type of white blood cell and part of the mammalian immune system, and haematocytes, which are cells that carry out a similar function in insects, react in the same way to infecting microbes. Both the insect and mammalian cells produce chemicals with a similar structure which move to the surface of the cells to kill the invading microbe. The immune cells then enclose the microbe and release enzymes to break it down.

Insects such as fruit flies (*Drosophila*), Greater Wax Moths (*Galleria*) and a type of Hawkmoth (*Manduca*) can be used to test the efficacy of new antimicrobial drugs or to judge how virulent fungal pathogens are. It is now routine practice to use insect larvae to perform initial testing of new drugs and then to use mice for confirmation tests. As well as reducing by up to 90% the number of mice required, this method of testing is quicker as tests with insects yield results in 48 hours whereas tests with mice usually take 4-6 weeks.

"We will continue to explore the similarities between insect and mammalian immune responses so that insects can be used as models to study different disease states in humans," said Dr Kavanagh.

"In addition we have shown that immune cells in insects and mammals are structurally and functionally similar despite being separated by over 400 million years of evolution."

'Liposuction leftovers' easily converted to IPS cells, Stanford study shows

STANFORD, Calif. - Globes of human fat removed during liposuction conceal versatile cells that are more quickly and easily coaxed to become induced pluripotent stem cells, or iPS cells, than are the skin cells most often used by researchers, according to a new study from Stanford's School of Medicine.

"We've identified a great natural resource," said Stanford surgery professor and co-author of the research, Michael Longaker, MD, who has called the readily available liposuction leftovers "liquid gold." Reprogramming adult cells to function like embryonic stem cells is one way researchers hope to create patient-specific cell lines to regenerate tissue or to study specific diseases in the laboratory.

"Thirty to 40 percent of adults in this country are obese," agreed cardiologist Joseph Wu, MD, PhD, the paper's senior author. "Not only can we start with a lot of cells, we can reprogram them much more efficiently. Fibroblasts, or skin cells, must be grown in the lab for three weeks or more before they can be reprogrammed. But these stem cells from fat are ready to go right away."

The fact that the cells can also be converted without the need for mouse-derived "feeder cells" may make them an ideal starting material for human therapies. Feeder cells are often used when growing human skin cells outside the body, but physicians worry that cross-species contamination could make them unsuitable for human use.

The findings will be published online Sept. 7 in the Proceedings of the National Academy of Sciences. Longaker is the deputy director of Stanford's Stem Cell Biology and Regenerative Medicine Institute and director of children's surgical research at Lucile Packard Children's Hospital. Wu is an assistant professor of cardiology and radiology, and a member of Stanford's Cardiovascular Institute.

Even those of us who are not obese would probably be happy to part with a couple of pounds (or more) of flab. Nestled within this unwanted latticework of fat cells and collagen are multipotent cells called adipose, or

fat, stem cells. Unlike highly specialized skin-cell fibroblasts, these cells in the fat have a relatively wide portfolio of differentiation options - becoming fat, bone or muscle as needed. It's this pre-existing flexibility, the researchers believe, that gives these cell an edge over the skin cells.

"These cells are not as far along on the differentiation pathway, so they're easier to back up to an earlier state," said first author and postdoctoral scholar Ning Sun, PhD, who conducted the research in both Longaker's and Wu's laboratories. "They are more embryonic-like than fibroblasts, which take more effort to reprogram."

These reprogrammed iPS cells are usually created by expressing four genes, called Yamanaka factors, normally unexpressed (or expressed at very low levels) in adult cells.

Sun found that the fat stem cells actually express higher starting levels of two of the four reprogramming genes than do adult skin cells - suggesting that these cells are already primed for change. When he added all four genes, about 0.01 percent of the skin-cell fibroblasts eventually became iPS cells but about 0.2 percent of the fat stem cells did so - a 20-fold improvement in efficiency.

The new iPS cells passed the standard tests for pluripotency: They formed tumors called teratomas when injected into immunocompromised mice, and they could differentiate into cells from the three main tissue types in the body, including neurons, muscle and gut epithelium. The researchers are now investigating whether the gene expression profiles of the fat stem cells could be used to identify a subpopulation that could be reprogrammed even more efficiently.

"The idea of reprogramming a cell from your body to become anything your body needs is very exciting," said Longaker, who emphasized that the work involved not just a collaboration between his lab and Wu's, but also between the two Stanford institutes. "The field now needs to move forward in ways that the Food and Drug Administration would approve - with cells that can be efficiently reprogrammed without the risk of cross-species contamination - and Stanford is an ideal place for that to happen."

"Imagine if we could isolate fat cells from a patient with some type of congenital cardiac disease," said Wu. "We could then differentiate them into cardiac cells, study how they respond to different drugs or stimuli and see how they compare to normal cells. This would be a great advance."

In addition to Sun, Wu and Longaker, other Stanford collaborators on the research include postdoctoral scholars Nicholas Panetta, MD, Deepak Gupta, MD, and Shijun Hu, PhD; graduate student Kitchener Wilson; medical student Andrew Lee; research assistant Fangjun Jia, PhD; associate professor of pathology and of pediatrics Athena Cherry, PhD; and professor of cardiothoracic surgery Robert Robbins, MD.

The research was supported by the Mallinckrodt Foundation, the American Heart Association, the California Institute for Regenerative Medicine, the National Institutes of Health, the Stanford Cardiovascular Institute, the Oak Foundation and the Hagey Laboratory for Pediatric Regenerative Medicine.

Fat reprograms genes linked to diabetes

* 12:44 07 September 2009 by Andy Coghlan

A gene that helps muscle cells burn fat can be radically altered and switched off if the cells carrying it are exposed to fat. The finding suggests that the same process may occur when people eat too much fat-rich junk food, resulting in drastic changes to this "fat burning" gene.

"Somehow, the environment plays on the genes we have," says lead researcher, Juleen Zierath of the Karolinska Institute in Stockholm, Sweden. She says her team's findings provide new clues to how this happens, and may help explain how type II diabetes develops in adulthood.

One possibility, she says, is that the altered cells become so engorged with unburnt fat, they become "diabetic", no longer accepting signals from the hormone insulin, which normally triggers the absorption of glucose from the bloodstream.

But proof that components in the diet can permanently alter genes is itself a breakthrough, providing the first evidence that the food we eat may change the function of our DNA. This is a process known as "epigenetics".

Fat switches off genes

In this study the DNA itself remained unchanged, except for a masking process called methylation which can permanently mothball a gene by capping individual chemical units, or bases.

Earlier in the same set of experiments, the researchers discovered that muscle cells from people with type II diabetes already showed these telltale epigenetic alterations to their DNA, particularly in the PGC-1 gene, which orchestrates metabolic programmes critical to the burning of fat in mitochondria, the chambers in cells that generate energy. By contrast, the healthy muscle cells from non-diabetics functioned normally.

The most significant result came when one team member, Romain Barrés, exposed the healthy muscle cells to the edible fatty acid, palmitic acid. He found that the PGC-1 gene became methylated, just as it is in people with diabetes.

"The palmitic acid essentially switches off the gene," says Zierath. The same thing happened on exposure to tumour necrosis factor-alpha, a substance produced by white blood cells to help fight infection.

Can't burn fat

But the fact fat produced the effect is highly significant, because it means that over-consumption of junk food could produce the same response. "It suggests that if you eat a fat-rich diet, something in that - either the fat itself or the build up of metabolites - triggers the methylation of genes. The net effect is that it switches off the gene," says Zierath. This, in turn, could lead to the gradual shutdown of mitochondria, an effect already observed in muscle cells from type II diabetics.

The team's analyses also reveal that the shutdown of PGC-1 led to inactivation of other genes vital for burning or transporting fat, such as those that produce the enzymes citrate synthase and carnitine palmitoyltransferase-2.

What you eat

The next step, says Zierath, is to find out how different diets affect the methylation status of PGC-1 and other genes vital for burning energy. In one study, she hopes to take muscle biopsies from obese patients before and after they undergo bariatric surgery to cut appetite by reducing the size of their stomachs.

Through this and other experiments to probe the effects of diet on gene function, Zierath and her colleagues hope to tease out a potential mechanism by which type II diabetes develops.

One intriguing unknown is whether methylation of genes triggered by exposure to fat is inheritable. If it is, it means that the "disease" would be handed down from parents to their children and could explain previous research indicating that what you eat could affect all your descendants.

Journal reference: Cell Metabolism, DOI: 10.1016/j.cmet.2009.07.011

Half of the fish consumed globally is now raised on farms, study finds

Aquaculture, once a fledgling industry, now accounts for 50 percent of the fish consumed globally, according to a new report by an international team of researchers. And while the industry is more efficient than ever, it is also putting a significant strain on marine resources by consuming large amounts of feed made from wild fish harvested from the sea, the authors conclude. Their findings are published in the Sept. 7 online edition of the Proceedings of the National Academy of Sciences (PNAS).

"Aquaculture is set to reach a landmark in 2009, supplying half of the total fish and shellfish for human consumption," the authors wrote. Between 1995 and 2007, global production of farmed fish nearly tripled in volume, in part because of rising consumer demand for long-chain omega-3 fatty acids. Oily fish, such as salmon, are a major source of these omega-3s, which are effective in reducing the risk of cardiovascular disease, according to the National Institutes of Health.

"The huge expansion is being driven by demand," said lead author Rosamond L. Naylor, a professor of environmental Earth system science at Stanford University and director of the Stanford Program on Food Security and the Environment. "As long as we are a health-conscious population trying to get our most healthy oils from fish, we are going to be demanding more of aquaculture and putting a lot of pressure on marine fisheries to meet that need."

Fishmeal and fish oil

To maximize growth and enhance flavor, aquaculture farms use large quantities of fishmeal and fish oil made from less valuable wild-caught species, including anchoveta and sardine. "With the production of farmed fish eclipsing that of wild fish, another major transition is also underway: Aquaculture's share of global fishmeal and fish oil consumption more than doubled over the past decade to 68 percent and 88 percent, respectively," the authors wrote.

In 2006, aquaculture production was 51.7 million metric tons, and about 20 million metric tons of wild fish were harvested for the production of fishmeal. "It can take up to 5 pounds of wild fish to produce 1 pound of salmon, and we eat a lot of salmon," said Naylor, the William Wrigley Senior Fellow at Stanford's Woods Institute for the Environment and Freeman Spogli Institute for International Studies.

One way to make salmon farming more environmentally sustainable is to simply lower the amount of fish oil in the salmon's diet. According to the authors, a mere 4 percent reduction in fish oil would significantly reduce the amount of wild fish needed to produce 1 pound of salmon from 5 pounds to just 3.9 pounds. In contrast, reducing fishmeal use by 4 percent would have very little environmental impact, they said.

"Reducing the amount of fish oil in the salmon's diet definitely gets you a lot more bang for the buck than reducing the amount of fishmeal," Naylor said. "Our thirst for long-chain omega-3 oils will continue to put a lot of strain on marine ecosystems, unless we develop commercially viable alternatives soon."

Naylor and her co-authors pointed to several fish-feed substitutes currently being investigated, including protein made from grain and livestock byproducts, and long-chain omega-3 oils extracted from single-cell microorganisms and genetically modified land plants. "With appropriate economic and regulatory incentives, the transition toward alternative feedstuffs could accelerate, paving the way for a consensus that aquaculture is aiding the ocean, not depleting it," the authors wrote.

Vegetarian fish

Fishmeal and fish oil are important staples at farms that produce carnivorous fish, including salmon, trout and tuna. But vegetarian species, such as Chinese carp and tilapia, can be raised on feed made from plants instead of wild-caught fish. That's one reason why farm-raised vegetarian fish have long been considered environmentally friendly.

In the early 1990s, vegetarian fish farms began adding small amounts of fishmeal in their feed to increase yields. However, between 1995 and 2007, farmers actually reduced the share of fishmeal in carp diets by 50 percent and in tilapia diets by nearly two-thirds, according to the PNAS report. Nevertheless, in 2007, tilapia and carp farms together consumed more than 12 million metric tons of fishmeal - more than 1.5 times the amount used by shrimp and salmon farms combined.

"Our assumption about farmed tilapia and carp being environmentally friendly turns out to be wrong in aggregate, because the sheer volume is driving up the demand," Naylor said. "Even the small amounts of fishmeal used to raise vegetarian fish add up to a lot on a global scale." Removing fishmeal from the diet of tilapia and carp would have a very positive impact on the marine environment, she added.

Regulating fisheries

On the policy front, Naylor pointed to California's Sustainable Oceans Act and the proposed National Offshore Aquaculture Act, which call for reductions in the use of fishmeal and fish oil in feeds. She also applauded plans by the National Oceanographic and Atmospheric Administration to develop a comprehensive national policy that addresses fisheries management issues posed by aquaculture. "No matter how much is done from the demand side, it is essential that there be regulation on the supply side as well," Naylor said. "You won't prevent the collapse of anchoveta, sardine and other wild fisheries unless those fisheries are carefully regulated."

Other co-authors of the PNAS study are Ronald W. Hardy, University of Idaho; Dominique P. Bureau and Katheline Hua, University of Guelph (Canada); Alice Chiu, Stanford; Matthew Elliott, Sea Change Management; Anthony P. Farrell, and Ian Forster, Centre for Aquaculture and Environmental Research (Canada); Delbert M. Gatlin, Texas A&M University and the Norwegian Center of Excellence; Rebecca J. Goldberg, Pew Charitable Trusts; and Peter D. Nichols, Commonwealth Scientific and Industrial Research Organization (Australia).

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Earth-sized planets are just right for life

* 07 September 2009 by David Shiga

THE discovery of extrasolar super-Earths - rocky planets about five to ten times the mass of Earth - has raised hopes that some may harbour life. Perhaps it's a vain hope though, since it now seems that Earth is just the right size to sustain life.

Life is comfortable on Earth in part because of its relatively stable climate and its magnetic field, which deflects cosmic radiation capable of damaging organic molecules as well as producing amazing auroras (see right).

The long-term stability of Earth's climate depends on the way the planet's crust is broken up into plates, which continually slide over and under one another in a process called plate tectonics. Carbon scrubbed from the atmosphere by natural chemical reactions gets buried and recycled within the Earth because of plate tectonics, part of a cycle that stabilises atmospheric carbon dioxide concentrations.

Now it seems rocky worlds have to be about the size of Earth to have both plate tectonics and magnetic fields, says Vlada Stamenkovic of the German Aerospace Center in Berlin. His team will present the work at the European Planetary Science Congress in Potsdam, Germany, on 15 September.

Heat from Earth's core creates the convection currents needed for plate tectonics. Such currents generate the force to tear the crust, produce multiple plates and move those plates around.

Stamenkovic's team found that the pressure and viscosity inside a super-Earth would be so high that a stagnant, insulating layer would form outside the core, weakening the convective currents needed to drive plate tectonics thus making the process unlikely. A 2007 study that concluded super-Earths were prone to plate tectonics did not account for the increase in viscosity that produces the stagnant layer (New Scientist, 13 October 2007, p 20).

The researchers also found that the slow transfer of heat out of the core in super-Earths would prevent a sufficiently rapid circulation of their molten cores, robbing them of a magnetic field.

Planets about 0.5 to 2.5 times the mass of Earth are most likely to support plate tectonics. The limits are fuzziest for magnetic field generation, but also favour Earth-sized planets. "Earth is special," says Stamenkovic.

But astrobiologist David Grinspoon of the Denver Museum of Nature and Science in Colorado points out that Venus seems to have recycled its crust in volcanic outbursts despite a lack of plate tectonics. While this has not stabilised Venus's climate, he says, the possibility that other forms of crustal recycling on super-Earths might do so should not be ruled out. "There may be super-Earths that have intelligent life that has concluded that no life is possible on puny planets such as ours," says Grinspoon.

Really?

The Claim: Cinnamon Oil Kills Bacteria.

By ANAHAD O'CONNOR

THE FACTS In a country obsessed with germs and sickness, antibacterial soaps and sanitizers are becoming more and more common. But because such products contribute to the growing problem of antibiotic-resistant bacteria, some researchers recommend sanitizers made with cinnamon oil, which has been shown in many studies to have powerful antimicrobial properties.

A recent study by a team of surgeons, for example, found that a solution made with cinnamon oil killed a number of common and hospital-acquired infections, like streptococcus and methicillin-resistant *Staphylococcus aureus*, or MRSA. The study found it was just as effective as several antiseptics widely used in hospitals. Another study by French researchers in 2008 had similar results, showing that at concentrations of 10 percent or less, cinnamon oil was effective against *Staphylococcus*, *E. coli* and several antibiotic-resistant strains of bacteria.

Dr. Lawrence D. Rosen, a pediatrician in New Jersey who dispenses natural health advice on his blog, wholechildcenter.org, recommends a tried-and-true recipe for homemade hand sanitizer called thieves oil. "I add cinnamon bark, lemon oil and eucalyptus," he said, adding, "The recipe goes back to the Middle Ages, where it was used by these thieves who would go around stealing jewelry from dead bodies, and they never got sick."

Cinnamon oil, when applied topically, is generally safe. But in some people it can cause an allergic reaction.

THE BOTTOM LINE Cinnamon oil has antiseptic properties.

Personal Health

Updating the Rules for Skin Cancer Checks

By JANE E. BRODY

Now, before you again don warm clothes, is a good time to note how much sun damage you incurred this summer. Are body parts that were not covered darker or more freckled than the skin you were born with? If so, you failed to cover your exposed skin and protect it adequately with sunscreen when out on both sunny and cloudy days.

Eventually, depending on your susceptibility and the extent of unprotected sun exposure, you could wind up with skin cancer, the nation's most common cancer by far. Even if you escape cancer, you will certainly speed the aging of your skin, and by midlife you might have a wrinkled, leathery surface that makes you look older than your years.

But unless you've already had one of the common skin cancers or a melanoma, the United States Preventive Services Task Force does not recommend a yearly head-to-toe checkup for skin cancer by you or a doctor.

In updated guidelines issued last February and printed in *The Annals of Internal Medicine*, the task force found insufficient evidence to justify periodic "screening for skin cancer by primary care clinicians or by patient self-examination."

You may wonder what the harm could be in such a checkup. Haven't you been repeatedly told that early detection is the secret to preventing a cancer that can threaten your life or well-being?

Research supports such testing for cancers of the cervix or breast. But in assessing whether routine screening for any disease is justifiable, experts must weigh the evidence for both benefits and risks. And the task force, an arm of the government's Agency for Healthcare Research and Quality, concluded that there was "a critical gap in the evidence" to assess the risks of routine skin cancer screening.

The task force found no direct evidence that whole-body skin exams by primary care physicians or patients "improves patient outcomes" and that studies were lacking to determine the extent of harm that could come from such screening. The possible risks it listed were "misdiagnosis, overdiagnosis and the resultant harms from biopsies and overtreatment."

In other words, there is not enough information to say whether the benefits of routine skin cancer screening outweigh the potential risks associated with examining and treating lesions that turn out not to be cancer.

When to See the Doctor

This is not to say that if you notice something suspicious anywhere on your skin - like a mole that is changing, a rough spot on a sun-exposed part of your body, or a sore that bleeds or does not heal - you should ignore it, hoping it will disappear on its own. Most dermatologists recommend periodic skin checkups, especially to catch early, curable melanomas, and any such lesion should be brought to a doctor's attention without delay.

Dr. Darius R. Mehregan, chairman of dermatology at Wayne State University School of Medicine in Michigan, agrees that for most adults an annual skin cancer checkup by a physician is not needed. Still, in an

interview, Dr. Mehregan suggested that patients should do a monthly self-check for the “A, B, C, D and E” of skin cancer starting around age 50. This means looking for lesions with any of these characteristics: A for asymmetry, B for irregular border, C for multiple colors, D for a diameter greater than six millimeters (about a quarter-inch) and E for evolving (that is, growing or changing).

Dr. Gary N. Fox, who practices dermatology in Defiance, Ohio, a farming area where skin cancers are rampant, also sees little to be gained from routinely screening people who do not have risk factors for skin cancer. But in an interview, Dr. Fox emphasized the importance of insisting on a biopsy if someone had a lesion that “causes sufficient patient or doctor concern, even if it has been there for 20 years.”

Furthermore, Dr. Fox said, unless the doctor doing the biopsy is very experienced in pathology, the biopsied tissue should be examined by a dermatopathologist, who is specially trained to diagnose skin disease. If there is any doubt about the finding, he said, “another pathologist should look at it since it doesn’t hurt to ask for a second opinion.” Sometimes, he explained, a mole can be hard to distinguish from a melanoma.

Dr. Fox also cautioned doctors against freezing a lesion to see if it went away unless there was no doubt about its nature. For example, the common sun-induced lesion called actinic keratosis, in which cancer cells are confined to the top of the skin, can safely be frozen.

But he adds that anyone who has had a number of actinic keratoses should be regularly re-examined, since more are likely to occur and they can develop into an invasive cancer.

Looking for Melanoma

Of course, if you have already had one skin cancer - a basal-cell or squamous-cell carcinoma or, more serious, a melanoma - you should be regularly examined as well. For example, Dr. Fox said, a person who has had one basal-cell cancer has a 50 percent chance of developing a new one within three to five years. He suggested repeat exams at three to four months, at six to eight months, and again at a year during the first year, and annually thereafter.

Since melanomas run in families, Dr. Fox added, anyone with a family history of the disease should start regular skin exams in their 20s. Likewise, Dr. Mehregan said, people who have many moles should get an early start on screening because it is difficult for patients to determine when a melanoma arises in a mole.

Dr. Fox explained that the main goal was to catch and treat melanoma “in situ” - that is, still confined to the site of origin and not life-threatening. He emphasized that a full skin exam for melanoma should be head to toe: the scalp (with hair parted by a hair dryer on cool setting) and all body surfaces, including the underarms, buttocks, genitals, palms, soles and nails.

However, he said, a check for the ordinary sun-related skin cancers - basal and squamous cell carcinomas - can be limited to sun-exposed body parts: the face, the trunk, the back, the arms, the legs and, in someone partly or completely bald, the scalp.

The best way to avoid skin cancer, these experts said, is to be diligent about sun protection. Wear a tightly woven hat with a wide brim and routinely use a full-spectrum sunscreen with an SPF rating of 30 (above that, there is little additional benefit), even when sitting behind glass or under an umbrella. And apply it generously: Dr. Mehregan notes that the SPF rating is based on using a tablespoon of the product for one arm.

Sun-protective clothing can help as well. Reapply sunscreen after sweating heavily or swimming, even if the product claims to be water-resistant.

Tool to Offer Fast Help for H.I.V. Exposure

By RONI CARYN RABIN

Time is of the essence in treating someone who may have been exposed to the AIDS virus. Starting Wednesday, emergency room doctors throughout New York State will be just a computer click away from concise guidelines for starting prompt drug treatment that can reduce the risk of becoming infected.

The guidelines come in the form of a computer application, or widget, developed by a team of doctors from St. Vincent’s Hospital in Manhattan with financing from the state’s AIDS Institute. They are to be given to more than 200 emergency departments this week and distributed more widely over time.

Non-Occupational Post Exposure Prophylaxis (nPEP) 1 Occupational PEP (oPEP) 2 Pediatric PEP 3 Acute HIV Infection (AHI) 4

New York State AIDS Clock
A new HIV infection occurs every one hour and fifty minutes in New York State. *
Number of HIV transmissions in New York State since January 1, 2009
3 1 9 2
Number of New York State residents reported living with HIV/AIDS as of December, 2007:
121,237
Number of HIV/AIDS cases in New York State living and dead as of December, 2007:
230,661
*Transmission calculations based on New York State and New York City HIV 2006 incidence data. The clock is set to zero on January 1, midnight. The AIDS clock will be re-calibrated to reflect 2007 HIV incidence rates when data becomes available.

Jayme R. Feldman, MSN, CPNP
Pediatric Nurse Practitioner at St. Vincent Catholic Medical Center

Text-based PEP & AHI Guidelines 5 Text-based HEP B & C Guidelines 6 HIV Consent Forms & PEP Reimbursement for Sexual Assault 7 HIV Testing 8

GUIDELINES With financing from New York State, doctors from St. Vincent’s Hospital in Manhattan developed a computer application headed to emergency departments.

The doctors who developed the widget call it a “one-stop shopping” approach to PEP, or post-exposure prophylactic treatment. It walks users through a screening process to determine whether they are candidates for treatment, provides specific information about the 28-day course of antiretroviral drugs, and even links to consent forms in 22 languages, including Creole, Laotian and Yoruba.

The widget is continually updated with the latest medical recommendations, and the home page includes a counter that keeps track of the number of new H.I.V. infections in the state.

“There’s a gap in knowledge in the health care sector about these topics,” said Dr. Tony Urbina, medical director of H.I.V./AIDS education at St. Vincent’s, who developed the widget with Paul Galatowitsch, also of St. Vincent’s. “You’d be surprised at how many patients come to us and say, ‘I went to an emergency room, and the doctor didn’t know what I was talking about, and I didn’t get the drugs,’ ” Dr. Urbina said.

With the widget, he continued, “all of the information is right there at your fingertips, and it’s also reliable and updated by the State Health Department,” instead of searching for it online, on sites that might not be reliable.

The application makes clear that the first dose of antiretroviral drugs should be given as soon as possible, and patients who think they may have been exposed to the virus through sex, drug use, contact with blood or in their work should be given high-priority, emergency status.

“Here in our emergency department, when we educate our staff,” Dr. Urbina said, “we say, ‘Treat this as a gunshot wound in terms of urgency.’ ”

Post-exposure prophylactic treatment works by inhibiting the virus from multiplying and by keeping the infection localized, so the immune system can prevent it from entering the bloodstream.

Clinical trials of health care workers exposed to H.I.V. through their jobs suggest that people can reduce their risk of infection by 80 percent if they begin drug treatment immediately.

Ideally, the first dose should be given within what doctors call the “golden two-hour period” after exposure, but state health officials say the treatment is effective if started within 36 hours. (The Centers for Disease Control and Prevention puts the window at 72 hours.)

Where Did All the Flowers Come From?

By CARL ZIMMER

Throughout his life, Charles Darwin surrounded himself with flowers. When he was 10, he wrote down each time a peony bloomed in his father’s garden. When he bought a house to raise his own family, he turned the grounds into a botanical field station where he experimented on flowers until his death. But despite his intimate familiarity with flowers, Darwin once wrote that their evolution was “an abominable mystery.”

Darwin could see for himself how successful flowering plants had become. They make up the majority of living plant species, and they dominate many of the world’s ecosystems, from rain forests to grasslands. They also dominate our farms. Out of flowers come most of the calories humans consume, in the form of foods like corn, rice and wheat. Flowers are also impressive in their sheer diversity of forms and colors, from lush, full-bodied roses to spiderlike orchids to calla lilies shaped like urns.



RARE PLANT *Amborella trichopoda*, a small shrub found only on the island of New Caledonia in the South Pacific, represents the oldest living lineage of flowering plants. Sangtae Kim/University of Florida

The fossil record, however, offered Darwin little enlightenment about the early evolution of flowers. At the time, the oldest fossils of flowering plants came from rocks that had formed from 100 million to 66 million years ago during the Cretaceous period. Paleontologists found a diversity of forms, not a few primitive forerunners.

Long after Darwin’s death in 1882, the history of flowers continued to vex scientists. But talk to experts today, and there is a note of guarded optimism. “There’s an energy that I haven’t seen in my lifetime,” said William Friedman, an evolutionary biologist at the University of Colorado, Boulder.

The discovery of new fossils is one source of that new excitement. But scientists are also finding a wealth of clues in living flowers and their genes. They are teasing apart the recipes encoded in plant DNA for building different kinds of flowers. Their research indicates that flowers evolved into their marvelous diversity in much the same way as eyes and limbs have: through the recycling of old genes for new jobs.

Until recently, scientists were divided over how flowers were related to other plants. Thanks to studies on plant DNA, their kinship is clearer. “There was every kind of idea out there, and a lot of them have been refuted,” said James A. Doyle, a paleobotanist at the University of California, Davis.

It is now clear, for example, that the closest living relatives to flowers are flowerless species that produce seeds, a group that includes pine trees and ginkgos. Unfortunately, the plants are all closely related to one another, and none is more closely related to flowers than any of the others.

The plants that might document the early stages in the emergence of the flower apparently became extinct millions of years ago. “The only way to find them is through the fossils,” Dr. Doyle said.

In the past few years scientists have pushed back the fossil record of flowers to about 136 million years ago. They have also found a number of fossils of mysterious extinct seed plants, some of which produce seeds in structures that look faintly like flowers. But the most intriguing fossils are also the most fragmentary, leaving paleobotanists deeply divided over which of them might be closely related to flowers. “There’s no consensus,” Dr. Doyle said.

But there is a consensus when it comes to the early evolution of flowers themselves. By studying the DNA of many flowering plants, scientists have found that a handful of species represent the oldest lineages alive today. The oldest branch of all is represented by just one species: a shrub called *Amborella* that is found only on the island of New Caledonia in the South Pacific. Water lilies and star anise represent the two next-oldest lineages alive today.

If you could travel back to 130 million years ago, you might not be impressed with the earliest flowers. “They didn’t look like they were going anywhere,” Dr. Doyle said.

Those early flowers were small and rare, living in the shadows of far more successful nonflowering plants. It took many millions of years for flowers to hit their stride. Around 120 million years ago, a new branch of flowers evolved that came to dominate many forests and explode in diversity. That lineage includes 99 percent of all species of flowering plants on Earth today, ranging from magnolias to dandelions to pumpkins. That explosion in diversity also produced the burst of flower fossils that so puzzled Darwin.

All flowers, from *Amborella* on, have the same basic anatomy. Just about all of them have petals or petal-like structures that surround male and female organs. The first flowers were probably small and simple, like modern *Amborella* flowers. Later, in six lineages, flowers became more complicated. They evolved an inner ring of petals that became big and showy, and an outer ring of usually green, leaflike growths called sepals, which protect young flowers as they bud.

It would seem, based on this recent discovery, that a petal is not a petal is not a petal. The flowers of, say, the paw-paw tree grow petals that evolved independently from the petals on a rose. But the genes that build flowers hint that there is more to the story.

In the late 1980s, scientists discovered the first genes that guide the development of flowers. They were studying a small plant called *Arabidopsis*, a botanical lab rat, when they observed that mutations could set off grotesque changes. Some mutations caused petals to grow where there should have been stamens, the flower’s male organs. Other mutations transformed the inner circle of petals into sepals. And still other mutations turned sepals into leaves.

The discovery was a remarkable echo of ideas first put forward by the German poet Goethe, who not only wrote “*Faust*” but was also a careful observer of plants. In 1790, Goethe wrote a visionary essay called “*The Morphology of Plants*,” in which he argued that all plant organs, including flowers, started out as leaves. “From first to last,” he wrote, “the plant is nothing but a leaf.”

Two centuries later, scientists discovered that mutations to genes could cause radical transformations like those Goethe envisioned. In the past two decades, scientists have investigated how the genes revealed through such mutations work in normal flowers. The genes encode proteins that can switch on other genes, which in turn can turn other genes on or off. Together, the genes can set off the development of a petal or any other part of an *Arabidopsis* flower.

Scientists are studying those genes to figure out how new flowers evolved. They have found versions of the genes that build *Arabidopsis* flowers in other species, including *Amborella*. In many cases, the genes have been accidentally duplicated in different lineages.

Finding those flower-building genes, however, does not automatically tell scientists what their function is in a growing flower. To answer that question, scientists need to tinker with plant genes. Unfortunately, no plant is as easy to tinker with as *Arabidopsis*, so answers are only beginning to emerge.

Vivian Irish, an evolutionary biologist at Yale, and her colleagues are learning how to manipulate poppies because, Dr. Irish points out, “poppies evolved petals independently.” She and her colleagues have identified flower-building genes by shutting some of them down and producing monstrous flowers as a result.

The genes, it turns out, are related to the genes that build *Arabidopsis* flowers. In *Arabidopsis*, for example, a gene called AP3 is required to build petals and stamens. Poppies have two copies of a related version of the

gene, called *paleoAP3*. But Dr. Irish and her colleagues found that the two genes produced different effects. Shutting down one gene transforms petals. The other transforms stamens.

Evolution of Flowers

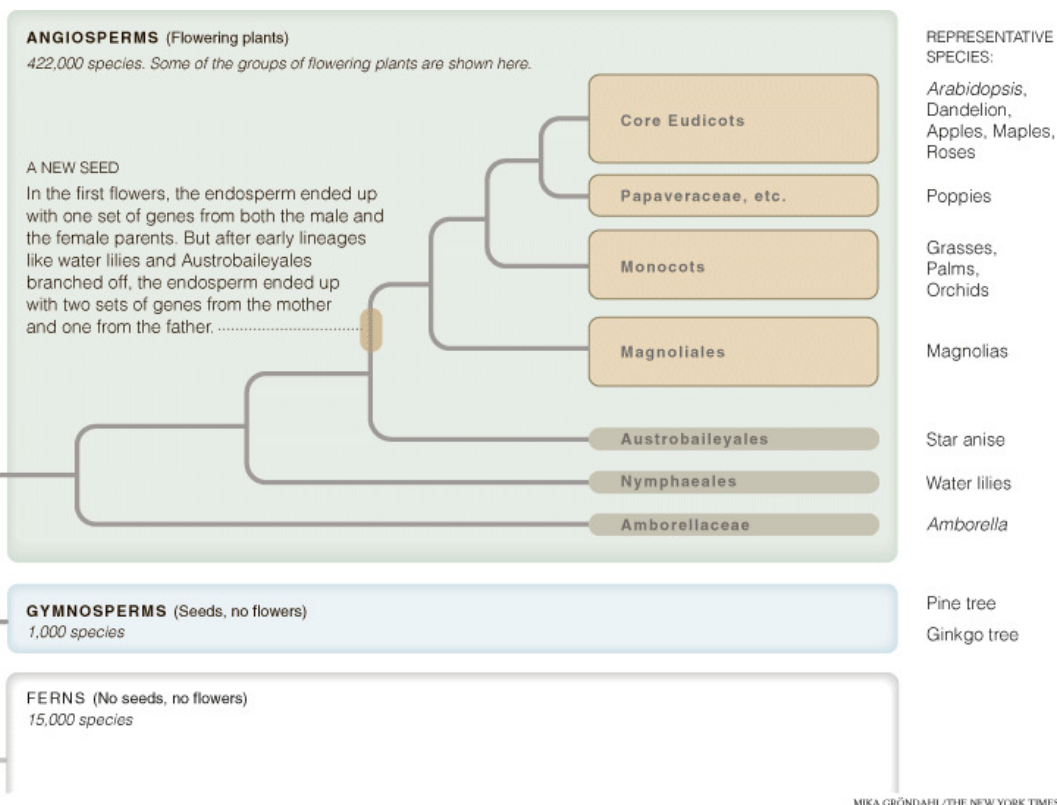
Recent studies of plant DNA have shown how flowering plants evolved since they separated from gymnosperms, plants that produce seeds but no flowers.



Amborella belongs to the oldest lineage of flowering plants on Earth today.

PHOTOGRAPH BY THOMAS J. LEMIEUX

Sources: James Doyle, University of California, Davis; William Friedman, University of Colorado, Boulder; Vivian Irish, Yale University



The results, Dr. Irish said, show that early flowers evolved a basic tool kit of genes that marked off different regions of a stem. Those geography genes made proteins that could then switch on other genes involved in making different structures. Over time, the genes could switch control from one set of genes to another, giving rise to new flowers. Thus, the petals on a poppy evolved independently from the petals on *Arabidopsis*, but both flowers use the same kinds of genes to control their growth.

If Dr. Irish is right, flowers have evolved in much the same way our own anatomy evolved. Our legs, for example, evolved independently from the legs of flies, but many of the same ancient appendage-building genes were enlisted to build those different limbs. “I think it is pretty cool that animals and plants have used similar strategies,” Dr. Irish said, “albeit with different genes.”

Dr. Irish said, however, that her studies of petals were only part of the story. “Lots of things happened when the flower arose,” she said. Flowers evolved a new arrangement of sex organs, for example. “A pine tree has male cones and female cones,” she said, “but flowers have male and female organs on the same axis.”

Once the sex organs were gathered together, they underwent a change invisible to the naked eye that might have driven flowers to their dominant place in the plant world.

When a pollen grain fertilizes an egg, it provides two sets of DNA. While one set fertilizes the egg, the other is destined for the sac that surrounds the egg. The sac fills with endosperm, a starchy material that fuels the growth of an egg into a seed. It also fuels our own growth when we eat corn, rice or other grains.

In the first flowers, the endosperm ended up with one set of genes from the male parent and another set from the female parent. But after early lineages like *Amborella* and water lilies branched off, flowers bulked up their endosperm with two sets of genes from the mother and one from the father.

Dr. Friedman, of the University of Colorado, Boulder, has documented the transition and does not think it was a coincidence that flowering plants underwent an evolutionary explosion after gaining an extra set of genes in their endosperm. It is possible, for example, that with extra genes, the endosperm could make more proteins.

“It’s like having a bigger engine,” Dr. Friedman said.

Other experts agree that the transition took place, but they are not sure it is the secret to flowers’ success. “I don’t know why it should be so great,” Dr. Doyle said.

As Dr. Friedman has studied how the extra set of genes evolved in flowers, he has once again been drawn to Goethe’s vision of simple sources and complex results.

Flowers with a single set of female DNA in their endosperm, like water lilies, start out with a single nucleus at one end of the embryo sac. It divides, and one nucleus moves to the middle of the sac to become part of the endosperm. Later, a variation evolved. In a rose or a poppy, a single nucleus starts out at one end of the sac. But

when the nucleus divides, one nucleus makes its way to the other end of the sac. The two nuclei each divide, and then one of the nuclei from each end of the sac moves to the middle.

Duplication, a simple process, led to greater complexity and a major change in flowers.

"Nature just doesn't invent things out of whole cloth," Dr. Friedman said. "It creates novelty in very simple ways. They're not radical or mysterious. Goethe already had this figured out."

'Hygiene hypothesis' challenged

Day care doubles early respiratory problems, does not prevent later asthma and allergy

New research hints that the common belief that kids who go to daycare have lower rates of asthma and allergy later in life might be nothing more than wishful thinking. While young children in daycare definitely do get more illnesses and experience more respiratory symptoms as a result, any perceived protection these exposures afford against asthma and allergy seem to disappear by the time the child hits the age of eight.

"We found no evidence for a protective or harmful effect of daycare on the development of asthma symptoms, allergic sensitization, or airway hyper-responsiveness at the age of eight years," wrote Johan C de Jongste, M.D., Ph.D., of Erasmus University in the Netherlands and principle investigator of the study. "Early daycare was associated with more airway symptoms until the age of four years, and only in children without older siblings, with a transient decrease in symptoms between four and eight years."

The results are published in the September 15 issue of the American Journal of Respiratory and Critical Care Medicine, a journal of the American Thoracic Society.

The researchers prospectively followed a birth cohort of nearly 4,000 Dutch children over the course of eight years in the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) Study. Parents completed questionnaires during pregnancy, at three and 12 months, and then yearly until the child reached the age of eight, and reported their children's airway symptoms annually. At the age of eight, more than 3,500 of the children were also assessed for specific allergies. Some also underwent testing for lung function and airway hyper-responsiveness.

Daycare use was assessed each year, and the children were categorized in early attendees (first attendance before two years of age), late attendees (first attendance between two and four years of age) and non-attendees.

They found that children who started daycare early were twice as likely to experience wheezing in the first year of life compared to those who didn't go to daycare. However, as the children aged, there was a shift: by age five, there was a trend for less wheezing among early attendees: they were about 80 percent as likely as non-attendees to wheeze, but this was not statistically significant. What's more, the shift reversed itself by age eight, when there was no association between early daycare attendance and wheezing at all. Late daycare attendees had similar, but less pronounced and statistically nonsignificant effects. The effects of daycare on wheeze were not different between boys and girls, but were more marked in children with older siblings.

"Children with older siblings and early daycare had more than fourfold higher risk of frequent respiratory infections and more than twofold risk of wheezing in the first year compared to children without older siblings and daycare," said Dr. de Jongste. "Importantly, children exposed to both early daycare and older siblings experienced most infections and symptoms in early childhood, without a protective effect on wheeze, inhaled steroid prescription or asthma symptoms until the age of eight years."

Despite the widespread acceptance of the idea that these early exposures pay off in later health benefits, the data in this study do not support that belief. If anything, this study suggests that these exposures cause more airway symptoms early in life with no counterbalancing benefit later.

"Early daycare merely seems to shift the burden of respiratory morbidity to an earlier age where it is more troublesome than at a later age," said Dr. de Jongste. "[E]arly daycare should not be promoted for reasons of preventing asthma and allergy."

Healthy older brains not significantly smaller than younger brains, new imaging study shows

Previous samples might have unknowingly included people with early brain disease

WASHINGTON -- The belief that healthy older brains are substantially smaller than younger brains may stem from studies that did not screen out people whose undetected, slowly developing brain disease was killing off cells in key areas, according to new research. As a result, previous findings may have overestimated atrophy and underestimated normal size for the older brain.

The new study tested participants in Holland's long-term Maastricht Aging Study who were free of neurological problems such as dementia, Parkinson's disease or stroke. Once participants were deemed otherwise healthy, they took neuropsychological tests, including a screening test for dementia, at baseline and every three years afterward for nine years.

According to the report in the September *Neuropsychology*, published by the American Psychological Association, participants were also given MRI scans at Year 3 to measure seven different parts of the brain, including the memory-laden hippocampus, the areas around it, and the frontal and cingulate areas of the cognitively critical cortex.

After examining behavioral data collected from 1994 to 2005 (with scans taken between 1997 and 1999 depending on when people entered the study), the researchers divided participants into two groups: one group with 35 cognitively healthy people who stayed free of dementia (average starting age 69.1 years), and the other group with 30 people who showed substantial cognitive decline but were still dementia-free (average starting age 69.2 years).

That cognitive decline was measured by drops of at least 30 percent on two or more of six core tests of verbal learning and fluency, recall, processing speed, and complex information processing, and/or drops of 3 or more points, or scores of 24 or lower (raising suspicion for cognitive impairment), on the Mini-Mental State Examination screening tool for dementia.

In contrast to the 35 people who stayed healthy, the 30 people who declined cognitively over nine years showed a significant effect for age in the hippocampus and parahippocampal areas, and in the frontal and cingulate cortices. In short, among the people whose cognition got worse, older participants had smaller brain areas than younger participants.

Thus, the seeming age-related atrophy in gray matter more likely reflected pathological changes in the brain that underlie significant cognitive decline than aging itself, the authors wrote. As long as people stay cognitively healthy, the researchers believe that the gray matter of areas supporting cognition might not shrink much at all. "If future longitudinal studies find similar results, our conception of 'normal' brain aging may become more optimistic," said lead author Saartje Burgmans, who is due to receive her PhD later this year.

The findings should caution scientists about drawing conclusions from brain studies that don't screen participants over time, using precise and objective definitions, the authors added.

Article: "The Prevalence of Cortical Gray Matter Atrophy May Be Overestimated In the Healthy Aging Brain," Saartje Burgmans, PhD student, Martin P. J. van Boxtel, PhD, MD, Eric F. P. M. Vuurman, PhD, Floortje Smeets, PhD student, and Ed H. B. M. Gronenschild, PhD, Maastricht University; Harry B. M. Uylings, PhD, Maastricht University and VU University Medical Center Amsterdam; and Jelle Jolles, PhD, Maastricht University; Neuropsychology, Vol. 23, No. 5.

(Full text of the article is available from the APA Public Affairs Office and at <http://www.apa.org/journals/releases/neu235541.pdf>)

Diamonds are for softies – boron is harder

* 08 September 2009 by Philip Ball

You don't often break a diamond. So when in 2003 Dave Mao cracked a tooth of his diamond anvil, he knew something extraordinary must have happened. Together with his daughter Wendy and other colleagues at the Geophysical Laboratory of the Carnegie Institution for Science in Washington DC, he was using the device to test materials at pressures many millions of times higher than those at the Earth's surface - higher even than in our planet's core - by squeezing them between two tiny diamond jaws.

Behind the glitz, diamond is just a form of carbon. It is, however, by common consent the hardest material known. The substance in the Maos' test cell had also begun as pure carbon. It was plain old graphite - the soft, slippery stuff that is used for pencil leads and lubricants. Clearly, something had happened in the anvil cell to make it awesomely hard.

It seemed the Maos might accidentally have succeeded where many before had failed. Had they made the first superhard material that matched or even surpassed diamond? Probably not, as it turned out. Six years and several twists later, though, that feat might at last have been achieved, though not with pure carbon. If the latest reports are right, the hardness crown has changed hands at last.

Why the fuss? Diamond's hardness has served us well enough over the years. Diamond-studded saws and drills have been around since at least the time of the Napoleonic wars. They are not even particularly expensive any more, since researchers at the General Electric Company in Schenectady, New York, discovered in the 1950s that you can make synthetic diamonds by subjecting softer carbon-rich materials to immense temperatures and pressures.

Unfortunately, diamond doesn't always cut it. In particular, it does not cut steel: the carbon just dissolves in the hot iron, reacting to form iron carbide. This susceptibility to heat and chemical attack is one reason why we are on the lookout for alternatives to diamond, says Artem Oganov, a materials physicist at Stony Brook University in New York. Diamond is also electrically insulating, which can be a limitation. "It would be good to have a range of superhard materials that have other properties," says Oganov, such as metallic or semiconducting characteristics.

Finding rivals has been a frustrating business. In part that is because although all of us know a hard object when we bump into one, working out what makes things hard is - well, hard. "Intuitively, covalent bonds and high bond-strength are a requirement," says Mao. Covalent bonds are one of the ways in which atoms link up to build molecules, large and small. They form when the smeared-out cloud, or "orbital", occupied by an electron belonging to an atom overlaps with one belonging to another. In general, the better the overlap, the stronger the bond. Hardness typically seems to arise in materials that have strong, short bonds.

Most of us know a hard object when we bump into one - but not what makes it hard

So might there be some tweak to carbon's atomic arrangements that would optimise the strength of its bonds and make a material harder than diamond? In the late 1980s, Marvin Cohen, a materials physicist at the University of California, Berkeley, thought so. He theorised that the strong bonds linking atoms in a hypothetical crystalline compound of carbon and nitrogen dubbed beta carbon nitride should make it particularly hard. But despite extensive efforts, the material has been difficult to synthesise, and its hoped-for hardness has never been demonstrated.

And what of Dave and Wendy Mao's miraculously hardened graphite? Unfortunately, the usual technique for determining a material's structure - bouncing X-rays off the sample and looking at the resulting diffraction pattern - proved extremely difficult for the tiny quantities in the diamond anvil cell. Opening the device to take a closer look didn't help, either, because the material morphed back into graphite as soon as the pressure was released.

Whatever it is, a material like the Maos' altered graphite could have its uses. Imagine, for example, an impact-resistant "smart skin" that, while normally soft and flexible, becomes the hardest thing going under a large force. Until we know what a material looks like at the atomic scale, however, reliable fabrication remains a problem.

Mao and theorist Yanming Ma and colleagues at Jilin University in Changchun, north-east China, recently proposed that the transformed graphite has a structure they call monoclinic carbon. This M-carbon forms when graphite sheets buckle and form extra chemical bonds between the layers (Physical Review Letters, vol 102, p 175506). The resulting structure, they calculated, should be almost as hard as diamond - although not quite. It is also strikingly similar to a form of carbon made by shining strong laser light onto graphite, reported in May this year by Katsumi Tanimura and colleagues at Osaka University, Japan (Physical Review Letters, vol 102, p 087402). The Japanese team did not attempt to assess the hardness of their material.

This piece of unfinished business aside, only one material has been claimed so far to crack the diamond ceiling - diamond itself. A nanocrystalline form of diamond, sometimes called aggregated diamond nanorods, was described in 2003 by Tetsuo Irifune and his colleagues at Ehime University in Japan. Since then, Natalia Dubrovinskaia and her colleagues at the University of Bayreuth in Germany have found that a tip made of these nanorods could scratch regular diamond, seemingly indicating a greater hardness.

So much for carbon. But who says we need it? In a quest for completely different superhard materials, Richard Kaner at the University of California, Los Angeles, and his team have been exploring the nether regions of the periodic table. Their first stop was the element osmium, each atom of which has eight "valence" electrons available for covalent bonding - the highest number known. More electrons, they reasoned, meant stronger bonds and perhaps superhardness. In 2005 the strategy seemed to bear fruit as the team discovered that osmium diboride, a repeating structure of one osmium atom bound to two boron atoms, is indeed very hard - although still only about a quarter as hard as diamond.

Two years later, they claimed that rhenium diboride was even harder, though still not a match for diamond. Rhenium is osmium's neighbour in the periodic table, and although its valence electron density is smaller, crucially it could make shorter, and therefore stronger, bonds. Kaner's claim has not gone undisputed.

Meanwhile, attention was switching back to the lighter end of the periodic table, home to many elements that can form short, strong bonds. One such is boron, which sits just one berth over from carbon. The idea that boron has superhardness potential goes back at least to 1965, when Robert Wentorf, one of the General Electric team that made synthetic diamond, claimed to have made superhard crystals of boron at a pressure of 100,000 atmospheres and a temperature of 1500 °C. He couldn't work out what the material's structure was, though, and the idea was shelved for 40 years.

"People were basically scared of boron," says Oganov by way of explanation. Boron forms several complex structures that are hard to tell apart. What's more, it reacts with nearly everything, and even a trace of impurities can drastically change the structure and properties of the boron crystal.

It was only in February this year that a team led by Oganov published a structure for the superhard boron crystal - a repeating pattern of 28 boron atoms they called B28 (Nature, vol 457, p 863). In May, Dubrovinskaia and her team announced that they had made large crystals of B28 that were about half as hard as diamond (Physical Review Letters, vol 102, p 185501). Close, but still no diamond necklace.

Boron and on

Pure boron is not the last word, though. Boron nitride - in which boron is combined with nitrogen - forms analogues of all the known carbon phases. There is a soft variant called h-BN, which is made of sheets of hexagonal rings just like graphite, and finds similar use as a lubricant. Then there's cubic boron nitride, or c-BN, which has a structure similar to diamond, and for a long time has played second fiddle only to diamond in hardness.

There is a third version, too, known as wurtzite or w-BN, which is comparable to a diamond-like form of carbon known as lonsdaleite. It had been made since the 1970s by using high pressure or explosive shock waves to squeeze h-BN, but had only been fabricated in quantities too small for its hardness to be measurable by any conventional means. In 2007, however, Dubrovinskaia and her colleagues succeeded in making a mosaic of w-BN crystals which they claimed had a hardness comparable to that of diamond (Applied Physics Letters, vol 90, p 101912).

They thought that the material's hardness came about because its crystals were tiny - just 10 or so nanometres across. Many crystalline materials get harder as the grains that make up their crystals get smaller, because grain boundaries prevent the movement of defects in the packing of atoms. But earlier this year, Changfeng Chen of Jiao Tong University in Shanghai, China, and his colleagues offered another explanation. They think that w-BN may be inherently hard, because it can transform into another, stronger structure when another material presses into it. The pressure causes chemical bonds to flip into a different arrangement which looks like that of c-BN, but has its network of atomic bonds ideally positioned to resist stress (Physical Review Letters, vol 102, p 055503).

"It's a bit like someone changing their body posture in response to applied stress so that they can carry a higher load," says Chen. As a result, the material becomes even harder than diamond, at least in theory. What's more, Chen and colleagues figured that the same thing that happens to w-BN should happen for lonsdaleite, its carbon counterpart. That could actually be harder to scratch and indent than diamond itself.

Meanwhile Vladimir Solozhenko, now at the University of Paris, and his co-workers had the idea that it might be best to throw all the most promising elements that have popped up in most hard materials to date - carbon, boron and nitrogen - into the pot. In 2001 they reported that one particular combination, BC₂N, has a hardness midway between c-BN and diamond (Diamond and Related Materials, vol 10, p 2228).

Until all such options have been explored, there is still plenty to play with, and no reason to think that diamond is as hard as it gets. In any case, new materials don't have to surpass diamond in order to be useful: c-BN has been used as an abrasive and in cutting tools for many years. Though only half as hard as diamond, it is by far the best material for grinding through steel.

It is true, too, that the real challenge in industries that use superhard materials, including construction, mining and aerospace engineering, is to find materials that are not just hard, but cheap and easy to make as well. In the end, perhaps, the real crown will go not to the material that cuts diamond, but to the one that undercuts it. *Philip Ball is a freelance science writer based in London*

Peer Review Survey 2009: Preliminary findings

Should peer review detect fraud and misconduct? What does it do for science and what does the scientific community want it to do? Will it illuminate good ideas or shut them down? Should reviewers remain anonymous?

These questions are raised by one of the largest ever international surveys of authors and reviewers, the Peer Review Survey 2009, whose preliminary findings are released today.

Peer review is fundamental to integration of new research findings. It allows other researchers to analyse findings and society at large to weigh up research claims. It results in 1.3 million learned articles published every year, and it is growing rapidly with the expansion of the global research community. With that growth come new concerns – about getting the next generation of researchers to review in sufficient numbers, about maintaining the system's integrity and whether it can be truly globalised; and also new ideas - about alternative quality measures, technologies to prevent plagiarism, rewarding reviewers and training them.

Sense About Science has promoted understanding of peer review to help people to work out whether research claims have been independently scrutinised. But with all the proposed changes and expansion in research publication, what do researchers think about peer review and its future? To find out, Sense About Science developed the Peer Review Survey 2009, in consultation with editors and publishers and administered with a grant from Elsevier; the survey included some questions from the Peer Review Survey 2007 for comparison, and new questions about future improvements, public awareness and pressures on the system.

Tracey Brown, Managing Director: "The 2007 survey had raised some of the issues. We sought to broaden that, particularly to find out whether the demand for all this free, independent scrutiny from the research

community is sustainable, and what the future of quality control is likely to be. It's a matter of public as well as scientific interest."

Preliminary findings include:

1. Playing an active role in the community is top of reasons to review:

90% say they review because they believe they are playing an active role in the community; only 16% say that increasing their chances of having future papers accepted is a reason to review.

2. Researchers want to improve, not replace peer review: 84% believe that without peer review there would be no control in scientific communication, but only a third (32%) think it is the best that can be achieved; 20% of researchers believe that peer review is unsustainable because of too few willing reviewers.

91% say that their last paper was improved through peer review; the discussion was the biggest area of improvement.

73% of reviewers (a sub-group) say that technological advances have made it easier to do a thorough job than 5 years ago.

Whilst 86% enjoy reviewing, 56% say there is a lack of guidance on how to review;

68% think formal training would help. On average, reviewers turn down two papers a year.

Just 15% of respondents felt that 'formal' peer review could be replaced by usage statistics.

61% of reviewers have rejected an invitation to review an article in the last year, citing lack of expertise as the main reason – this suggests that journals could better identify suitable reviewers.

3. High expectations: 79% or more of researchers think that peer review should identify the best papers, determine their originality and importance, improve those papers and, though lower scoring, also determine whether research is plagiarised or fraudulent.

While 43% of respondents thought peer review was too slow,

65% of authors (a further sub-group) reported that they had received a decision on their most recent paper within 3 months.

4. Reviewers want anonymity: 58% would be less likely to review if their signed report was published.

76% favour the double blind system where just the editor knows who the reviewers are.

5. Understanding of peer review: Researchers agree that peer review is well understood by the scientific community but just 30% believe the public understands the term.

6. Papers aren't recognising previous work: 81% think peer review should ensure previous research is acknowledged; 54% think it currently does. This reflects current concerns in the research community.

7. Detecting plagiarism and fraud might be a noble aim but is not practical: A majority think peer review should detect plagiarism (81%) or fraud (79%) but fewer (38% & 33%) think it is capable of this.

8. Reviewers divided over incentives: Just over half of reviewers think receiving a payment in kind (e.g. subscription) would make them more likely to review; 41% wanted payment for reviewing, but this drops to just 2.5% if the author had to cover the cost. Acknowledgement in the journal is the most popular option.

The preliminary results of the survey will be presented at Science Fact or Science Fiction: Should Peer Review Stop Plagiarism, Bias or Fraud? at the British Science Festival, Surrey University on Tuesday 8th September 2009, 10:00am. Tracey Brown of Science About Science, David Adam of The Guardian and Peter Hayward of Lancet Infectious Diseases will debate the challenges of publishing research. Further information: Alice Tuff ATuff@senseaboutscience.org 44 (0)20 7478 4380

NOTES 1. *The Peer Review Survey was an electronic survey conducted between 28th July 2009 and 11th August 2009; 40,000 researchers were randomly selected from the ISI author database, which contains published researchers from over 10,000 journals. Altogether 4,037 researchers completed our survey. The error margin was ±1.5% at 95% confidence levels; reviewers answered a subset of questions aimed specifically at reviewers (3,597 - a subset of the base) the error margin for this group was ±1.6% at 95% confidence levels.*

2. The full findings and report are due to be published in November 2009 and will be available at <http://www.senseaboutscience.org.uk/index.php/site/project/29/>.

3. Björk et al (2008) 'Global annual volume of peer reviewed scholarly articles and the share available via different Open Access options' Proceedings ELPUB2008 Conference on Electronic Publishing – Toronto, Canada – June 2008

Study: Parenthood Makes Moms More Liberal, Dads More Conservative

Matt Shipman | News Services | 919.515.6386

Parenthood is pushing mothers and fathers in opposite directions on political issues associated with social welfare, from health care to education, according to new research from North Carolina State University.

“Parenthood seems to heighten the political ‘gender gap,’ with women becoming more liberal and men more conservative when it comes to government spending on social welfare issues,” says Dr. Steven Greene, an associate professor of political science at NC State and co-author of the study. Greene and Dr. Laurel Elder of Hartwick College used data on the 2008 presidential election from the American National Election Studies to

evaluate the voting behavior of men and women who have children at home. Parents who have grown children were not part of the study.

“Basically, women with children in the home were more liberal on social welfare attitudes, and attitudes about the Iraq War, than women without children at home,” Greene says, “which is a very different understanding of the politics of mothers than captured by the ‘Security Mom’ label popular in much media coverage. But men with kids are more conservative on social welfare issues than men without kids.” Men with kids did not differ from men without kids in their attitudes towards Iraq.

Greene also notes that, “despite media speculation that Sarah Palin, given her status as a self-proclaimed ‘Hockey Mom’ and working mother of five, would be effective at attracting the votes and admiration of parents, especially mothers, the research showed no evidence of a ‘Sarah Palin effect’ (between parents and non-parents), even when looking exclusively at Republicans.” Greene explains that this means there was no difference in how parents viewed Sarah Palin versus how non-parents viewed Sarah Palin.

The researchers evaluated the effect of parenting on voting behavior because parenthood has become increasingly politicized in recent decades. For example, Greene says, the Republican party identified itself as the “family values” party during the 1990s.

Greene and Elder had previously looked at similar data for elections going back through 1980, and their new research shows that the trend is strengthening for men with children to become more conservative, while the trend for moms to become more liberal is holding steady.

“It appears that the Democratic position, that government has a role in addressing social problems, appeals to women with children,” Greene says, “Whereas men with children are drawn to the Republican arguments that government should not play a major role on social welfare issues.”

Greene presented the research, “‘Mortgage Moms’ and ‘More Responsible Fathers’: Parenthood and Issue Attitudes in the 2008 Presidential Election,” at the American Political Science Association’s annual meeting in Toronto, Sept. 5.

Seizure drug enhances sleep for women with hot flashes

Gabapentin, a drug initially used to treat seizures, improves sleep quality in menopausal women with hot flashes, University of Rochester Medical Center researchers report online and in the September issue of the *Journal of Women's Health*.

Approximately 40 percent of menopausal women experience sleep disruption, often in the form of difficulty with sleep initiation and frequent nighttime awakenings. The study is the first to show sustained benefits in sleep quality from gabapentin, which Rochester researchers already have demonstrated alleviates hot flashes.

"Gabapentin improves sleep quality but does not have the potential dependency problems of some other sleep medications and does not involve the use of hormone replacement therapy," said Michael E. Yurcheshen, M.D., assistant professor of Neurology and the lead author of the article.

"It has minimal side effects and it is a generic drug," said Yurcheshen, who is based at the Strong Sleep Disorders Center. "That makes it a very attractive treatment for these problems in this patient population."

For the current study, researchers used data from a previously published randomized, double-blind, placebo-controlled trial of gabapentin in 59 postmenopausal women who experienced seven to 20 hot flashes daily. The subjects took either 300 milligrams of gabapentin three times a day or a placebo. The research used a factor analysis of the Pittsburgh Sleep Quality Index, a well-known and validated questionnaire, to evaluate sleep. The results showed overall improvement in the sleep quality score, even after 12 weeks of treatment.

Gabapentin's impact on the sleep quality factor in menopausal women may reflect improvement in hot flashes, stabilization of sleep architecture, or a decrease in the amount of time to transition from wakefulness to sleep, the researchers wrote. It is also possible that gabapentin improved sleep quality by addressing underlying sleep pathology, such as restless legs syndrome. "We really are not sure which mechanism is responsible, but this study suggests that it does work to improve sleep quality," Yurcheshen said.

The gabapentin research reported in the *Journal of Women's Health* is the most recent in a series of Rochester studies into relief of hot flashes. In 2000, a Medical Center neurologist treating a menopausal woman for migraines first observed that the seizure medication seemed to cure her hot flashes. Since then, a clinical trial confirmed those results in women suffering from hot flashes due to menopause. Another Rochester study showed that gabapentin provides control of hot flashes in women with breast cancer who suffer hot flashes as a result of their cancer treatment. A third study found that gabapentin is as effective in reducing the number of hot flashes as the hormone estrogen, which used to be the gold standard treatment for menopause symptoms. *A co-author on the paper, Thomas Guttuso Jr., M.D., is listed as the inventor on a patent owned by the University of Rochester for the use of gabapentin in the treatment of hot flashes. The patent has been licensed to three companies. Guttuso is a former Medical Center neurologist who is now on the faculty at the State University of New York at Buffalo.*

In addition to Yurcheshen and Guttuso, the authors of the article include Michael P. McDermott, Ph.D., associate professor of Biostatistics at the Medical Center, Robert G. Holloway, M.D., M.P.H., professor of Neurology at the Medical Center, and Michael Perlis, Ph.D., associate professor of Psychology at the University of Pennsylvania.

K-12 education should include engineering

WASHINGTON -- The introduction of K-12 engineering education has the potential to improve student learning and achievement in science and mathematics, increase awareness about what engineers do and of engineering as a potential career, and boost students' technological literacy, according to a new report from the National Academy of Engineering and the National Research Council. The report examines the status and nature of efforts to teach engineering in U.S. schools.

"The problem solving, systems thinking, and teamwork aspects of engineering can benefit all students, whether or not they ever pursue an engineering career," said Linda Katehi, chancellor of the University of California, Davis, and chair of the committee that wrote the report. "A K-12 education that does not include at least some exposure to engineering is a lost opportunity for students and for the nation."

Engineering education at the K-12 level should emphasize engineering design and a creative problem-solving process, the committee said. It should include relevant concepts in mathematics, science, and technology, as well as support the development of skills many believe essential for the 21st century, including systems thinking, collaboration, and communication.

While science, technology, engineering, and mathematics instruction is collectively referred to as "STEM education," the report finds that the engineering component is often absent in policy discussions and in the classroom. In fact, engineering might be called the missing letter in STEM, the report says.

In preparing the report, the committee conducted an in-depth analysis of 15 K-12 engineering curricula; reviewed scientific literature related to learning engineering concepts and skills; evaluated evidence on the impact of K-12 engineering education initiatives; and collected preliminary information about pre-collegiate engineering education programs in other countries.

The committee found that engineering education opportunities in K-12 schools have expanded considerably in the past 15 years. Since the early 1990s, the report estimates, about 6 million children have been exposed to some formal engineering coursework. However, this number is still small compared with the overall number of students in K-12 schools (approximately 56 million in 2008). The committee noted that many challenges remain to expanding the availability and improving the quality of these programs, including the absence of content standards to guide development of instructional materials, limited pre-service education for engineering teachers, and structural and policy impediments to including this new subject in an already crowded school curriculum.

With these challenges in mind, the committee recommended that:

- * the National Science Foundation or U.S. Department of Education fund research to determine how science inquiry and mathematical reasoning can be connected to engineering design in curricula and professional development;
- * foundations and federal agencies with an interest in K-12 engineering education conduct long-term research to confirm and refine findings of studies of the impacts of engineering education;
- * the American Society of Engineering Education begin a national dialogue on preparing K-12 engineering teachers, and on the pros and cons of establishing a formal credentialing process; and
- * philanthropic foundations or federal agencies with an interest in STEM education and school reform identify models of implementation for K-12 engineering education that will work for different American school systems.

The committee also noted the importance of clarifying the meaning of "STEM literacy" and of developing curricula that would particularly appeal to groups typically underrepresented in engineering, such as girls, African Americans, and Hispanics.

The study was sponsored by Stephen D. Bechtel, Jr., chairman (ret.) and director, Bechtel Group Inc., with additional support from the National Science Foundation and Parametric Technology Inc. The National Academy of Sciences, National Academy of Engineering, Institute of Medicine, and National Research Council make up the National Academies. They are independent, nonprofit institutions that provide science, technology, and health policy advice under an 1863 congressional charter. A committee roster follows.

Copies of ENGINEERING IN K-12 EDUCATION: UNDERSTANDING THE STATUS AND IMPROVING THE PROSPECTS are available from the National Academies Press; tel. 202-334-3313 or 1-800-624-6242 or on the Internet at [HTTP://WWW.NAP.EDU](http://www.nap.edu). In addition, a podcast of the public briefing held on Sept. 8 to release this report is available at [HTTP://NATIONAL-ACADEMIES.ORG/PODCAST](http://national-academies.org/podcast).

Infertility and the Battle of the Sexes

TAU study offers an evolutionary explanation for today's fertility problems

About 10% of all couples hoping for a baby have fertility problems. Environmentalists say pollution is to blame and psychiatrists point to our stressful lifestyles, but evolutionary biologist Dr. Oren Hasson of Tel Aviv University's Department of Zoology offers a different take. The reproductive organs of men and women are currently involved in an evolutionary arms race, he reports in a new study. And the fight isn't over yet.

"The rate of human infertility is higher than we should expect it to be," says Dr. Hasson. "By now, evolution should have improved our reproductive success rate. Something else is going on." Combining empirical evidence with a mathematical model developed in cooperation with Prof. Lewi Stone of the department's Biomathematics Unit, the researchers suggest that the bodies of men and women have become reproductive antagonists, not reproductive partners. The conclusions of this research were published recently in the journal *Biological Reviews*.

Favoring the "super-sperm"

Over thousands of years of evolution, women's bodies have forced sperm to become more competitive, rewarding the "super-sperm" - the strongest, fastest swimmers - with penetration of the egg. In response, men are over-producing these aggressive sperm, producing many dozens of millions of them to increase their chances for successful fertilization.

But these evolutionary strategies demonstrate the Law of Unintended Consequences as well, says Dr. Hasson. "It's a delicate balance, and over time women's and men's bodies fine tune to each other. Sometimes, during the fine-tuning process, high rates of infertility can be seen. That's probably the reason for the very high rates of unexplained infertility in the last decades."

The unintended consequences have much to do with timing. The first sperm to enter and bind with the egg triggers biochemical responses to block other sperm from entering. This blockade is necessary because a second penetrating sperm would kill the egg. However, in just the few minutes it takes for the blockade to complete, today's over-competitive sperm may be penetrating, terminating the fertilization just after it's begun.

Sexual evolution explained

Women's bodies, too, have been developing defenses to this condition, known as "polyspermy." "To avoid the fatal consequences of polyspermy, female reproductive tracts have evolved to become formidable barriers to sperm," says Dr. Hasson. "They eject, dilute, divert and kill spermatozoa so that only about a single spermatozoon gets into the vicinity of a viable egg at the right time."

Any small improvement in male sperm efficiency is matched by a response in the female reproductive system, Dr. Hasson argues. "This fuels the 'arms race' between the sexes and leads to the evolutionary cycle going on right now in the entire animal world."

Advice for doctors and marriage counselors

Sperm have also become more sensitive to environmental stressors like anxious lifestyles or polluted environments. "Armed only with short-sighted natural selection," Dr. Hasson argues, "nature could not have foreseen those stressors. This is the pattern of any arms race. A greater investment in weapons and defenses entails greater risks and a more fragile equilibrium."

Dr. Hasson says that IVF specialists can optimize fertility odds by more carefully calculating the number of sperm placed near the female ova. And nature itself may have its say as well. Sexually adventurous women, like females of many birds and mammals who raise their offspring monogamously but take on other sexual partners, help create a more fertile future. But not always, says Hasson and Stone's mathematical model - certain types of infertile sperm race to the egg as competitively as any healthy sperm, and may block the sperm of a fertile lover.

But whatever the source of infertility, Dr. Hasson, who also works as a marriage counselor, can't recommend cheating, not even as an evolutionary psychologist. Infertile marriages can be stressful, but unlike birds, we have the capacity for rational thinking. He advises infertile couples to openly communicate about all their options, and seek counseling if necessary.



No sex tonight honey, I haven't taken my statins

* 15:28 08 September 2009 by **Linda Geddes**

High cholesterol isn't just bad for the heart – it could also make it harder for women to become sexually aroused. That might mean that cholesterol-lowering drugs like statins would help to treat so-called female sexual dysfunction (FSD).

Hyperlipidemia, or raised levels of cholesterol and other fats in the blood, is associated with erectile dysfunction in men, because the build-up of fats in blood vessel walls can reduce blood flow to erectile tissue. Since some aspects of female sexual arousal also rely on increased blood flow to the genitals, Katherine Esposito and her colleagues at the Second University of Naples in Italy compared sexual function in premenopausal women with and without hyperlipidemia.

Women with hyperlipidemia reported significantly lower arousal, orgasm, lubrication, and sexual satisfaction scores than women with normal blood lipid profiles. And 32 per cent of the women with abnormal profiles scored low enough on a scale of female sexual function to be diagnosed with FSD, compared with 9 per cent of women without normal levels. Women's sexual desire was not affected by hyperlipidemia, however.

Underlying condition

In a separate paper, Annamaria Veronelli at the University of Milan, Italy, and her colleagues found that female sexual dysfunction was also associated with diabetes, obesity and an underactive thyroid gland.

"These two papers suggest that there are strong connections between women's sexual arousal and organic diseases in the same way that men's sexual problems arise," says Geoffrey Hackett, a urologist at the Holly Cottage Clinic in Fisherwick, UK. "This is currently not even considered in women."

Hackett therefore suggests that a loss of sexual arousal in women might be an indicator of other underlying conditions, so such problems should be raised with a doctor.

Journal references: Journal of Sexual Medicine, DOI: 10.1111/j.1743-6109.2009.01284.x and DOI: 10.1111/j.1743-6109.2009.01242.x

Don't be fooled: swine flu still poses a deadly threat

* 17:01 08 September 2009 by **Debora MacKenzie**

Swine flu has still not grown more severe, as many feared it would but as the pandemic's second, autumn wave begins in the northern hemisphere, the virus is posing a different threat. While H1N1 mostly causes mild disease, some people – estimates suggest fewer than 1 per cent – become deathly ill, very fast.

At a meeting last week in Winnipeg, Canada, experts warned that these cases could overwhelm hospitals. "These were the sickest people I've ever seen," says Anand Kumar, an intensive care expert at the University of Manitoba in Winnipeg.

Kumar helped manage a wave of severe cases in the city in June, mostly in young Canadian aboriginals, who required the most advanced care. "This pandemic is like two diseases," he says. "Either you're off work a few days, or you go to hospital, often to the intensive care unit. There's no middle ground."

In the southern hemisphere, 15 to 33 per cent of hospitalised cases went to ICU in the past two months. "That's very high for flu," says Richard Wenzel of Virginia Commonwealth University in Richmond. "When this flu is bad, it's very bad."

Lung attack

In these cases the virus rapidly destroys the lungs' alveoli, where gas transfer occurs, often causing acute respiratory distress syndrome (ARDS), which usually kills in half of all cases. Antoine Flahault of the School of Public Health in Rennes, France, found that this past winter in Mauritius and New Caledonia, H1N1 caused ARDS 100 times as often as ordinary flu.

The direct viral damage inflicted on the lungs by severe H1N1 contrasts with SARS and bird flu, whose impact is mainly due to a runaway, body-wide immune response, says Kwok Yung Yuen of the University of Hong Kong, China. This means early suppression of H1N1 with antivirals is crucial, which in turn requires spotting cases fast.

Who will get severe H1N1? Kumar is coordinating a multi-hospital study of severe H1N1 to find out, but says preliminary results suggest severity is linked to HLA, a genetic variation in immune systems. This could be why flu is worse in some ethnic groups.

What haunts ICU doctors now is whether they will have enough beds for the coming second wave. If not, they will have to decide who to prioritise. ICU space is already tight, and studies in the UK and US have found it may not be enough. Australia managed to increase ICU capacity just enough to cope during its flu season, which is ending, says Kumar. "If we don't prepare, it could be really bad," he warns.

Study: Hairstylists Can Help Identify Older Clients Who Need Health Services

COLUMBUS, Ohio – Hairstylists may have a unique opportunity to help steer their elderly clients to needed health services, according to a small, exploratory study.

More than 80 percent of 40 Columbus-area stylists surveyed said that older clients often or always shared their problems during appointments.

“Hair stylists are in a great position to notice when their older clients are starting to suffer from depression, dementia, or self-neglect,” said Keith Anderson, co-author of the study and assistant professor of social work at Ohio State University.

“While not expecting too much beyond the scope of their jobs, we may be able to help stylists direct elderly people in trouble to community services.”

Anderson conducted the study with Andrea Cimbali and Jeffrey Maile, graduate students in social work at Ohio State. Their results appear in the current issue of the *Journal of Applied Gerontology*.

Anderson said he decided to do the study after reading sometimes-joking references in the popular press to “salon therapy,” in which clients discussed their relationship, family and health problems to their stylists, who act as sympathetic ears and sometimes as pseudo-therapists.

“I wondered if stylists really did have these close relationships with their clients,” Anderson said.

“And if they did, I thought there might be opportunities to use these relationships to help older adults.”

Anderson focused on older adults in this study because of his research interest in gerontology.

The study included 40 stylists from the Columbus area who responded to a mail survey. The participants reported that, on average, about one-third of their clients were 60 years old or older.

Anderson said the results suggest that most stylists do develop close long-term relationships with their older clients. About 85 percent of stylists described their relationships with older clients as “close” or “very close.” About 72 percent said their role was like one of “family” to some of their older customers.

“This is one reason why I think hair stylists are especially suited to seeing problems in their customers,” Anderson said.

“Their older clients may sit in a chair for an hour or longer while they’re having their hair done, and this may happen once or twice a month. So stylists are in a good position to recognize when things change with a client, and when they may need help.”

Health and family problems are the issues most often brought up by elderly customers – more than three-quarters of stylists have heard such complaints, the survey revealed. And more than a third of stylists said clients have discussed problems with depression or anxiety.

The vast majority of stylists said their response to hearing their clients’ problems is to offer sympathy and support, and to try to cheer them up.

But fewer than half said they have given advice, and only about one-quarter have tried to get the client to speak to someone who can help them.

That’s not because they are not willing to help, Anderson said. About two-thirds said they are willing to refer an older client to appropriate services.

But the problem, Anderson said, is that more than half – 52 percent -- said they were not familiar with community services that may be helpful to older adults.

“It seems like a perfect setup – stylists have access to older adults who may need someone to point them to the help they need. But at least this sample of stylists suggests they don’t know what services are out there to help these folks,” he said. But could hairstylists identify older clients who needed professional help?

At least the stylists surveyed thought they could. The researchers asked participants to rate on a scale of 1 to 10 (with 10 being the highest) their ability to recognize symptoms of depression, dementia and neglect in their older clients. In all three cases, stylists rated their ability between 7.6 and 7.8.

Anderson said the question then becomes how to get stylists more involved in helping their older clients. He noted that there’s already a national domestic violence awareness program called “Cut It Out” that recruits hair stylists to recognize indicators of domestic violence and get victims help. Something similar could be done to assist older adults with mental health and related problems.

Anderson said he recognizes that stylists have a job to do, and can’t devote too much of their time and education to issues unrelated to hair styling.

Only 45 percent of the stylists surveyed said they were interested in receiving mental health training.

But stylists could play an important role by even just learning about local community services and offering brochures to older adults that have information on how to access the help they need.

“We can’t expect them to do everything, but our results suggest that most stylists care about their clients and would be willing to help them,” he said.

Worldwide isotope shortage continues to pose significant challenges ***SNM survey of nuclear pharmacies finds patient rescheduling, delayed tests***

RESTON, Va. - SNM recently conducted a survey of nuclear pharmacies - pharmacies that supply the critical radioisotope Technetium-99m, which is used in more than 16 million nuclear medicine tests each year in the United States - to assess, anecdotally, the impact of the worldwide medical isotope shortage. According to the survey, 60 percent of radiopharmacies have been impacted by the most recent shortage. Technetium-99m is a product of Molybdenum-99, which has been in short supply recently.

Nuclear physicians and pharmacists are making changes to cope with the shortage, while striving to provide patients with the highest levels of care possible. For example, 75 percent of physicians are rescheduling patient tests by at least one day. In more than one out of three of these cases, tests have been delayed for longer than one month.

"This situation is untenable," said Robert W. Atcher, Ph.D., M.B.A, chair of SNM's Domestic Isotope Availability Task Force. "Nuclear scans and procedures that use Tc-99m are used to detect and diagnose many common cancers and cardiac conditions."

"In some cases, waiting even a day can severely impact care, especially if the condition is progressing rapidly," said Michael M. Graham, M.D., Ph.D., president of SNM. "Getting information early on in the disease progression is critical, and is one of the real benefits of molecular imaging."

In addition to delays, more than 80 percent of nuclear physicians and specialists are decreasing the dosage, which can lead to "longer exposure and less effective imaging scans," added Atcher.

Technetium-99m (Tc-99m) is a medical isotope derived from Mo-99 which is produced in reactors. Only six reactors in the world produce Mo-99 that is approved for use in the US. These reactors undergo routine maintenance. Recently, however, they have been experiencing chronic mechanical issues due to the age of the reactors and extended operation beyond their expected lifetime. When one reactor goes unexpectedly offline, this creates a limited supply of Mo-99, which is critically needed for nuclear medicine procedures. The most recent extended shortage began in May 2009, when the NRU reactor in Chalk River, Canada - the world's largest reactor that produces Mo-99 - went off-line. The situation has been exacerbated by the recent announcement that the NRU reactor will remain off-line at least through 2010.

While the shortage began three months ago, radiopharmacists are increasingly feeling pressure to find alternative agents to offset the Mo-99 shortage. A recent outage of a second reactor for planned maintenance made the shortage worse.

"Radiopharmacists are doing the best they can with the limited resources at their disposal," said Jeffrey P. Norenberg, Pharm.D., Executive Director of the National Association of Nuclear Pharmacies and a member of SNM's Domestic Isotope Availability Task Force. "But clearly, patients deserve better because better agents like Tc-99m exist. Governments should work together to prevent such shortages from ever happening again."

There are no reactors in the United States that produce Mo-99, making the isotope shortage especially acute. Nuclear medicine experts are trying to keep up with demand, while using less effective products. "It's a juggling act," Atcher said.

Rain of meteorites makes the moon hum

* 18:54 08 September 2009 by Rachel Courtland

THE man in the moon is humming a tune, but thankfully the noise won't drown out sensors on future missions peeking at the lunar interior.

A steady barrage of small meteorite impacts should cause the moon to "ring", but no seismometers sent to the moon to date have been sensitive enough to hear it. So Philippe Lognonné at the Institute of Earth Physics of Paris and colleagues decided to work out how loud the ring is.

The team estimated the meteorite population in the solar neighbourhood, and calculated the likely seismic signals that would be created by a range of meteorite sizes and velocities as they strike the moon.

Apollo calibration

To determine how the vibrations from these impacts would be seen by seismometers, the team used data taken by Apollo seismometers four decades ago. These measured the vibrations created by the landings of lunar modules and spent rocket stages.

Since the precise locations and timing of these landings were known, they could be used to gauge how long it would take vibrations caused by meteorite impacts to travel through the moon, and how much the signals might dim.

Their calculations revealed space rocks with masses ranging from a gram to a kilogram do indeed create a hum, but it is subtle. Earth's hum – created by pounding waves – is more than 1000 times louder.

"This shows that all planets may hum, those with and those without atmosphere," says Lognonné.

It's oh so quiet

The moon-hum's quietness means future lunar seismometers should be able to peek deep within the moon without the hum creating problematic background noise, says Lognonné.

Instead seismometers can focus on measuring waves created by moonquakes, tremors created by a variety of sources, including the tidal tug of the Earth. Because seismic waves are sensitive to the type, arrangement and density of rocks they pass through, studying the quakes can reveal more about the moon's interior.

The network of seismometers left by the Apollo missions has been shut down since 1977, so Lognonné hopes more sensitive instruments will be sent to the moon soon. These could reach deeper than the Apollo network to measure the size of the moon's core. "The area within 500 kilometres of the centre of the moon is complete unknown to seismology," Lognonné says.

"I think [the study] is a great idea," says Clive Neal of the University of Notre Dame in Indiana, who was not associated with the research. "Estimating the actual background noise is critical for designing the next generation of seismometers to go to the moon."

The first instrument may be a seismometer proposed for Japan's Selene-2 moon mission, which aims to send a lander to the surface, perhaps as early as 2015. *Journal reference: Journal of Geophysical Research (in press)*

Link found between common sexual infection and risk of aggressive prostate cancer

A new study from Harvard School of Public Health (HSPH) and Brigham and Women's Hospital researchers has found a strong association between the common sexually transmitted infection, *Trichomonas vaginalis*, and risk of advanced and lethal prostate cancer in men. The study appears online on September 9, 2009, on the Journal of the National Cancer Institute website and will appear in a later print edition.

"Prostate cancer is the most common cancer among men in western countries, and the second leading cause of cancer-specific mortality. Identifying modifiable risk factors for the lethal form of prostate cancer offers the greatest opportunity to reduce suffering from this disease," said Jennifer Stark, an HSPH researcher and lead author of the study.

One potential risk factor is inflammation, which appears to play an important role in the development and progression of prostate cancer, but the source of inflammation of the prostate is not clear. *Trichomonas vaginalis*, which infects an estimated 174 million people globally each year and is the most common non-viral sexually transmitted infection, can infect the prostate and could be a source of inflammation. With respect to prostate cancer prevention, it is noteworthy that up to three-quarters of men infected with *Trichomonas vaginalis* may not realize they are infected, since they may not have any symptoms.

A previous study had found an association between risk of prostate cancer and *Trichomonas vaginalis* infection, but was not large enough to determine if there was a link between the infection and advanced and lethal disease.

In the present study, the researchers analyzed blood samples from 673 men with prostate cancer who were participants in the Physicians' Health Study and compared infection status based on antibody levels to 673 control subjects who were not diagnosed with prostate cancer. The blood samples were collected in 1982, on average a decade before cancer diagnosis.

The results showed that *Trichomonas vaginalis* infection was associated with a more than two-fold increase in the risk of prostate cancer that was advanced stage at diagnosis, and a nearly three-fold increase in prostate cancer that would result in death. "The fact that we found a strong association between serologic evidence of infection with *Trichomonas vaginalis*, a potentially modifiable risk factor, and risk of advanced and lethal disease represents a step forward in prostate cancer, especially given that so few risk factors for aggressive prostate cancer have been identified," said Lorelei Mucci, assistant professor in the department of epidemiology at HSPH and senior author of the study.

The authors note that further research needs to be done to confirm the findings. If confirmed, the findings from the large-scale, prospective study would identify infections as one of the few known modifiable factors for aggressive prostate cancer. Moreover, since the infection is easily treated with an inexpensive antibiotic regimen, the results from the study suggest that prevention or early treatment of *Trichomonas vaginalis* infection could be a target for prostate cancer prevention.

Support for this study was provided by the National Cancer Institute, the National Heart, Lung, and Blood Institute, the Harvard University Milton Fund, the Dana-Farber/Harvard Cancer Center Prostate SPORE, and the Prostate Cancer Foundation.

"Prospective Study of Trichomonas vaginalis Infection and Prostate Cancer Incidence and Mortality: Physicians' Health Study," Jennifer R. Stark, Gregory Judson, John F. Alderete, Vasanthakrishna Mundodi, Ashwini S. Kucknoor, Edward L. Giovannucci, Elizabeth A. Platz, Siobhan Sutcliffe, Katja Fall, Tobias Kurth, Jing Ma, Meir J. Stampfer, Lorelei A. Mucci, Journal of the National Cancer Institute, online September 9, 2009

75 percent would consider letting an unsupervised trainee perform surgery if it could be done quicker

Three-quarters of surgical patients would consider allowing a competent unsupervised trainee junior doctor perform their entire operation if it meant they could have it done more quickly, according to a survey published in the September issue of BJUI. The responses were high regardless of how complex the surgery was, with 80 per cent of those facing minor surgery and 68 per cent of those facing major surgery saying they would consider the suggestion. Eighty patients took part in the survey at the John Radcliffe Hospital in Oxford, UK, after a hundred questionnaires were distributed to patients who had just undergone urological surgery. Just under two-thirds (65 per cent) were men, their average age was 69 and 42.5 per cent were in for major surgery.

"We were surprised by the results, as only 50 per cent of patients felt it was appropriate in general for trainees - even those just about to take up a consultant post - to operate unsupervised and this figure went down to 10 per cent when it came to their own operation" says specialist trainee Mr Robert Ritchie.

"But when waiting times were factored into the equation, it became very clear that patients were prepared to rethink their views if it meant having their operation more quickly."

Most of the respondents (90 per cent) felt that trainees needed to operate under supervision to improve their skills and 77 per cent were happy for a supervised trainee to do their operation. The majority (96 per cent) felt they should be told if a trainee was involved in their procedure.

"The opportunity to learn, repeat and perfect surgical skills is an essential component of any surgical training programme and allowing trainee surgeons to operate on patients is important" says Mr Ritchie.

"However, surgical training often fails to take into account individual patients and their right to know who is doing their operation. National Health Service consent forms currently state that the hospital cannot say who will be performing the operation, only that the surgeon will be competent to perform the procedure.

"This can be at odds with informed consent, which under common law requires that patients should be provided with clear and accurate information about the risks of any proposed investigation or treatment.

"It also appears to be at odds with General Medical Council (GMC) Guidelines. These say that surgeons must tell patients who will be mainly responsible for their care and what their roles are. They also state that the surgeon must make sure that the patient agrees to the participation of other professionals in their operation."

Mr Ritchie and his co-author, consultant urologist Mr John Reynard, are calling for a fundamental change in the level of information provided to patients about the identity of the surgeon carrying out their operation, to bring practice in line with this GMC guidance.

"Whether informing patients that trainees will be involved in their operation will lead to a reduction in training opportunities is unclear" says Mr Reynard. "A study of orthopaedic patients published in 2004 showed that 74 per cent were happy for a trainee to perform all or part of their procedure, but a 2005 study of cataract patients showed that only 16 per cent agreed to go ahead if a supervised trainee was directly involved."

The authors say that it is reassuring that patients understand the need for junior doctors to perform procedures as part of their training. But they also feel that it is important to try and address the issues around consent, without this resulting in a loss of training opportunities.

"The results of our study create a challenge for the consultant who has to balance his or her role as a trainer with the responsibility for overall care of the patient" adds Mr Reynard.

"We recommend that both the trainer and trainee see patients before surgery and take the opportunity to explain their respective roles in the operating theatre. It is a good time to stress how important training is in ensuring that high standards of surgical care and operative skills are maintained for present and future generations. "It is also clearly time for consultant surgeons who allow unsupervised trainees to operate to reappraise this practice."

Notes to editors Consent for surgery: will you be doing my operation, doctor? Ritchie R W and Reynard J. BJUI. 104, 766-768. (September 2009).

Killer birds bite off bats' heads

* 00:00 09 September 2009 by Sanjida O'Connell

It sounds like the avian equivalent of an Ozzy Osbourne legend. Great tits have been discovered killing and eating bats by pecking their heads open. Although bats have been reported preying on songbirds before, this is the first time great tits have been observed to prey on bats.

Péter Estók of the Max-Planck-Institute for Ornithology, Germany, first saw a bat being captured by a tit in a Hungarian cave in 1996. Ten years later, he and fellow bat ecologist Björn Siemers recorded 18 examples of pipistrelle bat predation by great tits, over the course of two winters in the same cave in the Bükk Mountains.

Bat hunting

The birds seek out bats as they wake from hibernation and usually eat them in the cave, though sometimes they carry them to a nearby tree.

"The birds don't kill the bats before they start eating them," says Siemers, "but the bats eventually die when the birds peck open their brain case."

As the bats are still very cold, only a degree above ambient temperature, they are extremely slow and easy for the birds to subdue. Nevertheless, it is a considerable feat for the tits given that a pipistrelle weighs approximately 5 grams and a great tit only four times as much.



This pipistrelle bat has had its head pecked open by a great tit (Image: Péter Estók)

Sly birds

The scientists ran an experiment to supply the tits with food, and discovered that this reduced consumption.

"This shows that the birds are predated the bats for food in times of scarcity. It shows how inventive this species can be," says Siemers.

Estók and Siemers also ran a playback experiment where they recorded and played the calls that the bats made as they woke from hibernation. The great tits were attracted to the calls.

"For a bat, these calls are very low frequency, a maximum of 15 kilohertz, but at a high frequency for the tits, above scientifically established hearing levels for this species, yet they react to them," says Siemers.

Who started it?

Gareth Jones, an expert on bat behaviour at the University of Bristol, says the finding is unexpected and novel. "I don't know of any other studies of predation of hibernating bats by small birds. It's a big jump for the tits, given that their normal prey are caterpillars."

As the birds have been anecdotally observed to eat bats in this cave for a decade, Siemers speculates that this is an example of cultural transmission. There are also four anecdotal reports of bats being eaten by tits in Sweden and Poland. Jones says, "Presumably this is learned behaviour, but it is much too strong an inference to suggest that it could be culturally transmitted from Poland to Hungary."

Journal reference: Biology Letters, DOI: 10.1098/rsbl.2009.0611 (in press)

New research confirms potential deadly nature of emerging new monkey malaria species in humans

Researchers in Malaysia have identified key laboratory and clinical features of an emerging new form of malaria infection. The research, funded by the Wellcome Trust, confirms the potentially deadly nature of the disease.

Malaria kills more than a million people each year. It is caused by malaria parasites, which are injected into the bloodstream by infected mosquitoes. Of the four species of malaria that commonly cause disease in humans, *Plasmodium falciparum*, found most commonly in Africa, is the most deadly. *P. malariae*, found in tropical and sub-tropical regions across the globe, has symptoms that are usually less serious.

Recently, researchers at the University Malaysia Sarawak, led by Professors Balbir Singh and Janet Cox-Singh, showed that *P. knowlesi*, a malaria parasite previously thought to mainly infect only monkeys – in particular long-tailed and pig-tailed macaques found in the rainforests of Southeast Asia – was widespread amongst humans in Malaysia. Subsequent reports in neighbouring Southeast Asian countries have led to the recognition of *P. knowlesi* as the fifth cause of malaria in humans.

Now, in a study published in the journal *Clinical Infectious Diseases*, Professors Singh and Cox-Singh, together with colleagues from University Malaysia Sarawak, Kapit Hospital and the University of Western Australia, have published the first detailed prospective study of the clinical and laboratory features of human *P. knowlesi* infections.

"*P. knowlesi* malaria can easily be confused with *P. malariae* since these two parasites look similar by microscopy, but the latter causes a benign form of malaria," says Professor Singh. "In fact, because the *P. knowlesi* parasites reproduce every twenty four hours in the blood, the disease can be potentially fatal, so early diagnosis and appropriate treatment is essential. Understanding the most common features of the disease will be important in helping make this diagnosis and in planning appropriate clinical management."

The researchers initially recruited over 150 patients admitted to Kapit Hospital in Sarawak, Malaysian Borneo, between July 2006 and January 2008 who had tested positive with a blood film slide for *Plasmodium* species. Using molecular detection methods, *P. knowlesi* was found to be by far the most common infection amongst these patients, accounting for over two-thirds of all cases.

As with other types of malaria in humans, *P. knowlesi* infections resulted in a wide spectrum of disease. Most cases of infection were uncomplicated and easily treated with chloroquine and primaquine, two commonly used anti-malarial drugs. However, around one in ten patients had developed complications and two died. Complications included breathing difficulties and kidney problems (including kidney failure in a small number of cases), which are also common in severe *P. falciparum* cases. Although the researchers saw a case fatality rate of just under 2%, which makes *P. knowlesi* malaria as deadly as *P. falciparum* malaria, they stress that an accurate fatality rate is hard to determine given the relatively small number of cases studied so far.

All of the *P. knowlesi* patients – including those with uncomplicated malaria – had a low blood platelet count. In other human forms of malaria, this would only be expected in less than eight out of ten cases. In addition, the *P. knowlesi* platelet counts tended to be significantly lower than for other malarias. However, even though blood platelets are essential for blood clotting, no cases of excessive bleeding or problems with clotting were identified. The researchers believe the low blood platelet count could be used as a potential feature for diagnosis of *P. knowlesi* infections.

Recently, there have been cases of European travellers to Malaysia and an American traveller to the Philippines being admitted into hospital with *knowlesi* malaria following their return home.

"The increase in tourism in Southeast Asia may mean that more cases are detected in the future, including in Western countries," says Professor Singh. "Clinicians assessing a patient who has visited an area with known or possible *P. knowlesi* transmission should be aware of the diagnosis, clinical manifestations, and rapid and potentially serious course of *P. knowlesi* malaria."

New look at Alzheimer's could revolutionise treatment

* 09 September 2009 by Andy Coghlan

GENES that increase the risk of Alzheimer's and a blood protein that speeds up cognitive decline are radically changing our view of the devastating illness. Reported this week, both findings suggest new causes for Alzheimer's, boosting prospects for its treatment and prevention.

"What we've found is absolutely fascinating, and will change the course of research into Alzheimer's," says Julie Williams of Cardiff University, UK, who led one of two genetics studies. She says the findings "show us the prime pathways into the disease".

For the past 20 years, researchers have been trying to treat Alzheimer's by blocking the accumulation of waxy plaques in the brain, with little success (see "Plaque drug trials fail"). While the exact role of these plaques is still unclear, the new studies suggest that disruptions of the immune system, the way cells metabolise fat, and wear and tear on the circulatory system may be as much to blame for Alzheimer's, or perhaps even the root cause.

This could help steer Alzheimer's research towards drugs that maintain the health of immune and vascular systems, while prevention strategies might include eating a low-fat, vegetable-rich diet and exercising.

Links have recently been discovered between cognitive decline and inflammation, which is a collection of processes involving the immune and vascular systems that protect the body from a range of harmful stimuli. To explore these links, Clive Holmes of the University of Southampton, UK, measured blood levels of tumour necrosis factor alpha in 222 people with Alzheimer's. TNF-alpha is released by white blood cells during inflammation. The volunteers also took a cognitive test first when they had their blood tested, and then three more times over a six-month period.

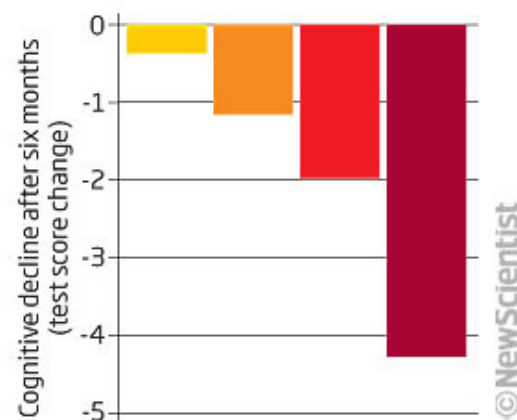
At the end of this time, cognitive decline was four times greater in those who started out with the highest TNF-alpha levels when compared with participants who had no TNF-alpha, whose cognition remained almost stable (see graph). A rapid decline in cognitive ability was also evident in people who had routine infections or accidents such as falling over, all of which can trigger inflammation (Neurology, vol 73, p 678). Interestingly, these inflammation "events" were seldom in the brain itself, but the rest of the body and bloodstream.

Holmes says that the results in people echo earlier experiments in mice, which showed that inflammation, and particularly high concentrations of TNF-alpha in the blood, accelerated Alzheimer's-like decline and death. He found that in the mice, microglial cells, responsible for removing dead neurons and destroying infectious

Inflammation and the brain

Immune chemical tumour necrosis factor-alpha (TNF- α) and "events" that trigger inflammation both accelerated Alzheimer's

- Low TNF- α , no event
- Low TNF- α , event
- High TNF- α , no event
- High TNF- α , event



agents, overreacted to TNF-alpha. He speculates that this might have caused microglial cells to kill live brain cells and that this is how inflammation contributes to, or even causes, Alzheimer's in people.

Backing this idea is the discovery of three gene variants that are more common in people with Alzheimer's than in the general population. Two separate research teams were involved, one led by Williams, the other by Philippe Amouyel of the Pasteur Institute in Lille, France (Nature Genetics, DOI: 10.1038/ng440 and DOI: 10.1038/ng.439). Both teams scanned between 300,000 and 500,000 single letter variations of the genetic code in thousands of people with Alzheimer's.

Until now, the main gene associated with Alzheimer's has been a faulty version of apolipoprotein E. Because faulty APOE causes people to make too much beta amyloid, the substance found in the waxy plaques of people with Alzheimer's, this reinforced theories that Alzheimer's is caused by plaques.

While the new research further confirmed that APOE is the most important gene variant predicting susceptibility to Alzheimer's, it also threw up three new gene variants that are abnormally common in people with Alzheimer's.

One of these variants is in the clusterin gene that clears the brain of protein junk, including beta amyloid. It is also responsible for dampening down aspects of the immune response, including one immunological chain reaction called the complement cascade, which rids the body of unwanted cells, toxins and proteins that have been snared by antibodies. Another is a variant of the CR1 gene, also vital for controlling the complement cascade.

It is not clear yet whether the variants cause these genes to be under or over-active. But because both genes are intimately involved in controlling the immune system, the discovery of their link with Alzheimer's fits with Holmes's result, and opens up a range of alternative causes and treatments.

The normal version of CR1 helps prune synapses, the brain connections destroyed in Alzheimer's. In people with the mutated form of CR1, this process may go into overdrive and destroy too many connections. Similarly, mutant clusterin may not damp down the immune system enough, causing it to attack, not protect, the brain.

Another possibility is that both gene variants affect a person's ability to repair blood vessels. As people get older, blood vessels become more damaged, particularly in the brain. The complement cascade is involved in fixing this damage, so the CR1 and clusterin gene variants may impair the repair process.

If this is true, better cardiovascular health might guard against the damaging effects of these mutant genes - and perhaps prevent Alzheimer's, says John Hardy of University College London, a pioneer of the plaque hypothesis. "This is pushing very much on the idea that we should focus on heart fitness," he says.

Meanwhile, the third gene to be implicated in Alzheimer's was a variant of the PICALM gene, which draws fats and proteins into brain cells, and may also be active around synapses. The researchers suggest that the variant associated with Alzheimer's may cause too much fat to be drawn into cells, killing them.

Both this hypothesis and the blood vessel one are backed up by a study published last month. Nikos Scarmeas of Columbia University Medical Center in New York and colleagues found that the risk of Alzheimer's was reduced by a third in volunteers who were physically active, while those who ate a diet rich in fruit and vegetables lowered their risk by 40 per cent. Those doing both lowered their risk by a massive 60 per cent (Journal of the American Medical Association, vol 302, p 627). What's more, in January research by Deborah Gustafson of the University of Gothenberg in Sweden linked obesity to a higher risk of Alzheimer's disease.

Williams says it is time to shift the focus away from the plaques. "We need to put the immune response, inflammation and the release of fats and cholesterol at the heart of future research." Hardy is less gung-ho as he suspects the plaque hypothesis will eventually produce drugs that work. But he agrees that preventing damage to blood vessels should now be explored as an Alzheimer's strategy.

Holmes points out that there are existing drugs for rheumatoid arthritis that neutralise TNF-alpha and might be worth trying. Tantalisingly, one such drug, etanercept, may already have helped people with Alzheimer's. The results, published last year, were dismissed by many. Maybe it's time to revisit that verdict.

Plaque drug trials fail

Alzheimer's has long been blamed on the fatty amyloid plaques that accumulate in the brain, but recent clinical trials suggest other processes may be at work.

Last year, Clive Holmes and his colleagues at the University of Southampton, UK, examined the brains of dead patients who'd received a vaccine that primes the immune system to attack amyloid plaques. Although the plaques had gone in most patients, in life their symptoms hadn't diminished (The Lancet, vol 372, p 216).

Also disappointing was the performance of tarenflurbil (Flurizan), a drug designed to attack plaques. Myriad Genetics of Salt Lake City, Utah, announced last year that it was suspending the \$200 million trial of the drug, the largest ever of an Alzheimer's treatment, after it failed to deliver significant improvements in memory, cognition or people's ability to care for themselves.

Meanwhile, drugs targeting other processes have shown success. The most tantalising news comes from trials of dimebolin, a hayfever treatment developed decades ago in Russia. Results from a trial published last year in *The Lancet* (vol 372, p 207) showed that patients taking the drug scored 7 points higher in standard tests of cognitive abilities compared with those on placebo, a substantial improvement on a scale of 70. As hay fever is caused by the body's inflammation process going awry, this result chimes with gene and hospital studies published this week that suggest inflammation plays a role in Alzheimer's (see main story).

A skull that rewrites the history of man

It has long been agreed that Africa was the sole cradle of human evolution. Then these bones were found in Georgia...

By Steve Connor, Science Editor

The conventional view of human evolution and how early man colonised the world has been thrown into doubt by a series of stunning palaeontological discoveries suggesting that Africa was not the sole cradle of humankind. Scientists have found a handful of ancient human skulls at an archaeological site two hours from the Georgian capital, Tbilisi, that suggest a Eurasian chapter in the long evolutionary story of man.

The skulls, jawbones and fragments of limb bones suggest that our ancient human ancestors migrated out of Africa far earlier than previously thought and spent a long evolutionary interlude in Eurasia – before moving back into Africa to complete the story of man.



One of the skulls discovered in Georgia, which are believed to date back 1.8 million years

Experts believe fossilised bones unearthed at the medieval village of Dmanisi in the foothills of the Caucasus, and dated to about 1.8 million years ago, are the oldest indisputable remains of humans discovered outside of Africa.

But what has really excited the researchers is the discovery that these early humans (or "hominins") are far more primitive-looking than the *Homo erectus* humans that were, until now, believed to be the first people to migrate out of Africa about 1 million years ago.

The Dmanisi people had brains that were about 40 per cent smaller than those of *Homo erectus* and they were much shorter in stature than classical *H. erectus* skeletons, according to Professor David Lordkipanidze, general director of the Georgia National Museum. "Before our findings, the prevailing view was that humans came out of Africa almost 1 million years ago, that they already had sophisticated stone tools, and that their body anatomy was quite advanced in terms of brain capacity and limb proportions. But what we are finding is quite different," Professor Lordkipanidze said.

"The Dmanisi hominins are the earliest representatives of our own genus – *Homo* – outside Africa, and they represent the most primitive population of the species *Homo erectus* to date. They might be ancestral to all later *Homo erectus* populations, which would suggest a Eurasian origin of *Homo erectus*."

Speaking at the British Science Festival in Guildford, where he gave the British Council lecture, Professor Lordkipanidze raised the prospect that *Homo erectus* may have evolved in Eurasia from the more primitive-looking Dmanisi population and then migrated back to Africa to eventually give rise to our own species, *Homo sapiens* – modern man. "The question is whether *Homo erectus* originated in Africa or Eurasia, and if in Eurasia, did we have vice-versa migration? This idea looked very stupid a few years ago, but today it seems not so stupid," he told the festival.

The scientists have discovered a total of five skulls and a solitary jawbone. It is clear that they had relatively small brains, almost a third of the size of modern humans. "They are quite small. Their lower limbs are very human and their upper limbs are still quite archaic and they had very primitive stone tools," Professor Lordkipanidze said. "Their brain capacity is about 600 cubic centimetres. The prevailing view before this discovery was that the humans who first left Africa had a brain size of about 1,000 cubic centimetres."

The only human fossil to predate the Dmanisi specimens are of an archaic species *Homo habilis*, or "handy man", found only in Africa, which used simple stone tools and lived between about 2.5 million and 1.6 million years ago.

"I'd have to say, if we'd found the Dmanisi fossils 40 years ago, they would have been classified as *Homo habilis* because of the small brain size. Their brow ridges are not as thick as classical *Homo erectus*, but their teeth are more *H. erectus* like," Professor Lordkipanidze said. "All these finds show that the ancestors of these people were much more primitive than we thought. I don't think that we were so lucky as to have found the first travellers out of Africa. Georgia is the cradle of the first Europeans, I would say," he told the meeting.

"What we learnt from the Dmanisi fossils is that they are quite small – between 1.44 metres to 1.5 metres tall. What is interesting is that their lower limbs, their tibia bones, are very human-like so it seems they were very good runners," he said.

He added: "In regards to the question of which came first, enlarged brain size or bipedalism, maybe indirectly this information calls us to think that body anatomy was more important than brain size. While the Dmanisi people were almost modern in their body proportions, and were highly efficient walkers and runners, their arms moved in a different way, and their brains were tiny compared to ours.

"Nevertheless, they were sophisticated tool makers with high social and cognitive skills," he told the science festival, which is run by the British Science Association.

One of the five skulls is of a person who lost all his or her teeth during their lifetime but had still survived for many years despite being completely toothless. This suggests some kind of social organisation based on mutual care, Professor Lordkipanidze said.

Study Spells Out Spread of Brain Illness in Animals

By SANDRA BLAKESLEE

Researchers are reporting that they have solved a longstanding mystery about the rapid spread of a fatal brain infection in deer, elk and moose in the Midwest and West.

The infectious agent, which leads to chronic wasting disease, is spread in the feces of infected animals long before they become ill, according to a study published online Wednesday by the journal Nature. The agent is retained in the soil, where it, along with plants, is eaten by other animals, which then become infected.

The finding explains the extremely high rates of transmission among deer, said the study's lead author, Dr. Stanley B. Prusiner, director of the Institute for Neurodegenerative Diseases at the University of California, San Francisco.

First identified in deer in Colorado in 1967, the disease is now found throughout 14 states and 2 Canadian provinces. It leads to emaciation, staggering and death.

Unlike other animals, Dr. Prusiner said, deer give off the infectious agent, a form of protein called a prion, from lymph tissue in their intestinal linings up to a year before they develop the disease. By contrast, cattle that develop a related disease, mad cow, do not easily shed prions into the environment but accumulate them in their brains and spinal tissues.

There is no evidence to date that humans who hunt, kill and eat deer have developed chronic wasting disease. Nor does the prion that causes it pass naturally to other animal species in the wild. Besides mad cow and chronic wasting disease, the prion diseases include Creutzfeldt-Jakob, which leads to dementia and death in humans. Each of these diseases is caused by a different strain, and all strains behave somewhat differently.

In the case of chronic wasting disease, "it turns out prions exploit the oldest trick in the book used by pathogens and parasites," said Mike Miller, a veterinarian at the Colorado Division of Wildlife who is an expert on chronic wasting disease. "Fecal-oral transmission is very effective," Dr. Miller continued.

Each deer excretes about two pounds of fecal pellets a day. As wild herds move around, or captive herds are trucked between states, more soil becomes infected. In captive herds, up to 90 percent of animals develop the disease, Dr. Prusiner said. In wild herds, a third of animals can be infected.

"This is an important finding," said Judd M. Aiken, a leading prion expert who is director of the Alberta Veterinary Research Institute in Canada and who was not involved in the new study. "Most of us suspected that prions might be spread in feces, but we needed proof." "The fact that prions are shed at a preclinical stage of the disease is very significant," Dr. Aiken added.

The study was carried out in two parts. First, Dr. Miller and his team infected five mule deer by feeding them brain tissue from an infected animal. They took fecal samples before infection and at three to six months afterward. The deer came down with chronic wasting disease 16 to 20 months later.

Four to nine months after infection, the deer began shedding prions in low levels in their feces, even though they had no symptoms. Surprisingly, an infected deer could shed as many prions at this stage as would accumulate in its brain during terminal disease.

In the second part of the experiment, Erdem Tamguney, an assistant professor at Dr. Prusiner's institute, created a strain of mice with deerlike prions in their brains. When Dr. Tamguney inoculated the brains of these mice with feces from infected but asymptomatic deer, half developed symptoms of chronic wasting disease. Fourteen out of 15 fecal samples transmitted the disease to some of the mice.

Dr. Aiken said prions tended to bind to clay in soil and to persist indefinitely. When deer graze on infected dirt, prions that are tightly bound to clay will persist for long periods in their intestinal regions. So there is no chance chronic wasting disease will be eradicated, he said. Outside the laboratory, nothing can inactivate prions bound to soil. They are also impervious to radiation.

'Dung of the devil' plant roots point to new swine flu drugs

Scientists in China have discovered that roots of a plant used a century ago during the great Spanish influenza pandemic contains substances with powerful effects in laboratory experiments in killing the H1N1 swine flu virus that now threatens the world. The plant has a pleasant onion-like taste when cooked, but when raw it has sap so foul-smelling that some call it the "Dung of the Devil" plant. Their report is scheduled for the Sept. 25 issue of ACS' Journal of Natural Products, a monthly publication.

In the study, Fang-Rong Chang and Yang-Chang Wu and colleagues note that the plant, *Ferula assa-foetida* (asafoetida,) grows mainly in Iran, Afghanistan and mainland China. People used it as a possible remedy during the 1918 Spanish flu pandemic that killed between 20 to 100 million people. Until now, however, nobody had determined whether the plant does produce natural antiviral compounds.

Chang and Wu identified a group of chemical compounds in extracts of the plant that showed greater potency against influenza A (H1N1) than a prescription antiviral drug available for the flu. "Overall, the present study has determined that sesquiterpene coumarins from *F. assa-foetida* may serve as promising lead components for new drug development against influenza A (H1N1) viral infection," the authors write.

Article #1 For Immediate Release "**Influenza A (H1N1) Antiviral and Cytotoxic Agents from *Ferula assa-foetida***"
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Ancient figurines were toys not mother goddess statues, say experts as 9,000-year-old artefacts are discovered

By David Derbyshire

They were carved out of stone and squeezed out of clay 9,000 years ago, at the very dawn of civilisation.

Now archaeologists say these astonishing Stone Age statues could have been the world's first educational toys.

Nearly 2,000 figures have been unearthed at Çatalhöyük in Turkey - the world's oldest known town - over the last few decades. The most recent were found just last week.

Made by Neolithic farmers thousands of years before the creation of the pyramids or Stonehenge, they depict tiny cattle, crude sheep and flabby people.



Rare find: *The 9000-year-old figurines dug up in Turkey are thought to have been used as educational toys*

In the 1960s, some researchers claimed the more rotund figures were of a mysterious large breasted and big bellied "mother goddess", prompting a feminist tourism industry that thrives today.

But modern day experts disagree. They say the "mother goddess" figures - which were buried among the rubbish of the Stone Age town - are unlikely to have been religious icons.

Many of the figures thought to have been women in the 1960s, are just as likely to be men.

Archaeologist Prof Lynn Meskell, of Stanford University, said: "The majority are cattle or sheep and goats. They could be representatives of animals they were dealing with - and they could have been teaching aides.

"All were found in the trash - and they were not in niches or platforms or placed in burials."

Out of the 2,000 figurines dug up at the site, less than five per cent are female, she told the British science Festival in Surrey University, Guildford. "These are things that were made and used on a daily basis," she said. "People carried them around and discarded them."

Çatalhöyük is one of the most important archaeological sites in the world. Established around 7,000 BC, it was home to 5,000 people living in mud brick and plaster houses. Their buildings were crammed so tightly together, the inhabitants clambered over the roofs and used ladders to get into their homes.



Amazing artefacts: *Many of the figurines resemble animals like sheep and goats*

The town dwellers were early farmers who had domesticated a handful of plants and kept wild cattle for meat and milk. Cattle horns were incorporated into the walls of their homes.

The town contains the oldest murals - paintings on plastered walls. Unlike later towns, there is no obvious hierarchy - no homes for priests or leaders, no temples and no public spaces. The dead were buried in spaces under homes, rather than in cemeteries. Some researchers believe it was an equalitarian society.

The town survived for around 2,000 years. It is not known what happened to its inhabitants, but they may have been killed by invaders or driven away by the loss of nearby farmland.

Ancient oceans offer new insight into the origins of animal life

Analysis of a rock type found only in the world's oldest oceans has shed new light on how large animals first got a foothold on the Earth.

A scientific team led by Professor Robert Frei at the University of Copenhagen in Denmark, and including scientists from Newcastle University, UK, and universities in Uruguay and Southern Denmark, have for the first time managed to plot the rise and fall of oxygen levels in the Earth's atmosphere over the last 3.8 billion years.

By analysing the isotopes of chromium in iron-rich sediments formed in the ancient oceans, the team has found that a rise in atmospheric oxygen levels 580 million years ago was closely followed by the evolution of animal life. Published today in the academic journal *Nature*, the data offers new insight into how animal life – and ultimately humans – first came to roam the planet.

"Because animals evolved in the sea, most previous research has focussed on oceanic oxygen levels," explains Newcastle University's Dr Simon Poulton, one of the authors of the paper. "Our research confirms for the first time that a rise in atmospheric oxygen was the driving force for oxygenation of the oceans 580 million years ago, and that this was the catalyst for the evolution of large complex animals."

The study

Distinctive chromium isotope signals occur when continental rocks are altered and weathered as a result of oxygen levels rising in the atmosphere. The chromium released by this weathering is then washed into the seas and deposited in the deepest oceans - trapped in iron-rich rocks on the sea bed.

Using this new data, the research team has not only been able to establish the trigger for the evolution of animals, but have also demonstrated that oxygen began to pulse into the atmosphere earlier than previously thought. "Oxygen levels actually began to rise 2.8 billion years ago" explains Dr Poulton.

"But instead of this rise being steady and gradual over time, what we saw in our data was a very unstable situation with short-lived episodes of free oxygen in the atmosphere early in Earth's history, followed by plummeting levels around 2 billion years ago. "It was not until a second rise in atmospheric oxygen 580 million years ago that larger complex animals were able to get a foothold on the Earth."

Cement's basic molecular structure finally decoded

By Denise Brehm Civil & Environmental Engineering

In the 2,000 or so years since the Roman Empire employed a naturally occurring form of cement to build a vast system of concrete aqueducts and other large edifices, researchers have analyzed the molecular structure of natural materials and created entirely new building materials such as steel, which has a well-documented crystalline structure at the atomic scale.

Oddly enough, the three-dimensional crystalline structure of cement hydrate - the paste that forms and quickly hardens when cement powder is mixed with water - has eluded scientific attempts at decoding, despite the fact that concrete is the most prevalent man-made material on earth and the focus of a multibillion-dollar industry that is under pressure to clean up its act. The manufacture of cement is responsible for about 5 percent of all carbon dioxide emissions worldwide, and new emission standards proposed by the U.S. Environmental Protection Agency could push the cement industry to the developing world.

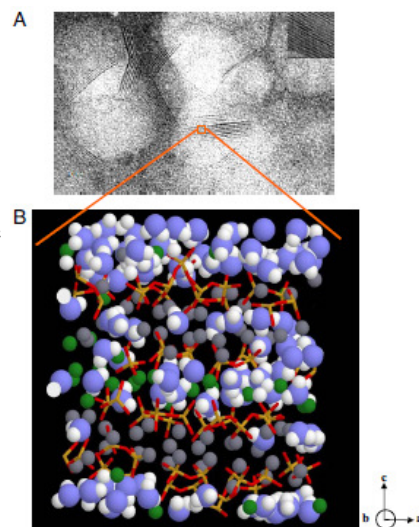


Fig. 1. (A) TEM image of clusters of C-S-H. The inset is a TEM image of tobermorite 14 Å from (45). (B) the molecular model of C-S-H: the blue and white spheres are oxygen and hydrogen atoms of water molecules, respectively; the green and gray spheres are inter and intra-layer calcium ions, respectively; yellow and red sticks are silicon and oxygen atoms in silica tetrahedra. (courtesy of A. Baronnet, CINaM, CNRS and Marseille Université', France)

"Cement is so widely used as a building material that nobody is going to replace it anytime soon. But it has a carbon dioxide problem, so a basic understanding of this material could be very timely," said MIT Professor Sidney Yip, co-author of a paper published online in the *Proceedings of the National Academy of Sciences* (PNAS) during the week of Sept. 7 that announces the decoding of the three-dimensional structure of the basic unit of cement hydrate by a group of MIT researchers who have adopted the team name of Liquid Stone.

"We believe this work is a first step toward a consistent model of the molecular structure of cement hydrate, and we hope the scientific community will work with it," said Yip, who is in MIT's Department of Nuclear Science and Engineering (NSE). "In every field there are breakthroughs that help the research frontier moving forward. One example is Watson and Crick's discovery of the basic structure of DNA. That structural model put biology on very sound footing."

Scientists have long believed that at the atomic level, cement hydrate (or calcium-silica-hydrate) closely resembles the rare mineral tobermorite, which has an ordered geometry consisting of layers of infinitely long chains of three-armed silica molecules (called silica tetrahedra) interspersed with neat layers of calcium oxide.

But the MIT team found that the calcium-silica-hydrate in cement isn't really a crystal. It's a hybrid that shares some characteristics with crystalline structures and some with the amorphous structure of frozen liquids, such as glass or ice.

At the atomic scale, tobermorite and other minerals resemble the regular, layered geometric patterns of kilim rugs, with horizontal layers of triangles interspersed with layers of colored stripes. But a two-dimensional look at a unit of cement hydrate would show layers of triangles (the silica tetrahedra) with every third, sixth or ninth triangle turned up or down along the horizontal axis, reaching into the layer of calcium oxide above or below.

And it is in these messy areas - where breaks in the silica tetrahedra create small voids in the corresponding layers of calcium oxide - that water molecules attach, giving cement its robust quality. Those erstwhile "flaws" in the otherwise regular geometric structure provide some give to the building material at the atomic scale that transfers up to the macro scale. When under stress, the cement hydrate has the flexibility to stretch or compress just a little, rather than snapping.

"We've known for several years that at the nano scale, cement hydrates pack together tightly like oranges in a grocer's pyramid. Now, we've finally been able to look inside the orange to find its fundamental signature. I call it the DNA of concrete," said Franz-Josef Ulm, the Macomber Professor in the Department of Civil and Environmental Engineering (CEE), a co-author of the paper. "Whereas water weakens a material like tobermorite or jennite, it strengthens the cement hydrate. The 'disorder' or complexity of its chemistry creates a heterogenic, robust structure. "Now that we have a validated molecular model, we can manipulate the chemical structure to design concrete for strength and environmental qualities, such as the ability to withstand higher pressure or temperature," said Ulm.

CEE Visiting Professor Roland Pellenq, director of research at the Interdisciplinary Center of Nanosciences at Marseille, which is part of the French National Center of Scientific Research and Marseille University, pinned down the exact chemical shape and structure of C-S-H using atomistic modeling on 260 co-processors and a statistical method called the grand canonical Monte Carlo simulation.

Like its name, the simulation requires a bit of gambling to find the answer. Pellenq first removed all water molecules from the basic unit of tobermorite, watched the geometry collapse, then returned the water molecules singly, then doubly and so on, removing them each time to allow the geometry to reshape as it would naturally. After he added the 104th water molecule, the correct atomic weight of C-S-H was reached, and Pellenq knew he had an accurate model for the geometric structure of the basic unit of cement hydrate.

The team then used that atomistic model to perform six tests that validated its accuracy.

"This gives us a starting point for experiments to improve the mechanical properties and durability of concrete. For instance, we can now start replacing silica in our model with other materials," said Pellenq. *Other team members are graduate student Rouzbeh Shahsavari of CEE and Markus Buehler, MIT's Esther and Harold E. Edgerton Career Development Associate Professor of Civil and Environmental Engineering; Krystyn Van Vliet, MIT's Thomas Lord Associate Professor of Materials Science and Engineering; and NSE postdoctoral associate Akihiro Kushima. This research was funded by the Portuguese cement manufacturer, Cimpor Corp., enabled through the MIT-Portugal Program.*

Model backs green tea and lemon claim, lessens need to test animals

West Lafayette, Ind. - An animal study at Purdue University has shown that adding ascorbic acid and sugar to green tea can help the body absorb helpful compounds and also demonstrates the effectiveness of a model that could reduce the number of animals needed for these types of studies.

Mario Ferruzzi, associate professor of food science and nutrition, adapted a digestion model with human intestinal cells to show that adding ascorbic acid to green tea would increase the absorbability of catechins found in the tea. Catechins, a class of polyphenols common in tea, cocoa and grape, are antioxidants thought to fight heart disease, stroke, cancer, diabetes and other health problems.

Ferruzzi, Elsa Janle, a Purdue associate research professor of foods and nutrition, and Catrina Peters, a Purdue graduate student in nutrition, were able to demonstrate that adding ascorbic acid, sucrose or both together increases by as much as three times the amount of catechins that can be absorbed into the bloodstream. The results of the in vivo study compared well with those predicted by the in vitro model.

"This model may be used as a pre-emptive screening tool at very little cost before you do expensive tests on animals or humans," said Ferruzzi, whose findings were published in the early online edition of the journal Food Research International. "If you want to get human screening off the ground, it takes months. If you want to use this model, it takes hours."

The model charts how the digestive stability, solubility and absorption of polyphenols changes based on modifications to a beverage's formula. It will not be exact in terms of measurements, but when compared to the in vivo test in rats, the model's predictions matched directionally to the in vivo study and were relatively close proportionately.

Ferruzzi said testing with the model could allow researchers to predict how a new product formula might change the product's properties, reducing the number of animals needed for testing to only products that showed desired characteristics in the model. The model also can be adapted to simulate the digestive characteristics of other animals or humans as originally intended.

"As long as we know the typical gastrointestinal conditions of an animal and the volumes, we can adapt the model to mimic those conditions," Ferruzzi said. "You don't have to do expensive precursor studies."

The in vivo study backed up the model study that showed adding sugar and vitamin C to green tea enhanced the body's ability to absorb polyphenols. Ferruzzi said that adding lemon juice or other citrus juice to tea would do the trick, or consumers could look for ready-to-drink products that contain 100 percent of the recommended amount of vitamin C or ascorbic acid on the ingredient list. "Having that vitamin C seems to do it," Ferruzzi said. "And if you don't want to squeeze a lemon into your cup, just have a glass of juice with your green tea."

Connie Weaver, head of the National Institutes of Health Purdue University-University of Alabama at Birmingham Botanical Research Center for Age-Related Diseases, which funded the research, said the study's focus was an important part of understanding how to get the most out of compounds considered beneficial.

"There is a lot of interest in bioactive materials to protect people from disease and promote better health," Weaver said. "What's been totally ignored is the way these materials are found in foods in combination with other ingredients. How they're involved in the food matrix can affect how you absorb these health promoters."

Ferruzzi said the next step in the research is to stage a human clinical trial.

Archaeologists discover oldest-known fiber materials used by early humans *Flax fibers could have been used for warmth and mobility; for rope, baskets, or shoes*

CAMBRIDGE, Mass. – A team of archaeologists and paleobiologists has discovered flax fibers that are more than 34,000 years old, making them the oldest fibers known to have been used by humans. The fibers, discovered during systematic excavations in a cave in the Republic of Georgia, are described in this week's issue of Science.

The flax, which would have been collected from the wild and not farmed, could have been used to make linen and thread, the researchers say. The cloth and thread would then have been used to fashion garments for warmth, sew leather pieces, make cloths, or tie together packs that might have aided the mobility of our ancient ancestors from one camp to another.

The excavation was jointly led by Ofer Bar-Yosef, George Grant MacCurdy and Janet G. B. MacCurdy Professor of Prehistoric Archaeology in the Faculty of Arts and Sciences at Harvard University, with Tengiz Meshveliani from the Georgian State Museum and Anna Belfer-Cohen from the Hebrew University. The microscopic research of the soil samples in which numerous flax fibers were discovered was done by Eliso Kvavadze of the Institute of Paleobiology, part of the National Museum of Georgia.

"This was a critical invention for early humans. They might have used this fiber to create parts of clothing, ropes, or baskets - for items that were mainly used for domestic activities," says Bar-Yosef. "We know that this is wild flax that grew in the vicinity of the cave and was exploited intensively or extensively by modern humans."

The items created with these fibers increased early humans chances of survival and mobility in the harsh conditions of this hilly region. The flax fibers could have been used to sew hides together for clothing and shoes, to create the warmth necessary to endure cold weather. They might have also been used to make packs for carrying essentials, which would have increased and eased mobility, offering a great advantage to a hunter-gatherer society. Some of the fibers were twisted, indicating they were used to make ropes or strings. Others had been dyed. Early humans used the plants in the area to color the fabric or threads made from the flax.

Today, these fibers are not visible to the eye, because the garments and items sewed together with the flax have long ago disintegrated. Bar-Yosef, Kvavadze and colleagues discovered the fibers by examining samples of clay retrieved from different layers of the cave under a microscope.

The discovery of such ancient fibers was a surprise to the scientists. Previously, the oldest known were imprints of fibers in small clay objects found in Dolni Vestonice, a famous site in the Czech Republic some 28,000 years old. The scientists' original goal was to analyze tree pollen samples found inside the cave, part of a study of environmental and temperature fluctuations over the course of thousands of years that would have affected the lives of these early humans. However, while looking for this pollen, Kvavadze, who led the analysis of the pollen, also discovered non-pollen polymorphs – these flax fibers.

Bar-Yosef and his team used radiocarbon dating to date the layers of the cave as they dug the site, revealing the age of the clay samples in which the fibers were found. Flax fibers were also found in the layers that dated to about 21,000 and 13,000 years ago.

Bar-Yosef's team began the excavations of this cave in 1996, and has returned to the site each year to complete this work. "We were looking to find when the cave was occupied, what was the nature of the occupation by those early hunter-gatherers, where did they go hunting and gathering food, what kind of stone tools they used, what types of bone and antler tools they made and how they used them, whether they made beads and pendants for body decoration, and so on," says Bar-Yosef. "This was a wonderful surprise, to discover these ancient flax fibers at the end of this excavation project."

Bar-Yosef and Kvavadze's co-authors are Belfer-Cohen, Meshveliani, Elizabeth Boaretto of the Weizmann Institute of Science and Bar-Ilan University, Nino Jakeli of the Georgian State Museum, and Zinovi Matskevich of the Department of Anthropology at Harvard.

The research was funded by the American School of Prehistoric Research at the Peabody Museum, Harvard University.

Ketamine reduces suicidality in depressed patients

Philadelphia, PA, 10 September 2009 - Drug treatment options for depression can take weeks for the beneficial effects to emerge, which is clearly inadequate for those at immediate risk of suicide. However, intravenous (IV) ketamine, a drug previously used as an anesthetic, has shown rapid antidepressant effects in early trials.

Researchers have now explored ketamine's effects on suicidality in patients with treatment-resistant depression, and are publishing their results in the September 1st issue of *Biological Psychiatry*. Ketamine acutely reduced suicidal thoughts when patients were assessed 24 hours after a single infusion. This reduction in suicidality was maintained when patients received repeated doses over the next two weeks.

Corresponding author Rebecca Price commented on these encouraging findings: "If these findings hold up in larger samples of high-risk suicidal patients, IV ketamine could prove an attractive treatment option in situations where waiting for a conventional antidepressant treatment to take effect might endanger the patient's life."

Since this was a preliminary study in a small group of depressed patients, further research is needed to replicate these results. However, the findings are promising and could result in improved treatment for suicidal patients in the future.

Notes to Editors: The article is "Effects of Intravenous Ketamine on Explicit and Implicit Measures of Suicidality in Treatment-Resistant Depression" by Rebecca B. Price, Matthew K. Nock, Dennis S. Charney, and Sanjay J. Mathew. Price, Charney, and Mathew are affiliated with the Department of Psychiatry, Mount Sinai School of Medicine, New York, New York. Charney is also with the Departments of Neuroscience, and Pharmacology & Systems Therapeutics, also at Mount Sinai. Price is also from the Department of Psychology, Rutgers, the State University of New Jersey, Piscataway, New Jersey. Nock is affiliated with the Department of Psychology, Harvard University, Cambridge, Massachusetts. The article appears in *Biological Psychiatry*, Volume 65, Issue 5 (September 1, 2009), published by Elsevier.

No change in the link between deprivation and death since 1900s

Research: Comparisons between geographies of mortality and deprivation from the 1900s and 2001: Spatial analysis of census and mortality statistics

The link between deprivation and premature death is as strong today as it was in the early 1900s according to research published on *bmj.com* today. The study, the first of its kind to directly compare modern deprivation and mortality with conditions a century ago in the whole of England and Wales, has been undertaken by Ian Gregory, Senior Lecturer at Lancaster University.

Using the census mortality data from 634 districts in the 1900s, Gregory has explored the links between deprivation and mortality in Edwardian England and Wales to premature death and poverty in 2001.

The twentieth century saw huge improvements in mortality rates in England and Wales. In the 1900s, 33% of deaths occurred in the under 5s and only 13% occurred over the age of 75 – one hundred years later deaths aged under 5 are less than 1% and 65% of deaths now occur in those over 75. Life expectancy has also improved, rising from 46 for males to 77 and 50 for females to 81.

In the 1900s the main causes of death were respiratory, infectious and parasitic diseases but in 2001 this changed to cancers, heart diseases and strokes. The experience of poverty changed too, while in the 1900s it meant not having the bare necessities for existence, a century later relative poverty meant comparing an individual's income or deprivation with those experienced by society as a whole.

Despite the dramatic decline in mortality in the twentieth century the link between mortality and deprivation across England and Wales "remains as strong today as it was a century ago", says Gregory.

The author argues that links between mortality and deprivation are deeply entrenched and that patterns from the Edwardian era are strong predictors of ill health today. Gregory maintains that modern diseases "have a possible long-term link to unhealthy living conditions in the distant past". He says: "The strong association

between modern deaths from lung cancer and 1900s mortality suggests that this might in part be a cultural effect caused by the long term prevalence of smoking in poorer areas."

Graffiti-free historic buildings

Many a historic landmark is defaced with graffiti, but the spray paint can only be removed – if at all – using caustic solutions which risk damaging the underlying surface. A new breathable coating provides efficient, all-round protection against attacks by taggers.

It takes seconds to spray on graffiti, but hours or weeks to remove – especially from porous natural stone or brickwork as found in the majority of historic monuments. The paint penetrates deep into the pores from which it is impossible to remove, even with a pressure hose or multi-component solvents. Often the only answer, other than living with the graffiti, is to etch away a part of the wall. Special anti-graffiti polymer coatings have been on the market for several years. They create a hydrophobic seal that closes the pores, preventing the paint from adhering to the undersurface and allowing it to be wiped off. But as a result the building can no longer breathe, augmenting the risk of mold development or salt efflorescence. Because they cannot be removed easily, such coatings also run counter to the principles of conservation, which require that any changes must be reversible.

"There are conflicting requirements for this kind of polymer coating – it mustn't seal the pores, because it is important that there should be a continuous exchange of air between the building and the external environment, and at the same time it has to prevent the spray paint from penetrating the pores. The coating needs to be sufficiently resistant to withstand both weathering and mechanical cleaning. Moreover, since we're dealing with historic landmarks, it must be possible to completely remove the coating from the walls if required, to restore them to their original condition with little effort and without damaging the structure," says Professor André Laschewsky, who heads the relevant research group at the Fraunhofer Institute for Applied Polymer Research IAP in Potsdam.

As part of an EU-sponsored project, Laschewsky's team and partners from the Center of Polymer and Carbon Materials of the Polish Academy of Sciences in Gliwice and Zabrze have developed a polymer coating that meets these requirements. "Our innovative polymer film seals the pores in the substrate, so that graffiti paint doesn't penetrate. But its micro-porous structure also creates a hydrophobic barrier that allows water vapor to escape from the building while at the same time preventing the infiltration of rainwater," says Laschewsky. The coating can be removed from the surface using a diluted brine solution which modifies its chemical composition and allows it to be washed off. Coordinated by the LABEIN Foundation in Spain and the German Federal Institute for Materials Research and Testing the partners have coated samples of ancient stone and brick and repeatedly covered them with graffiti – which was removed completely each time.

Dandelion rubber

Most natural rubber comes from rubber trees in Southeast Asia, but this source is now under threat from a fungus. Researchers have optimized the Russian dandelion to make it suitable for large-scale rubber production.

Anyone who has picked dandelions as a child will be familiar with the white liquid that seeps out of the stalks as you break them off. Viscous, sticky – and a much sought-after material: natural latex. Around 30,000 everyday products contain natural rubber, everything from car tires, catheter tubes, latex gloves to tops for drinks bottles. Car tires, for instance, would not be elastic enough without the incorporation of natural rubber. The bulk of this material comes from rubber trees in Southeast Asia. Rubber produced in this way can, however, cause allergic reactions, which is clearly an issue with clinical products. A fungus is also creating concern for rubber cultivators. In South America the infection is now so widespread that large-scale cultivation has become virtually impossible. The disease now also appears to have taken root in Southeast Asia's rubber belt. Fungicides still provide at least temporary protection. But if the fungus disease was to reach epidemic proportions, chemical crop protection would be rendered useless – experts fear that the natural latex industry could collapse if that were to happen.

Researchers are therefore turning to other sources – such as the Russian dandelion. Germans, Russians and Americans produced rubber from this plant during the Second World War. Once it is cut, latex seeps out, albeit difficult to use as it polymerizes immediately. Scientists from the Fraunhofer Institute for Molecular Biology and Applied Ecology IME in Aachen have now come a step nearer to large-scale rubber production from dandelions. "We have identified the enzyme responsible for the rapid polymerization and have switched it off," says Prof. Dr. Dirk Prüfer, Head of Department at the IME. "If the plant is cut, the latex flows out instead of being polymerized. We obtain four to five times the amount we would normally. If the plants were to be cultivated on a large scale, every hectare would produce 500 to 1000 kilograms of latex per growing season." The dandelion rubber has not caused any allergies so far, making it ideal for use in hospitals.

In the lab the researchers have genetically modified the dandelion. Their next step will involve cultivating the optimized plants using conventional breeding techniques. In around five years, Prüfer estimates, they may well have achieved their goal. In any case, the dandelion is not just suitable for rubber production: the plant also produces substantial quantities of inulin, a natural sweetener.

Don't stand by me: When involving an interested party may not be in your best interest

New research explores the role of personal connections in failing projects

CHICAGO (September 10, 2009) – When business leaders leave organizations following poor decisions, constituents often find comfort in replacing them with insiders – others familiar with the problem and original choices. But, new research shows that such decisions are best left to a completely unrelated, outside party, contrary to the natural inclination to go to an insider – someone with personal connections to the old boss.

"Vicarious entrapment: Your sunk costs, my escalation of commitment" will appear in an upcoming issue of *Journal of Experimental Social Psychology* and is co-authored by Adam Galinsky and Brian Gunia of the Kellogg School of Management at Northwestern University and Niro Sivanathan of the London Business School. The study found that when new decision makers share a psychological connection with an initial decision maker, they may invest further in the failing programs of the first – even to their own financial detriment.

In this research, the authors explored a phenomenon they coined "vicarious entrapment." They proposed that the success of a two-decision solution was dependent on not just a physical separation, but a psychological separation of the decision makers. If the delegated decision maker was even subtly connected to the original – by sharing similar attributes like the same birthday or simply empathizing with the first decision maker, for example – he/she honored the original decision maker's commitments and made further investments in that person's losing decisions.

"We know humans are social beings driven to find attachments and connections to others. Research has shown that once a psychological connection forms between two individuals, they are more likely to cooperate and favor each other financially," said Galinsky, the Morris and Alice Kaplan Professor of Ethics and Decision in Management at the Kellogg School. "The current research suggests that they are also more likely to escalate on each others' failing decisions."

Galinsky and his colleagues' experiments examined psychological connectedness in three contexts: financial investments, personnel decisions and auctions. Even when participants faced a direct financial cost to themselves – and even among economics students trained in the irrationality of honoring sunk costs – the delegated decision maker followed the original decisions once a psychological connection was made with the original decision maker.

In one experiment on personnel decisions, participants awarded a larger raise to an underperforming candidate originally "hired" by another initial decision-maker, but only when they had taken the perspective of and empathized with the first decision-maker. Likewise, participants who shared the same birthday (i.e., had something "in-common") with an original auction bidder made many more bids and lost significantly more money than those who took over for a bidder with a different birthday.

"Business, and even political organizations trying to navigate their way out of decisions gone wrong should carefully consider integrating a true outsider – someone with no connections to prior leadership" said Gunia, also of the Kellogg School. "Although outsiders may take longer to understand the problem, their psychological disconnection with the past may enable them to act more decisively once they do. Our research suggests that an individual who shares even the most subtle connections with predecessors may act less independently."

UCLA researchers develop biomarker for rapid relief of major depression

Brain-wave patterns may predict how effective medication will be

It is a long, slow slog to treat major depression. Many antidepressant medications are available, but no single biomarker or diagnostic test exists to predict which one is right for an individual. As a result, for more than half of all patients, the first drug prescribed doesn't work, and it can take months to figure out what does.

Now, based on the final results of a nationwide study led by UCLA, clinicians may be able to accurately predict within a week whether a particular drug will be effective by using a non-invasive test that takes less than 15 minutes to administer. The test will allow physicians to quickly switch patients to a more effective treatment, if necessary.

The study, called the Biomarkers for Rapid Identification of Treatment Effectiveness in Major Depression, or BRITE-MD, measured changes in brain-wave patterns using quantitative electroencephalography (QEEG), a non-invasive, computerized measurement that recognizes specific alterations in brain-wave activity. These changes precede improvement in mood by many weeks and appear to serve as a biomarker that accurately

predicts how effective a given medication will be. The study results appear in two articles published in the September issue of the journal *Psychiatry Research*.

Nine sites around the country collaborated on the study, which enrolled a total of 375 people who had been diagnosed with major depressive disorder (MDD). Each individual was given a baseline QEEG at the beginning of the trial and then prescribed the antidepressant escitalopram, commonly known as Lexapro, one of a class of drugs known as selective serotonin re-uptake inhibitors that are commonly prescribed for depression. After one week, a second QEEG was taken. The researchers examined a biomarker called the antidepressant treatment response (ATR) index — a specific change in brain-wave patterns from the baseline QEEG.

Subjects were then randomly assigned to continue with escitalopram or were given a different drug. A total of 73 patients who remained on escitalopram were tracked for 49 days to see if their results matched the prediction of the ATR biomarker. The ATR predicted both response and remission with an accuracy rate of 74 percent, much higher than any other method available. The researchers also found that they could predict whether subjects were more likely to respond to a different antidepressant, bupropion, also known as Wellbutrin XL.

"Until now, other than waiting, there has been no reliable method for predicting whether a medication would lead to a good response or remission," said Dr. Andrew Leuchter, professor of psychiatry at the Semel Institute for Neuroscience and Human Behavior at UCLA and lead author of the study. "And that wait can be as long as 14 weeks. So these are very exciting findings for the patient suffering from depression. The BRITE results are a milestone in our efforts to develop clinically useful biomarkers for predicting treatment response in MDD."

Major depressive disorder is a leading cause of disability, costing society in excess of \$80 billion annually; approximately two-thirds of these costs reflect the enormous disability associated with the disorder. An estimated 15 million people in the United States experience a depressive episode each year, and nearly 17 percent of adults will experience major depression in their lifetime.

"BRITE study results suggest that the ATR biomarker could potentially provide the greatest clinical benefit for those patients who might be receiving a medication that is unlikely to help them," Leuchter said. "Our results suggest that it may be possible to switch these patients to a more effective treatment quickly. This would help patients and their physicians avoid the frustration, risk and expense of long and ineffective medication trials."

Leuchter noted that research has shown that depression patients who do not get better with a first treatment experience prolonged suffering, are more likely to abandon treatment altogether and may become more resistant to treatment over time. "So the benefits to the individual and to society are enormous," he said.

An added benefit of the biomarker test, according to Leuchter, is that it is non-invasive, painless and fast — about 15 minutes — and only involves the placement of six electrodes around the forehead and on the earlobes. *Aspect Medical Systems, which developed the ATR biomarker, provided financial support for the study. Aspect also participated in the design and conduct of the study; the collection, management, analysis and interpretation of the data; and the preparation and review of the manuscript. Final approval of the form and content of the manuscript rested with the authors. Other UCLA authors included Dr. Ian Cook, Dr. Karl S. Burgoyne and Dr. James T. McCracken. Leuchter is chair of Aspect's neuroscience advisory board and has provided scientific consultation to them.*

Mighty Mouse takes off – thanks to magnets

* Updated 21:21 11 September 2009 by **Lisa Grossman**

With the aid of a strong magnetic field, mice have been made to levitate for hours at NASA's Jet Propulsion Laboratory (JPL) in Pasadena, California. The floating rodents could provide a valuable insight into how astronauts are affected by extended spells in zero gravity.

Strawberries and frogs have previously been levitated using the same method. It works because a strong magnetic field distorts the movement of electrons in water molecules, which in turn produces a magnetic field that opposes the one applied. The net result is a repulsive effect which, if suitably oriented and strong enough, can overcome the pull of gravity.

Yuanming Liu and colleagues at JPL in Pasadena, California, used a purpose-built levitation device containing a coil of wire, or solenoid, cooled to a few degrees above absolute zero so that it became superconducting. Running a current through the solenoid creates a magnetic field of 17 teslas, about 300,000 times that of the Earth.

The magnetic field varies along the length of the coil. A water-containing object placed at the base of the coil develops an opposing magnetic field that generates a force twice that of Earth's gravity at the bottom, Earth-like gravity in the middle, and zero gravity at the top. Liu's system can levitate water-based objects for hours or even days at a time.

Out of control

When the team placed a young mouse weighing 10 grams in a non-magnetic cage and moved it into the levitation zone, sure enough, the mouse began to float. "We were pretty excited to see it," Liu says. "There was

a lingering doubt that, even though you can levitate water, you may not be able to levitate a mouse." The mouse was not so thrilled. "It tried to grab on to something. I guess it wasn't used to floating," says Liu. "It bumped on the cage and started spinning. It obviously didn't like it that much."

Drug assisted

Mildly sedated, the mouse seemed less concerned during a subsequent trial. Even non-sedated mice got used to zero gravity after a while, spending up to three hours hanging in the air, and even eating and drinking.

The levitating mice could provide a testing ground for studying the effects of space travel on humans, such as bone and muscle loss, and changes in blood flow. Liu's machine is better suited to such experiments than the "vomit comet" planes that simulate microgravity, or the International Space Station. The magnetic levitator makes it possible to dial in anything between Earth and zero gravity for as long as needed, and at lower cost.

"They're pushing the state of the art for the technology of magnetic levitation," says Jim Valles of Brown University, who manipulates cells with magnetic fields. "It's really remarkable that they've been able to build a device big enough to be able to do a mammal, that maybe stands a chance of showing the prolonged effects that space flight could produce."

Health implications

The effects on the health of an animal spending hours or days in such an intense magnetic field are unknown, though rats subjected to a field of 9.4 teslas – just over half as strong as the one used on the mice – suffered no obvious ill effects. Liu's system is too small to be used on people, but could you build something similar to levitate humans one day? "Theoretically I think you could," says Liu, "but the cost would be prohibitive."

Giant stone-age axes found in African lake basin

A giant African lake basin is providing information about possible migration routes and hunting practices of early humans in the Middle and Late Stone Age periods, between 150,000 and 10,000 years ago.

Oxford University researchers have unearthed new evidence from the lake basin in Botswana that suggests that the region was once much drier and wetter than it is today. They have documented thousands of stone tools on the lake bed, which sheds new light on how humans in Africa adapted to several substantial climate change events during the period that coincided with the last Ice Age in Europe.



Four giant stone hand axes were recovered from the dry basin of Lake Makgadikgadi in the Kalahari Desert.

Researchers from the School of Geography and the Environment at the University of Oxford are surveying the now-dry basin of Lake Makgadikgadi in the Kalahari Desert, which at 66,000 square kilometres is about the same size of present day Lake Victoria.

Their research was prompted by the discovery of the first of what are believed to be the world's largest stone tools on the bed of the lake. Although the first find was made in the 1990s, the discovery of four giant axes has not been scientifically reported until now. Four giant stone hand axes, measuring over 30 cm long and of uncertain age, were recovered from the lake basin.

Equally remarkable is that the dry lake floor where they were found is also littered with tens of thousands of other smaller stone-age tools and flakes, the researchers report.

Professor David Thomas, Head of the School of Geography and the Environment at the University of Oxford, said: 'Many of the tools were found on the dry lake floor, not around its edge, which challenges the view that big lakes were only attractive to humans when they were full of water. 'As water levels in the lake went down, or during times when they fluctuated seasonally, wild animals would have congregated round the resulting watering holes on the lake bed. It's likely that early human populations would have seen this area as a prolific hunting ground when food resources in the region were more concentrated than at times when the regional climate was wetter and food was more plentiful and the lake was full of water.'

This work is part of an ongoing project investigating the complex history of major changes in climate in Africa. Co-researcher Dr Sallie Burrough has dated the sediment and shorelines of the lake basin, which has shown that the mega lake was filled with water on multiple occasions in the last 250,000 years. The research team has also investigated islands on the floor of the lake - remnants of former sand dunes - which suggest the region's climate has also been both windier and markedly drier than it is today.

Professor Thomas said: 'The interior of southern Africa has usually been seen as being devoid of significant archaeology. Surprisingly, we have found and logged incredibly extensive Middle Stone Age artefacts spread over a vast area of the lake basin. 'The record the basin is revealing is one of marked human adaptation in the

past. Early humans saw the opportunity to use the lake basin when it was not full of water, but at least seasonally dry. It shows that humans have adapted to climate change and variability in a sustained way.'

Many archaeologists believe that equivalent lakes in the North African Sahara desert played an important part in the 'Out of Africa' human expansion theory, as the ancestors of all modern humans would have chosen a wet route out of Africa. The new research is the first time that this giant Botswanan lake basin in southern Africa has been the focus of scientific research, and these findings could provide new evidence to support the theory about a hominid migration through and expansion from Africa.

Professor Thomas and Dr Burrough are planning further research into how the lake was formed and how it came and went. They say that the most likely explanation is that sustained periods of greater rainfall in the Angolan Highlands resulted in much greater flow in the Zambezi River, with the water being diverted into the lake basin due to a quirk of geology.

New research, beginning in 2010 and funded by the Leverhulme Trust, will investigate possible links between the lake basin and the Zambezi River, while initial discussions are in hand for setting up a major international geo-archaeologist programme to further unravel the complexities of human-climate-environment interactions in this important and under-researched region. *Provided by Oxford University (news : web)*

Muscle: 'hard to build, easy to lose' as you age

Have you ever noticed that people have thinner arms and legs as they get older? As we age it becomes harder to keep our muscles healthy. They get smaller, which decreases strength and increases the likelihood of falls and fractures. New research is showing how this happens — and what to do about it.

A team of Nottingham researchers has already shown that when older people eat, they cannot make muscle as fast as the young. Now they've found that the suppression of muscle breakdown, which also happens during feeding, is blunted with age.

The scientists and doctors at The University of Nottingham Schools of Graduate Entry Medicine and Biomedical Sciences believe that a 'double whammy' affects people aged over 65. However the team think that weight training may "rejuvenate" muscle blood flow and help retain muscle for older people.

These results may explain the ongoing loss of muscle in older people: when they eat they don't build enough muscle with the protein in food; also, the insulin (a hormone released during a meal) fails to shut down the muscle breakdown that rises between meals and overnight. Normally, in young people, insulin acts to slow muscle breakdown. Common to these problems may be a failure to deliver nutrients and hormones to muscle because of a poorer blood supply.

The work has been done by Michael Rennie, Professor of Clinical Physiology, and Dr Emilie Wilkes, and their colleagues at The University of Nottingham. The research was funded by the UK's Biotechnology and Biological Sciences Research Council (BBSRC) as part of ongoing work on age-related muscle wasting and how to lessen that effect.

Research just published in *The American Journal of Clinical Nutrition* compared one group of people in their late 60s to a group of 25-year-olds, with equal numbers of men and women. Professor Rennie said "We studied our subjects first — before breakfast — and then after giving them a small amount of insulin to raise the hormone to what they would be if they had eaten breakfast, of a bowl of cornflakes or a croissant."

"We tagged one of the amino acids (from which proteins are made) so that we could discover how much protein in leg muscle was being broken down. We then compared how much amino acid was delivered to the leg and how much was leaving it, by analysing blood in the two situations.

"The results were clear. The younger people's muscles were able to use insulin we gave to stop the muscle breakdown, which had increased during the night. The muscles in the older people could not."

"In the course of our tests, we also noticed that the blood flow in the leg was greater in the younger people than the older ones," added Professor Rennie. "This set us thinking: maybe the rate of supply of nutrients and hormones is lower in the older people? This could explain the wasting we see."

Following this up led Beth Phillips, a PhD student working with Professor Rennie, to win the Blue Riband Award for work she presented at the summer meeting of The Physiological Society in Dublin. In her research Beth confirmed the blunting effect of age on leg blood flow after feeding, with and without exercise. The team predicted that weight training would reduce this blunting. "Indeed, she found that three sessions a week over 20 weeks 'rejuvenated' the leg blood flow responses of the older people. They became identical to those in the young," said Professor Rennie.

"I am extremely pleased with progress," he said. "Our team is making good headway in finding more and more out about what causes the loss of muscle with age. It looks like we have good clues about how to lessen it with weight training and possibly other ways to increase blood flow."

Master gene creates armies of natural-born killers

* 18:00 13 September 2009 by Andy Coghlan

Discovery of the master gene behind the front-line troops of the body's immune system could promise a host of new treatments for disease. Called E4BP4, the gene kick-starts production of natural killer (NK) cells in the bone marrow.

Mice genetically engineered to lack the gene were able to make all other components of the immune system – such as B cells which produce antibodies and T cells which attack pre-selected targets – but not NK cells. This suggests that E4BP4 is indispensable for their production. "Now we know which gene is at the top of the hierarchy, it opens the door to the whole machinery for making them," says Hugh Brady of Imperial College London.

Brady and colleagues hope it may now be possible to develop drugs that artificially boost production of NK cells, helping patients to combat infections or cancer. Patrolling the bloodstream, the spleen and the lymph nodes, NK cells are the body's first line of defence against disease, rapidly identifying and destroying cells that have turned cancerous or been invaded by viruses.

Less well studied than B and T cells, NK cells account for about a fifth of all the body's white blood cells. "They're very much the cinderellas of the blood system," says Brady. "But if you get an infection, these are the guys who get there first, and they're the first line of tumour immunosurveillance."

Treatment hope

Now that a mouse incapable of making NK cells is available, it will be possible to mount experiments that reveal exactly what they can and can't do, says Brady. And with that knowledge, it might be possible to develop new treatments to boost NK cell activity, or other components of the immune system.

"This is an exciting discovery that could open the doors for new ways to treat cancer in the future," says Josephine Querido, senior information officer at Cancer Research UK. "Our immune system is an immensely powerful weapon in helping the body to fight disease, and this research helps to explain how a crucial part of these defences work."

The other intriguing finding, says Brady, is that although mice couldn't make NK cells if they lacked two copies of the E4BP4 gene (one from each parent), they did make half the usual number of NK cells if they had one copy of the gene. If the same is true in humans, it may explain why some people are unusually prone to infection or cancer. *Journal reference: Nature Immunology, DOI: 10.1038/ni.1787*

Ice cream may target the brain before your hips, UT Southwestern study suggests

DALLAS – Blame your brain for sabotaging your efforts to get back on track after splurging on an extra scoop of ice cream or that second burger during Friday night's football game.

Findings from a new UT Southwestern Medical Center study suggest that fat from certain foods we eat makes its way to the brain. Once there, the fat molecules cause the brain to send messages to the body's cells, warning them to ignore the appetite-suppressing signals from leptin and insulin, hormones involved in weight regulation. The researchers also found that one particular type of fat – palmitic acid – is particularly effective at instigating this mechanism.

"Normally, our body is primed to say when we've had enough, but that doesn't always happen when we're eating something good," said Dr. Deborah Clegg, assistant professor of internal medicine at UT Southwestern and senior author of the rodent study appearing in the September issue of *The Journal of Clinical Investigation*.

"What we've shown in this study is that someone's entire brain chemistry can change in a very short period of time. Our findings suggest that when you eat something high in fat, your brain gets 'hit' with the fatty acids, and you become resistant to insulin and leptin," Dr. Clegg said. "Since you're not being told by the brain to stop eating, you overeat."

Dr. Clegg said that in the animals, the effect lasts about three days, potentially explaining why many people who splurge on Friday or Saturday say they're hungrier than normal on Monday.

Though scientists have known that eating a high-fat diet can cause insulin resistance, little has been known about the mechanism that triggers this resistance or whether specific types of fat are more likely to cause increased insulin resistance. Dr. Clegg said she suspected the brain might play a role because it incorporates some of the fat we eat – whether it is from healthy oils or the not-so-healthy saturated fat found in butter and beef – into its structure.

Based on this suspicion, her team attempted to isolate the effects of fat on the animals' brains. Researchers did this by exposing the animals to fat in different ways: by injecting various types of fat directly into the brain, infusing fat through the carotid artery or feeding the animals through a stomach tube three times a day. The animals received the same amount of calories and fat; only the type of fat differed. The types included palmitic acid, monounsaturated fatty acid and oleic acid.

Palmitic acid is a common saturated fatty acid occurring in foods such as butter, cheese, milk and beef. Oleic acid, on the other hand, is one of the most common unsaturated fatty acids. Olive and grapeseed oils are rich in oleic acid.

"We found that the palmitic acid specifically reduced the ability of leptin and insulin to activate their intracellular signaling cascades," Dr. Clegg said. "The oleic fat did not do this. The action was very specific to palmitic acid, which is very high in foods that are rich in saturated-fat."

Dr. Clegg said that even though the findings are in animals, they reinforce the common dietary recommendation that individuals limit their saturated fat intake. "It causes you to eat more," she said.

The other key finding, she said, is that this mechanism is triggered in the brain – long before there might be signs of obesity anywhere else in the body.

The next step, Dr. Clegg said, is to determine how long it takes to reverse completely the effects of short-term exposure to high-fat food.

Other UT Southwestern researchers involved in the study included Dr. Carol Elias, assistant professor of internal medicine, and Drs. Boman Irani and William Holland, postdoctoral research fellows in internal medicine. Researchers from the University of Cincinnati, Tennessee Valley Healthcare System, Vanderbilt University School of Medicine and the University of Paris also contributed to the study.

The study was supported by the National Institute of Diabetes and Digestive and Kidney Diseases.