Hair of Tasmanian tiger yields genes of extinct species

All the genes that the exotic Tasmanian Tiger inherited only from its mother will be revealed by an international team of scientists in a research paper to be published on 13 January 2009 in the online edition of Genome Research. The research marks the first successful sequencing of genes from this carnivorous marsupial, which looked like a large tiger-striped dog and became extinct in 1936. The research also opens the door to the widespread, nondestructive use of museum specimens to learn why mammals become extinct and how extinctions might be prevented.

"Our goal is to learn how to prevent endangered species from going extinct," said Webb Miller, a Penn State professor of biology and of computer science and engineering and a member of the research team that includes scientists from the United States, Sweden, Spain, Denmark, the United Kingdom, and Germany. "I want to learn as much as I can about why large mammals become extinct because all my friends are large mammals," Miller said. "However, I am expecting that publication of this paper also will reinvigorate discussions about possibly bringing the extinct Tasmanian Tiger back to life."

The team's research relies on new gene-sequencing technology and computational methods developed by Miller and Stephan C. Schuster, a professor of biochemistry and molecular biology at Penn State. The new methods involve extracting DNA from the hair of extinct specimens, not from bone, which has been used in previous studies of extinct species. The team's work reveals that hair is a powerful time capsule for preserving DNA over long periods and under a wide range of conditions. "I think of hair as a shrine for ancient DNA," Schuster said. "It is sealed so well that not even air or water are able to penetrate the DNA stored inside. Most importantly, bacteria cannot reach the DNA as long as the structure of the hair remains sound."

"Tasmanian Tiger" is a common name of the extinct thylacine species (Thylacinus cynocephalus), which is more closely related to kangaroos and koalas than to dogs or tigers. The last known specimen died in a Tasmanian zoo in 1936. Thylacines have played a central role in discussions about the possibility of bringing extinct species back to life, but despite the availability of many bones and other remains, previous attempts to read thylacine DNA had been unsuccessful.

Miller, Schuster, and their colleagues were the first to report the genome-wide sequence of an extinct animal, the woolly mammoth, in November 2008. They next collaborated with Anders Goetherstroem, at Uppsala University in Sweden, to target the Tasmanian Tiger because, like the mammoth, it was a coveted goal of ancient-DNA researchers, who considered its sequencing unfeasable due to the inadequate quality of the DNA available from specimens. "The speculation was that the only reason we were able to extract DNA from mammoth hair is that the mammoths had remained frozen in the Arctic permafrost, but our success with the Tasmanian Tiger shows that hair can protect DNA for long periods under a variety of environmental conditions," Schuster said.

In their new paper in Genome Research, Miller, Schuster, and their colleagues describe the completion of the mitochondrial genome sequences of two Tasmanian Tigers, one at the Smithsonian Museum and the other at the Swedish Museum of Natural History. One specimen was prepared by a taxidermist as a skin and the other one was submerged in ethanol. The team extracted DNA from small amounts of the hair of both specimens, then used their methods to sequence independent copies of each region of the DNA molecule from many different fragments of DNA in the hairs. The scientists assured the high fidelity of their results by independently determining each position in the sequences an average of 50 times.

The scientists sequenced all the DNA in the hair samples from the two Tasmanian Tigers, including mitochondrial DNA, which is the focus of the Genome Research paper, and nuclear DNA, which the team plans to analyze in future work. "This study, in which we sequenced the complete mitochondrial genome of the thylacine species, also shows that it is feasible to sequence its complete nuclear genome," Schuster said.

The new gene sequences permitted the team to accurately determine how the Tasmanian Tiger is related to other marsupials. They compared the sequences to a mitochondrial genome sequence they determined from a living reference species, a marsupial called a numbat. "The two thylacine sequences were extremely similar to each other, with only 5 differences in 15,492 nucleotides," Miller reports. The researchers say this similarity suggests that, as the species neared extinction, there was too little genetic diversity to resist bacterial and other environmental stresses. "Low genetic diversity is appearing as a common theme in the extinct species being studied by our team," Schuster said.

The research also revealed that two previous sequences in public databases, both labeled as Tasmanian Tiger mitochondrial genes, were incorrect. "Our Smithsonian specimen was the male offspring of the female animal

named as the source of the earlier data, so the mitochondrial sequences, which are inherited only from the mother, should have been identical, but our analyses showed they are over 10 percent different," Schuster said.

The new study shows that the methods pioneered at Penn State are potentially useful for a new discipline involving the genome analysis of samples originating from museum archives, which Schuster calls "Museomics." "The collections dating back several hundred years and now housed in the world's museums of natural history are the treasure troves of science," Schuster said. "We hope to add DNA-sequence data to the taxonomic data provided by many of the important specimens that define the species we know today."

The team's experience in this study indicates that museum directors can be enthusiastic collaborators with genome scientists because the analysis of a specimen's hair does not damage the appearance of the museum's collections. "Whatever hairs fall off a specimen provide enough material for sequencing the animal's DNA," Schuster said. In contrast, sampling bone involves drilling holes in the museum's collection, which curators are understandably reluctant to permit. "The advantages of obtaining DNA from hair makes Museomics possible on a wide scale," Schuster said.

Miller and Schuster said their future research plans include studies of the world's only remaining large marsupial carnivore, the Tasmanian Devil. "Our preliminary genetic research with the Tasmanian Devil indicates that its genome may have alarmingly less genetic diversity than did the woolly mammoth and the Tasmanian Tiger when they became extinct, so we now have directed a portion of our research program to studying the Tasmanian Devil in the hope of preventing this magnificent mammalian species from becoming extinct."

This research received financial support from Penn State University, the Gordon and Betty Moore Foundation, the Pennsylvania Department of Health, and the Ramon Areces Foundation in Spain.

Ground-based bacteria may be making it rain

*** 12 January 2009 by Devin Powell**

BACTERIA may be able to make it rain without ever leaving the ground - if the powerful detergents they produce can reach the clouds, that is.

Previous studies have suggested that bacteria can affect cloud formation. For example, an analysis of snow samples has hinted that bacteria swept up into the atmosphere trigger precipitation so that they can return to the ground.

Now Barbara Nozière of Stockholm University, Sweden, and colleagues suggest that surfactants secreted by many species of bacteria could also influence the weather. While these are normally used to transport nutrients through membranes, the team have shown that they also break down the surface tension of water better than any other substance in nature. This led them to suspect that if the detergent was found in clouds it would stimulate the formation of water droplets. If the detergent from bacteria was found in clouds, it would stimulate the formation of water drops, causing rainfall

To find out if they were present in the atmosphere, Nozière collected air samples over a coastal region, an ocean, a forest and a jungle at locations in Brazil, Sweden and Finland. Particles in all the samples contained minute amounts of detergent with a chemical structure that resembled the surfactants. It also broke down the water into droplets in the same way. "The only thing we know of that could cause this strong an effect is the bacterial surfactants," Nozière said in a presentation at last month's meeting of the American Geophysical Union in San Francisco.

Nozière suggests that the bacteria may be helping to keep the atmosphere healthy and active. She also speculates that they evolved the ability to summon water from the sky to help them survive.

The next step will be to work out how these substances get up to the clouds, says Andi Andreae of the Max Planck Institute of Chemistry in Mainz, Germany. Only a small proportion of cloud-forming particles come from the ground, carried by the wind. "This bacterial gunk could hitch a ride on particles that travel from the surface to the clouds and supercharge them," he says.

Primate culture is just a stone's throw away from human evolution, study finds

For 30 years, scientists have been studying stone-handling behavior in several troops of Japanese macaques to catch a unique glimpse of primate culture. By watching these monkeys acquire and maintain behavioral traditions from generation to generation, the scientists have gained insight into the cultural evolution of humans.

Primatologists Michael A. Huffman, Charmalie A.D. Nahallage, and Jean-Baptiste Leca from the Primate Research Institute in Kyoto, Japan assessed social learning exhibited by these macaques during stone-handling, a behavior that has been passed down from elder to younger since it was observed in some of the troops in 1979. Stone-handling, in this study, included rubbing and clacking stones together, pounding them onto hard surfaces, picking them up, and cuddling, carrying, pushing, rolling and throwing them.

The scientists found, for example, that an infant's proximity to their mother had a significant impact on the development of the infant's stone-handling abilities. In other words, infants with mothers who frequently exhibited stone-handling behaviors spent more time with their mother, about 75% of their time, during the first three months of life, and they also participated in stone-handling earlier in life than the other infants. These findings suggest that the mothers' frequent stone-handling caught the infants' attention, and as a result, the infants acquired the behavior more quickly than other infants.

Furthermore, as the primatologists reported in the December 2008 issue of Current Directions in Psychological Science, a publication of the Association for Psychological Science, the stone-handling behavior changed with each generation as individual macaques contributed their own patterns of stone-handling, such as stone-throwing.

"The recent emergence of a unique behavior, stone-throwing, may serve to augment the effect of intimidation displays," concluded the authors. "Research on such transformation may shed light on the evolution of stone-tool use in early hominids." *Author Contact: Michael A. Huffman huffman@pri.kyoto-u.ac.jp*

Why we procrastinate and how to stop

It's a new year and many of us have started thinking about various resolutions: updating that resume, cleaning out the attic, starting that exercise routine. But the sad reality is that most of us will not follow through on these commitments, not because we're insincere, but because tomorrow is always a better time to get going.

Procrastination is a curse, and a costly one. Putting things off leads not only to lost productivity but also to all sorts of hand wringing and regrets and damaged self-esteem. For all these reasons, psychologists would love to figure out what's going on in the mind that makes it so hard to actually do what we set out to do. Are we programmed for postponement and delay?

Led by Sean McCrea of the University of Konstanz in Germany, an international team of psychologists wanted to see if there might be a link between how we think of a task and our tendency to postpone it. In other words, are we more likely to see some tasks as psychologically "distant"-- and thus making us save them for later rather than tackling them now?

The psychologists handed out questionnaires to a group of students and asked them to respond by e-mail within three weeks. All the questions had to do with rather mundane tasks like opening a bank account and keeping a diary, but different students were given different instructions for answering the questions. Some thought and wrote about what each activity implied about personal traits: what kind of person has a bank account, for example. Others wrote simply about the nuts and bolts of doing each activity: speaking to a bank officer, filling out forms, making an initial deposit, and so forth. The idea was to get some students thinking abstractly and others concretely. Then the psychologists waited. And in some cases, waited and waited. They recorded all the response times to see if there was a difference between the two groups, and indeed there was a significant difference.

The findings, reported in Psychological Science, a journal of the Association for Psychological Science, were very clear. Even though all of the students were being paid upon completion, those who thought about the questions abstractly were much more likely to procrastinate--and in fact some never got around to the assignment at all. By contrast, those who were focused on the how, when and where of doing the task e-mailed their responses much sooner, suggesting that they hopped right on the assignment rather than delaying it.

The authors note that "merely thinking about the task in more concrete, specific terms makes it feel like it should be completed sooner and thus reducing procrastination." They conclude that these results have important implications for teachers and managers who may want their students and employees starting on projects sooner. In addition, these findings are also relevant for those of us resolving to have better time management skills in the New Year!

For more information about this study, please contact: Sean McCrea (sean.mccrea@uni-konstanz.de)
Wray Herbert discusses this study in his blog, "We're Only Human…" (http://www.psychologicalscience.org/onlyhuman/)

Top 11 compounds in US drinking water

*** 15:38 12 January 2009 by Rowan Hooper**

A comprehensive survey of the drinking water for more than 28 million Americans has detected the widespread but low-level presence of pharmaceuticals and hormonally active chemicals.

Little was known about people's exposure to such compounds from drinking water, so Shane Snyder and colleagues at the Southern Nevada Water Authority in Las Vegas screened tap water from 19 US water utilities for 51 different compounds. The surveys were carried out between 2006 and 2007.

The 11 most frequently detected compounds - all found at extremely low concentrations - were:

· Atenolol, a beta-blocker used to treat cardiovascular disease

· Atrazine, an organic herbicide banned in the European Union, but still used in the US, which has been implicated in the decline of fish stocks and in changes in animal behaviour
· Carbamazepine, a mood-stabilising drug used to treat bipolar disorder, amongst other things
· Estrone, an oestrogen hormone secreted by the ovaries and blamed for causing gender-bending changes in fish
· Gemfibrozil, an anti-cholesterol drug
· Meprobamate, a tranquiliser widely used in psychiatric treatment
· Naproxen, a painkiller and anti-inflammatory linked to increases in asthma incidence
· Phenytoin, an anticonvulsant that has been used to treat epilepsy
· Sulfamethoxazole, an antibiotic used against the Streptococcus bacteria, which is responsible for tonsillitis and other diseases
· TCEP, a reducing agent used in molecular biology
· Trimethoprim, another antibiotic

The concentrations of pharmaceuticals in drinking water were millions of times lower than in a medical dose, and Snyder emphasises that they pose no public health threat. He cautions, though, that "if a person has a unique health condition, or is concerned about particular contaminants in public water systems, I strongly recommend they consult their physician".

Christian Daughton of the EPA's National Exposure Research Laboratory says that neither this nor other recent water assessments give cause for health concern. "But several point to the potential for risk - especially for the fetus and those with severely compromised health."

Daughton says the contamination surveys help people realise how they are intimately and inseparably connected with their environment. "The occurrence of pharmaceuticals in the environment also serves to make us acutely aware of the chemical sea that surrounds us," he says.

Modern life

While the US government regulates the levels of pathogens in US drinking water, there are no rules for pharmaceuticals and other compounds, apart from one: the herbicide atrazine. The atrazine levels measured by Snyder and colleagues were well within federal limits.

Snyder says water utilities could make drinking water purer. But the costs of "extreme purification" - far beyond what is needed for safety alone - are huge in terms of increased energy usage and carbon footprint. Ultra-pure water might not even be safe, adds Snyder.

The widespread occurrence of pharmaceuticals and endocrine disruptors reflects improved detection techniques, rather than greater pollution, says Snyder. Contamination is a fact of modern life, he adds.

"As we continue to populate and aggregate, our wastes will certainly accumulate where we live," he says. "We as a species have decided to live a modern life, with pharmaceuticals, plastics, transportation - therefore we must accept that there will be a certain degree of contamination."

Journal reference: Environmental Science and Technology, in press

The Maya suffered for their looks

Norman Hammond, Archaeology Correspondent

We may think we make sufficient sacrifices for our idea of beauty, what with false eyelashes, body perforations supporting various bits of metalwork from earrings to tongue studs, toupees and hair extensions, Spanx and padded bras. The Ancient Maya went much farther, however, reshaping their children's skulls and inlaying their own teeth with jade.

"The Maya went to extreme lengths to transform their bodies," Professor Mary Miller reports in the new year issue of Archaeology, the US journal. "They invested vast wealth and endured unspeakable pain to make themselves beautiful."

As an example, Professor Miller cites K'inich Janaab' Pakal, who ruled the western Maya city of Palenque from AD615 to 683, and after his death at the age of 80 was interred in a great carved sarcophagus below the Temple of the Inscriptions. His skeleton shows that soon after his birth, his head was strapped between two cradle-boards to compress it from back to front, not unlike the crystal-skulled aliens in the recent Indiana Jones film.

This left an indentation above his browline, which was emphasised by an artificial nasal bridge, probably of clay or plaster, built up on to his forehead. Although this does not survive in the burial, a stucco portrait head found below the sarcophagus shows it clearly. The head also shows that Pakal's hair was cut in a series of bluntly trimmed tresses, with longer strands on top flopping forward, which Professor Miller interprets as

imitating the leaves and corn silk on a maize plant: at the site of Cacaxtla, Maya-style murals show maize cobs on the plant as human heads. Pakal was shown as ever-youthful, like the maize that springs up anew each year.

Pakal's front teeth were filed into an inverted T-shape, marking him as also being the Sun God, something shown on his jade burial mask as well. For many Maya, notably those of the elite, dental decoration was seen as highly desirable.

Teeth, especially the upper incisors and canines were filed and notched in a variety of designs, giving in some cases a distinctly crooked smile. Most striking, however, were the dental inlays: a shallow hole was drilled into the front face of the tooth enamel (using a reed or bone hollow drill and an abrasive such as sand or jade dust), sometimes reaching the dentine within.

Small discs of jade, obsidian or haematite were then cemented into the holes: the plant adhesive was so powerful that many burials found by archaeologists today still have the inlays firmly in place. Up to three discs were inserted into a single tooth, and jade and the other materials were combined to give a flash of apple-green, dull red and shiny black across the mouth; inlays and filing were also combined. Dental decoration was probably applied as a rite of passage to adulthood, according to Professor Stephen Houston, of Brown University, Rhode Island.

The Maya also painted their bodies, in life and in death. Narrative scenes on polychrome vases show pigments applied to face, chest and buttocks. In death, Pakal's corpse was treated with alternating layers of red and black pigments, Professor Miller reports. Red to the Maya was the colour of the sunrise, black of the sunset, alternating with each other in the diurnal cycle.

Some facial designs are in the form of long strings of dots, especially around the mouth, and when this is shown in sculpture or vase-painting it may be intended to show tattooing rather than just make-up. "Beauty was a way to display social, if not moral, value among the ancient Maya," Professor Miller concludes. "The wealth they invested and pain they endured to create bodies that reflected their social beliefs make our modern-day obsession with beauty seem less excessive." *Archaeology Vol 62 No. 1: 36-42*

Medical study shows epidurals and spinal anesthetics are safer than previously reported

The largest ever prospective study [1,2] into the major complications [3] of epidurals and spinal anaesthetics published in the British Journal of Anaesthesia today (Monday 12 January 2009) concludes that previous studies have over-estimated the risks of severe complications of these procedures. The study concludes that the estimated risk of permanent harm following a spinal anaesthetic or epidural is lower than 1 in 20,000 and in many circumstances the estimated risk is considerably lower.

The study finds that the risk of permanent injury (of whatever severity) is about 1 in 23-50,000. In betting terms, the odds of being badly injured by an epidural or spinal anaesthetic are considerably better than 20,000-to-1 against. The risk of being paralysed by one of these injections is 2-3 times rarer than of suffering any permanent harm. The risk for women requiring pain relief for labour or Caesarean section is lower still, the most pessimistic estimate of permanent harm is 1 in 80,000 and it may be much lower. A similarly low risk was found in procedures performed for chronic pain and in children.

The study also finds that the risk of harm when an epidural is used for surgery is considerably higher than the estimated risk of using it during childbirth: between 1 in 6,000 and 1 in 12,000. However, while these figures may appear high, they too are still considerably lower than many previous estimates, and Dr Tim Cook, a consultant anaesthetist at the Royal United Hospital, Bath who led the project believes there are other reasons to explain these figures: "It has been known for a long time that these complications occur more often after surgery. The reason is likely to be that many of these patients are elderly with medical problems and that the process of having surgery itself increases risks. Major surgery leads to severe pain and may mean that an epidural has to stay in place for several days. Epidurals are generally only used for the biggest most painful operations and it is probably the least fit patients who have the most to gain from these techniques. What the project has shown is that many complications of epidurals occur after major surgery in elderly unhealthy patients. The risks must also be balanced against the generally accepted benefits of epidurals."

The project's results are based on the voluntary participation of every hospital in England, Scotland, Wales and Northern Ireland. A national census identified over 700,000 spinals and epidurals performed in the UK National Health Service each year. All major complications of these procedures were identified by the project team for one year. Each complication was reviewed by an expert panel, which assessed the cause and severity of all permanent injuries. In the year of the study, depending on interpretation, there were 14-30 patients who suffered permanent injury: injuries ranging from numbness in a part of the legs to paraplegia or death. Of the harmed patients 5-13 were paralysed and 3-6 died. Most complications were judged to be unavoidable.

Dr Tim Cook says, "The results are reassuring for patients with all procedures and settings being lower risk than many previous estimates. It is likely that this study will become widely quoted as the definitive estimate of these rare but potentially catastrophic complications."

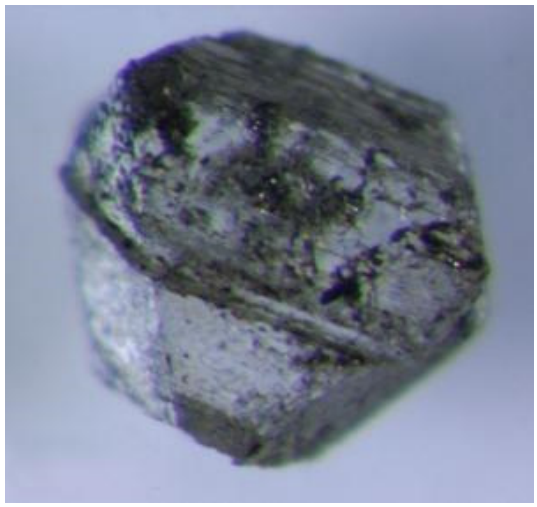
However, Dr Cook believes anaesthetists should not be complacent: "Although complications related to epidurals are rare, the profession still needs to examine how and why these complications arise and make steps to reduce their frequency. For instance, it is likely that the number of complications could be further reduced by a greater appreciation that prolonged weakness of the legs after an epidural or spinal is not normal and should be investigated by an experienced doctor to ensure a major complication is not developing."

Writing in an editorial that accompanies the paper in the British Journal of Anaesthesia, Dr Donal Buggy, a consultant anaesthetist at the Mater Hospital, Dublin, describes the report as, "a triumph not only for its authors and the NHS anaesthetists who delivered it, but also for UK NHS risk management systems, audit databases, and processes." Dr Buggy asserts that "the primary achievement of the project is that it enables anaesthetists and patients to more accurately define the risk of the specific rare but devastating complications of these procedures."

Ancient supercontinent was a diamond factory

* 18:10 12 January 2009 by **Catherine Brahic**

Talk about deep, dark secrets. Rare "ultra-deep" diamonds are valuable - not because they look good twinkling on a newlywed's finger - but because of what they can tell us about conditions far below the Earth's crust.



The Eurelia diamonds are the latest ultra-deep diamonds to have been found (Image: R Tappert)

Now a find of these unusual gems in Australia has provided new clues to how they were formed.

The diamonds, which are white and a few millimetres across, were found by a mineral exploration company just outside the village of Eurelia, some 300 kilometres north of Adelaide, in southern Australia. From there, they were sent to Ralf Tappert, a diamond expert at the University of Adelaide.

Tappert and colleagues say minerals found trapped inside the Eurelia diamonds could only have formed more than 670 kilometres (416 miles) beneath the surface of the Earth - a distance greater than that between Boston and Washington, DC.

Clues from the deep

"The vast majority of diamonds worldwide form at depths between 150 km and 250 km, within the mantle roots of ancient continental plates," says Tappert. "These diamonds formed in the Earth's lower mantle at depths greater than 670 km, which is much deeper than 'normal' diamonds."

Fewer than a dozen ultra-deep diamonds have been found in various corners of the globe since the 1990s. Sites range from Canada and Brazil to Africa - and now Australia.

"Deep diamonds are important because they are the only natural samples that we have from the lower mantle," says Catherine McCammon, a geologist at the University of Bayreuth in Germany. "This makes them an invaluable set of samples - much like the lunar rocks are to our studies of the moon."

The Eurelia gems contain information about the carbon they were made from. Their heavy carbon isotope signatures suggest the carbon was once contained in marine carbonates lying on the ocean floor.

'Oddball' gems

Location, though, provides researchers with a common thread for the Brazilian, African and Australian deep diamonds, which could explain how they were born. All six groups of diamonds were found in areas that would once have lined the edge of the ancient supercontinent Gondwana.

"Deep diamonds have always been treated like oddball diamonds," says Tappert. "We don't really know what their origin is. With the discovery of the ones in Australia we start to get a pattern."

Their geographic spread suggests that all these ultra-deep diamonds were formed in the same way: as the oceanic crust dived down beneath Gondwana - a process known as subduction - it would have dragged carbon down to the lower mantle, transforming it into graphite and then diamond along the way.

Eventually, kimberlites - volcanic rocks named after the town of Kimberley in South Africa - are propelled to the surface during rapid eruptions, bringing the gems up to the surface.

Surprisingly young

According to John Ludden of the British Geological Survey, if the theory were proven true, it would mean the Eurelia diamonds are much younger than most diamonds are thought to be.

"Many of the world's diamonds are thought to have been sampled from subducted crust in the very early Earth, 3 billion years ago," says Ludden.

Yet Tappert's theory suggests these diamonds would have been formed about 300 million years ago. "This may well result in a revision of exploration models for kimberlites and the diamonds they host, as to date exploration has focused on very old rock units of the early Earth," Ludden told New Scientist.

McCammon says Tappert's theory is "plausible" but just "one among possible models". She says not all deep diamonds fit the Gondwana model, but adds that the new gems "proved a concrete idea that can be tested by others in the community". *Journal reference: Geology (vol 37, p 43)*

Finger length may reveal your financial acumen

* 22:00 12 January 2009 **by Linda Geddes**

Successful financial traders may be born, not made. That's the implication of a new study which found that traders who excel at short-term or "high-frequency" trading may have been exposed to higher levels of testosterone in the uterus.

These traders can hold their stock for minutes, or mere seconds, before selling - requiring high levels of confidence and fast reaction times.

Last year, John Coates at the University of Cambridge, UK, and his colleagues found that traders who started their days with elevated testosterone made more money than those who didn't.

But successful traders aren't all macho and aggressive risk-takers - characteristics typically associated with high testosterone. "The good ones are very calm, they don't lose their temper, and probably the most extreme sport they do is fly fishing," says Coates. "They're not cavemen."

Because individual responses to testosterone can be affected by how much of the hormone you were exposed to in the uterus, Coates wondered if this could also be exerting an effect. So he recruited 49 male traders from the City of London and looked at their index-to-ring-finger ratio - a marker of prenatal testosterone exposure.

Profitable digits

He found that traders with a longer ring fingers, and therefore higher prenatal testosterone, made on average six times the profits of traders exposed to low levels of the hormone, and tended to remain traders for longer.

Previous studies have also suggested a link between a low index-to-ring-finger ratio and autism, and better sporting ability.

"This study provides evidence for human beings of what we know from studies of animals, that exposure to sex hormones early in life predisposes the nervous systems and resulting behavior to develop in certain ways," says Bruce McEwen of the Rockefeller University in New York. "In this case the development of the risk taking, visual-motor skills, etc that make for success in this kind of rapid stock trading."

"However, it takes environment, or the experiences and opportunities that a person has, to further shape the brain to this particular career path," he adds.

And while finger length may provide some indication of your suitability to financial trading, Coates cautions bosses against using it to make hiring decisions.

Goodbye CV?

Other factors undoubtedly play a role, and the effects of high prenatal testosterone may be a disadvantage in other types of trading. For example, other studies have suggested that people with a high index-to-ring-finger ratio make better mathematicians, so they may excel in more analytical city jobs.

"My hunch is that this correlation could reverse in types of trading where people position for long-term [as opposed to short-term] gains," says Coates.

However, John Manning, an evolutionary psychologist and author of The Finger Book (read our review) says it would be interesting to see if finger ratios correlate with other professions.

For example, you might expect a low index-to-ring-finger ratio to correlate with military ability, while a higher ratio might correlate with performance in personnel management, or in professions such as nursing, occupational therapy and the teaching of very young children, he says.

Journal reference: Proceedings of the National Academy of Sciences (DOI: 10.1073/pnas.0810907106)

Argonne scientists prove unconventional superconductivity in new iron arsenide compounds

Inelastic neutron scattering is sensitive to sign of superconducting gap

ARGONNE, Ill. (Jan. 9, 2009) — Scientists at U.S. Department of Energy's Argonne National Laboratory used inelastic neutron scattering to show that superconductivity in a new family of iron arsenide superconductors cannot be explained by conventional theories.

"The normal techniques for revealing unconventional superconductivity don't work with these compounds," physicist Ray Osborn said. "Inelastic neutron scattering is so far the only technique that does."

Conventional superconductivity can be explained by a theory developed by Bardeen, Cooper and Schrieffer (BCS) in 1957. In BCS theory, electrons in a superconductor combine to form pairs, called Cooper pairs, which are able to move through the crystal lattice without resistance when an electric voltage is applied. Even when the voltage is removed, the current continues to flow indefinitely, the most remarkable property of superconductivity, and one that explains the keen interest in their technological potential.

Normally, electrons repel each other because of their similar charge, but, in superconductors, they coordinate with vibrations of the crystal lattice to overcome this repulsion. But scientists don't believe the vibrational mechanism in the iron arsenides is strong enough to make them superconducting. This has led theorists to propose that this superconductivity has an unconventional mechanism, perhaps like high-temperature copper-oxide superconductors. Some iron arsenides are antiferromagnetic, rather than superconducting, so magnetism rather than atomic vibrations might provide the electron glue.

In BCS superconductors, the energy gap between the superconducting and normal electronic states is constant, but in unconventional superconductors the gap varies with the direction the electrons are moving. In some directions, the gap may be zero. The puzzle is that the gap does not seem to vary with direction in the iron arsenides. Theorists have argued that, while the size of the gap shows no directional dependence in these new compounds, the sign of the gap is opposite for different electronic states. The standard techniques to measure the gap, such as photoemission, are not sensitive to this change in sign.

But inelastic neutron scattering is sensitive. Osborn, along with Argonne physicist Stephan Rosenkranz, led an international collaboration to perform neutron experiments using samples of the new compounds made in Argonne's Materials Science Division, and discovered a magnetic excitation in the superconducting state that can only exist if the energy gap changes sign from one electron orbital to another.

"Our results suggest that the mechanism that makes electrons pair together could be provided by antiferromagnetic fluctuations rather than lattice vibrations," Rosenkranz said. "It certainly gives direct evidence that the superconductivity is unconventional."

Inelastic neutron scattering continues to be an important tool in identifying unconventional superconductivity, not only in the iron arsenides, but also in new families of superconductors that may be discovered in the future.

A paper ("Unconventional superconductivity in Ba0.6K0.4Fe2As2 from inelastic neutron scattering") on Osborn's and Rosenkranz's work has been published in volume 456, pages 930-932, of Nature. Funding for this research was provided by the U.S. Department of Energy, Office of Science, Office of Basic Energy Sciences.

Misuse of Vicks VapoRub may harm infants and toddlers

Toddler in respiratory distress after popular salve used

Vicks® VapoRub®, the popular salve used to relieve symptoms of cough and congestion, may be harmful for infants and toddlers. New research appearing in the January issue of CHEST, the peer-reviewed journal of the American College of Chest Physicians (ACCP), shows that Vicks® VapoRub® (VVR) may stimulate mucus production and airway inflammation, which can have severe effects on breathing in an infant or toddler. Research findings are consistent with current VVR labeling which indicates the product should not be used on children under 2 years of age.

"The ingredients in Vicks can be irritants, causing the body to produce more mucus to protect the airway," said Bruce K. Rubin, MD, FCCP, the study's lead author from the Department of Pediatrics at Wake Forest University School of Medicine, Winston Salem, NC. "Infants and young children have airways that are much narrower than those of adults, so any increase in mucus or inflammation can narrow them more severely."

Dr. Rubin and his colleagues at Wake Forest became interested in the effects of VVR on small children after they cared for an 18-month-old girl who developed severe respiratory distress after VVR was put directly under her nose. The research team then launched an investigation to determine the effects of VVR on the respiratory system. Using ferrets, which have an airway anatomy and cellular composition similar to humans, the team conducted tests that measured the effects of VVR on mucus secretion and build up in the airways, and fluid

build up in the lungs. Healthy ferrets and ferrets who had induced tracheal inflammation (simulating a person with a chest infection) underwent testing after they were exposed to VVR through intubation.

Results showed that in vitro VVR exposure increased mucus secretion 59 percent over baseline, while in vivo VVR exposure increased mucus secretion 14 percent in normal airways and 8 percent in the inflamed airway, in addition to the increase in secretion due to the inflammation. Mucus clearance, as measured by ciliary beat frequency in the trachea, also decreased by 36 percent during in vitro testing.

VVR is not indicated for patients under age 2. However, Dr. Rubin realizes that some parents are still choosing to use VVR to relieve their sick young child's symptoms, usually rubbing the salve on the feet or chest.

"I recommend never putting Vicks in, or under, the nose of anybody—adult or child. I also would follow the directions and never use it at all in children under age 2," said Dr. Rubin. Even when directions are followed, VVR may make people with congestion feel more comfortable, but it does nothing to increase airflow or actually relieve congestion. "Some of the ingredients in Vicks, notably the menthol, trick the brain into thinking that it is easier to breathe by triggering a cold sensation, which is processed as indicating more airflow. Vicks may make you feel better but it can't help you breathe better." Dr. Rubin also feels that although the study only tested Vick's VapoRub, similar products, including generic brands, could cause the same adverse reaction in infants and toddlers.

In addition to VVR, decongestants are not recommended for young children; however, there are other treatments that are safe and effective.

"Cough and cold medicines and decongestants are dangerous and neither effective nor safe for young children. Medications to dry up nasal passages also have problems," said Dr. Rubin. "The best treatments for congestion are a bit of saline (salt water) and gentle rubber bulb suction, warm drinks or chicken soup, and, often, just letting the passage of time heal the child." Dr. Rubin also notes that if a child is struggling to breathe, it is a medical emergency and would require the child to be seen by a doctor as quickly as possible.

"Parents should consult with a physician before administering any over-the-counter medicine to infants and young children," said James A. L. Mathers, Jr., MD, FCCP, President of the American College of Chest Physicians. "Furthermore, the American College of Chest Physicians and several other health-care organizations have concluded that over-the-counter cough and cold medicines can be harmful for infants and young children and are, therefore, not recommended."

Use of antidepressants associated with improvement in symptoms of fibromyalgia

The use of antidepressant medications by patients with fibromyalgia syndrome is associated with a reduction in pain, sleep disturbances and depressed mood and improvement of health-related quality of life, according to an analysis of previous studies, which is published in the January 14 issue of JAMA.

Fibromyalgia syndrome (FMS), which consists of chronic widespread pain and tenderness, with other symptoms including fatigue and sleep difficulties, has an estimated prevalence of 0.5 percent to 5.8 percent in North America and Europe. "Patients with FMS experience disability and reduced health-related quality of life (HRQOL). Fibromyalgia syndrome is also associated with high direct and indirect disease-related costs. Effective treatment of FMS is therefore necessary for medical and economic reasons," the authors write.

Winfried Häuser, M.D., of Klinikum Saarbrücken, Saarbrücken, Germany, and colleagues conducted a meta-analysis to evaluate the effects of treatment with antidepressants on FMS-related symptoms. The researchers identified 18 randomized controlled trials, involving 1,427 participants, for inclusion in the study.

Overall, there was strong evidence for a reduction of pain, fatigue and depressed mood and improved sleep and HRQOL with the use of antidepressants by patients with FMS.

The researchers found large effect sizes of tricyclic and tetracyclic antidepressants (TCAs) for reducing pain, fatigue, and sleep disturbances; small effect sizes of selective serotonin reuptake inhibitors (SSRIs) for reducing pain; small effect sizes of serotonin and noradrenaline reuptake inhibitors (SNRIs) for reducing pain, sleep disturbances, and depressed mood; and small effect sizes of monoamine oxidase inhibitors (MAOIs) for reducing pain.

"Before treatment is initiated, [accompanying] diseases related to potential adverse effects of the drugs and patients' preferences should be considered. Goals of pharmacological therapy should be defined (no cure, but possible symptom reduction). Since evidence for a long-term effect of antidepressants in FMS is still lacking, their effects should be re-evaluated at regular intervals to determine whether benefits outweigh adverse effects," the authors write. "The identification of patient characteristics associated with positive and negative therapeutic outcomes are needed to better target antidepressant therapy for FMS."

(JAMA. 2009;301[2]:198-209. Available pre-embargo to the media at www.jamamedia.org)

High caffeine intake linked to hallucination proneness

High caffeine consumption could be linked to a greater tendency to hallucinate, a new research study suggests.

People with a higher caffeine intake, from sources such as coffee, tea and caffeinated energy drinks, are more likely to report hallucinatory experiences such as hearing voices and seeing things that are not there, according to the Durham University study.

'High caffeine users' – those who consumed more than the equivalent of seven cups of instant coffee a day - were three times more likely to have heard a person's voice when there was no one there compared with 'low caffeine users' who consumed less than the equivalent of one cup of instant coffee a day.

The researchers say the findings will contribute to the beginnings of a better understanding of the effect of nutrition on hallucinations. Changes in food and drink consumption, including caffeine intake, could place people in a better position to cope with hallucinations or possibly impact on how frequently they occur, say the scientists.

In the study, funded by the Economic and Social Research Council and the Medical Research Council, 200 students were asked about their typical intake of caffeine containing products, such as coffee, tea and energy drinks as well as chocolate bars and caffeine tablets. Their proneness to hallucinatory experiences, and their stress levels, were also assessed. Seeing things that were not there, hearing voices, and sensing the presence of dead people were amongst the experiences reported by some of the participants.

The researchers, whose paper is published in the academic journal Personality and Individual Differences, say their finding could be down to the fact that caffeine has been found to exacerbate the physiological effects of stress. When under stress, the body releases a stress hormone called cortisol. More of this stress hormone is released in response to stress when people have recently had caffeine. It is this extra boost of cortisol which may link caffeine intake with an increased tendency to hallucinate, say the scientists.

Lead author, Simon Jones, a PhD student at Durham University's Psychology Department, said: "This is a first step towards looking at the wider factors associated with hallucinations. Previous research has highlighted a number of important factors, such as childhood trauma, which may lead to clinically relevant hallucinations. Many such factors are thought to be linked to hallucinations in part because of their impact on the body's reaction to stress. Given the link between food and mood, and particularly between caffeine and the body's response to stress, it seems sensible to examine what a nutritional perspective may add."

Co–author Dr Charles Fernyhough, also from Durham University's Psychology Department, noted "Our study shows an association between caffeine intake and hallucination-proneness in students. However, one interpretation may be that those students who were more prone to hallucinations used caffeine to help cope with their experiences. More work is needed to establish whether caffeine consumption, and nutrition in general, has an impact on those kinds of hallucination that cause distress."

Mr Jones added: "Hallucinations are not necessarily a sign of mental illness. Most people will have had brief experiences of hearing voices when there is no one there, and around three per cent of people regularly hear such voices. Many of these people cope well with this and live normal lives. There are, however, a number of organisations, such as the Hearing Voices Network, who can offer support and advice to those distressed by these experiences." R*esearch in this area continues and the public can take part in studies at www.dur.ac.uk/s.r.jones*

Facts about caffeine (Source: Wikipedia)

* Caffeine is a central nervous system stimulant, having the effect of temporarily warding off drowsiness and restoring alertness.
* With ninety per cent of North Americans consuming some of form caffeine every day, it is the world's most widely used drug.
* In its pure state, caffeine is a crystalline white powder.
* Caffeine is completely absorbed by the stomach and small intestine within 45 minutes of ingestion.
* When taken in moderation, studies have shown that caffeine can increase the capacity for mental or physical labour.

- Caffeine use can lead to a condition called caffeine intoxication. Symptoms include nervousness, irritability, anxiety, muscle twitching, insomnia, headaches, and heart palpitations. This is not commonly seen when daily caffeine intake is less than 250mg.

Little or no evidence that herbal remedies relieve menopausal symptoms

Herbal medicines for menopausal symptoms, Drug and Therapeutics Bulletin, Vol. 47, No. 1, January 2009

There is no strong evidence either way for several herbal remedies commonly taken to relieve troublesome menopausal symptoms, concludes the January issue of the Drug and Therapeutics Bulletin (DTB). And for some, there is hardly any evidence at all.

Between 30% and 70% of women in industrialised countries will experience vasomotor symptoms around the menopause, such as hot flushes and night sweats, prompted by the sharp fall in oestrogen levels.

On average, such symptoms last for around four years, but in around one in 10 women, they can last more than 12 years.

Herbal remedies commonly used to relieve menopausal symptoms include black cohosh, red clover, Dong quai, evening primrose oil, and ginseng. Others include wild yam extract, chaste tree, hops, sage leaf, and kava kava.

But little good quality evidence on the effectiveness of herbal medicines, or how they might react with prescription medicines is available, says DTB.

And, in general, safety has been under researched, which is a major concern given that herbal remedies are often assumed to be "safe" just on the grounds that they are "natural," says DTB.

Published studies are often poorly designed, include too few participants, or don't last long enough to be of real value.

Furthermore, the chemical make-up of various preparations of the same herb may differ, which can make it difficult to compare trial results.

The drugs regulator, the Medicines and Healthcare products Regulatory Agency (MHRA), has given a Traditional Herbal Registration to Menoherb, which contains black cohosh, under a scheme designed to boost the safety of herbal products on sale.

But clinical trial data on black cohosh are "equivocal," says DTB, with some studies suggesting that the remedy works well, while others suggest that it does not relieve symptoms effectively.

Liver toxicity is also a potential side effect of black cohosh.

There is "no convincing evidence" that red clover extract is effective, says DTB, and little evidence one way or another for dong quai, evening primrose oil, wild yam, chaste tree, hops, or sage.

This review appears in the new look DTB, which has been given its first major design make-over since it was first published in 1962.

Pagination has also increased from eight to 12, in a "deliberate attempt to address healthcare professionals' needs for clear, succinct information and practical advice on medicines, other treatments and the overall management of disease," says an editorial, another new feature of the redesign.

Other additions include the use of colour and a new layout, which will allow for illustrations, to make DTB both even more informative and more enjoyable to read.

Commenting on the move, DTB editor Dr Ike Iheanacho, said:

"For over 45 years, DTB has strived to produce rigorously researched information and advice for healthcare professionals, to help ensure patients get the best possible care. The newly redesigned version of the publication aims to continue and build on this tradition."

Butterflies use penis to gauge sex competition

* 13 January 2009 by **Devin Powell**

BUTTERFLY sex is not as elegant an affair as you might think. It seems that male monarch butterflies conduct an all-out sperm war based on a crude measure of how much sperm is stored inside a female from a previous mating.

During sex the males physically restrain the females for an entire day while injecting them with a fluid which contains fertile sperm as well as seemingly functionless cells without nuclei.

Michelle Solensky of The College of Wooster in Ohio paired male monarch butterflies with a selection of females that had had different numbers of partners.

She found that males could selectively increase or decrease the amount of fertile sperm in their deposits. For example, they deposited slightly more into a female for each of her previous mates (Animal Behaviour, DOI: 10.1016/j.anbehav.2008.10.026). "This may explain earlier observations that the last male to mate has a reproductive advantage," says Solenksy.

She then arranged for some female butterflies to receive a large deposit from a single male, and others to have a small deposit from three different males adding up to a similar volume.

When males later mated with the females, they used the same amount of sperm irrespective of which experimental group the female butterfly had been in. This showed that the males were adjusting their sperm on the basis of volume - not the number of previous partners.

"I don't know of any other creatures that respond to the amount of sperm inside their mates," says Solensky. "The new aspect for butterflies is that they can assess the intensity of sperm competition without ever witnessing previous matings," says Simone Immler at the University of Sussex in the UK.

Because monarch butterflies do not use chemical signals like pheromones, Solensky suspects that sensors on the male penis detect the volume directly, like the dipstick in a car's oil tank. If so, the cells that lack nuclei may act to bump up the volume of the deposit and discourage rivals.

Sensors on the male monarch butterfly's penis may detect the volume of sperm directly, like the dipstick in a car's oil tank

This behaviour backs a theory that males of some species can boost their sperm levels to raise the odds of passing on their genes. Male fish, for example, release more sperm into the water when they sense a nearby rival.

Even men who spend more time bonding with their girlfriend unconsciously release more sperm during sex. "Males can be just as choosy as females; sperm may be cheaper to make than an egg, but it still isn't free," says Solensky.

Delusions associated with consistent pattern of brain injury

A new study provides a novel theory for how delusions arise and why they persist. NYU Langone Medical Center researcher Orrin Devinsky, MD, performed an in-depth analysis of patients with certain delusions and brain disorders revealing a consistent pattern of injury to the frontal lobe and right hemisphere of the human brain. The cognitive deficits caused by these injuries to the right hemisphere, leads to the over compensation by the left hemisphere of the brain for the injury, resulting in delusions. The article entitled "Delusional misidentifications and duplications: Right brain lesions, left brain delusions" appears in the latest issue of the journal of Neurology.

"Problems caused by these brain injuries include impairment in monitoring of self, awareness of errors, and incorrectly identifying what is familiar and what is a work of fiction," said Dr. Devinsky, professor of Neurology, Psychiatry and Neurosurgery and Director of the NYU Epilepsy Center at NYU Langone Medical Center. "However, delusions result from the loss of these functions as well as the over activation of the left hemisphere and its language structures, that 'create a story', a story which cannot be edited and modified to account for reality. Delusions result from right hemisphere lesions, but it is the left hemisphere that is deluded."

Often bizarre in content and held with absolute certainty, delusions are pathologic beliefs that remain fixed despite clear evidence that they are incorrect. "Delusions are common problems in a variety of psychiatric and neurological disorders," said Dr. Devinsky. "Psychiatric disorders with delusions, for example- schizophrenia, have been proven to have functional and structural brain pathology. But now improved diagnostic techniques are allowing us to have increased identification of neurologic disorders among other patient populations with delusions."

In the study, the author finds that most neurologic patients with delusions usually have lesions in the right hemisphere and/or bifrontal areas. For example, the neurological disorders of Confabulation (incorrect or distorted statements made without conscious effort to deceive), Capgras (the ability to consciously recognize familiar faces but not emotionally connect with them) and Prosopagnosia (patients who may fail to recognize spouses or their own face but generate an unconscious response to familiar faces) result from right sided lesions.

The right hemisphere of the brain dominates self recognition, emotional familiarity and ego boundaries. After injury, the left hemisphere tends to have a creative narrator leading to excessive, false explanations. The resistance of delusions to change despite clear evidence that they are wrong likely reflects frontal dysfunction of the brain, which impairs the ability to monitor self and to recognize and correct inaccurate memories and familiarity assessments. Thus, right hemisphere lesions may cause delusions by disrupting the relation between and the monitoring of psychic, emotional and physical self to people, places, and even body parts. This explains why content specific delusions involve people places or things of personal significance and distort ones relation to oneself, the author explains.

"Our knowledge of delusions is limited by our ability to comprehend the patients irrational thought process," said Dr. Devinsky. "The pathogenesis of delusions likely includes many mechanisms that span overlapping psychological, cognitive and neurological disorders. Future research should explore the psychological, cognitive, and pyschologic-anatomic systems that change during the emergence and resolution of delusions as well as strategies to treat delusions."

Examples of Various Research Reviewed

In one study, nine patients with right hemisphere infarctions at a stroke rehabilitation unit had frequent delusion. While size of the stroke did not correlate when compared to the control group, the presence of brain atrophy was a significant predictor of delusions. When delusions occurred, it was usually caused by a right hemisphere lesion. Also, one study pointed out that delusional patients with Alzheimer's disease usually have significantly more right frontal lobe damage.

Other research showed that Reduplicative Paramnesia and Capgras syndrome cases with unilateral brain lesions strongly implicate the right hemisphere, usually the frontal lobe of the brain. Among 69 patients with Reduplicative Paramnesia, lesions were primarily in the right hemisphere in 36 cases (52%), bilateral in 28 (41%) and left hemisphere in 5 (7%) -- a sevenfold increase of right over left-sided lesions. Similarly in 26 Capras patients, lesions were primarily in the right hemisphere in 8 (32 %), bilateral in 16 (62 %) and left sided in 2 (7%)- a four-fold increase of right – over left-sided lesions. For both delusional syndromes, many bilaterial cases had maximal damage in the right hemisphere.

Among another study of 29 cases of delusional misidentification syndromes, all patients had right hemisphere pathology, while 15 (52 %) had left hemisphere damage. Fourteen had exclusively right hemisphere damage but none had isolated left hemisphere damage. When lateralized lesions are found, right hemisphere lesions are more common in other delusional misidentification and content specific delusions. Frontal lesions are strongly implicated in misidentification syndromes. Exclusively frontal lesions were associated with delusions in 10 of 29 (34.5) cases- four with right frontal and six with bifrontal lesions. None had lesions sparing the frontal lobes.

Human beta cells can be easily induced to replicate, according to study in Diabetes

PITTSBURGH, Jan 13 – Researchers at the University of Pittsburgh School of Medicine have successfully induced human insulin-producing cells, known as beta cells, to replicate robustly in a living animal, as well as in the lab. The discovery not only could improve models and methods for studying diabetes, but also opens up new possibilities for treating the condition.

"Most scientists thought that these important pancreatic cells could not be induced to regenerate, or could only replicate very slowly," explained senior author Andrew F. Stewart, M.D., professor of medicine and chief of the Division of Endocrinology and Metabolism at the University of Pittsburgh School of Medicine. "This work provides proof-of-principle that the production of human beta cells can be stimulated, and that the newly generated cells function effectively both in the lab and in a living animal." The findings are in the early online version of Diabetes, one of the journals of the American Diabetes Association.

Lead authors Nathalie Fiaschi-Taesch, Ph.D., assistant professor in Pitt's endocrinology division, and Todd A. Bigatel, M.D., a graduate of the postdoctoral fellowship program, identified molecules that play key roles in human beta, or islet, cell replication, building on previous work conducted by co-author Irene Cozar-Castellano, Ph.D., also an instructor of endocrinology, who performed similar studies using mouse cells.

They found that, unlike rodents, human beta cells contain a significant amount of a protein called cdk-6. When cdk-6 production was increased using a viral vector carrying the cdk-6 gene, the cells replicated. Stimulation was further enhanced by increasing production of another cell cycle molecule called cyclin D1. Untreated human islets did not replicate.

"After we transplanted some of these engineered human beta cells under the outer layer of a kidney in a diabetic mouse, we saw that replication continued and blood sugar levels normalized," explained Dr. Fiaschi-Taesch. "When we took out the kidney that contained the insulin-producing cells, the mouse immediately developed diabetes again."

The prospect of being able to study human beta cells and their replication in vivo, meaning in a living animal, could greatly improve diabetes study models, and could lead to techniques to generate new beta cells in patients with diabetes. In the future, it also could allow more effective therapeutic transplants of insulin-producing cells – either by expanding the numbers of cells available from a single cadaveric donor or from a gene-enhanced version of the patient's own cells, or by establishing permanent cell lines from existing beta cells or stem cells, Dr. Stewart pointed out.

He added that cell cycle replication molecules might also be targets for drugs that could transiently turn on beta cell replication to increase insulin production.

The team's work was funded by grants from the National Institutes of Health, the American Diabetes Association and the Juvenile Diabetes Research Foundation.

Chasing thundersnow could lead to more accurate forecasts

MU researcher releasing weather balloons during winter storms in search of phenomenon

COLUMBIA, Mo. – The job of one University of Missouri researcher could chill to the bone, but his research could make weather predicting more accurate. Patrick Market, associate professor of atmospheric science in the College of Agriculture, Food and Natural Resources, is chasing storms in the dead of winter in order to release weather balloons that will produce data about the little-known phenomenon of thundersnow.

"One of the things we don't understand is how the cloud becomes electrified," Market said. "We hope to determine how the atmosphere is becoming unstable."

Market and his storm-chasing students are searching for winter storms in order to release weather balloons into the storm every 90 minutes over a 24-hour period. The balloons carry boxes with a barometer to measure pressure, a thermometer to measure temperature, and a hydrometer to measure humidity. Market uses a GPS to monitor wind speed and direction of the balloons. This information covers the five things that are most important for a meteorologist to know for accurate predictions, according to Market.

"It has been decades since a detailed study with modern weather balloons has been done to see how the atmosphere destabilizes for summer thunderstorms, much less the winter storms," Market said. "So we are taking this tried-and-true tool of the meteorology trade and applying it to the very specific instance of heavy snowfall in the winter."

Once the weather balloons are launched, they provide detailed readings of every layer of the atmosphere. More detailed readings and data provide better and more accurate forecasting.

"We get thunderstorms in all seasons. That means something is making the atmosphere unstable," Market said. "Thunderstorms are often associated with heavy rainfall or heavy snowfall. It's just as important to get it right in the spring, summer or winter."

The phenomenon known as thundersnow is not understood very well. It is defined as a snowstorm with thunder and lightning that can bring heavy snowfalls of 8 to 12 inches. Tracking such storms can be quite a challenge.

"Often, these winter storms cause us to travel through inclement weather in order to get to the area where the weather balloons should be launched," Market said. "During travel, the heater in the vehicle cannot be on because the instruments need to be kept cold."

Novel Drugs Selectively Target Pathway Important In Rheumatoid Arthritis

Methotrexate (MTX), a folate antagonist that blocks folic acid activity, is the most widely used disease-modifying antirheumatic drug (DMARD) for rheumatoid arthritis. It enters the cell via several pathways, one of which involves folate receptor β (FRβ), which is highly specific for cells present in the joints of patients with rheumatoid arthritis (RA). During the last two decades, a second generation of folate antagonists has been designed to address some of the limitations of MTX, which include adverse side effects and resistance. A new study examined the capacity of several of these new drugs to determine whether they could selectively target cells that express FRβ. The study was published in the January issue of Arthritis & Rheumatism (http://www3.interscience.wiley.com/journal/76509746/home).

Led by Gerrit Jansen of the VU University Medical Center in Amsterdam, researchers analyzed FRβ expression from biopsy samples from the knee joints of RA patients before and after four months of treatment with MTX and from controls. These experiments confirmed that FRβ expression is highly specific to activated macrophages (a type of immune cell that plays a role in the inflammatory response in RA) in the synovial membrane of RA patients.

The researchers went on to examine new folate antagonists to determine which ones would most likely be beneficial in treating synovial inflammation. Several of these agents showed a markedly higher binding affinity for FRβ compared to MTX, which has a high affinity for entering cells via another pathway known as reduced folate carrier (RFC). This pathway is found throughout the body, however, and is therefore not specific for synovial cells. Researchers also examined whether two of the newer drugs would inhibit growth of FRβ-expressing cells and found that one of them, BCG 945, accomplished this at low concentrations. Interestingly, the uptake of BCG 945 was inhibited by the addition of folic acid. “In this context, it may be anticipated that, for example, fortification of food with folate may reduce the activity of this folate antagonist, whereas restriction in dietary folate intake could further enhance the therapeutic efficacy of these types of drugs,” the authors state. BGC 945 was originally discovered at the Institute of Cancer Research in London, and is now known as ONX 0801. Onyx Pharmaceuticals has an exclusive worldwide license to this compound.

They note that although MTX is the drug of first choice in the treatment of RA, its efficacy can be improved. “Further evaluation of folate antagonists with properties of high binding affinity for FRβ and low affinity for

the RFC may pave the road for a more selective targeted therapy of activated synovial macrophages," they conclude.

In an accompanying editorial in the same issue, Christoph Fiehn of the Center for Rheumatic Diseases in Germany notes that folate antagonists remain the key to RA treatment, both now and in the future. "Antifolate drugs that, unlike MTX, are FRβ-specific would have a stronger effect on synovial macrophages and a weaker effect on other types of cells that take up MTX by the ubiquitously expressed RFC," he explains. "A higher therapeutic effect and a lower rate of side effects of FRβ-specific antifolates as compared with MTX could possibly be the result."

Articles: "Folate Receptor β as a Potential Delivery Route for Novel Folate Antagonists to Macrophages in the Synovial Tissue of Rheumatoid Arthritis Patients," Joost W. van der Heijden, Ruud Oerlemans, Ben A.C. Dijkmans, Huiling Qi, Conny J. van der Laken, Willem F. Lems, Ann L. Jackman, Maarten C. Kraan, Paul P. Tak, Manohar Ratnam, Gerrit Jansen, Arthritis & Rheumatism, January 2009; 60:1; pp.12-21.

"The Future of Folic Acid Antagonist Therapy in Rheumatoid Arthritis," Christoph Fiehn, Arthritis & Rheumatism, January 2009; 60:1; pp. 1-4.

Bug enzyme generates fuel from water

* 17:01 13 January 2009 **by Colin Barras**

Light-powered, bacterial enzyme-containing nanoparticles that release hydrogen from water could lead the way to new strategies for generating the energy-rich gas.

The lack of low-cost ways to create hydrogen gas is one of the main barriers to the dream of economies fuelled by hydrogen not oil.

A class of enzymes called hydrogenases are used by organisms to convert hydrogen ions to hydrogen gas during anaerobic - without oxygen - respiration. These enzymes have long interested chemists searching for alternatives to existing, expensive, platinum-catalysed hydrogen generation.

The metal-containing enzymes are all crippled in varying degrees by the presence of oxygen and are also damaged by the very hydrogen they produce. That makes them difficult and expensive to use on industrial scales, says chemist Erwin Reisner, at Oxford University in the UK.

Bacterial gift

Now Reisner and colleague Fraser Armstrong have discovered that one bacterial hydrogenase is much more resistant to both gases.

The nickel, iron and selenium-rich enzyme, first isolated by Juan Fontecilla-Camps at the University of Joseph Fourier in Grenoble, France, is produced by a sulphate-reducing bacterium.

Its efficiency is relatively unaffected by the presence of hydrogen gas, and it continues to work even if the surrounding air contains 1% oxygen by volume - ordinarily even a few parts per million of oxygen would block hydrogenase activity.

The new enzyme also binds strongly to titanium dioxide nanoparticles, making it easy to produce a kind of light-powered, hydrogen-generating dust.

'Promising trial'

The dust particles are each attached both to the enzyme and to light-absorbing dye molecules that are used in some solar cells. In the presence of an electron-donating buffer solution, the dye absorbs light and releases excited electrons, which then pass to the enzyme. Suitably energised, the hydrogenase then converts hydrogen ions from water molecules into hydrogen gas - just as they would during the bacteria's respiration.

After a small sample of the nanoparticles spent 8 hours in a buffer solution under a tungsten-halogen lamp, the headspace gas above the solution was 4.6% hydrogen by volume - a result Armstrong calls "promising for a first trial". In a control experiment without the enzyme only trace quantities of hydrogen were present.

The reaction falls short of "true water splitting", says Armstrong. This would require another catalyst to release oxygen gas from the water molecules and provide the electrons to fuel the dye, making the buffer solution redundant. Developing that complete system is Reisner and Armstrong's next goal, they say.

Catalyst inspiration

The turnover rates for hydrogen gas cycling are comparable with platinum catalysts under certain conditions, so studying the new hydrogenase might inform the "design" of simpler catalysts that are as effective as platinum, but considerably cheaper.

Marc Fontecave at the Atomic Energy Commission in Grenoble, France, is working on such catalytic molecules. "What we need is catalysts working under aerobic conditions and not just 1% oxygen," he says. "Obviously, I'm more confident at the present stage in this type of catalyst than in hydrogenases."

Chris Pickett at the University of East Anglia in the UK agrees, but is still impressed with what has been achieved with the natural hydrogenase. "It is the enzyme systems which are showing what can be done and which are currently making the pace," he says. *Journal reference: Chemical Communications (DOI: 10.1039/b817371k)*

Scientists uncover evolutionary keys to common birth disorders

Study of changes in MSX gene family over 600 million years leads to new understanding of disease patterns

Boston-- The work of Forsyth scientist Peter Jezewski, DDS, Ph.D., has revealed that duplication and diversification of protein regions ('modules') within ancient master control genes is key to the understanding of certain birth disorders. Tracing the history of these changes within the proteins coded by the Msx gene family over the past 600 million years has also provided additional evidence for the ancient origin of the human mouth.

Dr. Jezewski has published an important study examining the Msx family that has ancient roots as a master control gene for patterned embryonic growth. Previous work by Dr. Jezewski, and other groups, identified mutations within the human MSX1 gene in two different birth disorders: either cleft lip and palate or skin derivative disorders ('ectodermal dysplasias') that include tooth and nail malformations. The mutations associated with the more severe clefting disorder are found within unique portions of the MSX protein, thus providing the first molecular explanation for this disease pattern. This work may eventually enable genetically susceptible families with environmental risk factors to prevent these common birth disorders.

Cleft lip and palate is one of the most common birth defects. Both genes and environment contribute to this condition. "If we can learn more about genetic susceptibility of these families, we can start to examine how environmental factors, like maternal smoking, may contribute to their manifestation," says Dr. Jezewski. "This information could lead to recommendations for appropriate behavioral changes within families who are genetically at risk."

Summary of Study

The study, "Domain duplication, divergence, and loss events in vertebrate Msx paralogs reveal phylogenomically informed disease markers," was published in BMC Evolutionary Biology January 14, 2009. This research was led by Dr. Peter Jezewski at The Forsyth Institute, and was conducted with collaborators at Boston University, Drs. John Finnerty and Maureen Mazza. The research team performed a battery of evolutionary analyses on 46 Msx proteins from a diverse collection of animals, ranging from sponges to humans. This analysis identified human sequence variants in Msx likely to underlie disease, and indicated why mutations in the same gene can lead to either orofacial clefting or ectodermal dysplasias.

These clinical insights were gleaned from work demonstrating that certain portions of the Msx proteins have remained constant over extremely long periods of time (>600 million years) while other Msx protein modules had duplicated and then subsequently diverged within the duplicated Msx sister genes, a previously unrecognized avenue for the evolution of morphological innovation. These observations will help to prioritize future clinical and functional research on these disease mutations. An outgrowth of these insights was the realization that the highly conserved protein modules that make up the Msx protein help to define a class of animal specific master control genes that each go on to specifically pattern the body plan of all modern animals.

Peter Alan Jezewski, D.D.S., Ph.D., is a research associate in the Department of Cytokine Biology at the Forsyth Institute and an instructor, Department of Oral Medicine, Infection and Immunity at the Harvard School of Dental Medicine. The Jezewski lab studies inheritance patterns of human oral-facial diseases particularly complex birth disorders as well as forms of aggressive periodontitis.

This work was supported in part by research grants from the National Institute of Dental and Craniofacial Research.

University of Leicester archaeologist uncovers evidence of ancient chemical warfare

CSI-style arguments suggest Persians routed Romans with poison gas

A researcher from the University of Leicester has identified what looks to be the oldest archaeological evidence for chemical warfare--from Roman times.

At the meeting of the Archaeological Institute of America, University of Leicester archaeologist Simon James presented CSI-style arguments that about twenty Roman soldiers, found in a siege-mine at the city of Dura-Europos, Syria, met their deaths not as a result of sword or spear, but through asphyxiation.

Dura-Europos on the Euphrates was conquered by the Romans who installed a large garrison. Around AD 256, the city was subjected to a ferocious siege by an army from the powerful new Sasanian Persian Empire. The dramatic story is told entirely from archaeological remains; no ancient text describes it. Excavations during the 1920s-30s, renewed in recent years, have resulted in spectacular and gruesome discoveries.

The Sasanians used the full range of ancient siege techniques to break into the city, including mining operations to breach the walls. Roman defenders responded with 'counter-mines' to thwart the attackers. In one of these narrow, low galleries, a pile of bodies, representing about twenty Roman soldiers still with their arms, was found in the 1930s. While also conducting new fieldwork at the site, James has recently reappraised this coldest of cold-case 'crime scenes', in an attempt to understand exactly how these Romans died, and came to be lying where they were found.

Dr James, Reader in the School of Archaeology and Ancient History at the University of Leicester, said: "It is evident that, when mine and countermine met, the Romans lost the ensuing struggle. Careful analysis of the disposition of the corpses shows they had been stacked at the mouth of the countermine by the Persians, using their victims to create a wall of bodies and shields, keeping Roman counterattack at bay while they set fire to the countermine, collapsing it, allowing the Persians to resume sapping the walls. This explains why the bodies were where they were found. But how did they die? For the Persians to kill twenty men in a space less than 2m high or wide, and about 11m long, required superhuman combat powers—or something more insidious."

Finds from the Roman tunnel revealed that the Persians used bitumen and sulphur crystals to get it burning. These provided the vital clue. When ignited, such materials give off dense clouds of choking gases. "The Persians will have heard the Romans tunnelling," says James, "and prepared a nasty surprise for them. I think the Sasanians placed braziers and bellows in their gallery, and when the Romans broke through, added the chemicals and pumped choking clouds into the Roman tunnel. The Roman assault party were unconscious in seconds, dead in minutes. Use of such smoke generators in siege-mines is actually mentioned in classical texts, and it is clear from the archaeological evidence at Dura that the Sasanian Persians were as knowledgeable in siege warfare as the Romans; they surely knew of this grim tactic."

Ironically, this Persian mine failed to bring the walls down, but it is clear that the Sasanians somehow broke into the city. James recently excavated a 'machine-gun belt', a row of catapult bolts, ready to use by the wall of the Roman camp inside the city, representing the last stand of the garrison during the final street fighting. The defenders and inhabitants were slaughtered or deported to Persia, the city abandoned forever, leaving its gruesome secrets undisturbed until modern archaeological research began to reveal them.

You can read more about Dr James' work at: http://www.le.ac.uk/archaeology/school/staff/staff_simonjames.html http://www.le.ac.uk/ar/stj/dura.htm http://www.le.ac.uk/archaeology/ResearchonDura-EuroposSyria.htm

Explaining the curse of work

* 14 January 2009 **by Mark Buchanan**

"Parkinson's law", first published in an article of 1955, states: work expands to fill the time available for its completion. Is it more than just a cynical slogan? (Image: OJO Images/Rex Features)

IT IS 1944, and there is a war on. In a joint army and air force headquarters somewhere in England, Major Parkinson must oil the administrative wheels of the fight against Nazi Germany. The stream of vital paperwork from on high is more like a flood, perpetually threatening to engulf him.

Then disaster strikes. The chief of the base, the air vice-marshal, goes on leave. His deputy, an army colonel, falls sick. The colonel's deputy, an air force wing commander, is called away on urgent business. Major Parkinson is left to soldier on alone.

At that point, an odd thing happens - nothing at all. The paper flood ceases; the war goes on regardless. As Major Parkinson later mused: "There had never been anything to do. We'd just been making work for each other."

That feeling might be familiar to many working in large organisations, where decisions can seem to be bounced between layers of management in a whirl of consultation, circulation, deliberation and delegation. It led Major Parkinson - in civilian dress, C. Northcote Parkinson, naval historian, theorist of bureaucracy and humorist- to a seminal insight. This is "Parkinson's law", first published in an article of 1955, which states: work expands to fill the time available for its completion.

Is there anything more to that "law" than just a cynical slogan? Physicists Peter Klimek, Rudolf Hanel and Stefan Thurner of the Medical University of Vienna in Austria think so. They have recreated mathematically just the kind of bureaucratic dynamics that Parkinson described anecdotally 50 years ago. Their findings put Parkinson's observations on a scientific footing, but also make productive reading for anyone in charge of organising... well, anything.

Parkinson based his ideas not just on his war experience, but also his historical research. Between 1914 and 1928, he noted, the number of administrators in the British Admiralty increased by almost 80 per cent, while the number of sailors they had to administer fell by a third, and the number of ships by two-thirds. Parkinson suggested a reason: in any hierarchical management structure, people in positions of authority need subordinates, and those extra bodies have to be occupied- regardless of how much there actually is to do.

Parkinson was crystallising, with tongue half in cheek, classic work done by the German sociologist Max Weber in the early 20th century. Weber described the attributes of an ideal bureaucracy and possible "degenerating" influences - such as any system of promotion not based wholly on merit. Parkinson's own analysis spawned other, more po-faced and politically charged critiques of public bureaucracies from economists such as William Niskanen, who served on US President Ronald Reagan's Council of Economic Advisers. Niskanen theorised that bureaucracies grow because officials seek to increase the budgets they

control and so boost their own salary, power and standing. He and other conservatives used such arguments to push for smaller government - but they could not give any supporting quantitative insight into the growth of bureaucracies.

The new work aims to do just that. "Parkinson's essays weren't quantitative," says Klimek, "but they're so clear that it's easy to cast them into specific mathematical models." From a simple system of equations using quantities such as the promotion and drop-out rates within a hierarchical body, a "phase diagram" can be computed to show what conditions breed ever greater bureaucracy. A high probability of promotion coupled with the hiring of more subordinates - the scenario Parkinson described- is unsurprisingly a recipe for particularly fast growth.

Parkinson was also interested in other aspects of management dynamics, in particular the workings of committees. How many members can a committee have and still be effective? Parkinson's own guess was based on the 700-year history of England's highest council of state- in its modern incarnation, the UK cabinet. Five times in succession between 1257 and 1955, this council grew from small beginnings to a membership of just over 20. Each time it reached that point, it was replaced by a new, smaller body, which began growing again. This was no coincidence, Parkinson argued: beyond about 20 members, groups become structurally unable to come to consensus.

A look around the globe today, courtesy of data collected by the US Central Intelligence Agency, indicates that Parkinson might have been onto something. The highest executive bodies of most countries have between 13 and 20 members. "Cabinets are commonly constituted with memberships close to Parkinson's limit," says Thurner, "but not above it." And that is not all, says Klimek: the size of the executive is also inversely correlated to measures of life expectancy, adult literacy, economic purchasing power and political stability. "The more members there are, the more likely a country is to be less stable politically, and less developed," he says.

Why should this be? To find out, the researchers constructed a simple network model of a committee. They grouped the nodes of the network - the committee members- in tightly knit clusters with a few further links between clusters tying the overall network together, reflecting the clumping tendencies of like-minded people known to exist in human interactions. To start off, each person in the network had one of two opposing opinions, represented as a 0 or a 1. At each time step in the model, each member would adopt the opinion held by the majority of their immediate neighbours.

Such a process can have two outcomes: either the network will reach a consensus, with 0s or 1s throughout, or it will get stuck at an entrenched disagreement between two factions. A striking transition between these two possibilities emerged as the number of participants grew - around Parkinson's magic number of 20. Groups with fewer than 20 members tend to reach agreement, whereas those larger than 20 generally splinter into subgroups that agree within themselves, but become frozen in permanent disagreement with each other. "With larger groups, there's a combinatorial explosion in the number of ways to form factions," says Thurner.

Santo Fortunato, a physicist who works on complex networks at the Institute for Scientific Interchange in Turin, Italy, thinks the result is convincing evidence for Parkinson's conjecture. But he would like to see further testing. "The outcome might well change significantly if you change the shape of the social network, or the way people's opinions influence one another," he says.

So might this kind of work offer a rational way to optimise our decision-making bodies? One curious detail provides an intriguing slant on this question. In the computer simulations, there is a particular number of decision-makers that stands out from the trend as being truly, spectacularly bad, tending with alarmingly high probability to lead to deadlock: eight.

Where this effect comes from is unclear. But once again, Parkinson had anticipated it, noting in 1955 that no nation had a cabinet of eight members. Intriguingly, the same is true today, and other committees charged with making momentous decisions tend to fall either side of the bedevilled number: the Bank of England's monetary policy committee, for example, has nine; the US National Security Council has six.

So perhaps we all subliminally know the kind of things that Parkinson highlighted and the computer simulations have confirmed. As Parkinson noted, we ignore them at our peril. Charles I was the only British monarch who favoured a council of state of eight members. His decision-making was so notoriously bad that he lost his head.

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Pet dogs rival humans for emotional satisfaction

* Updated 16:50 14 January 2009 **by Ewen Callaway**

Who needs children when a puppy can provide a similar emotional experience? After playing with their pets, dog owners experience a burst in a hormone linked to infant care, not to mention romantic love and friendship, new research finds.

Nicknamed the "cuddle chemical" and the "love drug", oxytocin has been found to dampen stress, combat depression, and breed trust in humans. Studies of voles, mice and rats also point to oxytocin's role in pair bonding and social memory.

For this reason, biologists Miho Nagasawa and Takefumi Kikusui, of Azuba University in Japan, wondered whether social contact between two different species could boost oxytocin levels, as well.

"Miho and I are big dog lovers and feel something changed in our bodies when gazed [upon] by our dogs," Kikusui says.

After playing with their pets, dog owners seem to experience a burst in oxytocin - a hormone linked to infant care and romantic love (Image: Henryk T Kaiser/Rex)

Look of love

They recruited 55 dog owners and their pets for a laboratory play session. Owners provided a urine sample to measure oxytocin levels, and then played with their dog for half an hour. Another urine test followed.

As a control on another occasion, some owners sat in a room with their dog and were told to completely avoid the gaze of their pets.

Kikusui's team videotaped the sessions and measured how long a dog spent eyeing its owner. Based on the analysis, the researchers split the pairs that were allowed to play into two groups: "long gaze", who locked eyes for an average of 2.5 minutes during the play session, and "short gaze", who made eye contact for fewer than 45 seconds, on average.

They found that these groupings reflected changes in owner's oxytocin levels. In participants that spent a long time making eye contact, oxytocin levels rose by more than 20% during the play session, on average. In the control group, owners that avoided their pooches' gaze saw their oxytocin levels drop slightly.

Mood enhancers

Kikusui thinks eye contact is a good proxy for the bond between owner and dog. Long-gaze owners tended to rate their relationship with their pet as more satisfying than short-gaze owners. And even when instructed to avoid eye contact during the control session, these owners experienced a mild boost in oxytocin.

A flood of the cuddle chemical could explain why playing with dogs can lift moods and even improve symptoms of anxiety and depression, Kikusui says.

More speculatively, oxytocin might have played a part in the domestication of dogs from wolves, about 15,000 years ago, the pair suggest. "Maybe during the evolutionary process, humans and dogs came to share the same social cues", such as eye contact and hand gestures, Kikusui says. "This is why dogs can adapt to human society."

One previous study found that humans who are administered oxytocin looked toward the eyes of people in photographs more often and for longer than subjects given a placebo.

However, Clive Wynne, a psychologist at the University of Florida in Gainseville, is skeptical that oxytocin release played a role in dog domestication. "Genetic evidence shows that wolves were turning into dogs thousands of years before anyone could suggest that people were involved," he says.

Still, he thinks that oxytocin could explain why some owners seem more devoted to their dogs than their families. "Think of the Helmsley women who gave a hell of a lot more money to her dogs than to her grandchildren," he says.

Journal reference: Hormones and Behavior (DOI: 10.1016/j.yhbeh.2008.12.002)

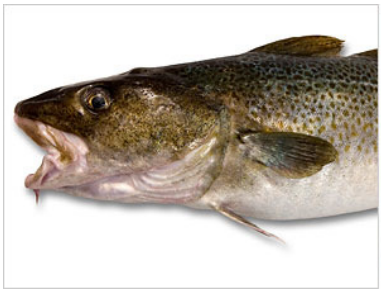
Research Ties Human Acts to Harmful Rates of Species Evolution

By CORNELIA DEAN

Human actions are increasing the rate of evolutionary change in plants and animals in ways that may hurt their long-term prospects for survival, scientists are reporting.

Hunting, commercial fishing and some conservation regulations, like minimum size limits on fish, may all work against species health.

Atlantic cod and Bighorn sheep are generally harvested by humans as mature adults, whereas predators would target the smaller or weaker.



The idea that target species evolve in response to predation is not new. For example, researchers reported several years ago that after decades of heavy fishing, Atlantic cod had evolved to reproduce at younger ages and smaller sizes.

The new findings are more sweeping. Based on an analysis of earlier studies of 29 species — mostly fish, but also a few animals and plants like bighorn sheep and ginseng — researchers from several Canadian and American universities found that rates of evolutionary change were three times higher in species subject to "harvest selection" than in other species. Writing in The Proceedings of the National Academy of Sciences, the researchers say the data they analyzed suggested that size at reproductive maturity in the species under pressure had shrunk in 30 years or so by 20 percent, and that organisms were reaching reproductive age about 25 percent sooner.

In Alberta, Canada, for example, where regulations limit hunters of bighorn sheep to large animals, average horn length and body mass have dropped, said Paul Paquet, a biologist at the University of Calgary who participated in the research. And as people collect ginseng in the wild, "the robustness and size of the plant is declining," he said.

The researchers said that reproducing at a younger age and smaller size allowed organisms to leave offspring before they were caught or killed. But some evidence suggests that they may not reproduce as well, said Chris Darimont, a postdoctoral fellow in environmental studies at the University of California, Santa Cruz, who led the work. The fish they studied that are reproducing earlier "on average have far, far, far fewer eggs than those who wait an additional year and grow a few more centimeters," he said in an interview.

Dr. Darimont said it was unknown whether traits would change back if harvesting were reduced, or how long that might take.

The researchers also noted that the pattern of loss to human predation like hunting or harvesting is opposite to what occurs in nature or even in agriculture.

Predators typically take "the newly born or the nearly dead," Dr. Darimont said. For predators, targeting healthy adults can be dangerous, and some predator fish cannot even open their mouths wide enough to eat adult prey. Animals raised as livestock are typically slaughtered relatively young, he said, and farmers and breeders retain the most robust and fertile adults to grow their herds or flocks.

But commercial fishing nets and other gear that comply with conservation regulations typically trap large fish while letting smaller ones escape. Trophy hunters typically seek out the largest animals. And for some fish in some areas, as much as 50, 60 or even 80 percent of the stock may be caught every year.

"Targeting large, reproducing adults and taking so many of them in a population in a given year — that creates this ideal recipe for rapid trait change," Dr. Darimont said.

Some fisheries scientists have said their studies of fish stock had not shown a correlation between fishing intensity and growth rates. And some wildlife conservationists question the idea that hunting can have harmful effects on species.

Dr. Paquet said that although he had confidence in the new findings, he knew there would be questions about the analytical methods he and his fellow researchers used. "That's expected," he said. "That's how science proceeds."

He said he had anticipated that the work would be "contentious" among trophy hunters. "Essentially, we are saying, 'You should not do this because it is having effects even you might not like,' " he said.

Daniel Pauly, who directs the Fisheries Center at the University of British Columbia, said the new findings "make sense."

Though Dr. Pauly said he had not seen the new work, he recalled similar changes in black chin tilapia, fish that live in brackish water. He said in an interview that he had studied the fish more than 30 years ago, when he was a young graduate student doing field work in Ghana.

After decades of heavy fishing, the size of the typical adult fish had shrunk to about 10 centimeters from about 15 centimeters. But at the time, he said, "I did not realize what was happening."

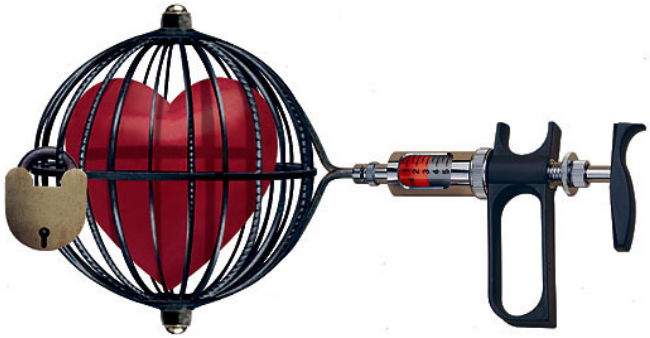
Some fisheries managers are already suggesting that conservation regulations should be changed to safeguard larger fish in protected species. "Lots of people argue for that because the big ones are so fecund," Dr.

Pauly said. But he said customers in fish markets typically prefer larger fish. And if fishers are not permitted to keep the big ones, they "must catch enormous quantities of fish to have a good tonnage."

Findings

Anti-Love Drug May Be Ticket to Bliss

By JOHN TIERNEY



In the new issue of Nature, the neuroscientist Larry Young offers a grand unified theory of love. After analyzing the brain chemistry of mammalian pair bonding — and, not incidentally, explaining humans' peculiar erotic fascination with breasts — Dr. Young predicts that it won't be long before an unscrupulous suitor could sneak a pharmaceutical love potion into your drink.

That's the bad news. The not-so-bad news is that you may enjoy this potion if you took it knowingly with the right person. But the really good news, as I see it, is that we might reverse-engineer an anti-love potion, a vaccine preventing you from making an infatuated ass of yourself. Although this love vaccine isn't mentioned in Dr. Young's essay, when I raised the prospect he agreed it could also be in the offing.

Could any discovery be more welcome? This is what humans have sought ever since Odysseus ordered his crew to tie him to the mast while sailing past the Sirens. Long before scientists identified neuroreceptors, long before Britney Spears' quickie Vegas wedding or any of Larry King's seven marriages, it was clear that love was a dangerous disease.

Love was correctly identified as a potentially fatal chemical imbalance in the medieval tale of Tristan and Isolde, who accidentally consumed a love potion and turned into hopeless addicts. Even though they realized that her husband, the king, would punish adultery with death, they had to have their love fix.

They couldn't guess what was in the potion, but then, they didn't have the benefit of Dr. Young's research with prairie voles at the Yerkes National Primate Research Center at Emory University. These mouselike creatures are among the small minority of mammals — less than 5 percent — who share humans' propensity for monogamy. When a female prairie vole's brain is artificially infused with oxytocin, a hormone that produces some of the same neural rewards as nicotine and cocaine, she'll quickly become attached to the nearest male. A related hormone, vasopressin, creates urges for bonding and nesting when it is injected in male voles (or naturally activated by sex). After Dr. Young found that male voles with a genetically limited vasopressin response were less likely to find mates, Swedish researchers reported that men with a similar genetic tendency were less likely to get married. In his Nature essay, Dr. Young speculates that human love is set off by a "biochemical chain of events" that originally evolved in ancient brain circuits involving mother-child bonding, which is stimulated in mammals by the release of oxytocin during labor, delivery and nursing.

"Some of our sexuality has evolved to stimulate that same oxytocin system to create female-male bonds," Dr. Young said, noting that sexual foreplay and intercourse stimulate the same parts of a woman's body that are involved in giving birth and nursing. This hormonal hypothesis, which is by no means proven fact, would help explain a couple of differences between humans and less monogamous mammals: females' desire to have sex even when they are not fertile, and males' erotic fascination with breasts. More frequent sex and more attention to breasts, Dr. Young said, could help build long-term bonds through a "cocktail of ancient neuropeptides," like the oxytocin released during foreplay or orgasm.

Researchers have achieved similar results by squirting oxytocin into people's nostrils — not terribly sexy, but it seems to enhance feelings of trust and empathy. Although Dr. Young is not concocting any love potions (he's looking for drugs to improve the social skills of people with autism and schizophrenia), he said there could soon be drugs that increase people's urge to fall in love.

"It would be completely unethical to give the drug to someone else," he said, "but if you're in a marriage and want to maintain that relationship, you might take a little booster shot yourself every now and then. Even now it's not such a far-out possibility that you could use drugs in conjunction with marital therapy."

I see some potential here, but also big problems. Suppose you took that potion and then suddenly felt an urge to run off with the next person you spent any time with, like your dentist? What if you went to a business convention and then, like an artificially stimulated prairie vole, bonded with the nearest stranger? What if, like Tristan, you developed an overwhelming emotional connection to your boss's spouse?

Even if the effects could somehow be targeted to the right partner, would you want to start building a long-term relationship with a short-term drug? What happens when it wears off?

A love vaccine seems simpler and more practical, and already there are some drugs that seem to inhibit people's romantic impulses (see TierneyLab, at www.nytimes.com/tierneylab). Such a vaccine has already been demonstrated in prairie voles.

"If we give an oxytocin blocker to female voles, they become like 95 percent of other mammal species," Dr. Young said. "They will not bond no matter how many times they mate with a male or hard how he tries to bond. They mate, it feels really good and they move on if another male comes along. If love is similarly biochemically based, you should in theory be able to suppress it in a similar way."

I doubt many people would want to permanently suppress love, but a temporary vaccine could come in handy. Spouses going through midlife crises would not be so quick to elope with their personal trainers; elderly widowers might consult their lawyers before marrying someone resembling Anna Nicole Smith. Love is indeed a many-splendored thing, but sometimes we all need to tie ourselves to the mast.

Q & A

Bite and Bite Again

By C. CLAIBORNE RAY

Q. When you wake up with several mosquito bites and find one very bloated mosquito in the room, why has it bitten you so many times in a short period?

A. A female mosquito takes a blood meal when it is carrying fertilized eggs, seeking a blood protein that allows the eggs to develop. Several reasons have been suggested for the multiple bites that many people (and animals) may experience from a single mosquito.

The simplest explanation is that the victim tossed and turned, interrupting the feeding before the mosquito had its fill. The mosquito has a sensory nerve that signals the brain when the midgut is full; otherwise feeding would continue until the bursting point.

Victoria Roberts

It is also possible that some blood types are not as easily thinned by the anticoagulant in the mosquito's saliva, so the mosquito has to make more tries to get a satisfying meal. Another factor may be the mosquito's search for an accessible vein near the skin surface, much like that of a nurse trying multiple sites to take a blood sample.

Some studies suggest that multiple feeding attempts occur more often when the mosquito is either acquiring or transmitting a disease organism, like the malaria parasite, because of a chemical feedback system between mosquito and prey. It has even been suggested that some mosquitoes can transmit chemicals that make the host less sensitive to inflammation after a series of bites, so that more blood can be taken.

Paper Details Sites on Mars With Plumes of Methane

By KENNETH CHANG

In early 2003, a plume of methane gas rose from the surface of Mars. The big unanswered question is, What belched?

Subsurface Martian cows are highly unlikely. But scientists are seriously considering the possibility of bacteria.

A team of researchers reported Thursday that the bursts of methane originated from three specific regions in the planet's northern hemisphere, where it was midsummer. The gas came out at a rate of 0.6 kilograms a second, the scientists said, and the plume contained 19,000 metric tons of methane.

"This is the first definitive detection of methane on Mars," Michael J. Mumma of the NASA Goddard Space Flight Center in Greenbelt, Md., the leader of the research team, said at a news conference, "and the first definitive maps and identification of active regions of release."

The findings appeared in a paper published online Thursday by the journal Science. Dr. Mumma said additional scientific papers describing other time periods of the observations, which span from 2001 to last year, were being prepared.

Methane — the simplest of hydrocarbon molecules, with one carbon atom and four hydrogen atoms — is fragile in air. It falls apart when hit by ultraviolet radiation in sunlight. That means any methane in the Martian air must be recent.

When the presence of methane was reported in 2004 by three teams of scientists, the findings generated surprise and skepticism because only a few explanations seemed to be plausible.

One was geothermal chemical reactions involving water and heat in volcanoes or underground hot springs. But evidence for recent volcanism on Mars is scarce. Also, volcanoes would be expected to spew other gases like sulfur dioxide, and those are not plentiful in the planet's atmosphere.

A second possibility is biological. On Earth, a class of bacteria known as methanogens breathes out methane as a waste product.

NASA's current Mars strategy is to look for signs of water and perhaps life in the planet's distant past. "Perhaps we need to also think in terms of present-day life holding on somewhere in the subsurface," said Lisa M. Pratt, a professor of geological sciences at Indiana University who participated in the news conference but was not involved with the research.

Even if the source turns out to be geological in origin or to have come from long-extinct bacteria, the sites would still be prime locations to look for other microbes that thrive on methane as food. "It gives us a bull's-eye to go after," Dr. Pratt said.

Because of the difficulty in measuring methane, many scientists wondered if the earlier reports really showed methane or if all three teams had been misled by their data.

Dr. Mumma's group used telescopes in Hawaii to examine the light reflected off Mars. Different molecules absorb different wavelengths of light, and the scientists reported seeing black lines in the spectrum corresponding to methane and to water vapor. As Mars rotated, bringing different areas into view of the telescope, the scientists could measure variations in the concentrations.

The concentrations in 2003 were densest over three regions — known as Terra Sabae, Nili Fossae and Syrtis Major — and as high as 45 parts per billion. The scientists said that mineralogy of the surface suggested these areas had flowing water in the far Martian past.

Nili Fossae had been under consideration for the landing site for NASA's next surface rover, the Mars Science Laboratory, but was not among the four finalists announced in November. Last month, scientists reported that the Mars Reconnaissance Orbiter had spotted exposed outcrops of carbonate rocks in Nili Fossae, perhaps the vestige of ancient lakes and seas.

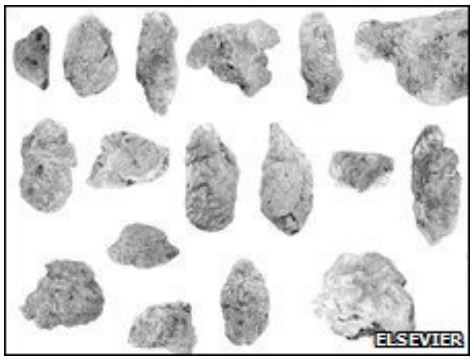
At the news conference, Michael Meyer, the lead scientist for the Mars program at NASA headquarters, said that a recent decision to delay the launching of the rover to 2011 from 2009 could allow reconsideration of Nili Fossae. An instrument aboard the science laboratory would be able to detect methane at levels of 100 parts per trillion.

Poo clue to ancient bird's diet

An analysis of the dried faeces of the giant moa, an extinct bird from New Zealand, has overturned ideas about what the flightless giants ate.

At three metres in height, it was thought moa grazed on trees and bushes, but the faeces turned up evidence only of tiny herbs. The study also showed that moa diets were significantly different to those of the species introduced later. The research appears in the current issue of Quaternary Science Reviews.

Alan Cooper, director of the Australian Centre for Ancient DNA and senior author on the study, has been collating DNA from a range of different species of moa in recent years.



Some of the coprolite samples reached 15cm in length

Prior efforts investigating ancient DNA in the region have shown how varied species of birds diverged with the breakup of the islands of the South Pacific, providing the researchers with a catalogue of DNA samples to which they can refer.

Knock-on effects

In the new research, Jamie Wood of the University of Otago and colleagues studied the leaf fragments, plant seeds, and DNA in more than 1,500 faecal fossils - known as coprolites - that have survived only because of the moa's behaviour. "When animals shelter in caves and rock shelters, they leave faeces which can survive for thousands of years if dried out," Professor Cooper says.

By analysing the DNA in the coprolites, the researchers were able to discern the diets of the varying species of moa that were scattered around New Zealand. "Over half the plants we detected in the faeces were under 30cm in height," says Dr Wood. "This suggests that some moa grazed on tiny herbs, in contrast to the current view of them as mainly shrub and tree browsers. "We also found many plant species that are currently threatened or rare, suggesting that the extinction of the moa has impacted their ability to reproduce or disperse."

'Quite remarkable'

The moa's evident diet is in sharp contrast to that of the herbivores that were introduced later to the islands, for whom the moa's diet would have been toxic - suggesting that the moa co-evolved with the native plants they ate.

"It's a fairly elegant approach that most people wouldn't have thought of doing," says Ian Barnes, a bio-archaeologist at Royal Holloway, University of London. "The ability to look at a species that went extinct several hundred years ago and get some insight into the real ecology of that animal - what it ate, whether they were in competition with each other, whether different species ate different stuff, how they divided the landscape up - is quite remarkable."

What is more, the approach could be applied in Australia to conduct similar studies - but the evidence has so far been lacking. "Given the arid conditions, Australia should probably have similar deposits from the extinct giant marsupials," says Professor Cooper. "A key question for us is 'where has all the Australian poo gone?'"

Game of two halves leads to brain asymmetry

A tug-of-war between the two sides of the brain causes it to become asymmetrical, according to research published today in the journal Neuron. Asymmetry in the brain is thought to be important to enable the two hemispheres to specialise and operate more efficiently.

Left-right asymmetry is present in the brains of most animals and is first evident at the time of early brain development. However, until now, scientists did not know the mechanisms that bring it about. Now, in a study funded primarily by the Wellcome Trust, researchers have shown that a competition between the two sides causes this asymmetry.

By studying brain development in zebrafish, PhD student Jenny Regan and her colleagues in Professor Stephen Wilson's team at UCL (University College London) have shown that a protein known as Fgf8 acts as a magnet to attract nerve cells to one side of the brain.

"Fgf8 is found in both sides of the brain, leading to a 'tug-of-war' competition between the two sides to attract the migrating group of nerve cells," says Dr Regan. "This isn't a fair fight, however – Fgf8 on the left-hand side has an ally to help it win the battle."

A second protein, known as Nodal, is present only on the left and teams up with Fgf8 to attract the group of nerve cells, triggering a cascade of events that lead to asymmetric development of the brain, with neurons on the left making different connections to those on the right. The combined action of Fgf8 and Nodal ensures that when the asymmetry develops, it is usually in the same direction – this helps to explain why there is consistent handedness between individuals. Nodal is known to also play a role in other areas of the body where asymmetry occurs, such as the heart and positioning of internal organs.

If Nodal is inhibited, the competition is fairer and the group of nerve cells has an equal probability of migrating to the right or left side, but a bias in the direction of migration can be restored by adding extra Fgf8 to one side of the brain.

"Brain asymmetry is essential for proper brain function," explains Professor Wilson. "It allows the two sides of the brain to become specialised, increasing its processing capacity and avoiding situations of conflict where both sides of the brain try to take charge.

"For example, faced with a predator, an animal would not want both sides of the brain to try to drive the escape as this might lead to conflict over which direction to turn. Instead, the animal might keep watch more with one eye (and consequently one half of the brain) and so each side of the brain might be dominant for particular activities."

Previous studies have shown that rearing chickens in the dark makes their brains less asymmetric. The chicks can still peck for food and watch out for predators, but only if doing one of these tasks at a time. When they try to do both, they are less efficient than fully asymmetric animals in which one eye specialises for one task and the other eye for the other task.

In humans, people with schizophrenia have disrupted brain asymmetries but as yet, it is not clear if there is a causal link between the asymmetry and schizophrenia. "The direction and handedness that brain asymmetry takes is not critical for survival, but the strong bias towards one direction may be to ensure that all members of a population have consistent behaviours," adds Professor Wilson. "This may be very important for social animals, such as humans and schooling fish."

Common soil mineral degrades the nearly indestructible prion

MADISON — In the rogues' gallery of microscopic infectious agents, the prion is the toughest hombre in town.

Warped pathogens that lack both DNA and RNA, prions are believed to cause such fatal brain ailments as chronic wasting disease (CWD) in deer and moose, mad cow disease in cattle, scrapie in sheep and Creutzfeldt-Jakob disease in humans. In addition to being perhaps the weirdest infectious agent know to science, the prion

is also the most durable. It resists almost every method of destruction from fire and ionizing radiation to chemical disinfectants and autoclaving, which reduce prion infectivity but fail to completely eliminate it.

Now, however, a team of Wisconsin researchers has found that a common soil mineral, an oxidized from of manganese known as birnessite, can penetrate the prion's armor and degrade the protein.

The new finding, which was reported earlier this month (Jan. 2) in the Journal of General Virology, is important because it may yield ways to decontaminate soil and other environments where prions reside.

"Prions are resistant to many of the conventional means of inactivating pathogens," says Joel Pedersen, a University of Wisconsin-Madison environmental chemist and the senior author of the new study. For example, autoclaving, a standard method for sterilization in the laboratory, will reduce the concentration of prions in solution, but fails to eliminate them altogether, as it does for virtually all other types of pathogens.

Because prions infect both wild and domesticated animals, the agent can contaminate barnyards and other areas where infected livestock are kept, as well as persist in natural environments where deer, elk and other animals can become infected by contact with contaminated soil.

Other studies have shown that prions can survive in the soil for at least three years, and that soil is a plausible route of transmission for some animals, Pedersen says. "We know that environmental contamination occurs in deer and sheep at least," he notes.

Prion reservoirs in the soil, Pedersen explains, are likely critical links in the chain of infection because the agent does not appear to depend on vectors - intermediate organisms like mosquitoes or ticks - to spread from animal to animal.

That the birnessite family of minerals possessed the capacity to degrade prions was a surprise, Pedersen says. Manganese oxides like birnessite are commonly used in such things as batteries and are among the most potent oxidants occurring naturally in soils, capable of chemically transforming a substance by adding oxygen atoms and stripping away electrons. The mineral is most abundant in soils that are seasonally waterlogged or poorly drained.

"A variety of manganese oxide minerals exist and one of the most common is birnessite. They are common in the sense that you find them in many soils, but in low concentrations," says Pedersen. "They are among the strongest oxidants in soil." The new study, which was led by Fabio Russo of the University of Naples and Christopher J. Johnson of UW-Madison, was conducted on prions in solution in the laboratory. The group's working hypothesis, according to Pedersen, is that the mineral oxidizes the prion, a chemical process that can be seen in things like iron oxidizing to form rust or how cut pears and apples turn brown when exposed to oxygen.

The next step, Pedersen says, is to mix the mineral with contaminated soil to see if it has the same effect. If it does, birnessite may become a useful tool for cleaning up contaminated farmyards and other places where the prion may be concentrated in the soil.

"I expect that its efficacy would be somewhat diminished in soil," says Pedersen. "It's something we'll explore."

In addition to Pedersen, Russo and Christopher Johnson, co-authors of the new study include Chad J. Johnson of the UW-Madison School of Veterinary Medicine, and Judd Aiken and Debbie McKenzie of the University of Alberta. The work was supported by grants from the National Science Foundation, the U.S. Environmental Protection Agency and the U.S. Department of Defense. −*Terry Devitt, 608-262-8282, trdevitt@wisc.edu*

Cornell-led team detects dust around a primitive star, shedding new light on universe's origins

ITHACA, N.Y. – A Cornell-led team of astronomers has observed dust forming around a dying star in a nearby galaxy, giving a glimpse into the early universe and enlivening a debate about the origins of all cosmic dust.

The findings are reported in the Jan. 16 issue of the journal Science (Vol. 323, No. 5912). Cornell research associate Greg Sloan led the study, which was based on observations with NASA's Spitzer Space Telescope. The researchers used Spitzer's Infrared Spectrograph, which was developed at Cornell.

Dust plays a key role in the evolution of such galaxies as our Milky Way. Stars produce dust – rich with carbon or oxygen – as they die. But less is known about how and what kind of dust was created in galaxies as they formed soon after the big bang.

Sloan and his colleagues observed dust forming around the carbon star MAG 29, located 280,000 light years away in a smaller nearby galaxy called the Sculptor Dwarf. Stars more massive than the sun end their lives as carbon stars, which in our galaxy are a rich source of dust.

The Sculptor Dwarf contains only 4 percent of the carbon and other heavy elements in our own galaxy, making it similar to primitive galaxies seen at the edge of the universe. Those galaxies emitted the light we now see soon after they and the universe formed. "What this tells us is that carbon stars could have been pumping dust soon after the first galaxies were born," Sloan said.

Scientists have debated where the dust in the early universe comes from. Supernovae have been a favorite suspect, but they may destroy more dust than they create.

"While everyone is focused on the questions of how much and what kind of dust supernovae make, they may not have appreciated that carbon stars can make at least some of the dust we are seeing," Sloan said. "The more we can understand the quantity and composition of the dust, the better we can understand how stars and galaxies evolve, both in the early universe and right next door."

Observing such stars as MAG 29 is not unlike using a time machine, Sloan said, in which astronomers can catch glimpses of what the universe looked like billions of years ago. "We haven't seen carbon-rich dust in this primitive of an environment before," Sloan said.

NASA's Jet Propulsion Laboratory, Pasadena, Calif., manages the Spitzer Space Telescope mission for NASA's Science Mission Directorate, Washington. Science operations are conducted at the Spitzer Science Center at the California Institute of Technology, also in Pasadena. Caltech manages JPL for NASA. For more information about Spitzer, visit http://www.spitzer.caltech.edu/spitzer and http://www.nasa.gov/spitzer .

Fish guts explain marine carbon cycle mystery

Research published today reveals the major influence of fish on maintaining the delicate pH balance of our oceans, vital for the health of coral reefs and other marine life.

The discovery, made by a team of scientists from the UK, US and Canada, could help solve a mystery that has puzzled marine chemists for decades. Published today (16 January 2009) in Science, the study provides new insights into the marine carbon cycle, which is undergoing rapid change as a result of global CO2 emissions.

Until now, scientists have believed that the oceans' calcium carbonate, which dissolves to make seawater alkaline, came from the external 'skeletons' of microscopic marine plankton. This study estimates that three to 15 per cent of marine calcium carbonate is in fact produced by fish in their intestines and then excreted. This is a conservative estimate and the team believes it has the potential to be three times higher.

Fish are therefore responsible for contributing a major but previously unrecognised portion of the inorganic carbon that maintains the ocean's acidity balance. The researchers predict that future increases in sea temperature and rising CO2 will cause fish to produce even more calcium carbonate.

To reach these results, the team created two independent computer models which for the first time estimated the total mass of fish in the ocean. They found there are between 812 and 2050 million tonnes (between 812 billion and 2050 billion kilos) of bony fish in the ocean. They then used lab research to establish that these fish produce around 110 million tonnes (110 billion kilos) of calcium carbonate per year.

Calcium carbonate is a white, chalky material that helps control the delicate acidity balance, or pH, of sea water. pH balance is vital for the health of marine ecosystems, including coral reefs, and important in controlling how easily the ocean will absorb and buffer future increases in atmospheric CO2.

This calcium carbonate is being produced by bony fish, a group that includes 90% of marine fish species but not sharks or rays. These fish continuously drink seawater to avoid dehydration. This exposes them to an excess of ingested calcium, which they precipitate into calcium carbonate crystals in the gut. The fish then simply excrete these unwanted chalky solids, sometimes called 'gut rocks', in a process that is separate from digestion and production of faeces.

The study reveals that carbonates excreted by fish are chemically quite different from those produced by plankton. This helps explain a phenomenon that has perplexed oceanographers: the sea becomes more alkaline at much shallower depths than expected. The carbonates produced by microscopic plankton should not be responsible for this alkalinity change, because they sink to much deeper depths intact, often becoming locked up in sediments and rocks for millions of years. In contrast, fish excrete more soluble forms of calcium carbonate that are likely to completely dissolve at much shallower depths (e.g. 500 to 1,000 metres).

Lead author Dr Rod Wilson of the University of Exeter (UK) said: "Our most conservative estimates suggest three to 15 per cent of the oceans' carbonates come from fish, but this range could be up to three times higher. We also know that fish carbonates differ considerably from those produced by plankton. Together, these findings may help answer a long-standing puzzle facing marine chemists, but they also reveal limitations to our current understanding of the marine carbon cycle."

And what about the future? The researchers predict that the combination of increases in sea temperature and rising CO2 expected over this century will cause fish to produce even more calcium carbonate. This is for two reasons. Firstly, higher temperatures stimulate overall metabolism in fish, which drives all their biological processes to run faster. Secondly, increasing CO2 in their blood directly stimulates carbonate production by the gut specifically.

Dr Rod Wilson continues: "We have really only just scratched the surface of knowing the chemistry and fate of fish carbonates. Given current concerns about the acidification of our seas through global CO2 emissions, it

is more important than ever that we understand how the pH balance of the sea is normally maintained. Because of the impact of global climate change, fish are likely to have an even bigger influence on the chemistry of our oceans in future. So, it is vitally important that we build on this research to help fully understand these processes and how this will affect some of our most precious marine ecosystems."

This study was carried out by the University of Exeter (UK), University of Miami (USA), University of Ottawa (Canada), University of British Columbia (Canada), Centre for Environment, Fisheries and Aquaculture Science (UK) and University of East Anglia (UK).

Dr Rod Wilson's research was supported by the Biotechnology and Biological Sciences Research Council (BBSRC).

Colourful pigs evolved through farming, not nature

* 01:00 16 January 2009 **by Andy Coghlan**

Pigs evolved bright coat colours rapidly after domestication thanks to the human a penchant for novelty, a new gene analysis suggests.

Farmers selected and bred the brightly coloured pigs to distinguish them from their brown and black wild cousins and probably also because they preferred the unusual colours.

At the other extreme, the gene analysis shows that wild pigs today are evolving through natural selection to maintain camouflage colours to escape detection by predators.

"Every time a gene mutation arose in the wild causing coat colour to change, it was eliminated immediately," says Greger Larson of Durham University, UK, and joint leader of the analysis with Leif Andersson of Uppsala University in Sweden. "So if a black piglet showed up, that was the one picked off by a predator."

Pig a colour

Domestication overrode natural selection with artificial selection from around 10,000 years ago, when humans began to domesticate pigs and other animals such as dogs, favouring animals with mutations resulting in brightly coloured coats. "What it comes down to is the real human penchant for novelty," says Larson.

To establish how colours might have arisen in pigs, the researchers analysed DNA from 68 domestic pigs of 51 breeds, and 15 wild boar. All samples were from animals in Europe and Asia.

In each sample, they examined variations in the gene melanocortin receptor-1 (MC1R) in melanocyte skin cells, which orchestrates the manufacture of melanin pigments. In each species, the gene governs coat colour by dictating the balance between production of dark coloured eumelanin and red-yellow coloured pheomelanin.

They found about 10 mutations in the domestic and wild pigs. But the mutations in the wild pigs were all "silent", insofar as they had no physical effect on the protein produced and therefore on the colour of the animal's coat. This shows that in the wild, colour change was selected against to avoid losing camouflage. "When you mess with the gene, you get over-expression of dark or light melanins, which alters the colour," Larson explains.

Tickled pink

By contrast, all the mutations in the domestic pigs altered coat colour. Black pigs overproduce eumelanin, for example, and pink pigs stop making melanin altogether, resulting in a "default" pink colour.

'Smiling' black and white pigs in a row: Black domestic pigs with white banding caused by mutations in their MC1R gene. This fancy color pattern would never survive in the wild, but is highly prized by people **Image: Jeff Veitch**

Some of the domesticated pigs had as many as three mutations in their MC1R, each new mutation adding something that couldn't have arisen without the previous ones. For example, in pigs which are pink with black spots, for example, three mutations are needed, and the mutation causing the black spots had to have come last, following on from mutations which gave the pink background colour.

This provided the clinching evidence that the coat colours were selected for after domestication, says Larson, because pink pigs wouldn't have survived long enough in the wild to have allowed the third mutation to arise. "It shows there was a big difference in the selection regimes practiced by Mother Nature and by humans," says Larson.

The analysis also revealed that black pigs in Europe owe their blackness to different mutations from the black pigs in Asia. "It proves independent domestication of pigs on two continents," says Larson.

David Fisher, who studies melanocytes as director of the melanoma programme at Massachusetts General Hospital in Boston, says the study was sound. "It's not difficult to imagine the potential advantages during animal domestication of being able to have an easily recognisable body feature, such as coat colour," he says.
Journal reference: PLoS Genetics, DOI: 0.1371/journal.pgen.1000341

Postnatal depression can be effectively treated and possibly prevented

Clinical effectiveness of health visitor training in psychologically informed approaches for depression in postnatal women: pragmatic cluster randomised trial in primary care, BMJ Online

Health visitors can be trained to identify women with postnatal depression and offer effective treatment, while telephone peer support (mother to mother) may halve the risk of developing postnatal depression, suggests research published on bmj.com today.

About 13% of women experience postnatal depression in the year following the birth of their child. But postnatal depression is frequently undetected and untreated, often because of poor recognition of symptoms, unawareness of treatment options or fear of stigmatisation.

Antidepressants have been shown to be an effective treatment for postnatal depression, but many women are reluctant to take drugs, especially when breast feeding. Psychological therapies may provide an alternative treatment, but their effectiveness is unclear.

In one of the largest trials of postnatal depression, Dr Jane Morrell and colleagues analysed whether psychological interventions were effective in treating the symptoms of postnatal depression. Over 4,000 mothers from 101 general practices in England consented to take part. Practices were randomised so women received either a cognitive behavioural approach or a person centred approach from specially trained health visitors or health visitor usual care.

Health visitors in the intervention group were trained to identify depressive symptoms and deliver cognitive behavioural or person centred sessions for an hour per week for up to eight weeks. Validated scales were used to assess depressive symptoms among the mothers. A threshold score of 12 or more identified women with symptoms of depression. Participants were followed up for 18 months and assessed every six months using a postal questionnaire.

At both six months and 12 months postnatally, the mothers who received care from the specially trained health visitors showed significantly greater reductions in depressive symptoms than those who received health visitor usual care. Mothers in the intervention group with depressive symptoms at six weeks were 40% less likely to have depressive symptoms at six months than those receiving health visitor usual care.

The researchers found no benefit of one psychological approach over the other.

In a second study, Dr Cindy-Lee Dennis and colleagues from Canada examined the effectiveness of telephone based peer support to prevent postnatal depression in high risk women.

After web-based screening of more than 21,000 women from seven health regions in Ontario, Canada, 701 were identified at high risk of postnatal depression and randomised to receive standard postnatal care or standard care and the support of a peer volunteer (who had experienced postnatal depression themselves).

Mothers who received peer support had half the risk of developing postnatal depression at 12 weeks after birth than those in the control group. Mothers were receptive to receiving telephone-based peer support and over 80% said they were satisfied with their experience and would recommend this support to a friend.

Women and family members need to be educated about postnatal depression so they can recognise the symptoms, and treatment needs to be convenient and accessible to new mothers, says Dr Cindy-Lee Dennis in an accompanying editorial.

She calls for a coordinated multidisciplinary approach to identify postnatal depression involving all health professionals who come into contact with new mothers including midwives, doctors, nurses and health visitors.

Global warming linked to European viral epidemic

An epidemic of the viral disease nephropathia epidemica (NE) has been linked to increases in the vole population caused by hotter summers, milder winters and increased seedcrop production by broadleaf trees. Research published in BioMed Central's open access International Journal of Health Geographics links outbreaks of this rodent-borne disease to known effects of global warming.

Dr Jan Clement from the Department of Microbiology & Immunology at Belgium's Rega Institute (University of Leuven) worked with a team of medical researchers and bioscience-engineers to investigate outbreaks of NE in Belgium. Dr. Clement founded the Belgian Hantavirus Reference Centre in 1985, and noted that of the 2,200 cases since then, 828 (37.6%) occurred in just the last three years, 2005-2007. The epidemic has been shown to extend to neighboring countries such as France, Germany, The Netherlands, and Luxembourg. He said, "This animal-borne disease, scarcely known before 1990, has been increasing in incidence in Belgium with a cyclic pattern, reaching epidemic proportions since 2005. The fact that the growing

combined effect of hotter summer and autumn seasons is matched by the growth of NE in recent years means this epidemic can be considered an effect of global warming".

NE is caused by infection with Puumala virus (PUUV), which is spread by the bank vole, a rodent common throughout most of Europe. The authors believe that warmer weather causes increases in the amount of 'mast', plant seeds from oak and beech trees, that forms the voles' staple diet. This plethora of food results in increases in the vole population and warm summers raise the chances that people will visit the forests where the voles live. According to Clement, "Since 1993, each NE peak has been preceded by increased autumnal mast formation the year before, resulting in yearly NE numbers significantly higher than those during the mast years themselves".

PUUV is a hantavirus, a group of viruses known to cause hemorrhagic fevers (fevers combined with bleeding disorders). NE is a relatively mild hemorrhagic fever that causes flu-like symptoms often with renal complications, sometimes also with pulmonary problems, needing Intensive Care treatment, such as acute dialysis and/or mechanical ventilation. In some rare cases it can, moreover, cause the shock with internal haemorrhaging and death for which these infections are infamous. Clement said, "In 1997, more than 9,000 people in the Russian republic of Bashkortostan contracted the disease, of which 34 cases were fatal".

Notes to Editors

1. Relating increasing hantavirus incidences to the changing climate: the mast connection Jan Clement, Jurgen Vercauteren, Willem W Verstraeten, Genevieve Ducoffre, Jose M Barrios, Anne-Mieke Vandamme, Piet Maes and Marc Van Ranst International Journal of Health Geographics (in press)

During embargo, article available here: ij-healthgeographics.com/imedia/6578210312195333_article.pdf?random=599710

After the embargo, article available at journal website: http://www.ij-healthgeographics.com/

Researchers detail how aging undermines bone healing

Goal: Make the old heal like the young

Researchers have unraveled crucial details of how aging causes broken bones to heal slowly, or not at all, according to study results published today in the Journal of Bone and Mineral Research. The research team also successfully conducted preclinical tests on a potential new class of treatments designed to "rescue" healing capability lost to aging.

In the worst cases, an age-related delay in healing keeps the two sides of a fractured bone from ever rejoining (non-union), leaving many confined to wheelchairs, unable to walk or to live independently. Of the estimated 5.6 million fractures in the United States each year, between five and ten percent (up to 560,000) will heal slowly or incompletely. Researchers have known for 30 years that aging interferes with fracture healing, and have been filling in the details since on the complex web of biochemicals, stem cells and genes that bring about healing. The field is now reaching the point where precision designed drugs are in different stages of animal and human trials.

The current study is focused on cyclooxygenase 2 (COX-2), an enzyme known from past studies to drive stem cells to differentiate into cartilage, which then matures into bone. Researchers at the University of Rochester Medical Center 20 years ago discovered the gene in humans that is responsible for producing the COX-2 enzyme and revealed the enzyme's role in causing inflammation, the reason drugs like the painkiller Vioxx were developed to shut down its action. Then about seven years ago another research team here determined that COX-2 also plays an essential role in bone formation during skeletal repair.

The current study shows for the first time that COX-2 levels drop dramatically with age, and that the drop most explains why stem cells no longer turn into cartilage as efficiently, an early step in the chain reaction of healing. While a role for COX-2 in bone repair had been detailed prior to the current study, the cell populations responsible for the supply of COX-2 to the fracture callus, the layer of pre-cartilage cells (cartilage progenitors) that form first around a fracture to guide bone building, had not. The team also confirmed for the first time that healing ability lost with age can be rescued by manipulating the COX-2 pathway with existing, experimental drugs. The study was in mice, but is especially relevant to human medicine because of the similarity between human and mouse COX-2 gene, and because the study mice were engineered by the National Institute on Aging, and have inspired several major insights into aging that have been validated in humans.

"The skeleton loses the ability to repair itself as we age," said Regis J. O'Keefe, M.D., Ph.D., chairman of the Department of Orthopaedics at the University of Rochester Medical Center and corresponding author of the article. "Our results position the COX-2 pathway as one of several under exploration with the common goal of accelerating healing in aging humans, and with the potential to come together in future combination therapies."

Turning Back the Clock

In the current study, healing rates were compared between a group of young mice (7-9 weeks old) and a group of old mice (52-56 weeks of age), with healing evaluated by imaging and gene expression studies.

Specifically, the current study found that the older mice experienced delayed fracture healing, decreased bone formation and decreased resupply of blood vessels to the healing site in aging mice. Expression of the gene that codes for production of the COX-2 was reduced by 75 percent in fractures between aged mice and young mice during the early healing phase five days after a fracture. COX-2 expression in young mice peaked at the exact time that stem cells were changing into cartilage within the fracture callus of young mice, and was reduced during that period in older mice.

In addition, experiments confirmed that COX-2 is expressed primarily in early stem cell precursors of cartilage that also express collagen, type II, alpha 1 (col2a1), the gene that codes for production of a key part of type II collagen in mice and humans, the fibrous, structural protein that lends strength to bone. Researchers observed in aged mice a dramatic decrease as well in the expression of other genes known to contribute to bone formation as well (e.g. osteocalcin and type X collagen). Altogether the results suggest that in aging animals gene expression is altered early in fracture repair with consequences for the entire healing cascade.

Researchers found further proof that COX-2 is responsible for loss of bone healing ability with age when they were able to reverse the process with a drug known to encourage the COX-2 signaling effect. COX-2 catalyzes the conversion of a fatty acid to prostaglandin E2 (PGE2), a hormone with many functions in the animal body depending on the type of cell they interact with, from blood vessel dilation to embryo implantation in the womb to bone healing. PGE2 is known to have it effect on cells by reacting with one of four receptor proteins (EP1–EP4) on the surface of cells, including the surfaces of bone marrow stem cells, cartilage cells and bone-producing cells (osteoblasts). Human cells send and receive signals that switch on life processes through workhorse proteins called receptors that enable messages to penetrate cells.

Prior work in other labs had established that the ability of PGE2 to create new bone growth occurs in particular through its interaction with the EP4 receptor. In the current study, the team showed that delayed fracture healing observed in aged mice could be rescued with local delivery of an experimental drug, CP-734432, which directly activates the EP4 receptor in place of the missing COX-2 (an EP4 agonist). The drug, provided to the team by Pfizer Inc., was also recently used to prevent osteoporosis in early animal studies. Local injection of an EP4 agonist to the fracture site of aged mice compensated for the reduced fracture repair observed with aging, with a significant reduction in immature cartilage seen and more efficient formation of mature bone.

Along with O'Keefe, the study effort was led by Amish Naik, Chao Xie, Michael Zuscik, Edward Schwarz, Hani Awad, J. Edward Puzas, Brendan Boyce and Xinping Zhang within the Center for Musculoskeletal Research, as well as by Paul Kingsley within the Department of Pediatrics, at the Medical Center. Major contributions were also made by Hichim Drissi within the Department of Orthopaedics at the University of Connecticut School of Medicine and Robert Guldberg from the Institute for Bioengineering and Bioscience at Georgia Institute of Technology. The study was funded by Public Health Service and the Howard Hughes Medical Institute.

Scripps Florida scientists find novel use for old compound in cancer treatment

Once-discarded drug proves effective in pediatric neuroblastoma models

The compound, α-difluoromethylornithine or DFMO, targets the activity of a specific enzyme and, even in very limited doses, is effective in protecting against the malignancy in animal models.

The study was published in the January 15, 2009 issue of the journal, Cancer Research (Volume 69, Issue 2).

"The drug, which was developed as a cancer therapy and later shelved because of toxicity concerns, has been around since the 1970s," said John Cleveland, Ph.D., chair of the Scripps Florida Department of Cancer Biology whose laboratory conducted the study. "But over the past five years, it has undergone a rebirth as a chemoprevention agent, first showing efficacy in animal models of human cancer and more recently in human prostate and colon cancer. Our study shows that it likely works in a large cast of tumors, even those having poor prognosis, like high-risk neuroblastoma."

Neuroblastoma is a childhood malignancy of the sympathetic nervous system (part of the nervous system that serves to accelerate the heart rate, constrict blood vessels, and raise blood pressure) that accounts for nearly eight percent of all childhood cancers and 15 percent of pediatric cancer-related deaths. Its solid tumors arise from developing nerve cells, most commonly in the adrenal gland, but also in the abdomen, neck, and chest. Neuroblastoma usually occurs in infants and young children, appearing twice as frequently during the first year of life than in the second. Tragically, children with stage IV, high-risk neuroblastoma have a less than a 40 percent chance of long-term survival.

The best-known genetic alteration involved in neuroblastoma is the amplification of the proto-oncogene—a molecule that when overexpressed can cause cancer - called MYCN. Amplification of MYCN occurs in about 20 percent of all neuroblastoma and is associated with the high-risk form of the disease. Targeting this and

related genes directly might be therapeutically tempting, the study noted, but highly problematic because the oncoproteins they produce are also required for the growth of most normal cell types.

As a result, Cleveland and colleagues focused on inhibiting ornithine decarboxylase (Odc), a protein that contributes to cancer cell growth and that is a target of the proto-oncogene MYCN. Increased levels of Odc are common in cancer, and forced Odc expression in animal models has been shown to lead to increased tumor incidence. Recent findings have shown that Odc overexpression is also an indication of poor prognosis in neuroblastoma. DFMO, the drug used by the Cleveland team, inhibits the activity of Odc.

To test the effect of DFMO on preventing neuroblastoma, the study used a transgenic mouse that faithfully models many of the hallmarks of MYCN-amplified neuroblastoma in humans.

"We were able to prevent neuroblastoma caused by MYCN, delaying the onset and incidence of this tumor type" said Cleveland. "What's even more compelling, we used low doses of the drug, and DFMO only had to be given for a moderate amount of time to prevent cancer." While DFMO selectively impaired the proliferation of MYCN-amplified neuroblastoma, it had no appreciable effect on non-MYCN-amplified neuroblastoma cell lines, indicating that the growth of the former is "addicted" to Odc.

"Our study offers a strong suggestion to the clinical cancer community that they should keep an open mind about the Odc-polyamine pathway, and that this particular pathway might represent a novel therapeutic angle to tackle this malignancy." Cleveland said. "While there are valid safety concerns about giving DFMO to pediatric patients suffering from advanced stage MYCN-amplified neuroblastoma, it may be time to revisit the issue as our study showed that transient treatment with DFMO is sufficient to provide chemoprevention and may show benefit for this otherwise lethal malignancy."

The first author of the study, "Targeting Ornithine Decarboxylase Impairs Development of Q2 MYCN-Amplified Neuroblastoma," is Robert J. Rounbehler of The Scripps Research Institute. In addition to Cleveland, other authors of the study are Weimin Li, Mark A. Hall, Chunying Yang, and Mohammad Fallahi at Scripps Florida. The study was supported by the National Institutes of Health and the State of Florida.

New family of antibacterial agents uncovered

Appearing in the Jan. 16, 2009, issue of JBC

As bacteria resistant to commonly used antibiotics continue to increase in number, scientists keep searching for new sources of drugs. In this week's JBC, one potential new bactericide has been found in the tiny freshwater animal Hydra.

The protein identified by Joachim Grötzinger, Thomas Bosch and colleagues at the University of Kiel, hydramacin-1, is unusual (and also clinically valuable) as it shares virtually no similarity with any other known antibacterial proteins except for two antimicrobials found in another ancient animal, the leech.
Hydramacin proved to be extremely effective though; in a series of laboratory experiments, this protein could kill a wide range of both Gram-positive and Gram-negative bacteria, including clinically-isolated drug-resistant strains like Klebsiella oxytoca (a common cause of nosocomial infections). Hydramacin works by sticking to the bacterial surface, promoting the clumping of nearby bacteria, then disrupting the bacterial membrane.

Grötzinger and his team also determined the 3-D shape of hydramacin-1, which revealed that it most closely resembled a superfamily of proteins found in scorpion venom; within this large group, they propose that hydramacin and the two leech proteins are members of a newly designated family called the macins.

"Hydramacin-1, Structure and Antibacterial Activity of a Protein from the Basal Metazoan Hydra" by Sascha Jung, Andrew J. Dingley, René Augustin, Friederike Anton-Erxleben, Mareike Stanisak, Christoph Gelhaus, Thomas Gutsmann, Malte U. Hammer, Rainer Podschun, Alexandre M. J. J. Bonvin, Matthias Leippe, Thomas C. G. Bosch, and Joachim Grötzinger
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Seasonal variation in blood pressure

A French study reported in the 12th January issue of Archives of Internal Medicine has found a strong correlation between blood pressure and outdoor temperature in a large sample of the elderly.(1) As a result, the investigators advise that, during periods of extreme temperatures, careful monitoring of blood pressure and antihypertensive treatment "could contribute to reducing the consequences of blood pressure variations in the elderly".

The study, which monitored 8801 participants over the age of 65 in the French Three-City study, found that systolic and diastolic blood pressure values differed significantly across the four seasons of the year and according to the distribution of outdoor temperature. The higher the temperature, the greater the decrease in blood pressure. Systolic blood pressure, for example, decreased with increasing temperature, with an 8.0 mmHg decrease between the lowest (< 7.9°C) and the highest (21.2°C) temperatures. Average systolic blood pressure was 5 mmHg higher in winter than in summer. High blood pressure, defined as a systolic blood pressure of 160

mmHg or higher, or a diastolic blood pressure of 95 mmHg or higher, was detected in 33.4 per cent of participants during winter and 23.8 percent during summer. These changes in blood pressure were greater in subjects 80 years or older than in younger participants.

Participants' blood pressure was measured at the beginning of the study (starting in 1999) and again about two years later. Outdoor temperatures on the day of measurement were obtained from local meteorological offices. Participants in the Three-City study were from Bordeaux, Dijon and Montpellier.

"Although our study does not demonstrate a causal link between blood pressure and external temperature, the observed relationship nevertheless has potentially important consequences for blood pressure management in the elderly," the authors state. "Because the risk of stroke or aneurysmal rupture is highest in the elderly, improved protection against these diseases by close monitoring of blood pressure and antihypertensive medication when outdoor temperature is very low could be considered."

Speaking on behalf of the European Society of Cardiology (ESC), Professor Frank Ruschitzka from the University Hospital, Zurich, says that the study reaffirms the place of the elderly as a target group for blood pressure monitoring. "The elderly, especially the increasing number of octogenarians, should not be neglected. They need extra care, and will benefit from monitoring and appropriate treatment. This study emphasises the need for year-round vigilance."

One possible explanation for the study findings, adds Professor Ruschitzka, lies in the emerging link between vitamin D and blood pressure. The elderly, especially those in care homes, are subject to vitamin D deficiency, largely as a result of their limited exposure to sunlight, and vitamin D deficiency can predispose to hyptertension via activation of the renin-angiotensin-aldosterone system. "The benefit of sunlight on vitamin D levels in the elderly is under appreciated," says Professor Ruschitzka. "Fifteen minutes exposure to sunlight can produce the equivalent of 2000 international units vitamin D."

A report from the Framingham Heart Study published in 2008 found that moderate vitamin D deficiency nearly doubles the risk of myocardial infarction, stroke and heart failure over a mean of 5.4 years in patients with high blood pressure.(2) The Nurses Health Study, also reporting in 2008, found that lower blood levels of vitamin D are independently associated with an increased risk of hypertension; women with the lowest levels had a 66 per cent higher incidence of hypertension than those with the highest levels.(3)

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2. Wang TJ, Pencina MJ, Booth SL, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation 2008; 117: 503-511.

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Free Antibiotics: The Wrong Prescription for Cold and Flu Season

Free Flu Shots Are a Better Option

With an epidemic of antibiotic-resistant infections growing, experts are warning grocery-store pharmacies that antibiotics giveaways are an unhealthy promotional gimmick. If grocery stores want to help customers and save them money during cold and flu season, the Infectious Diseases Society of America (IDSA) says, they should offer free influenza vaccinations instead.

Giant, Stop & Shop, and other grocery stores have recently begun offering free antibiotics at their pharmacies. Most concerning are promotions such as Wegmans' that link antibiotics to the winter cold-and-flu season - despite the fact that antibiotics will have no effect on these viral illnesses and carry risks of serious side effects.

"While it may make good marketing sense, promoting antibiotics at a time when we are facing a crisis of antibiotic resistance does not make good public health sense," said IDSA President Anne Gershon, MD. "On the other hand, grocery stores would be doing a tremendous service if they help more people get their flu shots."

A new study in the February 1 issue of Clinical Infectious Diseases shows that workers age 50-64 who received influenza vaccine lost substantially fewer days of work and worked fewer days while ill. But influenza vaccine is underutilized. Millions of doses were thrown away at the end of the last two flu seasons.

"The opposite is true for antibiotics," said Lauri Hicks, DO, medical director for the "Get Smart: Know When Antibiotics Work" program at the Centers for Disease Control and Prevention (CDC). "Each year tens of millions of antibiotics are prescribed for viral conditions, like the common cold, for which antibiotics are totally ineffective. Overuse of antibiotics is jeopardizing the effectiveness of these essential drugs."

For example, in some parts of the country methicillin-resistant Staphylococcus aureus (MRSA) is the leading cause of emergency room visits for skin and soft tissue infections. To make matters worse, there are very few new antibiotics under development to fight resistant bacteria.

In addition, the risks associated with antibiotics are under-appreciated. Allergic reactions and other adverse events cause an estimated 142,000 emergency room visits annually, according to a recent study by CDC.

"Most doctors know better than to prescribe antibiotics when they are not needed," Dr. Gershon added. "But many find it hard to say 'no' to sick patients who think antibiotics will GetSmartSmallmake them feel better. We are concerned that these pharmacy marketing efforts will encourage patients to ask for antibiotics prescriptions."

IDSA urges grocery store pharmacies to partner with the CDC's "Get Smart" program. CDC and its partners educate the public and health care providers about when antibiotics will and won't work and the dangers of antibiotic resistance. For more information, see the Get Smart website.

"Lowering customers' health care costs is an admirable goal," Dr. Gershon said. "But singling out antibiotics for promotion when we are facing a crisis of antibiotic resistance is the wrong way to do it. On the other hand, free influenza vaccinations could make a real contribution to public health."

Record number of wooden tablets unearthed from Heijo Palace remains in Nara

Click here for the original Japanese story

NARA -- Tens of thousands of wooden tablets dating back to the Nara period (710-794), have been found within the remains of the Heijo Palace here, it has been learned.

It is expected to be the biggest single find of wooden tablets, or mokkan, in the remains of the palace, a survey by the Nara National Research Institute for Cultural Properties has indicated.

"They were in a place where important government offices were located, and there is a possibility that we will find important historical data," an institute representative said.

The previous largest find of mokkan within the palace remains was in 1966, when some 13,000 items were unearthed. The latest find is expected to far exceed that figure, and it will reportedly take several years to wash the tablets and read the writing on them.

A wooden tablet from the Nara Period, still virtually intact, is pictured at the excavation site within the remains of the Heijo Palace in Nara. **(Mainichi)**

The research institute uncovered a hole containing a large number of wooden tablets while excavating the site last spring. The hole measured about 10 meters from east to west and 7 meters from north to south, and was about 1 meter deep at its deepest point. It was the biggest waste disposal pit in the palace grounds.

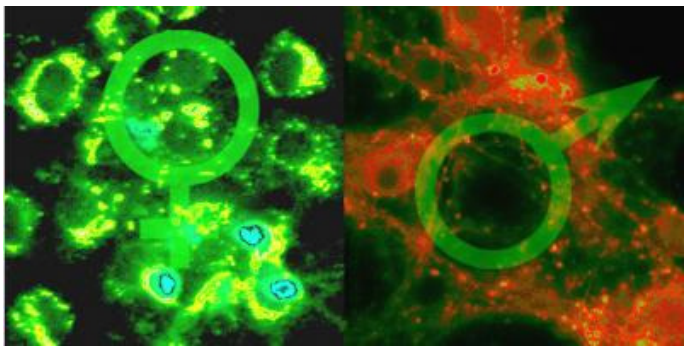
Most of the mokkan were in scraps, but investigations have uncovered writing relating to the imperial guard that protected the emperor, and the inscription "Hoki Period, Year 2," referring to the year 771. There is a possibility that the wooden tablets were discarded when military-related facilities were set up.

In 1989, around 74,000 wooden tablets, referred to as the Nijo Oji mokkan, were uncovered from a separate area of the Heijo capital, but to date the total number of wooden tablets found within the remains of the palace had stood at about 50,000.

Neurons show sex-dependent changes during starvation

Appearing in the Jan. 23, 2009, issue of JBCi

When it comes to keeping brains alive, it seems nature has deemed that females are more valuable then males. As reported in this weeks' JBC, researchers found that nutrient deprivation of neurons produced sex-dependent effects. Male neurons more readily withered up and died, while female neurons did their best to conserve energy and stay alive.



The idea that the sexes respond differently to nutrient depravation is not new, and revolves around the male preferences to conserve protein and female preferences to conserve fat. However, these metabolic differences have really only been examined in nutrient-rich tissues like muscles, fat deposits, and the liver.

After 24 hours of starvation, neurons from females (left panel) mobilize free fatty acids and form lipid droplets (bright green), keeping them alive. In contrast, neurons from males (right panel) begin eating themselves from the inside to break down proteins, presumably to use as fuel. **Robert S.B. Clark**

Robert Clark and colleagues at the Children's Hospital of Pittsburgh of University of Pittsburgh Medical Center examined whether this sex-dependent response in starvation could manifest in brain cells. They grew neurons taken separately from male and female rats or mice in lab dishes and subjected them to starvation over 72 hours.

After 24 hours, the male neurons experienced significantly more cell dysfunction (measured by analyzing cell respiration, which decreased by over 70% in male cells compared to 50% in female cells) and death. Visually, male neurons also displayed more abundant signs of autophagy, whereby a cell breaks down its components as a fuel source, while female neurons created more lipid droplets to store fat reserves.

As with other cell culture studies, the researchers note these results may not be truly indicative of what happens in living animals during starvation, but it allows them to look at the neurons independent of external factors like circulating hormones.

"Starving Neurons Show Sex Difference in Autophagy" by Lina Du, Robert W. Hickey, Hülya Bayır, Simon C. Watkins, Vladimir Tyurin, Fengli Guo, Patrick M. Kochanek, Larry W. Jenkins, Jin Ren, Greg Gibson, Charleen T. Chu, Valerian E. Kagan, and Robert S. B. Clark Article link: http://www.jbc.org/cgi/content/full/284/4/2383

Eyes reveal health secrets of the brain

*** 17 January 2009 by Duncan Graham-Rowe**

THE eyes may be the windows to the soul, but they also make pretty good peepholes into the brain. Thanks to an optical version of ultrasound, it is becoming possible to locate and monitor the growth of brain tumours, and to track neurodegenerative conditions like multiple sclerosis, Alzheimer's and Parkinson's disease - all by peering into the eye.

The brain is connected to each eye by an optic nerve, so any degeneration of the brain caused by such diseases can also damage cells along the nerve and in the retina, says Helen Danesh-Meyer, an eye surgeon and neuro-ophthalmologist at the University of Auckland Medical School in New Zealand. Indeed, a loss of visual function is one of the first symptoms in many people with a neurodegenerative condition.

Although evidence of a link between degeneration of the optic nerve and diseases such as Alzheimer's has been around since the late 1980s, without instruments capable of measuring the retinal changes accurately it is only recently that this knowledge could be put to use, says Danesh-Meyer.

The accuracy of ophthalmological tools has greatly improved in the last few years. Developments include a type of laser-camera technique called Heidelberg retina tomography (HRT), and a laser device called GDx, both of which can be used to scan the shape and thickness of optical nerve fibres at the back of the eye.

Both tools are now widely used to manage glaucoma, but in 2006 Danesh-Meyer became one of the first researchers to use them to study neurodegenerative diseases by looking at the region of the retina where ganglion cells meet to form the optic nerve - a region known as the optic nerve disc (OND). In a trial involving 40 Alzheimer's patients and 50 healthy volunteers, she was able to show that people with Alzheimer's had a distinctive enlargement to a cup-shaped part of their OND and a progressive thinning of the retinal nerve fibres within the disc.

Following this discovery, researchers have been using even more accurate instruments to track degenerative changes in the OND to monitor the progression of diseases like Alzheimer's, Parkinson's and MS. But it has been the emergence of optical coherence tomography (OCT) that appears most promising: it became commercially available in 2006 and is fast becoming a standard tool for the management of glaucoma and diabetic retinopathy. When applied to the OND, it produces highly detailed two and three-dimensional images of the subsurface retinal tissue, says Denise Valenti at Boston University, who has been using OCT to study Parkinson's and Alzheimer's.

The technique works very much like ultrasound, but bounces light off the tissue instead of sound waves. One beam of light is fired at the tissue and another at a reference mirror. When the reflected beams have travelled an identical distance, interference will make their combined beam brighter than if the distances are different. So by reflecting one beam off of different layers of tissue, and moving the reference mirror until the combined reflected beam is brightest, the technique can measure the depths of each section of tissue and build up a detailed image of its structure. It has proved particularly useful in ophthalmology because the semi-transparent nature of retinal tissue makes it possible for OCT to penetrate to greater depths - up to several millimetres. When applied to the OND it can give information about both the shape and thickness of retinal nerve fibres, allowing even subtle changes to be tracked.

Such changes can be used to monitor the progression of diseases non-invasively and relatively cheaply. Unlike MRI, which is expensive and can require patients to remain still for an hour or more, OCT is increasingly available in clinics and can be carried out in a few minutes. "It's extremely inexpensive compared to other tests," says Valenti.

One possibility is to use OCT to monitor the effectiveness of treatments for neurodegenerative diseases, says Danesh-Meyer: "These drugs can have a lot of side effects, so if they are not having a benefit then you won't want to continue with them."

Laura Balcer, a neurologist at the University of Pennsylvania School of Medicine in Philadelphia, has been using OCT on patients taking part in MS drug trials to try to establish if the system can accurately gauge drug efficacy. Such an objective tool would allow symptoms to be picked up that might otherwise go unreported, she says. For example, OCT has already shown that even in people with MS whose eye function is normal, there are marked differences in OND shape and fibre thickness compared with healthy people. "MS researchers are very excited about OCT," she says.

The technology is also proving its value as a tool for monitoring brain tumours, which can affect vision by pressing on the optic nerve. Such pressure will cause damage to different parts of the OND, depending on where in the brain the tumour is located, says Danesh-Meyer. What's more, the extent of the thinning of the nerve-disc fibre can also reveal whether vision will be restored upon removal of the tumour.

In the case of one patient who was 24 weeks pregnant following several IVF attempts, OCT monitoring allowed surgeons to hold off on removing her brain tumour until well into the third trimester, when the fetus had a better chance of survival. The usual treatment would have been to operate immediately to prevent permanent vision loss, but this would have risked inducing premature labour. By monitoring the compression on the optic nerve to ensure it did not reach the point at which permanent damage was inevitable, Danesh-Meyer was able to keep tabs on the tumour's growth and delay the surgery. As a result, the baby was born safely and the patient kept her vision.

The ultimate aim for many using OCT is to diagnose diseases before symptoms arise. The difficulty with this is that the thickness of retinal nerve fibres can vary from person to person, says Danesh-Meyer, so there is not always a clear baseline from which to compare patient scans.

Eventually though, the low cost and simplicity of the technology may make it feasible for people to be given an OCT scan of each eye at a young age, to give doctors a record of their healthy retinal nerve, says Danesh-Meyer. With regular screening, some neurological conditions could be spotted incredibly early. "We're really just at the cusp of knowing where this is all going."

Test Subjects Who Call the Scientist Mom or Dad

By PAM BELLUCK

Even before his son was born, Pawan Sinha saw unique potential.

At a birthing class, Dr. Sinha, a neuroscience professor at the Massachusetts Institute of Technology, stunned everyone, including his wife, by saying he was excited about the baby's birth "because I really want to study him and do experiments with him." He did, too, strapping a camera on baby Darius's head, recording what he looked at

Dr. Sinha is among a new crop of scientists using their children as research subjects.

Darius Sinha was an early participant in his father's research. **Courtesy of Pawan Sinha**

Other researchers have studied their own children in the past, but sophisticated technology allows modern-day scientists to collect new and more detailed data. The scientists also say that studying their children allows for more in-depth research and that the children make reliable participants in an era of scarce research financing.

"You need subjects, and they're hard to get," said Deborah Linebarger, a developmental psychologist who directs the Children's Media Lab at the University of Pennsylvania, who has involved her four children in her studies of the effect of media on children.

Arthur Toga, a neurology professor at the medical school at the University of California, Los Angeles, studying brain change, scanned his three children's brains using magnetic resonance imaging.

Stephen M. Camarata at the medical school at Vanderbilt, has involved all seven of his children in studies of learning problems and speech.

And Deb Roy, at M.I.T., embedded 11 video cameras and 14 microphones in ceilings throughout his house, recording 70 percent of his son's waking hours for his first three years, amassing 250,000 hours of tape for a language development study he calls the Human Speechome Project.

Some research methods are clearly benign; others, while not obviously dangerous, might not have fully understood effects. Ethicists said they would consider participation in some projects acceptable, even valuable,

but raised questions about the effect on the child, on the relationship with the parent, and on the objectivity of the researcher or the data.

"The role of the parent is to protect the child," said Robert M. Nelson, director of the Center for Research Integrity at Children's Hospital of Philadelphia. "Once that parent becomes an investigator, it sets up an immediate potential conflict of interest. And it potentially takes the parent-child relationship and distorts it in ways that are unpredictable."

Researchers themselves acknowledge the challenge of being simultaneously scientist and parent.

"I don't want them to feel uncomfortable, like I'm invading their privacy," said Dr. Linebarger, who ultimately set some boundaries. "When you mix being a researcher with being a parent, it can put your kids in an unfair place."

Children have been subjects for some well-known scientist-parents, including Jean Piaget, the child-development theorist. But some past examples would probably not pass ethical muster today.

Jonas Salk injected his children with his polio vaccine. Clarence Leuba, a psychologist, wondering if laughter in response to tickling was learned or innate, forbade tickling of his infant son and daughter, except when he tickled them, wearing a mask to hide his expression.

These days, scientists using human subjects are expected to seek approval from institutional review boards, which consider federal regulations on risk, coercion of subjects and researcher bias.

Some scientists said that in studies with multiple subjects they considered it unnecessary to report their child's participation, because they would face no greater risk than others. Some asserted that involving their children proved risks were minimal.

Dr. Toga said some nonscientists have said: "Why would a parent subject their kid to the dangers of M.R.I.? You should be ashamed of yourself."

His response: "All I'm doing is taking a picture. Nobody loves my kids more than me. Would I ever do something that would endanger them?"

Some researchers sign required parental consent forms, and some have spouses sign.

"I sign my own permission slips," said Gedeon Deak, whose three sons have participated in his cognitive science studies at University of California, San Diego. He tells review boards his subjects are a "sample of convenience," not randomly selected, but he has seen no need to specify that his sons are among the participants.

"If they're your kids and you want to ask them questions, you can," he said. "If you want to put your kid into a drug trial, that's different."

Michael Caligiuri, who oversees U.C.S.D.'s review boards, said researchers should disclose their child's role. He said panels might allow it but would probably require that investigators "can't be present" when their children participate and "can't view identifiable data" from their children.

Some scientists use their children only in pilot studies, not published ones, in case their child's performance skews the results.

Dr. Linebarger changed some of her procedures after her son Alec, at about age 5, answered a question by saying "his parents didn't listen to him and that sometimes he felt lonely," she recalled. "I was just floored," she said. "I sort of assumed that we have this wonderful son-mother relationship. I decided I needed to be more careful. I was worried I would be biasing anything I did."

Now, her husband handles forms, and staff members usually conduct the testing.

"We videotape and I look at it after, and sometimes I don't even like to do that," she said, because it is tempting to question them on their answers.

M.I.T.'s review board chairman, Leigh Firn, said that Dr. Roy's project did not raise concerns about risk since parents routinely videotaped children, but that its scale prompted questions about privacy — for his son, but also for visitors to his Arlington, Mass., home.

The board consulted an independent expert and urged safeguards. Cameras and microphones had to be easily turned off. Visitors signed consent forms. People can have their video segments erased — including his son, once he is 18. The expert recommended not videotaping toilet training, to avoid later embarrassment.

Dr. Roy has students who catalog recordings sign confidentiality agreements, and each handles only video or audio, in 15-minute, randomly ordered snippets. They are asked to report anything "potentially embarrassing," he said, but usually "when there's something juicy or controversial the recording is off, and if it isn't, good luck finding it." Plus, every room has an "oops button" to erase regretted utterances instantly.

Now, as he analyzes his son's vocabulary bursts, tracks how a single word progressed from "gaga" to "water," and studies interaction between his son and grown-ups, he said some scientists say: "My god, this is

such a valuable database. Why don't you share it more openly?" He said he had been denied a federal grant because he would not. Like Dr. Sinha, he is expanding the project to include other children, applying the research to autism.

Some researchers say scientist and parent roles sometimes intertwine.

"You put your kid in the scanner and you say please, please, please, let it be normal," Dr. Toga said.

Dr. Deak, who sometimes observes while students test his children, finds his investigator role "fighting with the natural thing of wanting your kid to get the answers right."

When one son, 4, answered questions about color and shape wearing an electrode-studded cap to measure brain waves, "I wasn't sure whether he'd be willing to put the cap on, whether he'd be willing to do the task," Dr. Deak said. He did, although "he needed more breaks than other kids. He wanted snacks."

And when Karen Dobkins, a U.C.S.D. psychology professor, enlisted her infant twins, Gabriel and Jacob, she said, "it was kind of painful, because one of my twin boys basically played the game really well, but my other son, we couldn't even use his data." She said that "made me worry that he had autism."

Her worries proved unfounded. Still, she said, "I took only the good data and copied it and put it in both of their baby books."

Some researchers say their children can become very practiced at taking tests, affecting their results.

At 18 months, Dr. Linebarger's daughter Callie was so blasé about research that she interrupted a study and said, "No questions, Mama," Dr. Linebarger recalled. "Later, when we were walking to get pizza and she was riding on my husband's shoulders," she said, "I tried to slip the questions in casually and she just looked at me with a smirk."

Some scientists' research stems from their children's experiences.

When his toddler, Claire, had inexplicable monthly fevers, Greg Licameli, an otolaryngologist at Children's Hospital Boston, had her tonsils removed (a colleague performed the surgery). The fevers stopped, and he began studying similar cases.

Dr. Camarata and his wife, Mary, devised research around their daughter Kathryn's habit of repeating word endings, their daughter Laura's verbal precociousness and their daughter Jane's reading trouble.

When his son Vincent had serious speech problems, he focused on language disorders.

Vincent, now 19 and in college, said he had "had a very good experience with my dad and his work. We'd go out and have lunch, go hiking, shoot skeet sometimes. It never felt like a drill, ever. It felt like fun."

Dr. Toga said research had allowed his children to "come to work with Dad," and get brain-scan printouts for show-and-tell. "They were so determined to please their father that they would lie still," he said.

His daughter Rebecca, now 18, said that at first, "it was kind of claustrophobic" in the noisy scanner, her head covered with a "cage kind of thing," her body tight in blankets. "The first time I kept talking because I was nervous, but then they just calmed me down and I got used to it," she said. By age 8 or 9, she fell asleep during a study.

Dr. Sinha's wife, Pam, although a scientist herself, did not rest easy.

She was "quite opposed to this idea of experimentation" on their son, Dr. Sinha said, so "it had to be done surreptitiously, whenever she would go out or when I would take him out in his little BabyBjorn."

It is still, he said, "a sore topic between us."

Medicine in the Ancient World

by Sarah Yeomans

Life in the ancient world was risky business. The perils of war, disease, famine and childbirth are a just a few examples of circumstances that contributed to a much lower average lifespan in the ancient world than we have in the modern era. People in antiquity were no less concerned about the prevention and cure of maladies than they are now, however, and entire cults, sanctuaries and professions dedicated to health dotted the spiritual, physical and professional landscapes of the ancient world. So what exactly did ancient cultures do to combat disease and injury, and did these methods have any real basis in science as we know it today? The answers may surprise you.

In many societies, the gods played an integral role in human health. In the Greek world, the god Asklepios was dedicated exclusively to healing.[a] Sanctuaries called *Asklepions* drew the ill and injured, who would often travel for days to seek the healing that they believed these ancient sanitariums could provide. Similar in some ways to the modern spa, Asklepions provided baths, healthy foods and sanctuary rooms intended specifically for sleep and meditation Most Asklepions were located in remote and beautiful areas, such as the famous sanctuaries of Epidauros in Greece and Pergamum in northwest Turkey. Animal

sacrifices and votive offerings were made at altars and temples to the god. Excavations at Asklepions have uncovered "anatomical votives," so named because they represent the body part that was injured or affected by illness.

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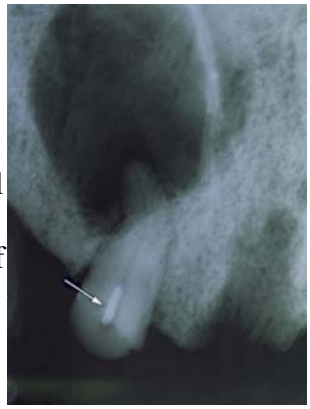
By the fifth century B.C., physicians and the god of healing had become intrinsically linked, with Asklepios as the divine patron of the medical profession. Hippocrates, the most famous physician of antiquity, lived during this time, and medical treatises that he authored would be used as medical textbooks for centuries to come. From such writings, as well as other inscriptions, we see that ancient physicians knew that lancing, draining and cleaning infected wounds promoted healing, and that they knew of certain herbs that had healing and disinfecting properties.[b] Wild ginger was known to be helpful for nausea, and a particular clay found on the Greek island of Lemnos was believed to be helpful for ailments such as dysentery. This clay, called *terra sigillata* for the stamped discs that were formed from it and sold as medicine, contains the counterpart to elements such as kaolin and bentonite, which are used in modern medicines to treat diarrhea.



Surgical techniques in the ancient world could be surprisingly advanced. The famous Roman physician Galen (c. 129–199 A.D.), who was born in the city of Pergamum near the Asklepion, is generally regarded as the most accomplished medical researcher of the Roman world, and some of his surgical procedures would not be seen again until modern times. He successfully conducted cataract surgeries by inserting a needle behind the lens of the eye in order to remove the cataract, and his described methods of preparing a clean operating theater reveal a keen awareness of contagion.[1] While some of Galen's practices and theories are still followed and praised by physicians today, others, such as his rejection of the stomach wall as having no role in digestion, have been proven by modern science to be erroneous.

By the seventh century A.D., medicine as a science that was relatively independent of religious restrictions had virtually disappeared in the west, as the use of cadavers for scientific dissection had been prohibited by the Church. However, Islamic scholars in the East were studying Greek medicine in depth.[c] Herbs such as henbane and Indian hemp (related to marijuana) were known for their anesthetic properties, and physicians stressed the effects of diet and environment on health. Perhaps one of the most famous eastern physicians was Abu 'Ali al-Husayn ibn 'Abd Allah ibn Sina (980–1037 A.D.), whose work *The Canon of Medicine* codified existing medical knowledge. *The Canon* includes descriptions, causes and diagnostic techniques for conditions such as rabies, stomach ulcers, different types of hepatitis, breast cancer, facial paralysis, diphtheria, leprosy, diabetes, cancer and gout. Later translations Latinized his name to Avicenna, and by the 13th century his work had become the standard medical reference text throughout Western Europe.

Archaeology has further illuminated medical practices in the ancient world. Certain skeletons discovered during excavations demonstrate evidence of rather astonishing surgical successes. Perhaps the most startling evidence of sophisticated ancient surgery can be found in skulls that show signs of trepanation, a procedure still used today that is performed by drilling a hole into the skull to relieve intracranial pressure. Trepanated skulls from ancient societies in Central and South America, Africa, Asia, Europe and the Near and Middle East have been found that perhaps date back as far as the Mesolithic period, about 12,000 years ago.[2] By examining the bone regrowth around the surgical hole in the skull, scientists are able to determine how long the patient survived after undergoing the procedure. Some patients died immediately, some lived only a few weeks, but others seem to have healed completely.

Excavations have also revealed evidence of sophisticated dental practices in antiquity. In a mass grave at Horvat en Ziq in the northern Negev desert of Israel, a skull dating to about 200 B.C. was found that contains one of the earliest known dental fillings. A 2.5-millimeter bronze wire had been inserted into the tooth's canal.[d] Elsewhere, skulls recovered from the catacombs in Rome, which were in use during the first through the fifth centuries A.D., exhibit some rather pricey dental work: Several were recovered that have gold fillings. Ironically, it is often the funerary monuments and graves of ancient doctors that attest to their care of the living. Tablets that decorated funerary altars of physicians often depicted the instruments of their profession—objects that look remarkably similar to instruments used by surgeons today. Scalpels, forceps, forked probes for examining wounds, needles for stitching wounds, small spoons for cleaning wounds and measuring medicines, catheters and even gynecological specula are all examples of instruments employed by the medical doctors of antiquity.

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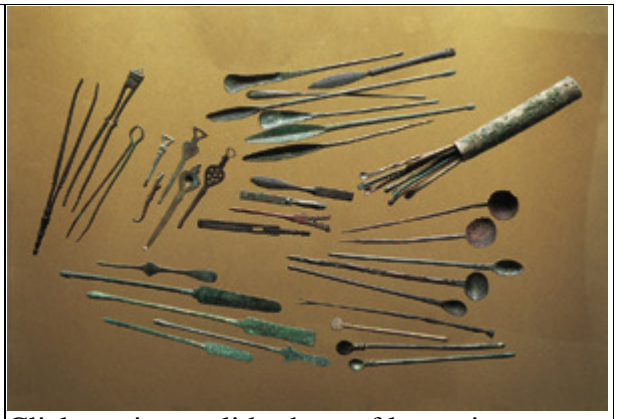

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Of course, calling on a higher power for assistance during a physical trial or illness was as common in the ancient world as it is today. Many modern hospitals have nondenominational worship spaces where people can pray and meditate; people in antiquity visited shrines and temples to do the same. Individuals preparing to undergo dangerous ordeals such as childbirth or battle would often invoke the protection of the divine. Even as medical science continues to evolve, the contemplation of mortality will likely continue to cause humans to look beyond the known for the explanations that even modern science cannot yet provide.

Notes

[a] Bronwen Wickkiser, "Asklepios Appears in a Dream," *Archaeology Odyssey*, July/August 2005.
[b] George B. Griffenhagen, "Origins: On the Pill," *Archaeology Odyssey*, May/June 2002.
[c] David W. Tschanz, "Origins: A Cure for the Common Cold?" *Archaeology Odyssey*, Summer 1998.
[d] Hector Avolos, "Ancient Medicine," *Bible Review*, June 1995.
[1] See Galen, *Galen on the Usefulness of the Parts of the Body*, trans. by Margaret Tallmadge May (Ithaca, NY: Cornell University Press, 1968) and A. Sorsby, *A. Modern Ophthalmology* (London: Butterworths, 1963).
[2] See S. Missios, "Hippocrates, Galen, and the Uses of Trepanation in the Ancient Classical World," *Neurosurgical Focus* 23(1):E11 (2007); P. Marino and M. Gonzales-Portillo," Preconquest Peruvian Neurosurgeons: A Study of Inca and Pre-Columbian Trephination and the Art of Medicine in Ancient Peru" *Neurology* 47:4, (2000), pp. 940–955.