Inexpensive hypertension drug could be multiple sclerosis treatment, Stanford study shows

STANFORD, Calif. - Turning serendipity into science, researchers at the Stanford University School of Medicine have found a link, in mice and in human brain tissue, between high blood pressure and multiple sclerosis. Their findings suggest that a safe, inexpensive drug already in wide use for high blood pressure may have therapeutic value in multiple sclerosis, as well.

While neurology professor Lawrence Steinman, MD, senior author of the new study, cautioned that extensive clinical trial work is needed to determine if the drug, known as lisinopril, can do in humans what it does in mice, he is excited that "we were able to show that all the targets for lisinopril are there and ready for therapeutic manipulation in the multiple-sclerosis lesions of human patients. Without that, this would be just another intriguing paper about what's possible in the mouse."

The paper will be published online Aug. 17 by the Proceedings of the National Academy of Sciences.

The genesis for the paper can be traced to about seven years ago, when Steinman learned he had high blood pressure. His doctor put him on lisinopril, which is used by millions of people all over the world and has an excellent safety profile. Chagrined, Steinman went home and, researcher that he is, immediately did a Google search on the drug. (Steinman is a renowned multiple sclerosis investigator whose earlier work on the inflammatory features of the disease spurred development of a blockbuster class of anti-inflammatory multiple-sclerosis therapeutics. The drug natalizumab, marketed under the trade name Tysabri, is one.)

Long ago, a glitch crept into Steinman's home computer: No matter what keywords he types into the search field, the computer automatically inserts the additional term, "multiple sclerosis." Thus, to his surprise, a list of medical literature popped up offering tantalizing, if vague, hints of a possible connection between multiple sclerosis and a fast-acting hormone, angiotensin, whose receptors abound on blood-vessel walls throughout the body.

In response to, say, a change in posture, angiotensin immediately causes blood vessels to constrict. "That raises your blood pressure so when you stand up to get out of a chair, you don't fall down and faint," said Steinman, who is also the George A. Zimmerman Professor in the medical school. But angiotensin overactivity causes chronic hypertension. Lisinopril controls blood pressure by blocking an enzyme that converts angiotensin's precursor into the active hormone. The drug also appears to have certain anti-inflammatory properties.

Multiple sclerosis is a chronic and occasionally lethal autoimmune disease in which the body's immune system mounts recurring assaults on the myelin sheathing of nerve cells in the brain. This causes nerves to malfunction and can lead to blindness and paralysis. Both multiple sclerosis and atherosclerosis involve inflammatory processes.

Eventually, Steinman and his colleagues decided to test the angiotensin/multiple-sclerosis relationship using modern scientific techniques. First, they examined the multiple-sclerosis lesions of brain samples from autopsied patients. In those lesions, well-established molecular-detection methods turned up significantly elevated levels of both the angiotensin receptor and the angiotensin-producing enzyme blocked by lisinopril.

Next, the investigators turned to an equally well-established animal model: a laboratory-bred strain of mouse that, after being immunized with a particular chemical, develops brain lesions very similar to those observed in multiple sclerosis. When, before immunization with the disease-triggering chemical, mice got lisinopril dosages equivalent to those prescribed for humans with high blood pressure, they didn't develop the paralysis characteristic of disease progression. Strikingly, if it was given after the mice developed full-blown symptoms, lisinopril reversed their paralysis.

The team also found that lisinopril administration reduced numerous molecular measures of inflammation that accompany multiple sclerosis in humans and its analog in the animal model. But, importantly, the drug didn't inhibit the mice's overall immune competence.

An additional observation was that lisinopril administration triggered proliferation of an important class of immune cells, called regulatory T cells, that prevent autoimmune diseases by dialing down the activity of other immune cells erroneously targeting cells and tissues that should be left alone. It's likely, Steinman said, that this proliferation was a key component in the protection provided by the drug, as an infusion of regulatory T cells from mice that had been given lisinopril was sufficient to prevent or reverse the disease process in mice that had been given none.

Steinman's results have major public-health implications, said Marc Feldmann, an Imperial College London immunologist who is familiar with the study but did not participate in it. He noted that the current therapies for multiple sclerosis (including Tysabri) are pricey monoclonal antibodies, costing tens of thousands of dollars annually for each patient treated. "If multiple-sclerosis patients can be treated with lisinopril at something like 1

percent of the price of treatment with Tysabri, then far more patients will receive adequate therapy, at a substantially lower cost to those paying for it," Feldmann said.

First authorship of the paper is shared by two postdoctoral researchers in Steinman's lab: Michael Platten, MD, and Sawsan Youssef, PhD. (Platten is now a neurology professor at University Hospital of Heidelberg, in Germany.) Other Stanford co-authors include May Han, MD, acting assistant professor of neurology and neurological sciences, and Raymond Sobel, MD, professor of pathology.

The study was financed by the National Institutes of Health, the National MS Society, the Phil N. Allen Trust, the German Research Foundation, the Helmholtz Association, the U.S. Public Health Service and the Biomedical Sciences Exchange Program.

MIT study: Heavier rainstorms ahead

Analysis shows climate change to yield more extreme rainfall

CAMBRIDGE, Mass. - Heavier rainstorms lie in our future. That's the clear conclusion of a new MIT and Caltech study on the impact that global climate change will have on precipitation patterns.

But the increase in extreme downpours is not uniformly spread around the world, the analysis shows. While the pattern is clear and consistent outside of the tropics, climate models give conflicting results within the tropics and more research will be needed to determine the likely outcomes in tropical regions.

Overall, previous studies have shown that average annual precipitation will increase in both the deep tropics and in temperate zones, but will decrease in the subtropics. However, it's important to know how the frequency and magnitude of extreme precipitation events will be affected, as these heavy downpours can lead to increased flooding and soil erosion.

It is the frequency of these extreme events that was the subject of this new research, which will appear online in the Proceedings of the National Academy of Sciences during the week of Aug. 17. The report was written by Paul O'Gorman, assistant professor in the Department of Earth, Atmospheric and Planetary Sciences at MIT, and Tapio Schneider, professor of environmental science and engineering at Caltech.

Model simulations used in the study suggest that precipitation in extreme events will go up by about 6 percent for every one degree Celsius increase in temperature. Separate projections published earlier this year by MIT's Joint Program on the Science and Policy of Global Change indicate that without rapid and massive policy changes, there is a median probability of global surface warming of 5.2 degrees Celsius by 2100, with a 90 percent probability range of 3.5 to 7.4 degrees.

Specialists in the field called the new report by O'Gorman and Schneider a significant advance. Richard Allan, a senior research fellow at the Environmental Systems Science Centre at Reading University in Britain, says, "O'Gorman's analysis is an important step in understanding the physical basis for future increases in the most intense rainfall projected by climate models." He adds, however, that "more work is required in reconciling these simulations with observed changes in extreme rainfall events." The basic underlying reason for the projected increase in precipitation is that warmer air can hold more water vapor. So as the climate heats up, "there will be more vapor in the atmosphere, which will lead to an increase in precipitation extremes," O'Gorman says.

However, contrary to what might be expected, extremes events do not increase at the same rate as the moisture capacity of the atmosphere. The extremes do go up, but not by as much as the total water vapor, he says. That is because water condenses out as rising air cools, but the rate of cooling for the rising air is less in a warmer climate, and this moderates the increase in precipitation, he says.

The reason the climate models are less consistent about what will happen to precipitation extremes in the tropics, O'Gorman explains, is that typical weather systems there fall below the size limitations of the models. While high and low pressure areas in temperate zones may span 1,000 kilometers, typical storm circulations in the tropics are too small for models to account for directly. To address that problem, O'Gorman and others are trying to run much smaller-scale, higher-resolution models for tropical areas.

Photos of cake can keep you slim, say psychologists

* 11:49 17 August 2009 **by Laura McGuinness**

Picture a thick wedge of rich, velvety Black Forest gateau. Hungry? Unlikely as it sounds, showing weight-conscious women pictures of sweet treats actually strengthens their resolve to eat healthily, rather than encouraging them to cheat.

Advertisers clearly believe images of tasty morsels persuade people to buy but psychologist Floor Kroese of Utrecht University in the Netherlands speculated that temptation might in fact heighten self-control.

To test out this theory, Kroese and her colleagues asked 54 female students to look at a picture of either a slice of chocolate cake or a flower under the guise of a memory test. The researchers then questioned the students about any plans to eat more healthily and offered them a choice between a chocolate or oatmeal cookie.

Women shown the cake picture gave a higher priority to their healthy eating intentions than their counterparts shown the flower. They were also significantly more likely to pick the oatmeal cookie – which earlier tests showed was generally perceived as the healthier option.

Let them look at cake

"Food temptations do not always trigger indulgence," says Kroese. "It seems that seeing a food temptation reminded people of their goal to watch their weight, and helped them act accordingly."

Previous studies suggested that smelling palatable, unhealthy foods makes people rate healthy eating as highly important, but this is the first research to look at how unhealthy food affects snacking behaviour.

Ayelet Fishbach of the Booth School of Business at the University of Chicago agrees with Kroese's conclusion. "In moderation, this positive impact of food temptations will overcome the negative impact – the urge to indulge," she says.

Kroese suggests that sticking pictures of tempting foods on the fridge door may help to bring weight-watching goals to mind. But she cautions that the results can only be applied to women wanting to lose weight: it is unclear whether they would hold in the general population.

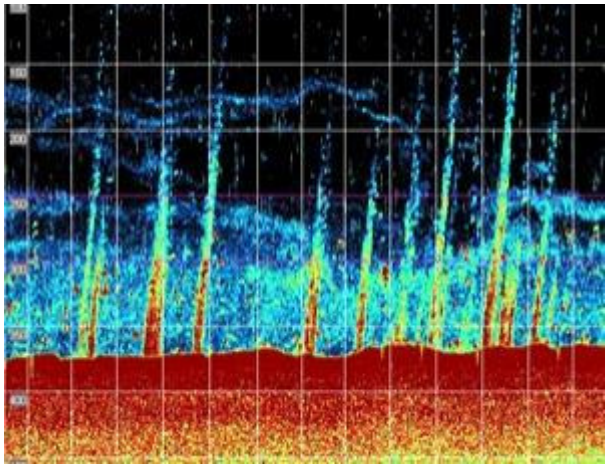
Her team is now looking into varying the strength of a temptation. Early findings suggest that while very tempting images seem to remind people of their weight-loss goals, weakly attractive images do not prompt the same mechanism to kick in. "Interestingly, this might mean that weak temptations could then be more dangerous," she says. *Journal reference: Appetite, DOI: 10.1016/j.appet.2009.08.002*

As Arctic Ocean warms, megatonnes of methane bubble up

*** 17:02 17 August 2009 by Michael Marshall**

It's been predicted for years, and now it's happening. Deep in the Arctic Ocean, water warmed by climate change is forcing the release of methane from beneath the sea floor.

Over 250 plumes of gas have been discovered bubbling up from the sea floor to the west of the Svalbard archipelago, which lies north of Norway. The bubbles are mostly methane, which is a greenhouse gas much more powerful than carbon dioxide.



Sonar image of methane plumes rising from the Arctic Ocean floor **(Image: National Oceanography Centre, Southampton)**

The methane is probably coming from reserves of methane hydrate beneath the sea bed. These hydrates, also known as clathrates, are water ice with methane molecules embedded in them.

The methane plumes were discovered by an expedition aboard the research ship James Clark Ross, led by Graham Westbrook of the University of Birmingham and Tim Minshull of the National Oceanography Centre, Southampton, both in the UK.

Warm gas

The region where the team found the plumes is being warmed by the West Spitsbergen current, which has warmed by 1 °C over the past 30 years.

"Hydrates are stable only within a particular range of temperatures," says Minshull. "So if the ocean warms, some of the hydrates will break down and release their methane."

None of the plumes the team saw reached the surface, so the methane was not escaping into the atmosphere and thus contributing to climate change – not in that area, at least. "Bigger bubbles of methane make it all the way to the top, but smaller ones dissolve," says Minshull.

Just because it fails to reach the surface doesn't mean the methane is harmless, though, as some of it gets converted to carbon dioxide. The CO2 then dissolves in seawater and makes the oceans more acidic.

And it is possible that other, more vigorous plumes are releasing methane into the atmosphere. The team studied only one group of plumes, which were in a small area and were erratic.

"Almost none of the Arctic has been surveyed in a way that might detect a gas release like this," Minshull says.

Methane megatonnes

Ronald Cohen of the Carnegie Institution for Science in Washington DC says it's a striking result: "What's amazing is that they see such enormous quantities of methane."

The methane being released from hydrate in the 600-square-kilometre area studied probably adds up to 27 kilotonnes a year, which suggests that the entire hydrate deposit around Svalbard could be releasing 20 megatonnes a year.

If methane began escaping at similar rates throughout the Arctic, it would dramatically increase methane levels in the atmosphere.

Globally, it's thought that around 500 to 600 megatonnes of methane are released into the atmosphere each year.

Matt Rigby of the Massachusetts Institute of Technology says, "If there is potential for clathrates to destabilise and release methane, it needs to be intensively studied."

Gas from where?

Cohen cautions that the Arctic methane may not be from hydrate, but could be coming from the methane's primary source, which might be deep within the Earth.

If that was the case, the warming of the West Spitsbergen current may not be to blame.

He says that the large amounts of methane being released make this unlikely, however: "If the methane is all primary, it would be an unprecedented amount." So the idea that the hydrates are at least partly to blame is more plausible. "It's not definitively proven, but it's certainly reasonable," he says.

Methane hydrate could be used as a new, somewhat greener fossil fuel, but extracting the methane without releasing any into the atmosphere remains a challenge.

Journal reference: Geophysical Research Letters, DOI: 10.1029/2009GL039191

Children with headache

Family quarrels and a lack of free time can promote headaches in children. This is what Jennifer Gassmann and her coauthors concluded in their study on risk factors, which appears in the current issue of the Deutsches Ärzteblatt International (Dtsch Arztebl Int 2009; 106[31-32]: 509-16).

This investigation was a component of a large-scale study entitled "Children, Adolescents, and Headache" (Kinder, Jugendliche und Kopfschmerz - KiJuKo), in which data were collected in four annual "waves" from 2003 to 2006. Out of a multitude of variables tested in the larger study, the authors chose to look at the ones that concerned the children's family and leisure time. Up to 30% of all children around the world complain of headache symptoms arising at least once per week.

Boys who experienced more than one family quarrel per week had a 1.8 times higher risk of developing headaches. The amount of free time available to them seemed to be even more important: boys who only sometimes had time to themselves had a 2.1 times higher risk of developing headaches.

Parents' behavior when their child complains of headache also seemed to play a major role. Either positive or negative reinforcement from the parents teaches the child that he or she can gain certain advantages from headache symptoms. The parents' responses had a particularly strong effect on the frequency of symptoms in girls: reinforcing parental responses raised their risk of recurrent headaches by 25%.

The sexes also differed with respect to the frequency of headache. Twice as many girls as boys had their symptoms at least once a week. The children's age, however, seemed to have no more than a minor effect on headache manifestations. ***http://www.aerzteblatt.de/v4/archiv/pdf.asp?id=65550***

Faster, cheaper way to find disease genes in human genome passes initial test

Method makes it feasible to search for disease genes in unrelated people with same condition

University of Washington (UW) researchers have successfully developed a novel genome-analysis strategy for more rapid, lower cost discovery of possible gene-disease links. By saving time and lowering expenses, the approach makes it feasible for scientists to search for disease-causing genes in people with the same inherited disorder but without any family ties to each other.

The strategy also might be extended to common medical conditions with complex genetics by making it more cost-effective and efficient to study the genomes of large groups of people.

Such large-scale research hasn't been undertaken because it has been prohibitively expensive, cumbersome, and time-consuming to sequence, compare and interpret entire human genomes.

The study, published today in Nature by lead author Sarah B. Ng, a graduate student in the UW Department of Genome Sciences, was conducted as a proof-of-concept to see if a more targeted analysis and newer technology could identify candidate genes for Mendelian disorders. These are diseases like cystic fibrosis or sickle cell anemia that are caused by a mutation in a single gene and are passed along through generations in a simple inheritance pattern. In this study, the rare Mendelian disorder picked to evaluate the strategy in unrelated, affected individuals was Freeman-Sheldon syndrome.

The study's senior author is Jay Shendure, UW assistant professor of genome sciences. In addition to the Shendure lab, the UW labs of Deborah Nickerson, Genome Sciences; Michael Bamshad, Pediatrics; and Evan Eichler, Genome Sciences, played key roles in the collaborative study.

To make progress in disease genetics, new strategies such as this are vital. Shendure gave an example: "The genetics of thousands of rare diseases remains unsolved because sufficient numbers of families with individuals

affected by those disorders are not easily available. Even with such families, mapping and identifying the causative gene can take many years."

From attempts to determine the genetics of cancer, diabetes, and heart disease, scientists now realize that common variations in the human genome account for only a small fraction of the risk of these common diseases. The new strategy allows researchers to investigate the contributions of rare variants and might be extended to larger population studies to untangle the complex genetics underlying the leading causes of death and disability.

Shendure explained the team's approach: "We decided to focus only on the 1 percent of the human genome which codes for proteins. This portion is called the exome. In other words, we determined the genetic variation in these areas, and ignored the rest. We used new technologies to capture these specific regions in the genomes of 12 people, 4 of whom were affected by the same Mendelian disorder. None of the subjects were relatives. We then decoded these selected parts of the genome through massively parallel DNA sequencing, a technology that allows one to sequence hundreds of millions of DNA fragments in parallel." Intersecting these data found that only a single gene, MYH3, contained novel mutations in the exomes of all four affected individuals.

The UW was one of three institutions, along with Harvard Medical School and the Broad Institute, funded in 2008 for The Exome Project by the National Heart, Lung and Blood Institute of the National Institutes of Health. The project aims at developing technologies to selectively sequence the human exome.

Shendure pointed out that a limitation of sequencing only exomes is that it doesn't reveal the regulatory, structural or other non-coding differences between human genomes.

Despite this limitation, genome-focused sequencing has several advantages: "Our focus on the protein-coding subset of the genome enables us do at least 20 times more samples than could be done with whole genome sequencing with equivalent effort," Shendure said. The data-gathering for this project started in November of 2008, and finished in February 2009. However, with the technical advances the researchers have achieved, a similar type of rare disease could be solved in a matter of weeks, and in the future even more rapidly.

As "second-generation" DNA sequencing technologies such as this expand in their use and overcome obstacles in the cost and time for collecting data, Shendure predicts different challenges will follow each step. For example, the amount of raw data that is collected by these sequencing instruments at the UW alone soon will be measured in petabytes. A petabyte is one quadrillion units of computer data, roughly the equivalent of 6 billion Web photos. New computational approaches for data analysis are a major part of the UW efforts, and they are expanding the new information that can be obtained with an exome-based approach.

"Massively parallel technologies that make it possible to study individual genomes have only recently emerged," Shendure said, "but hold significant promise for gaining new insights in human biology and medicine. This approach to human exome sequencing will be the key in scaling everyone's efforts to explore the genetics of both susceptibility and resistance to more complex human diseases such as heart disease, cancer, and infectious diseases."

In addition to Ng and Shendure, the research team for "Targeted Capture and Massively Parallel Sequencing of 12 Human Genomes" included Emily Turner, Peggy Robertson, Steven Flygare, Choli Lee, Tristan Shaffer, Michelle Wong, Evan Eichler, and Deborah Nickerson, all from UW Genome Sciences; Abigail Bigham and Michael Bamshad from UW Pediatrics, and Arindam Bhattacharjee from Agilent Technologies.

The research was supported by grants from the National Heart, Lung, and Blood Institute, the National Human Genome Research Institute, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, all part of the National Institutes of Health; the Washington Research Foundation, and the Agency for Science, Technology, and Research in Singapore.

Taking up music so you can hear

EVANSTON, Ill. - Anyone with an MP3 device - just about every man, woman and child on the planet today, it seems - has a notion of the majesty of music, of the primal place it holds in the human imagination.

But musical training should not be seen simply as stuff of the soul - a frill that has to go when school budgets dry up, according to a new Northwestern University study.

The study shows that musicians - trained to hear sounds embedded in a rich network of melodies and harmonies - are primed to understand speech in a noisy background, say in a restaurant, classroom or plane.

It is the first demonstration of musical training offsetting the deleterious effects of background noise, and the implications are provocative.

"The study points to a highly pragmatic side of music's magic," said Nina Kraus, Hugh Knowles Professor of Communication Sciences and Neurobiology and director of Northwestern's Auditory Neuroscience Laboratory, where the research was done.

The findings strongly support the potential therapeutic and rehabilitation use of musical training to address auditory processing and communication disorders throughout the life span.

Hearing speech in noise is difficult for everyone. But the difficulty is particularly acute for older adults, who are likely to have hearing and memory loss, and for poor readers who have normal hearing but whose nervous systems poorly transcribe sounds that ultimately are critical to good reading skills.

"Many older adults will say, 'I can hear what you're saying, but I don't understand you,'" Kraus said. "So they might have a little bit of a hearing loss, but often not enough to warrant the difficulty that a lot of older adults report."

Such populations could benefit from the reordering of the nervous system that occurs with musical training, according to the study. Because the brain changes with experience, musicians have better-tuned circuitry - the pitch, timing and spectral elements of sound are represented more strongly and with greater precision in their nervous systems.

"Musical training makes musicians really good at picking out melodies, the bass line, the sound of their own instruments from complex sounds," Kraus said. Now, for the first time, this study has confirmed that such fine tuning of the nervous system also makes musicians highly adept at translating speech in noise.

The finding has particular implications for hearing certain consonants which are vulnerable to misinterpretation by the brain and are a big problem for some poor readers in a noisy environment. The brain's unconscious faulty interpretation of sounds makes a big difference in how words ultimately will be read.

Thirty-one study participants, with normal hearing and a mean age of 23, were divided into one group with music experience and another without it. They had to listen to sentences presented in increasingly noisy conditions and repeat back what they heard.

Better perception in noise was linked with better working memory and tone discrimination ability. The results imply that musical training enhances the ability to hear speech in challenging listening environments by strengthening auditory memory and the representation of important acoustic features.

In one of the tests, for example, participants had to repeat back "The square peg will settle in the round hole." Such longer sentences that are syntactically correct but lack familiar cues measure working memory as well as the ability to distinguish sounds in noise.

The Auditory Neuroscience Lab at Northwestern has helped establish the relationship between sound encoding in the brain and linguistic abilities by showing that the very neural sound transcription processes that are deficient in children with dyslexia are enhanced in people with musical experience. Based on this collective work, poor readers may show greater benefits from training programs that include music as well as speech sounds.

By reinforcing the pervasive effects that musical experience has on sound-processing abilities, Kraus stressed, this study underscores the importance of music education being more accessible to the general population.

"Musician Enhancement for Speech-in-Noise" was published online in Ear and Hearing, the official journal of the American Auditory Society. The study's investigators are Alexandra Parbery-Clark, Erika Skoe, Carrie Lam and Nina Kraus. The National Science Foundation supported the study.

Researchers find genetic link between physical pain and social rejection

UCLA psychologists have determined for the first time that a gene linked with physical pain sensitivity is associated with social pain sensitivity as well.

Their study indicates that variation in the mu-opioid receptor gene (OPRM1), often associated with physical pain, is related to how much social pain a person feels in response to social rejection. People with a rare form of the gene are more sensitive to rejection and experience more brain evidence of distress in response to rejection than those with the more common form.

The research was published Aug. 14 in the early online edition of Proceedings of the National Academy of Sciences and will appear in the print version in the coming weeks.

The findings give weight to the common notion that rejection "hurts" by showing that a gene regulating the body's most potent painkillers - mu-opioids - is involved in socially painful experiences too, said study co-author Naomi Eisenberger, UCLA assistant professor of psychology and director of UCLA's Social and Affective Neuroscience Laboratory.

In the study, researchers collected saliva samples from 122 participants to assess which form of the OPRM1 gene they had and then measured sensitivity to rejection in two ways. First, participants completed a survey that measured their self-reported sensitivity to rejection. They were asked, for example, how much they agreed or disagreed with statements like "I am very sensitive to any signs that a person might not want to talk to me." Next, a subset of this group, 31 participants, was studied using functional magnetic resonance imaging (fMRI) at UCLA's Ahmanson–Lovelace Brain Mapping Center during a virtual ball-tossing game in which participants were ultimately socially excluded. Subjects were told that they would be connected over the Internet with two

other players who were also in fMRI scanners and that they would all be playing the interactive ball-tossing game. In reality, however, participants were playing with a preset computer program, not other people.

Initially, participants were included in the activity but were then excluded when the two other "players" stopped throwing the ball to them.

"What we found is that individuals with the rare form of the OPRM1 gene, who were shown in previous work to be more sensitive to physical pain, also reported higher levels of rejection sensitivity and showed greater activity in social pain–related regions of the brain - the dorsal anterior cingulate cortex and anterior insula - in response to being excluded," Eisenberger said.

The dorsal anterior cingulate cortex and anterior insula are brain regions often associated with the distress of physical pain. Previous research by Eisenberger and her colleagues has shown that these brain regions are also involved in the pain of social rejection.

"Although it has long been suggested that mu-opioids play a role in social pain - and there are convincing animal models that show this - this is the first human study to link this mu-opioid receptor gene with social sensitivity in response to rejection," Eisenberger said.

"These findings suggest that the feeling of being given the cold shoulder by a romantic interest or not being picked for a schoolyard game of basketball may arise from the same circuits that are quieted by morphine," said Baldwin Way, a UCLA postdoctoral scholar and the lead author on the paper.

Eisenberger argues that this overlap in the neurobiology of physical and social pain makes good sense.

"Because social connection is so important, feeling literally hurt by not having social connections may be an adaptive way to make sure we keep them," she said. "Over the course of evolution, the social attachment system, which ensures social connection, may have actually borrowed some of the mechanisms of the pain system to maintain social connections."

Shelley E. Taylor, UCLA distinguished professor of psychology, is also a co-author on the paper.

The research was funded by a National Institute of Mental Health (NIMH) postdoctoral fellowship, the National Institute on Aging, the NIMH and the Harry Frank Guggenheim Foundation.

Excessive exercise can be addicting, new study says

Animals that exercised excessively went into withdrawal when given a drug that blocks the action of heroin

WASHINGTON - Although exercise is good for your health, extreme exercise may be physically addicting. Rats given a drug that produces withdrawal in heroin addicts went into withdrawal after running excessively in exercise wheels, according to new research. Rats that ran the hardest had the most severe withdrawal symptoms.

The scientists who conducted the study reason that if excessive exercise is addicting, then maybe, to feel good, addicts could take moderate exercise instead of drugs. The findings also shed light on the potentially fatal eating disorder called anorexia athletica, in which exercise undertaken to shed pounds becomes as compulsive as taking drugs, resulting in even greater weight loss.

"Excessive running shares similarities with drug-taking behavior," the researchers wrote in the August issue of Behavioral Neuroscience, published by the American Psychological Association.

For those looking for an excuse to hit the couch, however, this study looked at excessive, not moderate, exercise. "As with food intake and other parts of life, moderation seems to be the key. Exercise, as long as it doesn't interfere with other aspects of one's life, is a good thing with respect to both physical and mental health," said lead author Robin Kanarek, PhD, of Tufts University.

For several weeks, 44 male and 40 female rats were allowed to either run in exercise wheels or remain inactive. To simulate anorexia athletica, the researchers divided the active and inactive rats into groups whose members were either given food for one hour a day or around the clock. Rats in all four groups were then given naloxone, a medicine for heroin overdose that produces immediate withdrawal symptoms.

Active and inactive rats responded very differently to naloxone, which was given in proportion to their weight. The active rats showed withdrawal symptoms like those seen in narcotics addicts: trembling, writhing, teeth chattering, and drooping eyelids.

The active rats who had access to food for only one hour a day both ran the most and displayed the most severe withdrawal symptoms. Like people with anorexia athletica, they ran so much that they lost significant amounts of weight. Additionally, the more a given rat had run, the worse its withdrawal symptoms after naloxone. In contrast, regardless of how much they ate, inactive rats responded very little to the drug.

Because of the way the active rats responded to naloxone, they seemed to have undergone the same changes in the brain's reward system as rats addicted to drugs. "Exercise, like drugs of abuse, leads to the release of neurotransmitters such as endorphins and dopamine, which are involved with a sense of reward," noted Kanarek.

Insights into behaviors that trigger the release of the brain's "reward" chemicals may lead to addiction treatments that incorporate moderate exercise, according to the researchers. The findings also suggest that active rats given limited food may make a good experimental model for studying and developing treatments for anorexia athletica, added Kanarek.

Because rats and humans share many nervous-system traits, researchers frequently carry laboratory findings like these out into the real world.

Article: "Running and Addiction: Precipitated Withdrawal in a Rat Model of Activity-Based Anorexia," Robin B. Kanarek, PhD, Kristen E. D'Anci, PhD, Nicole Jurdak, MS, and Wendy Foulds Mathes, PhD, Tufts University; Behavioral Neuroscience, Vol. 123, No. 4. (Full text of the article is available from the APA Public Affairs Office and at http://www.apa.org/journals/releases/bne1234905.pdf)

NASA Researchers Make First Discovery of Life's Building Block in Comet

NASA scientists have discovered glycine, a fundamental building block of life, in samples of comet Wild 2 returned by NASA's Stardust spacecraft.

"Glycine is an amino acid used by living organisms to make proteins, and this is the first time an amino acid has been found in a comet," said Dr. Jamie Elsila of NASA's Goddard Space Flight Center in Greenbelt, Md. "Our discovery supports the theory that some of life's ingredients formed in space and were delivered to Earth long ago by meteorite and comet impacts."

Elsila is the lead author of a paper on this research accepted for publication in the journal Meteoritics and Planetary Science. The research will be presented during the meeting of the American Chemical Society at the Marriott Metro Center in Washington, DC, August 16.

"The discovery of glycine in a comet supports the idea that the fundamental building blocks of life are prevalent in space, and strengthens the argument that life in the universe may be common rather than rare," said Dr. Carl Pilcher, Director of the NASA Astrobiology Institute which co-funded the research.

Proteins are the workhorse molecules of life, used in everything from structures like hair to enzymes, the catalysts that speed up or regulate chemical reactions. Just as the 26 letters of the alphabet are arranged in limitless combinations to make words, life uses 20 different amino acids in a huge variety of arrangements to build millions of different proteins.

Stardust passed through dense gas and dust surrounding the icy nucleus of Wild 2 (pronounced "Vilt-2") on January 2, 2004. As the spacecraft flew through this material, a special collection grid filled with aerogel – a novel sponge-like material that's more than 99 percent empty space – gently captured samples of the comet's gas and dust. The grid was stowed in a capsule which detached from the spacecraft and parachuted to Earth on January 15, 2006. Since then, scientists around the world have been busy analyzing the samples to learn the secrets of comet formation and our solar system's history.

"We actually analyzed aluminum foil from the sides of tiny chambers that hold the aerogel in the collection grid," said Elsila. "As gas molecules passed through the aerogel, some stuck to the foil. We spent two years testing and developing our equipment to make it accurate and sensitive enough to analyze such incredibly tiny samples."

Earlier, preliminary analysis in the Goddard labs detected glycine in both the foil and a sample of the aerogel. However, since glycine is used by terrestrial life, at first the team was unable to rule out contamination from sources on Earth. "It was possible that the glycine we found originated from handling or manufacture of the Stardust spacecraft itself," said Elsila. The new research used isotopic analysis of the foil to rule out that possibility.

Isotopes are versions of an element with different weights or masses; for example, the most common carbon atom, Carbon 12, has six protons and six neutrons in its center (nucleus). However, the Carbon 13 isotope is heavier because it has an extra neutron in its nucleus. A glycine molecule from space will tend to have more of the heavier Carbon 13 atoms in it than glycine that's from Earth. That is what the team found. "We discovered that the Stardust-returned glycine has an extraterrestrial carbon isotope signature, indicating that it originated on the comet," said Elsila.

The team includes Dr. Daniel Glavin and Dr. Jason Dworkin of NASA Goddard. "Based on the foil and aerogel results it is highly probable that the entire comet-exposed side of the Stardust sample collection grid is coated with glycine that formed in space," adds Glavin.

"The discovery of amino acids in the returned comet sample is very exciting and profound," said Stardust Principal Investigator Professor Donald E. Brownlee of the University of Washington, Seattle, Wash. "It is also a remarkable triumph that highlights the advancing capabilities of laboratory studies of primitive extraterrestrial materials."

The research was funded by the NASA Stardust Sample Analysis program and the NASA Astrobiology Institute. NASA's Jet Propulsion Laboratory, Pasadena, Calif., manages the Stardust mission for NASA's Science Mission Directorate, Washington. Lockheed Martin Space Systems, Denver, developed and operated the spacecraft.

To learn more about the mission, visit http://stardustnext.jpl.nasa.gov/ .

For more about the NASA Goddard astrobiology team, visit http://astrobiology.gsfc.nasa.gov/analytical .

Study shows how to boost value of Alzheimer's-fighting compounds

WEST LAFAYETTE, Ind. - The polyphenols found in red wine are thought to help prevent Alzheimer's disease, and new research from Purdue University and Mount Sinai School of Medicine has shown that some of those compounds in fact reach the brain.

Mario Ferruzzi, a Purdue associate professor of food science; Connie Weaver, Purdue's head of foods and nutrition; and Elsa Janle, a Purdue associate professor of foods and nutrition, found that the amount of polyphenols from grapeseed extract that can reach a rat's brain is as much as 200 percent higher on the 10th consecutive day of feeding as compared to the first. Many previous experiments, in which absorption was measured after single or sporadic doses, often found very little, if any, of the bioactive polyphenols reaching brain tissues. However, more chronic exposure appears to improve absorption.

"This shows that reasonable and chronic consumption of these products may be the way to go, rather than single, high doses, similar to drugs," said Ferruzzi, who collaborated on the research with Mount Sinai's Dr. Giulio Pasinetti. "It's like eating an apple a day, not a case of apples over two days every month."

A paper detailing the findings was published in the early online version of the September issue of the Journal of Alzheimer's Disease.

Polyphenols, compounds found in the skins and seeds of grapes, are thought to prevent the formation of beta-amyloid protein, which creates the plaque in the brain that causes Alzheimer's disease. Alzheimer's is a progressive brain disease that destroys memory and cognitive skills and affects as many as 4.5 million Americans, according to the National Institute on Aging.

Pasinetti, the Aidekman Family Professor in Neurology and director of the Center of Excellence for Novel Approaches to Neurotherapeutics, said discovering how polyphenols are absorbed and distributed to the brain can impact researchers' understanding of the amount of grape products or red wine a person would need to consume to most effectively combat Alzheimer's disease.

"The most important thing is that when we follow the repetitive administration of this compound, we were able to observe the transfer of the compound to the brain," Pasinetti said. "This may help us figure out the proper concentration necessary to get these chemicals to the brain."

Ferruzzi said the study dealt with polyphenols, but also could be important for determining proper doses of other compounds or drugs for patients. Testing of a pharmaceutical, for example, could show that the drug is too potent when given repetitively; whereas that might not be apparent if the drug is administered on non-consecutive days or weeks.

"It could become important in terms of side effects," Ferruzzi said. "You could be overdosing because the body is adapting and absorbing or metabolizing these compounds differently over time."

Pasinetti is the principal investigator for the Center of Excellence for Research and Complementary and Alternative Medicine in Alzheimer's Disease grant from the National Institutes of Health that funded the work. Ferruzzi said further studies will focus on the mechanisms that control absorption of compounds during chronic consumption. *Writer: Brian Wallheimer, 765-496-2050, bwallhei@purdue.edu*

ABSTRACT

Bioavailability of Gallic Acid and Catechins from Grape Seed Polyphenol Extract is Improved by Repeated Dosing in Rate: Implications for Treatment in Alzheimer's Disease

Mario G. Ferruzzi, Jessica K. Lobo, Elsa M. Janle, Naomi Whittaker, Bruce Cooper, James E. Simon, Qing-Li Wu, Cara Welch, Lap Ho, Connie Weaver and Giulio M. Pasinetti

The present study explored the bioavailability and brain deposition of a Grape Seed Polyphenolic Extract (GSPE) previously found to attenuate cognitive deterioration in a mouse model of Alzheimer's disease (AD). Plasma pharmacokinetic response of major GSPE phenolic components was measured following intragastric gavage of 50, 100 and 150 mg GSPE per kg BW. LC-MS analysis identified gallic acid (GA), catechin (C), epicatechin (EC) in plasma of rats gavaged acutely with GSPE. Additionally, 4-methylgallic acid (4-OMeGA), 3'-methylcatechin (3'-OMeC) and 3'-methylepicatechin (3'-OMeEC) were identified as circulating metabolites of GSPE phenolic constituents. Cmax for individual GSPE constituents and their metabolites increased in a dose-dependent fashion (with increasing GSPE oral dose). Repeated daily exposure to GSPE was found to significantly increase bioavailability (defined as plasma AUC0-8h) of GA, C and EC by 198, 253 and 282% relative to animals receiving only a single acute GSPE dose. EC and C were not detectable in brain tissues of rats receiving a single GSPE dose but reached levels of 290.7± 45.9 and 576.7± 227.7 pg/g in brain tissues from rats administered GSPE for 10 days. This study suggests that brain deposition of GA, C and EC is affected by repeated dosing of GSPE.

Tobacco plants yield the first vaccine for the dreaded 'cruise ship virus'

WASHINGTON, Aug. 18, 2009 - Scientists have used a new vaccine production technology to develop a vaccine for norovirus, a dreaded cause of diarrhea and vomiting that may be the second most common viral infection in the United States after the flu. Sometimes called the "cruise ship virus," this microbe can spread like wildfire through passenger liners, schools, offices and military bases.

The new vaccine is unique in its origin - it was "manufactured" in a tobacco plant using an engineered plant virus. Researchers are enlisting plants in the battle against norovirus, swine flu, bird flu, and other leading infectious diseases. This plant biotechnology opens the door to more efficient, inexpensive ways to bring vaccines quickly to the public, especially critical in times when viruses mutate into unpredictable new strains, said Charles Arntzen, Ph.D., who reported on the topic today at the 238th National Meeting of the American Chemical Society (ACS).

"The recent outbreak of H1N1 influenza virus has once again reminded us of the ability of disease-causing agents to mutate into new and dangerous forms," Arntzen points out. "It will be at least six months until a vaccine for this new strain will be available, and it will take even longer to create large stock piles of vaccine. For a case like the H1N1 influenza virus, you want to be able to move very rapidly and introduce a commercial vaccine in the shortest possible time. We think we have a major advantage in using engineered plant viruses to scale-up vaccine manufacture within weeks instead of months."

Noroviruses are always mutating, making it a moving target for vaccine developers. Arntzen says this has presented an obstacle for big pharmaceutical companies who might have considered developing a vaccine. Production costs can skyrocket when a single disease may frequently require new vaccines that must be developed and tested for safety and effectiveness. As a result, vaccines do not exist for many diseases that sicken enormous numbers of people each year. Arntzen notes that plant biotechnology could create a cheaper, quicker vaccine manufacturing technique uniquely suited to combat mutating viruses like norovirus and the flu.

Norovirus temporarily disables its victims, giving them severe diarrhea or nausea for up to three days. While not as life-threatening as the flu, Arntzen says it is equally important.

"It essentially closes down wings of hospitals, schools, day care centers and homes for the elderly. In the case of the military, it can shut down an entire ship and delay military operations while there is a cleanup in process. Because the disease spreads so rapidly, the major economic consequences are caused by the disruption of normal daily life and commerce," says Arntzen.

Norovirus will continue to evolve new strains, so Arntzen's team designed a vaccine manufacturing process quick enough to keep up with it and other shape-shifting viruses. "With plant-based vaccines, we can generate the first gram quantities of the drug and do clinical tests within eight to 10 weeks… We could easily scale that up for commercial use in a two to four month period," explains Arntzen.

Plant-based vaccine production also offers cost advantages. Building greenhouses is more cost effective than the sterilized facilities, expensive manufacturing technology and stainless steel tanks required for the insect or mammalian cell cultures used in most traditional vaccines.

"The other cost advantages relate to vaccine purification and formulation. Purification from plant extracts is simpler because there are no infectious agents to clean up. There are no viruses in plants which can infect humans, so you don't have to worry about viral removal," notes Arntzen.

The team re-engineered plant viruses to produce high levels of specially designed "virus-like" nanoparticles in tobacco plants. At about 25 nanometers in diameter, the particles are about the same size as the norovirus, but they consist only of the outer surface protein - the portion of the virus recognized by the human immune system. The particles contain none of the infectious material of the original virus, but they stimulate a robust immune response to fight off an actual infection.

To battle each new strain of the norovirus and to keep full resistance to older strains, Arntzen says the vaccine could be administered as a booster every 12 to 18 months. After successful experiments in mice, his team is developing a nasal delivery system for the virus-like particles. Arntzen expects to start clinical trials in late 2009 or early 2010.

Several companies, most notably pharmaceutical heavyweight Bayer, are investing in new facilities to create plant-based vaccines for cancer, as well as other pharmaceutical proteins. He suggests the first plant-based vaccines should be publicly available within four to five years.

"Mammalian and insect-based vaccines are tried and true - some have barely changed in nearly 60 years," says Arntzen. But that doesn't necessarily mean they are the best in terms of manufacturing costs or flexibility. It simply means that the industry is not accustomed to using plant biotechnology.

"Among other factors, the uncertainty on how such products would be viewed in the FDA approval process has created uncertainty in big pharma companies, and uncertainty is often a 'kiss of death' in product

development that can involve hundreds of millions of development cost." But, he adds, "the current pipeline of new products now working their way to FDA approval is sure to change these opinions in coming years."

Doctor-pharmacist partnership reduces hospitalization for heart failure

Collaborative medication management between doctors and pharmacists cut the heart failure hospitalization rate by nearly half.

The striking difference in hospitalization rates may have been underestimated in this study because patients who received the collaborative medicine review were sicker than those who didn't receive it.

DALLAS - Thinking "outside the medicine cabinet" is paying off in Australia, where a doctor-pharmacist partnership is reducing hospitalizations for heart failure — one of the most expensive conditions to treat - researchers report in Circulation: Heart Failure.

In the American Heart Association journal, researchers describe a collaborative model for ensuring heart failure patients take their medicines properly. The rate of hospitalization was cut by 45 percent in the first year of being part of a collaborative medicines review service.

"This is the first study to show these benefits in real-world practice rather than in a trial setting," said Elizabeth E. Roughead, Ph.D., lead author of the study and a pharmacist and associate professor in the School of Pharmacy and Medical Sciences at the University of South Australia in Adelaide. "If you have heart failure, getting a home visit with your pharmacist and then having a follow-up visit with your doctor about your medicines can keep you out of the hospital."

Researchers followed 273 heart failure patients over age 65 who underwent collaborative medicine review and compared them to 5,444 controls who didn't have their medicines reviewed. The participants were Australian veterans, who have extremely detailed medical records. All participants took one of three types of beta blocker drugs. Before these drugs are used, Australian physicians must sign paperwork confirming a heart failure diagnosis.

Those in the test group were slightly sicker than controls, and had more co-morbidities (eight other conditions vs. seven for the controls). Compared to controls, the group undergoing medicine review also had more prescriptions, more changes in medication prior to their home review, prescriptions from a higher number of caregivers and more hospitalizations.

After adjusting for a range of possible confounders, the researchers found that only 5.5 percent of the patients in the collaborative review group were hospitalized within a year, compared to 12 percent of the control group.

The collaborative approach features house calls with a twist: Pharmacists go to patients' homes and ask them to bring out all their prescription and non-prescription medications. The pharmacists are trained to notice signs of possible medication misuse, including under-dosing, overdosing and hoarding unneeded medicines from old prescriptions - a habit that increases the chance of accidentally taking the wrong medicine.

The pharmacists also look for over-the-counter medications and vitamins that could interact with the patients' prescription drugs. The average age of patients in both groups was 81.6 years, Roughead said.

Under the system used in Australia since 2001, a patient's general practitioner provides a referral to a pharmacist with the special collaborative training. The pharmacist conducts an interview, preferably in the patient's home, and reports findings from the review to the general practitioner. The report notes any known or potential problems the patient may have managing their medicines. The doctor then follows up with the patient if necessary. That follow-up could include showing the patient how, why and when to take their medicines or discussing proper ways to store the drugs as well as describing possible interactions between prescriptions, non-prescription medicines or vitamins found in the home by the pharmacist.

"Poor use of medicines can increase costs enormously," Roughead said. "This study indicates that investing in improvements in medication management can result in more cost-effective health care."

Co-authors include John D. Barratt, B. Pharm., B. App. Sc.; Emmae Ramsay, B.Sc.; Nicole Pratt, B.Sc.; Philip Ryan, M.B.B.S.; Robert Peck, B. Pharm.; Graeme Killer, M.B.B.S. and Andrew L. Gilbert, Ph.D. Author disclosures are on the manuscript. The Australian Government Department of Veterans' Affairs funded the research.

Overall antibiotic prescription rates for respiratory tract infections decreasing

From 1995 to 2006 the rate of antibiotic prescriptions for acute respiratory tract infections decreased significantly, attributable in part to a decline in ambulatory visits for ear infections in young children, according to a study in the August 19 issue of JAMA. But prescription rates for broad spectrum antibiotics, namely azithromycin and quinolones, increased substantially during the study period.

During the past decade, a variety of initiatives in the United States have advocated the judicious use of antibiotics, particularly for acute respiratory tract infection (ARTI), which is a common cause of health care

visits and antibiotic prescriptions, especially in young children. Antibiotic use can increase the likelihood for emergence of antibiotic-resistant bacteria. Infections caused by antibiotic-resistant microorganisms are associated with increased illness, death and substantial economic costs, according to background information in the article. Recent measurements of antibiotic prescription patterns in the United States have not been available.

Carlos G. Grijalva, M.D., M.P.H., of Vanderbilt University School of Medicine, Nashville, Tenn., and colleagues conducted a study to assess the national trends in antibiotic prescriptions for ARTI in ambulatory settings, using data from the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey (1995-2006).

For children younger than 5 years, annual ARTI-associated visit rates decreased by 17 percent (from 1,883 per 1,000 population in 1995-1996 to 1,560 per 1,000 population in 2005-2006) and annual antibiotic prescription rates in all visits decreased by 27 percent (from 1,552 to 1,128 per 1,000 population). This decrease was due to a 36 percent reduction in ARTI-associated antibiotic prescriptions (from 1,216 per 1,000 in 1995-1996 to 779 per 1,000 in 2005-2006). Annual otitis media (OM; ear infection) visit rates decreased by 33 percent (950 to 634 per 1,000 population) over the study period and rates of antibiotic prescriptions for OM decreased by 36 percent (1,216 to 779 per 1,000 population).

Among persons age 5 years or older, ARTI visit rates remained stable but associated antibiotic prescription rates decreased by 18 percent (from 178 to 146 per 1,000 population). Antibiotic prescription rates for non-OM ARTI for which antibiotics are rarely indicated decreased by 24 percent for this group.

"Overall, ARTI-associated prescription rates for penicillin, cephalosporin, and sulfonamide/tetracycline decreased. Prescription rates for azithromycin increased and it became the most commonly prescribed macrolide [a type of antibiotic] for ARTI and OM (10 percent of OM visits). Among adults, quinolone prescriptions increased," the authors write.

"Our results indicate that overall antibiotic prescription rates have decreased significantly. These changes coincided with efforts to reduce inappropriate antibiotic prescribing and the initiation of routine infant immunization with pneumococcal conjugate vaccine. Further efforts to improve antibiotic selection are needed." *(JAMA. 2009;302[7]:758-766. Available pre-embargo to the media at www.jamamedia.org)*

At last -- a quick and accurate way of diagnosing endometriosis

A quick and accurate test for endometriosis that does not require surgery has been developed by researchers from Australia, Jordan and Belgium, according to new research published online today (Wednesday 19 August) in Europe's leading reproductive medicine journal Human Reproduction [1].

Until now there has been no way of accurately diagnosing endometriosis apart from laparoscopy – an invasive surgical procedure – and this often leads to women waiting for years in pain and discomfort before their condition is identified correctly and treated.

Now researchers at the University of Sydney and Mu'tah University in Karak, Jordan, have discovered that if they take a small sample of the endometrium (the lining of the uterus), which can be done by inserting the device for taking the biopsy via the vagina, and then test for the presence of nerve fibres in the sample, they can diagnose whether or not endometriosis is present with nearly 100% accuracy.

Endometriosis, which has been estimated to affect 10-15% of women of reproductive age, is a chronic gynaecological disease in which cells from the endometrium establish themselves outside the uterus, within a woman's pelvic area. Symptoms associated with it include infertility, painful periods, pelvic pain and pain during sexual intercourse. Once laparoscopy has identified endometriosis as the cause of these symptoms, treatment involves surgical removal (usually via laparoscopy) of the abnormally sited endometrial cells. However, laparoscopy itself can be associated with complications and can adversely affect fertility in women who do not have endometriosis.

In a separate study also published online today in Human Reproduction, another research group from Belgium and Hungary has found that the density of nerve fibres in the endometrium was about 14 times higher in women with endometriosis than in healthy women, and that using specific markers to identify the presence of nerve fibres could predict with nearly 100% accuracy the presence of minimal to mild endometriosis [2].

In the first study, led by Professor Ian S. Fraser, head of the Queen Elizabeth II Research Institute for Mothers and Infants at the University of Sydney and Dr Moamar Al-Jefout, assistant professor in reproductive medicine at Mu'tah University, researchers took endometrial biopsies from 99 women who had consulted doctors about pelvic pain, infertility or both and who were undergoing laparoscopy for the condition.

The results from the endometrial biopsies were compared with the results of the laparoscopies, and the researchers found that in 64 women who had endometriosis confirmed by laparoscopy, all but one tested positive for the presence of nerve fibres in the endometrial biopsy. In the 35 women who were found not to have endometriosis by laparoscopy, no nerve fibres were found in 29 of the endometrial biopsies. In the other

six cases, the biopsy found there were nerve fibres present; three of these women had severely painful periods and painful sex, and also a history of infertility, and of the other three, one had adhesions that were considered too slight to be endometriosis, while the other had a previous history of endometriosis.

Women with endometriosis and painful symptoms had significantly higher nerve fibre density in comparison with women with infertility but no pain (2.3 nerve fibres per mm2 compared to 0.8 per mm2 respectively). The mean average of nerve fibre density in the women with a laparoscopic diagnosis of endometriosis was 2.7 per mm2.

The study showed that testing endometrial biopsies for the presence of nerve fibres was able to diagnose endometriosis with 83% specificity (the proportion of negative cases of endometriosis correctly identified) and 98% sensitivity (proportion of positive cases correctly identified). This double blind study confirmed the results of a pilot study published in 2007 by the same group [3].

Dr Al-Jefout said: "This study has shown that testing for nerve fibres in endometrial biopsies is a valid and highly accurate diagnostic test for endometriosis. This test is probably as accurate as assessment via laparoscopy, the current gold standard, especially as it is unclear how often endometriosis is overlooked, even by experienced gynaecologists. Endometrial biopsy is clearly less invasive than laparoscopy, and this test could help to reduce the current lengthy delay in diagnosis of the condition, as well as allowing more effective planning for formal surgical or long-term medical management. It may be particularly helpful in cases of infertility."

Currently, diagnosing endometriosis via laparoscopy involves the woman being booked into hospital for the surgical procedure, an anaesthetic, and the presence of doctors, nurses and expensive equipment. In some countries there are long waiting lists for operations. In contrast, taking an endometrial biopsy is relatively quick and easy to organise and perform, and results are available within about three days. However, Dr Al-Jefout said: "It needs to be emphasised that this test requires a carefully collected endometrial biopsy and an experienced immunohistochemical pathology laboratory to confirm or exclude the presence of nerve fibres."

He continued: "Our results indicate that a negative endometrial biopsy result would miss endometriosis in only one percent of women. Performing a planned laparoscopy only on a woman with a positive endometrial biopsy result would result in endometriosis being confirmed in eighty to ninety percent of these women. Thus, using this diagnostic test in an infertility workup would significantly reduce the number of laparoscopies performed without reducing the number of women whose endometriosis is diagnosed and surgically treated." In addition, he said it could be particularly useful in teenagers with spasmodic symptoms but a family history of endometriosis. "The usual diagnostic delay in this special group is greater than in older women. An endometrial biopsy to confirm or exclude the diagnosis of endometriosis will help initiating earlier treatment and possibly preventing the progress of endometriosis, thus improving life style and protecting their future fertility."

The researchers plan to continue using the test in patients and to search for other markers to help refine the test further. "Ideally, we would like to develop a blood test as an even simpler means of providing early information on the presence or absence of endometriosis in order to assist doctors in early diagnosis. However, this endometrial biopsy test has proven so effective that it is currently the only test which appears to have equivalent efficacy to a diagnostic laparoscopy carried out by an experienced gynaecologist," he concluded.

In the second study, led by Professor Thomas D'Hooghe, coordinator of the University of Leuven Fertility Centre (Belgium), researchers looked at 40 endometrial samples, half taken from women with minimal to mild endometriosis diagnosed by laparoscopy and histology (microscopic examination of tissue), and half from women without the condition. They analysed the tissues for several markers indicating the presence of four types of nerve fibres (sensory C, A ∂ , adrenergic and cholinergic nerve fibres).

Dr Attila Bokor, a doctoral fellow at the University of Leuven, who did the study as part of his PhD project said: "We observed nerve fibres in the endometrial samples of ninety percent (18 out of 20) of the women with endometriosis. The density varied throughout the samples, with few specimens showing counts above 30 per mm2, and with most between 0 and 10 per mm2. None, or very few, nerve fibres, were detected in any of the samples from women without endometriosis. The density of the small nerve fibres was about 14 times higher in endometrium from patients with minimal to mild endometriosis when compared with women with a normal pelvis."

Prof D'Hooghe said: "Our data show that the combination of three different neural markers increases the sensitivity, specificity and diagnostic accuracy of this method of testing for endometriosis. The test diagnosed endometriosis with 95% sensitivity and 100% specificity."

Dr Bokor and the team of Prof D'Hooghe will do a blinded validation study in September 2009 to confirm the results of their research. "If this confirms our findings, we believe our research can be a solid base for a

simple, reliable and relatively cheap method for non-invasive diagnosis of minimal and mild endometriosis, since trans-cervical endometrium sampling and immunohistochemical analysis are routine gynaecological and pathological procedures. Our research programme is also aimed at discovering new biomarkers that can enable a blood test for endometriosis to be developed," said Prof D'Hooghe.

[1] Diagnosis of endometriosis by detection of nerve fibres in an endometrial biopsy: a double blind study. Human Reproduction journal. doi:10.1093/humrep/dep275

[2] Density of small diameter sensory nerve fibres in endometrium: a semi-invasive diagnostic test for minimal to mild endometriosis. Human Reproduction journal. doi:10.1093/humrep/dep283

[3] A pilot study to evaluate the relative efficacy of endometrial biopsy and full curettage in making a diagnosis of endometriosis by the detection of endometrial nerve fibers. Al-Jefout M, Andreadis N, Tokushige N, Markham R, Fraser I. Am J Obstet Gynecol 2007 Dec 197(6):578.e1-4

Why humans can't navigate out of a paper bag

* 18 August 2009 **by Chris Berdik**

THE journey seemed simple enough, on the map anyway. Allison Fine left her home to drive to Vermont, just a few hours north on a major highway. She had studied the route and had a GPS gadget to help her. Nevertheless, she soon had absolutely no idea where she was.

"I don't know what happened," she says, "but I pulled over in tears, called my husband and said, 'find me on Google Maps and talk me to Vermont'." This he did, staying on the line for more than an hour.

Fine is an extreme case, but the feeling of getting hopelessly lost is something that most of us can relate to. In fact, along with our flair for language and our unparalleled intelligence, less-than-stellar navigational skills are among the things that can be considered uniquely human. While the vast majority of animals have no trouble finding their way around, most people, when stripped of maps or signs, are notoriously bad at it. A handful are so terrible at orienting themselves, even in places they know well, that they rarely leave the house alone (see "Lost in space"). "I try to study maps," says Fine. "But when I get out into the real world, it just looks completely different."

Until recently, little was known about how the human inner compass works. This is partly because "sense of direction" is not one neatly defined ability. Instead, it is made up of many different skills, such as awareness and memory of your surroundings, sensing your speed and direction changes over time, and tracking the location of objects and places relative to you as you move through an environment. These skills rely on many different parts of the brain, including those involved in vision, memory and imagination, which are tied together into a "cognitive map" by the hippocampus.

Now researchers have begun to unravel how this system works, and to ponder whether we have lost our way somewhere in evolution, or whether our inner homing pigeon is simply lying dormant, waiting to be released. Have we lost our way somewhere in evolution or is our inner homing pigeon simply lying dormant?

The first person to explore the idea of a cognitive map - a mental representation of an individual's physical surroundings - was Edward Tolman, a psychologist at the University of California, Berkeley, in 1948. Tolman observed that rats could take novel routes to food hidden in a maze when their learned route was blocked or they were moved to a new starting point. Since then, countless other species have shown an impressive talent for keeping track of where they are.

Take golden hamsters. They can make a straight dash for home even after being blindfolded and led in a winding path away from their nests. Similar skills have also been observed in geese, toads and spiders.

Equivalent tests with people, however, have seen our species come up seriously short. In "triangle completion" tasks, researchers lead people, either blindfolded or in a landmark-free virtual-reality environment, along two sides of a triangle and then tell them to find their way back to the starting point. In one such study, Jack Loomis, a cognitive psychologist at the University of California, Santa Barbara, found that the average error on the final turn was 24 degrees and most people significantly under or overshot the distance. As Loomis summed up: "None of the subjects exhibited good performance."

This weak innate ability to judge distance and direction makes for some pretty squishy mental maps, says William Warren, a cognitive neuroscientist at Brown University in Providence, Rhode Island. He fitted volunteers with virtual-reality headsets and showed them how to navigate virtual mazes. In half of the experiments, the mazes contained virtual, and invisible, "wormholes" that transported subjects close to a target that they would have known was some distance and a turn or two away. Yet the volunteers happily passed through these shortcuts to end up at a point that even a halfway-decent geometric reckoning would have told them was impossible. "The punchline," Warren says, "is that people didn't even notice anything amiss."

These findings, presented at this year's Vision Science Society conference in Naples, Florida, suggest that human cognitive maps pay little heed to geometric realities. Instead, we remember webs of landmarks such as

the store, our office, the church where we turn left on our way home, yet have little sense of how these fit together spatially.

Of course, some species find their way with the aid of specialised senses that we simply do not possess. Migratory birds can sense the Earth's magnetic field, for example, while some insects can see gradations in the polarity of sunlight. Yet even animals that lack any huge sensory advantage, such as hamsters, navigate better than many of us.

In a series of recent studies, Michael Kahana and his colleagues at the University of Pennsylvania in Philadelphia studied the brains of epileptic people, who already had electrodes implanted in their brains, as they played a taxi-driving video game. By noting which neurons fired when, the researchers discovered that human brains have specialised neurons dedicated to sense of direction, similar to those found in the hippocampus of rats, mice, monkeys and goldfish. So why can't we compute geometric space in the same way?

Losing our way

It could be that we lost this ability at some point in our evolution, sacrificing the kind of precision that other animals enjoy in return for cognitive flexibility, which allows us to make sense of our surroundings and find our way using reasoning and experience rather than geometry.

Indeed, studies of people that live closest to the land, such as the Bedouin in the Sahara, Arctic Inuit and Australian Aborigines, show that reasoning and experience can be very useful for finding your way. Such people can navigate perfectly well using subtle, learned directional cues from the landscape, even in what looks like the most barren expanse of snow or desert. Trading a mental tally of distance and direction for real understanding of the landscape in this way may have given us an evolutionary boost.

The trouble is, unlike an innate computation of distance and directional change, this connection to the landscape is all too easy to distort or lose entirely. Claudio Aporta, an anthropologist at Carleton University in Ottawa, Ontario, Canada, has observed how young Inuit hunters, who have begun to rely on GPS to navigate, have found themselves hopelessly lost for days when the technology fails, leading to several fatal and near-fatal incidents (Current Anthropology, vol 46, p 729). This was unheard of among the elders - until recently, the Inuit didn't even have a term for being lost. "It was just a matter of time before the weather cleared or they recognised a feature on the land and they would find their way," says Aporta.

That these skills are so easily lost could explain why the average westerner struggles to navigate without help. Most people now live in a world that has been made navigable by maps, street signs, transport networks and GPS. There is no need to understand the environment to get around.

Yet while these findings seem to show that we could all navigate like a Bedouin if we had to, other studies indicate that for some of us, substantial improvements may be impossible.

In 2006, Daniel Montello and Toru Ishikawa at the University of California, Santa Barbara, taught 24 people two landmark-studded routes which were connected by a winding but landmark-free route in 10 weekly sessions. After each session, they asked participants to point from one landmark to the others, which were always out of sight, and draw maps of the routes.

Three clear groups emerged: one that kept doing well throughout the experiment, one that did poorly from beginning to end and one that was intermediate. This final group was the largest, and the volunteers within it all improved at the tasks as the experiment progressed, although only one-third of this group became as good as the top performers (Cognitive Psychology, vol 52, p 93).

To Thomas Wolbers, a neuroscientist at the University of Edinburgh, UK, findings like these point to a genetic component to navigation ability. Several studies have found signs of such a link in rodents, and Wolbers is currently looking for similar evidence in a sample of 50,000 people. He expects to get initial findings in about a year.

Regardless of whether all or just some of us are a navigational lost cause, psychologist Colin Ellard at the University of Waterloo in Ontario, author of You Are Here, argues that there is an upside to our lack of natural navigation skills. He suggests that losing our relationship with physical space, coupled with the unique human ability to imagine ourselves in another location, may have given us the freedom to create a reality of our own. What other species could comprehend the World Wide Web or contemplate exploring new worlds, he asks. Losing our relationship with physical space may have allowed us to create a reality of our own

And while we may struggle to find our way back to the car after a shopping trip, we can take heart in the knowledge that, as a species, we have managed to find our way to the moon and back, and have sent satellites to just the right orbit so that we no longer need to think about where we are going. Show me a hamster that can do that. Some people are so prone to getting lost that they fear leaving the house alone.

Lost in space

Every so often, Sharon Roseman rounds a bend in her suburban Colorado neighbourhood and drives into a new world. It's a lot like the world she knows - same houses, same street names - but with one critical, maddening difference: everything in it has shifted 90 degrees. Familiar stores at well-known intersections are not where she feels they should be, and the Rocky mountains have migrated from the north to the east.

Roseman's world has been turning like this since she was 5 years old, and the only sure-fire way to set things right is to close her eyes and spin until everything "clicks" back into place, a remedy she jokingly calls her "Wonder Woman cure". Despite countless visits to a doctor, prescriptions and brain scans over more than 50 years, nobody has offered a diagnosis. Nobody, Roseman suspects, really believed her. Until now.

Giuseppe Iaria of the University of Calgary, Alberta, and Jason Barton at the University of British Columbia in Vancouver, both in Canada, may have finally put a name to Roseman's condition. They call it developmental topographical disorientation. While people with the disorder have no obvious brain injury or other cognitive problem, they are chronically unable to orient themselves, even in places they know well. The pair have found 400 or so people who may have the disorder, some of whom are so prone to getting lost they fear leaving the house alone.

In a paper published earlier this year, Iaria and Barton used real-world navigation tasks, map sketching and brain scans to document the case of "Patient One", a middle-aged woman in Vancouver who routinely gets lost, even in familiar environments (Neuropsychologia, vol 47, p 30). They found that Patient One had normal cognitive abilities, no brain damage, lesions or dyslexia, and no problems with memory, balance or visual perception.

In tests, she could follow a route by memorising a list of directions, says Iaria, but she had great difficulty creating an accurate mental representation of her environment. Drawing maps totally flummoxed her and she took three times as long as control subjects to come up with an accurate shortcut after learning the location of four landmarks in a virtual city.

Functional magnetic resonance images of her brain revealed that her hippocampus and retrosplenial cortex - areas that are activated in typical human brains as they form a cognitive map - showed no spike in activity as she tried to imagine a route. The researchers are now investigating the possibility that there may be a common developmental defect in the hippocampus that leaves some people chronically lost.

To test your own navigation skills or volunteer for Iaria and Barton's study visit www.gettinglost.ca/Test.html.

Show me the way to go home

In 1986, Kenneth Hill, a psychologist at Saint Mary's University in Halifax, Nova Scotia, Canada, joined thousands of volunteers searching for a 9-year-old boy lost in the Nova Scotia wilderness. After more than a week, they found the boy's body less than 3 kilometres from where he was last seen. Since then, Hill has focused his career on the study of how people behave when they are lost in the wild, in a bid to predict where people will turn up.

He has found that children under 7 years of age have the highest survival rates, because they do not build a mental map that might trigger counterproductive efforts to get reoriented. "Most of the time they just wander around for a while, and then they get cold and look for warmth," says Hill. Instead, it is people who believe they have a strong sense of direction that get into the most trouble. Some have been known to dismiss visual clues and even distrust a compass if it contradicts their mental map.

Search and rescue professionals have begun to use a similar approach. Rick Toman, director of search and rescue for the state of Massachusetts, uses a computer model that includes common trends among different types of people to inform the search. Autistic children are often fascinated by water, for example, so it pays to look near rivers and lakes, while suicidal people prefer elevated spots with good views. Missing married men are often easier to find, says Toman. They tend to turn up at a motel "with somebody they shouldn't be with".

Science ponders 'zombie attack'

By Pallab Ghosh Science correspondent, BBC News

If zombies actually existed, an attack by them would lead to the collapse of civilisation unless dealt with quickly and aggressively.

That is the conclusion of a mathematical exercise carried out by researchers in Canada. They say only frequent counter-attacks with increasing force would eradicate the fictional creatures. The scientific paper is published in a book - Infectious Diseases Modelling Research Progress.

In books, films, video games and folklore, zombies are undead creatures, able to turn the living into other zombies with a bite. But there is a serious side to the work.

There has been a revival of the zombie film in recent years

In some respects, a zombie "plague" resembles a lethal, rapidly spreading infection. The researchers say the exercise could help scientists model the spread of unfamiliar diseases through human populations.

In their study, the researchers from the University of Ottawa and Carleton University (also in Ottawa) posed a question: If there was to be a battle between zombies and the living, who would win?

Professor Robert Smith? (the question mark is part of his surname and not a typographical mistake) and colleagues wrote: "We model a zombie attack using biological assumptions based on popular zombie movies.

"We introduce a basic model for zombie infection and illustrate the outcome with numerical solutions."

To give the living a fighting chance, the researchers chose "classic" slow-moving zombies as our opponents rather than the nimble, intelligent creatures portrayed in some recent films. "While we are trying to be as broad as possible in modelling zombies - especially as there are many variables - we have decided not to consider these individuals," the researchers said.

Back for good?

Even so, their analysis revealed that a strategy of capturing or curing the zombies would only put off the inevitable. In their scientific paper, the authors conclude that humanity's only hope is to "hit them [the undead] hard and hit them often". They added: "It's imperative that zombies are dealt with quickly or else... we are all in a great deal of trouble."

According to the researchers, the key difference between the zombies and the spread of real infections is that "zombies can come back to life".

Professor Neil Ferguson, who is one of the UK government's chief advisers on controlling the spread of swine flu, said the study did have parallels with some infectious diseases.

"None of them actually cause large-scale death or disease, but certainly there are some fungal infections which are difficult to eradicate," said Professor Ferguson, from Imperial College London.

"There are some viral infections - simple diseases like chicken pox have survived in very small communities. If you get it when you are very young, the virus stays with you and can re-occur as shingles, triggering a new chicken pox epidemic."

Professor Smith? told BBC News: "When you try to model an unfamiliar disease, you try to find out what's happening, try to approximate it. You then refine it, go back and try again."

"We refined the model again and again to say... here's how you would tackle an unfamiliar disease."

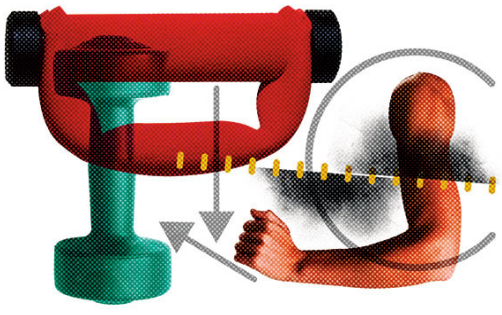
Professor Ferguson went on to joke: "The paper considers something that many of us have worried about - particularly in our younger days - of what would be a feasible way of tackling an outbreak of a rapidly spreading zombie infection.

"My understanding of zombie biology is that if you manage to decapitate a zombie then it's dead forever. So perhaps they are being a little over-pessimistic when they conclude that zombies might take over a city in three or four days."

Well

Weight Lifting May Help to Avert Lymph Problem

By TARA PARKER-POPE



Stuart Bradford

After a woman has surgery for breast cancer, she is typically given a long list of don’ts. Don’t lift anything heavier than 15 pounds, including your child. Don’t carry a heavy purse or grocery bags. Don’t scrub, push, pull or hammer.

The goal is to prevent lymphedema, a painful and unsightly swelling of an arm or leg that can occur near the site where lymph nodes have been removed or damaged by radiation. But new research suggests that much of that advice may be too restrictive. To prevent lymphedema after breast cancer, the best strategy may be more exercise, not less.

Last week, The New England Journal of Medicine reported on a study of 141 breast cancer patients who had lymphedema. Half adhered to the traditional restrictions, while the other half embarked on a slow, progressive program of weight lifting. To the researchers’ surprise, the weight lifters actually had significantly fewer flare-ups than the women who restricted their activity.

“Lymphedema is a very feared complication, and many women have made major alterations to their lifestyle in an effort to avoid it,” said Dr. Monica Morrow, chief of breast surgery at Memorial Sloan-Kettering Cancer Center in Manhattan. “This is a very welcome study that very clearly shows controlled weight lifting

does not make it worse and, in fact, improves symptoms. That should be a reason to re-evaluate a whole lot of things we tell people about lymphedema."

The findings don't mean that patients should disregard everything their doctors tell them about lymphedema, which can also occur with other cancers. Once lymph nodes have been damaged or removed, the lymphatic system is less able to cope with trauma or infection, and the painful swelling, tightness and heaviness of lymphedema can result. While physical therapy can ease the symptoms, some patients never fully recover.

Doctors say some of the standard guidelines are reasonable. Intravenous lines, for example, pose a risk of infection, and they should not be used on an arm affected by lymphedema. But other restrictions, like not carrying children or using a blood pressure cuff on the affected arm, may be too extreme.

An editorial accompanying the weight-lifting study in The New England Journal notes that the current "policy of avoidance" should be replaced by recommendations for rehabilitation, particularly because many women have to ignore the restrictions anyway - they are caring for young children, or their jobs require manual labor.

"Rather than saying, 'Don't ever lift more than 15 pounds, don't carry a suitcase,' instead we should empower women," said Wendy Demark-Wahnefried, a professor of behavioral science at the University of Texas M. D. Anderson Cancer Center, who wrote the editorial. "Give them the rehab and the exercise training they need after their treatment."

Kathryn H. Schmitz, an associate professor at the University of Pennsylvania School of Medicine and the study's lead author, notes that in the past, patients were wrongly advised to avoid activity after a heart attack or a back injury. "It's the same principle as back rehab and cardiac rehab," she said. "You're slowly and progressively increasing the stress that your system can handle. We're applying that to lymphedema."

Corrie Roberts of Philadelphia developed lymphedema in her left arm in June 2004, about 18 months after a mastectomy. She had taken the usual precautions, but during back surgery the anesthesiologist mistakenly used her left arm to insert the intravenous line.

After taking part in the weight-lifting study, she said the swelling and discomfort were finally under control. She uses an exercise room in her apartment building and lifts weights three to five days a week. "It sure was an improvement," said Ms. Roberts, 75. "As long as I keep the weight lifting up, I don't have swelling in my arm."

Dr. Schmitz is conducting a separate study to determine whether weight lifting can prevent symptoms in women who have never had lymphedema. Another study will focus on exercise programs for people with lower-limb lymphedema.

Experts warn that women should not embark on an exercise program on their own, but should ask their doctor about finding a rehabilitation center or exercise program for patients at risk for lymphedema. The women in the study began with very light weights and were regularly monitored for swelling or pain. Dr. Schmitz noted that not every woman is a candidate, and that a few women in the study developed swelling almost immediately after exerting the arm.

Centers that offer the weight-lifting program used in the New England Journal study can be found at www.uphs.upenn.edu/news. Patients can look for a personal trainer who has a cancer exercise certification from the American College of Sports Medicine. In addition, many Y's now have exercise programs for cancer patients through a partnership with the Lance Armstrong Foundation.

Women can also order the DVD "Strength and Courage: Exercises for Breast Cancer Survivors," which was developed by Dr. Sharon Cowden, a Pittsburgh pediatrician and golfer who had breast cancer, and Janette Poppenberg, a health fitness specialist certified by the American College of Sports Medicine.

DNA Evidence Can Be Fabricated, Scientists Show

By ANDREW POLLACK

Scientists in Israel have demonstrated that it is possible to fabricate DNA evidence, undermining the credibility of what has been considered the gold standard of proof in criminal cases.

The scientists fabricated blood and saliva samples containing DNA from a person other than the donor of the blood and saliva. They also showed that if they had access to a DNA profile in a database, they could construct a sample of DNA to match that profile without obtaining any tissue from that person. "You can just engineer a crime scene," said Dan Frumkin, lead author of the paper, which has been published online by the journal Forensic Science International: Genetics. "Any biology undergraduate could perform this."

Dr. Frumkin is a founder of Nucleix, a company based in Tel Aviv that has developed a test to distinguish real DNA samples from fake ones that it hopes to sell to forensics laboratories.

The planting of fabricated DNA evidence at a crime scene is only one implication of the findings. A potential invasion of personal privacy is another.

Using some of the same techniques, it may be possible to scavenge anyone's DNA from a discarded drinking cup or cigarette butt and turn it into a saliva sample that could be submitted to a genetic testing company that measures ancestry or the risk of getting various diseases. Celebrities might have to fear "genetic paparazzi," said Gail H. Javitt of the Genetics and Public Policy Center at Johns Hopkins University.

Tania Simoncelli, science adviser to the American Civil Liberties Union, said the findings were worrisome.

"DNA is a lot easier to plant at a crime scene than fingerprints," she said. "We're creating a criminal justice system that is increasingly relying on this technology."

John M. Butler, leader of the human identity testing project at the National Institute of Standards and Technology, said he was "impressed at how well they were able to fabricate the fake DNA profiles." However, he added, "I think your average criminal wouldn't be able to do something like that."

The scientists fabricated DNA samples two ways. One required a real, if tiny, DNA sample, perhaps from a strand of hair or drinking cup. They amplified the tiny sample into a large quantity of DNA using a standard technique called whole genome amplification. Of course, a drinking cup or piece of hair might itself be left at a crime scene to frame someone, but blood or saliva may be more believable.

The authors of the paper took blood from a woman and centrifuged it to remove the white cells, which contain DNA. To the remaining red cells they added DNA that had been amplified from a man's hair. Since red cells do not contain DNA, all of the genetic material in the blood sample was from the man. The authors sent it to a leading American forensics laboratory, which analyzed it as if it were a normal sample of a man's blood.

The other technique relied on DNA profiles, stored in law enforcement databases as a series of numbers and letters corresponding to variations at 13 spots in a person's genome.

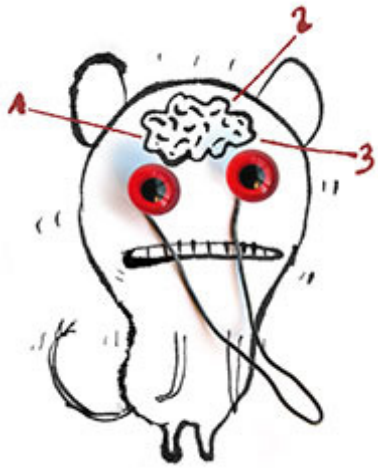
From a pooled sample of many people's DNA, the scientists cloned tiny DNA snippets representing the common variants at each spot, creating a library of such snippets. To prepare a DNA sample matching any profile, they just mixed the proper snippets together. They said that a library of 425 different DNA snippets would be enough to cover every conceivable profile.

Nucleix's test to tell if a sample has been fabricated relies on the fact that amplified DNA — which would be used in either deception — is not methylated, meaning it lacks certain molecules that are attached to the DNA at specific points, usually to inactivate genes.

Basics

Brain Is a Co-Conspirator in a Vicious Stress Loop

By NATALIE ANGIER



Serge Bloch

If after a few months' exposure to our David Lynch economy, in which housing markets spontaneously combust, coworkers mysteriously disappear and the stifled moans of dying 401(k) plans can be heard through the floorboards, you have the awful sensation that your body's stress response has taken on a self-replicating and ultimately self-defeating life of its own, congratulations. You are very perceptive. It has.

As though it weren't bad enough that chronic stress has been shown to raise blood pressure, stiffen arteries, suppress the immune system, heighten the risk of diabetes, depression and Alzheimer's disease and make one a very undesirable dinner companion, now researchers have discovered that the sensation of being highly stressed can rewire the brain in ways that promote its sinister persistence.

Reporting earlier this summer in the journal Science, Nuno Sousa of the Life and Health Sciences Research Institute at the University of Minho in Portugal and his colleagues described experiments in which chronically stressed rats lost their elastic rat cunning and instead fell back on familiar routines and rote responses, like compulsively pressing a bar for food pellets they had no intention of eating. Moreover, the rats' behavioral perturbations were reflected by a pair of complementary changes in their underlying neural circuitry. On the one hand, regions of the brain associated with executive decision-making and goal-directed behaviors had shriveled, while, conversely, brain sectors linked to habit formation had bloomed.

In other words, the rodents were now cognitively predisposed to keep doing the same things over and over, to run laps in the same dead-ended rat race rather than seek a pipeline to greener sewers. "Behaviors become habitual faster in stressed animals than in the controls, and worse, the stressed animals can't shift back to goal-directed behaviors when that would be the better approach," Dr. Sousa said. "I call this a vicious circle."

Robert Sapolsky, a neurobiologist who studies stress at Stanford University School of Medicine, said, "This is a great model for understanding why we end up in a rut, and then dig ourselves deeper and deeper into that

rut." The truth is, Dr. Sapolsky said, "we're lousy at recognizing when our normal coping mechanisms aren't working. Our response is usually to do it five times more, instead of thinking, maybe it's time to try something new."

And though perseverance can be an admirable trait and is essential for all success in life, when taken too far it becomes perseveration — uncontrollable repetition — or simple perversity. "If I were to try to break into the world of modern dance, after the first few rejections the logical response might be, practice even more," said Dr. Sapolsky, the author of "Why Zebras Don't Get Ulcers," among other books. "But after the 12,000th rejection, maybe I should realize this isn't a viable career option."

Happily, the stress-induced changes in behavior and brain appear to be reversible. To rattle the rats to the point where their stress response remained demonstrably hyperactive, the researchers exposed the animals to four weeks of varying stressors: moderate electric shocks, being encaged with dominant rats, prolonged dunks in water. Those chronically stressed animals were then compared with nonstressed peers. The stressed rats had no trouble learning a task like pressing a bar to get a food pellet or a squirt of sugar water, but they had difficulty deciding when to stop pressing the bar, as normal rats easily did.

But with only four weeks' vacation in a supportive setting free of bullies and Tasers, the formerly stressed rats looked just like the controls, able to innovate, discriminate and lay off the bar. Atrophied synaptic connections in the decisive regions of the prefrontal cortex resprouted, while the overgrown dendritic vines of the habit-prone sensorimotor striatum retreated.

According to Bruce S. McEwen, head of the neuroendocrinology laboratory at Rockefeller University, the new findings offer a particularly elegant demonstration of a principle that researchers have just begun to grasp. "The brain is a very resilient and plastic organ," he said. "Dendrites and synapses retract and reform, and reversible remodeling can occur throughout life."

Stress may be most readily associated with the attosecond pace of postindustrial society, but the body's stress response is one of our oldest possessions. Its basic architecture, its linked network of neural and endocrine organs that spit out stimulatory and inhibitory hormones and other factors as needed, looks pretty much the same in a goldfish or a red-spotted newt as it does in us.

The stress response is essential for maneuvering through a dynamic world — for dodging a predator or chasing down prey, swinging through the trees or fighting off disease — and it is itself dynamic. As we go about our days, Dr. McEwen said, the biochemical mediators of the stress response rise and fall, flutter and flare. "Cortisol and adrenaline go up and down," he said. "Our inflammatory cytokines go up and down."

The target organs of stress hormones likewise dance to the beat: blood pressure climbs and drops, the heart races and slows, the intestines constrict and relax. This system of so-called allostasis, of maintaining control through constant change, stands in contrast to the mechanisms of homeostasis that keep the pH level and oxygen concentration in the blood within a narrow and invariant range.

Unfortunately, the dynamism of our stress response makes it vulnerable to disruption, especially when the system is treated too roughly and not according to instructions. In most animals, a serious threat provokes a serious activation of the stimulatory, sympathetic, "fight or flight" side of the stress response. But when the danger has passed, the calming parasympathetic circuitry tamps everything back down to baseline flickering.

In humans, though, the brain can think too much, extracting phantom threats from every staff meeting or high school dance, and over time the constant hyperactivation of the stress response can unbalance the entire feedback loop. Reactions that are desirable in limited, targeted quantities become hazardous in promiscuous excess. You need a spike in blood pressure if you're going to run, to speedily deliver oxygen to your muscles. But chronically elevated blood pressure is a source of multiple medical miseries.

Why should the stressed brain be prone to habit formation? Perhaps to help shunt as many behaviors as possible over to automatic pilot, the better to focus on the crisis at hand. Yet habits can become ruts, and as the novelist Ellen Glasgow observed, "The only difference between a rut and a grave are the dimensions."

It's still August. Time to relax, rewind and remodel the brain.

Adding Layers of Skills to a Science Background

By STEVE LOHR

In good times or bad, the pace of technological change never seems to let up. This relentless engine of innovation, economists agree, is the wellspring of the nation's long-run prosperity. But it presents a daunting challenge to science and technology professionals who are trying to stay ahead, seeking a career that is unlikely to become outsourced, automated or obsolete.

The sour economy has only intensified those pressures. So colleges across the country are reporting a surge in applications since last fall, up as much as 50 percent, for continuing education programs intended for people

with science and engineering backgrounds. The offerings, in classroom settings and online, range from short courses of a few days to graduate degree programs that span years.

Some students want refresher courses, educators say, but most are trying to broaden their appeal by adding business and communications skills or by learning how to apply their technical talents in promising fields like renewable energy, transportation and health care.

"Technical expertise by itself is not sufficient, and that is more true now than it has ever been," said Bhaskar Pant, executive director of professional programs at Massachusetts Institute of Technology's school of engineering.

The technology workers most in demand in the future, according to James E. Spohrer, a researcher and director of university programs for I.B.M., will be "T-shaped people." Such people, Mr. Spohrer explains, possess a deep knowledge in one technical discipline topped off by a wide portfolio of skills, from project management to industry expertise, that makes them more valuable to employers.

CHANGE OF FOCUS Mark Spencer, who has a doctorate in chemistry, left NASA to be a photographer, then refreshed his credentials at M.I.T. so he could return to the technology field. **Jodi Hilton for The New York Times**

Katherine Heningburg, 28, an electrical engineer at General Dynamics in Scottsdale, Ariz., wants to become one of those broadly skilled technologists. Ms. Heningburg, who designs computer circuits for communications systems, is taking online courses from Arizona State University to earn both a master's degree in engineering and an M.B.A.

The added skills, she said, should prepare her to lead project teams, a step into management. "My goal is to bridge the gap between the business and technical side," Ms. Heningburg said. "And this will give me the ammunition I need to be marketable within my company, in my industry and beyond."

In many schools, hybrid courses that apply computing to business problems are increasingly popular among continuing education students. These blended courses are in new academic niches like knowledge services, data analytics and services science, which combines technology with business processes. These hybrid disciplines apply computing to businesses as diverse as online advertising and food distribution.

"All the business knowledge and data analytics is further up the economic ladder than pure technology alone," said Ram Akella, a professor of information systems and technology management at the University of California, Santa Cruz. "That work is not going to go offshore."

Sometimes, a return to school is a smart way to restart a science career. That was the motivation for Mark Spencer, 53, when last fall he began M.I.T.'s Career Re-engineering Program.

Mr. Spencer has a Ph.D. in chemistry and for more than a decade was a scientist at NASA's Ames Research Center in Moffett Field, Calif., specializing in atmospheric chemistry and climate modeling. But in 1995, Mr. Spencer, an avid amateur photographer, decided to pursue a long-held desire to try another career. He moved back to his home state, Massachusetts, and set up a photography studio.

MR. Spencer did well for years, as both the owner of a small business and as a photographer, winning a string of professional awards. Yet, he explained, the intellectual stimulation of photography waned over time, and the deep recession reduced sales of his business by 40 percent.

So Mr. Spencer immersed himself in courses at M.I.T. two days a week last fall and, as part of the program, started an internship this year at a technology and research firm, Agiltron. One division of the company does contract work for the government, and shortly after he arrived Mr. Spencer was asked to help prepare a contract proposal on deadline. He was hired the next day, well before the M.I.T program was over.

"I didn't get my full money's worth," he joked.

Mr. Spencer said he found the M.I.T. course work useful and stimulating. But like others, Mr. Spencer also pointed to the networking benefits of rejoining a university community and the value of the program as a sign to employers that you are motivated and willing to make an entrepreneurial investment in yourself.

"If my résumé started by saying I had run a photography studio for the last 15 years, there's no way I would have gotten in the door," Mr. Spencer said. "Having that M.I.T program at the top of the résumé really was crucial."

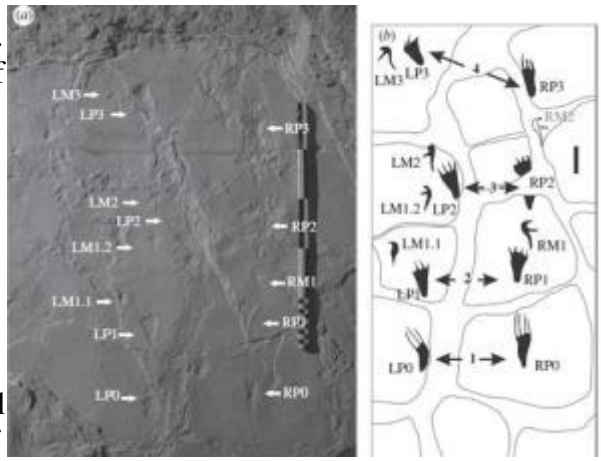
Pterosaur tracks show it touched down like a bird

* 00:01 19 August 2009 **by Colin Barras**

Pterosaurs may have been furry rather than feathery, but they may not have been so very different from birds in other respects. A set of footprints unearthed in France is the first to show one of the winged reptiles coming into land – and suggests they did so in much the same way as most modern birds.

While dinosaurs wandered the lands of the Mesozoic era, their relatives the pterosaurs occupied the skies. The flying reptiles remain something of a palaeontological puzzle – some even question whether the largest pterosaurs could fly at all.

An exceptional set of footprints preserved in 150-million-year-old rock near Crayssac in south-west France holds some answers to pterosaur behaviour. They record the moment a small pterosaur came into land, says Kevin Padian at the University of California, Berkeley.



A photograph and drawing of the pterosaur footprints. The lowest prints are of the rear limbs only. Towards the top of the trackway the pterosaur turned to the left and walked away on all fours (Image: Proceedings of the Royal Society B)

Padian's team says the prints are similar to those produced by a landing bird. Although most pterosaur tracks show the animals walking on all fours, the first prints in the newly discovered tracks are of the rear limbs only.

That's because the pterosaur used its wings to "stall" as birds do, says the team, so that the animal's body swung up from a horizontal flight position to near vertical, enabling it to land gently on its hind feet.

Flap stall

"The smaller ones, like the smallest birds, are all good flappers, so they [could] 'flap-stall' to land," says Padian. Larger pterosaurs might have stalled by simply holding their wings against the airflow. Either way, the pterosaurs would have needed sophisticated neural control on a par with modern birds, the researchers say.

After the flap stall, the tracks show the animal stabilised itself with its arms, as it hopped a little way forward before it began to walk away on all four limbs.

David Martill, a pterosaur specialist at the University of Portsmouth, UK, says that although the tracks record a "small moment, perhaps no more than three seconds, in the life of a pterosaur", they offer a real insight into the lives of the ancient animals.

But Michael Habib at Chatham University in Pittsburgh, Pennsylvania, points out that the real mystery of pterosaur flight remains unsolved.

"Any flying animal larger than a large insect will need to use some kind of controlled stall or hover mechanism to land," he says, but the new track "does not give us any new information about launch".

Hop aloft

Earlier this year Habib suggested that the largest pterosaurs took flight by using all four limbs to leap into the air – a technique similar to that used by some bats but quite unlike the take-off behaviour of modern birds.

Padian says Habib's theory may have been possible. "On the other hand, pterosaurs seem perfectly capable of standing on their back legs, so a two-legged [bird-style] take-off, whether from a standing pose or running, seems equally plausible – depending on the pterosaur."

Journal reference: Proceedings of the Royal Society B, DOI: 10.1098/rspb.2009.1161

The greenhouse gas that saved the world

Chemistry researchers uncover why the archean world was not frozen solid

When Planet Earth was just cooling down from its fiery creation, the sun was faint and young. So faint that it should not have been able to keep the oceans of earth from freezing. But fortunately for the creation of life, water was kept liquid on our young planet. For years scientists have debated what could have kept earth warm enough to prevent the oceans from freezing solid. Now a team of researchers from Tokyo Institute of Technology and University of Copenhagen's Department of Chemistry have coaxed an explanation out of ancient rocks, as reported in this week's issue of PNAS

A perfect greenhouse gas

"The young sun was approximately 30 percent weaker than it is now, and the only way to prevent earth from turning into a massive snowball was a healthy helping of greenhouse gas," Associate Professor Matthew S. Johnson of the Department of Chemistry explains. And he has found the most likely candidate for an archean atmospheric blanket. Carbonyl Sulphide: A product of the sulphur disgorged during millennia of volcanic activity.

"Carbonyl Sulphide is and was the perfect greenhouse gas. Much better than Carbon Dioxide. We estimate that a blanket of Carbonyl Sulphide would have provided about 30 percent extra energy to the surface of the planet. And that would have compensated for what was lacking from the sun", says Professor Johnson.

Strange distribution

To discover what could have helped the faint young sun warm early earth, Professor Johnson and his colleagues in Tokyo examined the ratio of sulphur isotopes in ancient rocks. And what they saw was a strange signal; A mix of isotopes that couldn't very well have come from geological processes.

"There is really no process in the rocky mantle of earth that would explain this distribution of isotopes. You would need something happening in the atmosphere," says Johnson. The question was what. Painstaking experimentation helped them find a likely atmospheric process. By irradiating sulphur dioxide with different wavelengths of sunlight, they observed that sunlight passing through Carbonyl Sulphide gave them the wavelengths that produced the weird isotope mix.

"Shielding by Carbonyl Sulphide is really a pretty obvious candidate once you think about it, but until we looked, everyone had missed it," says Professor Johnson, and he continues.

- "What we found is really an archaic analogue to the current ozone layer. A layer that protects us from ultraviolet radiation. But unlike ozone, Carbonyl Sulphide would also have kept the planet warm. The only problem is: It didn't stay warm".

Life caused ice-age

As life emerged on earth it produced increasing amounts of oxygen. With an increasingly oxidizing atmosphere, the sulphur emitted by volcanoes was no longer converted to Carbonyl Sulphide. Instead it got converted to sulphate aerosols: A powerful climate coolant. Johnson and his co-workers created a Computer model of the ancient atmosphere. And the models in conjunction with laboratory experiments suggest that the fall in levels of Carbonyl Sulphide and rise of sulphate aerosols taken together would have been responsible for creating snowball earth, the planetwide ice-age hypothesised to have taken place near the end of the Archean eon 2500 million years ago. And the implications to Johnson are alarming:

"Our research indicates that the distribution and composition of atmospheric gasses swung the planet from a state of life supporting warmth to a planet-wide ice-age spanning millions of years. I can think of no better reason to be extremely cautious about the amounts of greenhouse gasses we are currently emitting to the atmosphere".

Neural pathway missing in tone-deaf people

Syndrome may be similar to other speech and language disorders

Washington, DC — Nerve fibers that link perception and motor regions of the brain are disconnected in tone-deaf people, according to new research in the August 19 issue of The Journal of Neuroscience. Experts estimate that at least 10 percent of the population may be tone deaf – unable to sing in tune. The new finding identifies a particular brain circuit that appears to be absent in these individuals.

"The anomaly suggests that tone-deafness may be a previously undetected neurological syndrome similar to other speech and language disorders, in which connections between perceptual and motor regions are impaired," said Psyche Loui, PhD, of Beth Israel Deaconess Medical Center and Harvard Medical School, one of the study's authors.

The authors used an MRI-based technique called diffusion tensor imaging to examine connections between the right temporal and frontal lobes. This region, a neural "highway" called the arcuate fasciculus, is known to be involved in linking music and language perception with vocal production. Brain images of 20 people were taken, half of whom had been identified as tone-deaf through listening tests.

The arcuate fasciculus was smaller in volume and had a lower fiber count in the tone-deaf individuals. More notably, the superior branch of the arcuate fasciculus in the right hemisphere could not be detected in the tone-deaf individuals. The researchers speculated that this could mean the branch is missing entirely, or is so abnormally deformed that it appears invisible to even the most advanced neuroimaging methods.

“The findings are clear," said Nina Kraus, PhD, at Northwestern University, who was unaffiliated with the study. "They show that the arcuate fasciculus, a structure long-known to join perceptual and motor areas, has reduced connectivity in individuals with tone deafness. Beyond improving our understanding of the anatomical underpinnings of tone-deafness, this study provides new insight into a person's ability to detect pitch," Kraus said.

These findings add to previous work by the same researchers demonstrating that tone-deaf people could not consciously hear their own singing, and work by other researchers indicating abnormalities in brain regions that affect sound perception and production. *The research was supported by the National Science Foundation, the National Institutes of Deafness and Communication Disorders, and the Grammy Foundation.*

Key feature of immune system survived in humans, other primates for 60 million years

CORVALLIS, Ore. – A new study has concluded that one key part of the immune system, the ability of vitamin D to regulate anti-bactericidal proteins, is so important that is has been conserved through almost 60 million years of evolution and is shared only by primates, including humans – but no other known animal species.

The fact that this vitamin-D mediated immune response has been retained through millions of years of evolutionary selection, and is still found in species ranging from squirrel monkeys to baboons and humans, suggests that it must be critical to their survival, researchers say.

Even though the "cathelicidin antimicrobial peptide" has several different biological activities in addition to killing pathogens, it's not clear which one, or combination of them, makes vitamin D so essential to its regulation.

The research also provides further evidence of the biological importance of adequate levels of vitamin D in humans and other primates, even as some studies and experts suggest that more than 50 percent of the children and adults in the U.S. are deficient in "the sunshine vitamin."

"The existence and importance of this part of our immune response makes it clear that humans and other primates need to maintain sufficient levels of vitamin D," said Adrian Gombart, an associate professor of biochemistry and a principal investigator with the Linus Pauling Institute at Oregon State University.

In a new study in the journal BMC Genomics, researchers from OSU and the Cedars-Sinai Medical Center describe the presence of a genetic element that's specific to primates and involved in the innate immune response. They found it not only in humans and their more recent primate ancestors, such as chimpanzees, but also primates that split off on the evolutionary tree tens of millions of years ago, such as old world and new world primates.

The genetic material – called an Alu short interspersed element – is part of what used to be thought of as "junk DNA" and makes up more than 90 percent of the human genome. That genetic material, however, is now understood to often play important roles in regulating and "turning on" the expression of other genes.

In this case, the genetic element is believed to play a major role in the proper function of the "innate" immune system in primates – an ancient, first line of defense against bacteria, viruses and other pathogens, in which the body recognizes something that probably doesn't belong there, even though the specific pathogen may never have been encountered before.

"Many people are familiar with the role of our adaptive immune system, which is what happens when we mount a defense against a new invader and then retain antibodies and immunity in the future," Gombart said. "That's what makes a vaccine work. But also very important is the innate immune system, the almost immediate reaction your body has, for instance, when you get a cut or a skin infection."

In primates, this action of "turning on" an optimal response to microbial attack only works properly in the presence of adequate vitamin D, which is actually a type of hormone that circulates in the blood and signals to cells through a receptor. Vitamin D is produced in large amounts as a result of sun exposure, and is available in much smaller amounts from dietary sources.

Vitamin D prevents the "adaptive" immune response from over-reacting and reduces inflammation, and appears to suppress the immune response. However, the function of the new genetic element this research explored allows vitamin D to boost the innate immune response by turning on an antimicrobial protein. The overall effect may help to prevent the immune system from overreacting.

"It's essential that we have both an innate immune response that provides an immediate and front line of defense, but we also have protection against an overreaction by the immune system, which is what you see in sepsis and some autoimmune or degenerative diseases," Gombart said. "This is a very delicate balancing act, and without sufficient levels of vitamin D you may not have an optimal response with either aspect of the immune system."

After years of research, scientists are continuing to find new roles that vitamin D plays in the human body. It can regulate the actions of genes that are important to bone health, calcium uptake, and inhibition of cell growth. It helps regulate cell differentiation and, of course, immune function.

"The antimicrobial peptide that we're studying seems to be involved not just in killing bacteria, but has other biological roles," Gombart said. "It recruits other immune cells and sort of sounds the alarm that something is wrong. It helps promote development of blood vessels, cell growth and healing of wounds. And it seems to have important roles in barrier tissues such as skin and the digestive system. Vitamin D is very important for the health of the skin and digestive system, and putting the cathelicidin antimicrobial peptide gene under its regulation may be important in this function."

Any one, or some combination of those biological roles may be why vitamin D-mediated regulation of the antimicrobial peptide has been conserved in every primate species ever examined for its presence, researchers

said, and did not disappear long ago through evolutionary variation and mutation. The evolution of primates into many different families and hundreds of species has been carefully tracked through genetic, molecular sequence and fossil studies, but the presence of this regulatory element in primates is still largely the same as it's been for more than 50 million years.

The evolutionary survival of this genetic element and the placement of the cathelicidin antimicrobial peptide gene under the regulation of the vitamin D pathway "may enable suppression of inflammation while potentiating innate immunity, thus maximizing the overall immune response to a pathogen and minimizing damage to the host," the researchers wrote in their conclusion.

Vitamin D deficiency is an issue of growing concern among many scientists, due to changing lifestyle or cultural trends in which many people around the world get less sun exposure and often inadequate dietary levels of the vitamin. It's a special problem with the elderly, which often have reduced exposure to sunlight and less ability to produce vitamin D in their skin – and at least partly as a result, are more susceptible to bone fractures, chronic inflammation and infectious disease.

Scientists help explain effects of ancient Chinese herbal formulas on heart health

New research at The University of Texas Health Science Center at Houston suggests that ancient Chinese herbal formulas used primarily for cardiovascular indications including heart disease may produce large amounts of artery-widening nitric oxide. Findings of the preclinical study by scientists in the university's Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases (IMM) appear in the Sept. 15 print issue of the journal Free Radical Biology & Medicine.

Nitric oxide is crucial to the cardiovascular system because it signals the inner walls of blood vessels to relax, which facilitates the flow of blood through the heart and circulatory system. The messenger molecule also eliminates dangerous clots, lowers high blood pressure and reduces artery-clogging plaque formation.

The results from this study reveal that ancient Chinese herbal formulas "have profound nitric oxide bioactivity primarily through the enhancement of nitric oxide in the inner walls of blood vessels, but also through their ability to convert nitrite and nitrate into nitric oxide," said Nathan S. Bryan, Ph.D., the study's senior author and an IMM assistant professor.

Herbal formulas are a major component of traditional Chinese medicines (TCMs), which also include acupuncture and massage. "TCMs have provided leads to safe medications in cancer, cardiovascular disease and diabetes," said C. Thomas Caskey, M.D., IMM director and CEO. "The opportunity for Dr. Bryan's work is outstanding given that cardiac disease is the No. 1 cause of death in the United States."

In the study, researchers performed laboratory tests on DanShen, GuaLou and other herbs purchased at a Houston store to assess their ability to produce nitric oxide. Ancient Chinese herbal formulas used primarily for cardiovascular indications are made up of three to 25 herbs. The formulas can be administered as tablets, elixirs, soups and teas.

Most Chinese herbal formulas marketed in the United States are not considered drugs by the U.S. Food and Drug Administration, said Yong-Jian Geng, M.D., Ph.D., study co-author and cardiology professor at The University of Texas Medical School at Houston. They are considered dietary supplements and are not regulated as strictly as drugs.

Scientists also tested the capacity of the store-bought TCMs to widen blood vessels in an animal model. "Each of the TCMs tested in the assays relaxed vessels to various degrees," the authors stated.

"Further studies should be considered in humans, particularly those with cardiac indications," Geng said. "Hopefully, we will have more data to report in the near future."

While fully integrated into the healthcare systems in some parts of Asia, ancient Chinese herbal formulas are often considered alternative medicines in Western nations. Part of the reason, according to Bryan, may be that until recently little was known about how they work.

"The next step is to identify the active components of the TCMs that are responsible for producing the NO. We are currently trying to isolate and identify the active component or components," Bryan said.

Yaoping Tang, M.D., an IMM postdoctoral fellow, was the lead author of the study titled "Nitric oxide bioactivity of traditional Chinese medicines used for cardiovascular indications." Also collaborating on the study was Harsha Garg, an IMM senior research assistant.

Hidden treasure: Technique reveals buried image in famed illustrator's painting

WASHINGTON - Scientists today reported use of a new X-ray imaging technique to reveal for the first time in a century unprecedented details of a painting hidden beneath another painting by famed American illustrator N.C. (Newell Convers) Wyeth. The non-destructive look-beneath-the-surface method could reveal hidden images in

hundreds of Old Master paintings and other prized works of art, the researchers say. The scientists reported the research at the 238th National Meeting of the American Chemical Society (ACS).

Jennifer Mass, Ph.D., and colleagues note in the new study that many great artists re-used canvases or covered paintings with other paintings. They did this in order to save money on materials or to let the colors and shapes of a prior composition influence the next one, she says. Art historians believe that several of Wyeth's most valued illustrations have been lost from view in that way. Some regard N.C. Wyeth (1882-1945) as the greatest American illustrator of the 20th century.

One of these so-called lost illustrations depicts a dramatic fist fight and was published in a 1919 Everybody's Magazine article titled "The Mildest Mannered Man." Using simple X-ray techniques, other scientists previously showed that Wyeth had covered the fight scene with another painting, "Family Portrait." But until now, the fine detail and colors in the fight scene have been lost from view. Nobody has seen the true image except in black and white reproductions.

The illustration above is hidden beneath artist N. C. Wyeth's painting "Family Portrait" (below). **Brandywine River Museum**

The new instrument, called a confocal X-ray fluorescence microscope, was developed at the Cornell High Energy Synchrotron Source (CHESS) national X-ray facility. The instrument reveals minute details in hidden paintings without removing paint samples. It shoots X-ray beams into a painting and then collects fluorescent X-ray "signals" given off by the chemicals in the various paint layers. Scientists can link each signal to specific paint pigments. In addition to revealing the original image, the method is providing new information on Wyeth's materials and methods. The same technique may ultimately reveal hidden images in paintings by other famed artists, the researchers say.

Researchers are using a new X-ray technique to identify the original details and colors of the "fist-fight" image (above) hidden underneath this "Family Portrait" painting. **Brandywine River Museum**

Romantic, candle-lit dinners: An unrecognized source of indoor air pollution

WASHINGTON - Burning candles made from paraffin wax - the most common kind used to infuse rooms with romantic ambiance, warmth, light, and fragrance - is an unrecognized source of exposure to indoor air pollution, including the known human carcinogens, scientists reported here today. Levels can build up in closed rooms, and be reduced by ventilation, they indicated in a study presented at the 238th National Meeting of the American Chemical Society (ACS).

In the study, R. Massoudi Ph.D., and Amid Hamidi , Ph.D., said that that candles made from bee's wax or soy, although more expensive, apparently are healthier. They do not release potentially harmful amounts of indoor air pollutants while retaining all of the warmth, ambience and fragrance of paraffin candles (which are made from petroleum).

"An occasional paraffin candle and its emissions will not likely affect you," Hamidi said. "But lighting many paraffin candles every day for years or lighting them frequently in an un-ventilated bathroom around a tub, for example, may cause problems." Besides the more serious risks, he also suggested that some people who believe they have an indoor allergy or respiratory irritation may in fact actually be reacting to air pollutants from burning candles

New approach to wound healing may be easy on skin, but hard on bacteria

WASHINGTON, D.C. - In a presentation today (Aug. 19) to the American Chemical Society meeting, Ankit Agarwal, a postdoctoral researcher at the University of Wisconsin-Madison, described an experimental approach to wound healing that could take advantage of silver's anti-bacterial properties, while sidestepping the damage silver can cause to cells needed for healing.

Silver is widely used to prevent bacterial contamination in wound dressings, says Agarwal, "but these dressings deliver a very large load of silver, and that can kill a lot of cells in the wound." Wound healing is a particular problem in diabetes, where poor blood supply that inhibits healing can require amputations, and also in burn wards. Agarwal says some burn surgeons avoid silver dressings despite their constant concern with infection.

Using a new approach, Agarwal has crafted an ultra-thin material carrying a precise dose of silver. One square inch contains just 0.4 percent of the silver that is found in the silver-treated antibacterial bandages now used in medicine. In tests in lab dishes, the low concentration of silver killed 99.9999 percent of the bacteria but did not damage cells called fibroblasts that are needed to repair a wound.

Agarwal builds the experimental material from polyelectrolyte multilayers - a sandwich of ultra-thin polymers that adhere through electrical attraction. To make the sandwich, Agarwal alternately dips a glass plate in two solutions of oppositely charged polymers, and finally adds a precise dose of silver.

"This architecture is very easily tuned to different applications," Agarwal says, because it allows exact control of such factors as thickness, porosity and silver content. The final sandwich may range from a few nanometers to several hundred nanometers in thickness. (One nanometer is one-billionth of a meter; a human hair is about 60,000 nanometers in diameter.)

Nicholas Abbott, a professor of chemical and biological engineering who advises Agarwal, says during the past decade, "about a bazillion papers have been published on polyelectrolyte multilayers. It's been a tremendous investment by material scientists, and that investment is now ripe to be exploited."

The project was supported by seed funding from the Wisconsin Institutes of Discovery - a new unit devoted to advancing technology in five targeted areas, including tissue engineering — and benefited from contributions by Christopher Murphy, Jonathan McAnulty and Charles Czuprynski of UW-Madison's School of Veterinary Medicine; Ronald Raines of the Department of Biochemistry; and Michael Schurr, a burn surgeon at the School of Medicine and Public Health.

Although both mammalian cells and bacteria are sensitive to silver, bacteria are much more sensitive, leaving a sweet spot - a concentration of silver that can kill bacteria without harming cells needed for healing. In tests using mouse cells and sample bacteria, Agarwal has tuned the dose to find the sweet spot where the silver bullet destroys 99.9999 percent of the bacteria, but does not harm fibroblasts. Indeed, the system is so sensitive that increasing the silver dose from 0.4 percent to 1 percent of the level used in a commercial dressing severely damaged the fibroblasts.

To kill bacteria, silver must take the form of charged particles, or ions, and the tiny silver nanoparticles that Agarwal embeds in the sandwich can be designed to release ions for days or weeks as needed. In contrast, Agarwal says, commercial wound dressings contain a large dose of silver ions, which are released faster and with less control.

The required dose of silver can also be reduced because the new material would be designed to stay in close contact with the wound, Abbott says. "In a commercial dressing, the silver is part of the bandage that is placed on the wound surface. We envision this material becoming incorporated into the wound; the cells will grow over it and it will eventually decay and be absorbed into the body, much like an absorbable suture."

Tests on animals will be needed to before the new material can be tested on humans, says Abbott. "A commercial dressing needs to have a large quantity of silver so it can diffuse to the wound bed, and that quantity turns out to be toxic to mammalian cells in lab dishes. We are putting the silver where we need it, so we can use a small loading of silver, which does not exhibit toxicity to mammalian cells because the silver is precisely targeted."

Warning over codeine use after tonsillectomy

A report out of The University of Western Ontario, published in the New England Journal of Medicine, warns the use of codeine to treat pain following a tonsillectomy could prove fatal for some children. Dr. Gideon Koren, who holds the Ivey Chair in Molecular Toxicology at Western, zeroed in on the danger after investigating the death of a two year old boy following a relatively easy operation to remove his tonsils.

Koren is a pediatrics professor at both Western and the University of Toronto, and the Director of the Motherisk program at the Hospital for Sick Children in Toronto. Enlarged tonsils are usually treated with antibiotics, but Koren says tonsillectomies are still performed in the case of sleep apnea, where the child stops breathing while asleep.

In this particular case, the toddler had a history of snoring and sleep-study-confirmed sleep apnea. He was taken to an outpatient clinic, had the operation, and was taken home. The mother was given syrup of codeine and instructed how to administer it to her child for pain relief. On the second night after surgery, the child developed a fever and wheezing, and was found dead the next morning. Tests later showed the mother had given the proper dosage, and yet the child's body was found to have high levels of morphine. The coroner asked Koren to look at the case.

"The sudden death of a healthy child was quite sobering because tonsillectomies are done every day, all over North America," says Koren. "And more and more of them are done on an outpatient basis, with the child going

home the same day." The child was found to have the ultra-rapid metabolism genotype which causes the body to metabolize codeine at a faster rate, producing significantly higher amounts of morphine.
Last year Koren published research showing how mothers who are given codeine for pain following childbirth, can pass toxic levels of morphine to their babies though their breastmilk, if they carry this genotype. It's estimated just over one per-cent of Caucasians carry this gene, but the incidence could be as high as 30% in those of African origin.

Koren has another concern about giving codeine to children following a tonsillectomy for sleep apnea. "If the apnea doesn't go away, codeine will also suppress the child's breathing. This demonstrates the need to keep children in hospital under surveillance for at least 24 hours to see if the apnea persists."

Western graduate student Catherine Ciszkowski co-authored the paper with Koren. The Ivey Chair in Molecular Toxicology studies why drugs can be safe for most people, and yet life-threatening to some, and tries to find ways to predict those situations.

Major insights into evolution of life reported by UCLA molecular biologist

Humans might not be walking the face of the Earth were it not for the ancient fusing of two prokaryotes - tiny life forms that do not have a cellular nucleus. UCLA molecular biologist James A. Lake reports important new insights about prokaryotes and the evolution of life in the Aug. 20 advance online edition of the journal Nature.

Endosymbiosis refers to a cell living within another cell. If the cells live together long enough, they will exchange genes; they merge but often keep their own cell membranes and sometimes their own genomes.

Lake has discovered the first exclusively prokaryote endosymbiosis. All other known endosymbioses have involved a eukaryote — a cell that contains a nucleus. Eukaryotes are found in all multicellular forms of life, including humans, animals and plants. "This relationship resulted in a totally different type of life on Earth," said Lake, a UCLA distinguished professor of molecular, cell and developmental biology and of human genetics. "We thought eukaryotes always needed to be present to do it, but we were wrong."
In the Nature paper, Lake reports that two groups of prokaryotes - actinobacteria and clostridia - came together and produced "double-membrane" prokaryotes. "Higher life would not have happened without this event," Lake said. "These are very important organisms. At the time these two early prokaryotes were evolving, there was no oxygen in the Earth's atmosphere. Humans could not live. No oxygen-breathing organisms could live."

The oxygen on the Earth is the result of a subgroup of these double-membrane prokaryotes, Lake said. This subgroup, the cyanobacteria, used the sun's energy to produce oxygen through photosynthesis. They have been tremendously productive, pumping oxygen into the atmosphere; we could not breathe without them. In addition, the double-membrane prokaryotic fusion supplied the mitochondria that are present in every human cell, he said.

"This work is a major advance in our understanding of how a group of organisms came to be that learned to harness the sun and then effected the greatest environmental change the Earth has ever seen, in this case with beneficial results," said Carl Pilcher, director of the NASA Astrobiology Institute, headquartered at the NASA Ames Research Center in Moffett Field, Calif., which co-funded the study with the National Science Foundation. "Along came these organisms — the double-membrane prokaryotes — that could use sunlight," Lake said. "They captured this vast energy resource. They were so successful that they have more genetic diversity in them than all other prokaryotes.

"We have a flow of genes from two different organisms, clostridia and actinobacteria, together," he said. "Because the group into which they are flowing has two membranes, we hypothesize that that was an endosymbiosis that resulted in a double membrane. It looks as if a single-membrane organism has engulfed another. The genomes are telling us that the double-membrane prokaryotes combine sets of genes from the two different organisms."

For this study, Lake has looked back more than 2.5 billion years. He conducted an analysis of the genomics of the five groups of prokaryotes. Lake is interested in learning how every organism is related.

"We all are interested in our ancestors," he said. "A friend at UC Berkeley, Alan Wilson, was the first person to collect DNA from large numbers of people around the world. He showed that we are all related to a woman who lived in Africa 200,000 years ago. Some in the media called her Eve. He called her the Lucky Mother, the mother of us all.

"In our field, we have enormous amounts of data but cannot make sense of it all. Endosymbiosis allows us to start to understanding things; it tells us that many genes are exchanged.

"We have been overlooking how important cooperation is," Lake said. "If two prokaryotes get together, they can change the world. They restructured the atmosphere of the Earth. It's a message that evolution is giving us: Cooperation is a way to get ahead."

Actinobacteria have an unusual DNA composition, with a very high amount of "G" and "C" nucleotides - chemicals whose patterns carry the data required for constructing proteins. Nucleotides are designated by the

letters G (guanine), C (cytosine), A (adenine) and T (thymine); the sequence of nucleotides serves as a chemical code.

Some actinobacteria are pathogens, including ones that cause tuberculosis and leprosy. Some clostridia can photosynthesize, which no other single-membrane prokaryote does. Photosynthesis may have been developed in clostridia. Double-membrane prokaryotes include the pathogens that cause ulcers, as well as the organisms that led to the creation of the chloroplasts that are in all green plants and which make plant growth possible.

Where does white skin come from?

* 19 August 2009 **by Anil Ananthaswamy**

THE idea that early humans became fair-skinned as they migrated north out of Africa so they could make enough vitamin D to stay healthy has been questioned again, reopening a debate that many think is settled.

In equatorial Africa and in the tropics, melanin - the pigment that makes skin dark - provides protection against the intense sunlight. But melanin can also block the ultraviolet radiation (UVB) that triggers vitamin D production in the skin. This is an advantage in the tropics, where UVB radiation is barely filtered by the atmosphere above.

But UVB intensity falls dramatically at higher latitudes, where melanin can pose a problem for dark-skinned people. Vitamin D deficiency can lead to rickets and women with the disease often develop a deformed pelvis, making it difficult for them to reproduce.

According to the vitamin D hypothesis, when humans left Africa tens of thousands of years ago and reached Europe, natural selection weeded out the melanin. While people with lighter skin could produce adequate levels of vitamin D, those whose skin remained dark were more likely to suffer from rickets. The hypothesis arose when studies from the early 20th century showed that blacks in the US were two to three times as likely to suffer from the disease as whites.

"It is a very attractive hypothesis and very few people have taken issue with it," says Ashley Robins of the University of Cape Town Medical School, Observatory, South Africa.

Robins is one of the few, arguing that adequate vitamin D wouldn't necessarily have been a problem. Melanin is not an absolute screen against UVB, he says. Dark-skinned people in higher latitudes need to be exposed to about 6 to 10 times as much sunlight as white-skinned people for the vitamin D in their blood to reach acceptable levels. This equates to about 2 to 3 hours of sunlight about 3 times a week for Africans living in, say, the UK. "Early humans would have had that amount of exposure every day," says Robins. "And that would certainly have overwritten any melanin barrier. I'm pretty certain that you would not have got vitamin D deficiency and rickets."

Robins also points to studies showing that while black volunteers have significantly lower blood levels of vitamin D than white volunteers after a whole-body dose of UVB, the difference narrowed and even disappeared when levels of metabolites derived from vitamin D were compared (American Journal of Physical Anthropology, DOI: 10.1002/ajpa.21077). This suggests that in darker-skinned people, enzymes from the liver and kidneys were working harder to keep the levels of the active metabolites the same, regardless of the skin pigmentation. "There seems to be a compensatory mechanism," says Robins. "That's another reason why the vitamin D hypothesis fails."

But Michael Holick, an expert on vitamin D at the Boston University School of Medicine, says Robins is wrong. Rickets is a debilitating disease with serious consequences, says Holick. "De-pigmentation would have had to occur within a few generations. Otherwise, you would not have been able to procreate in northern European environments."

Asta Juzeniene, of the Oslo University Hospital in Montebello, Norway, points out that the consequences of vitamin D deficiency go beyond rickets. She says a lack of the vitamin has also been linked to diabetes, cancer, rheumatoid arthritis, multiple sclerosis and heart disease.

Juzeniene and her colleagues recently reviewed alternate hypotheses for why humans might have evolved lighter skin (Journal of Photochemistry and Photobiology B: Biology, vol 96, p 93). One highly controversial idea involves sexual selection: once sensitive light skin was no longer hazardous, as in Africa, it was selected for sexual attractiveness. The other idea is that dark skin was more prone to frostbite in higher latitudes, and hence would have come under negative selection pressure, a claim that comes from studies of soldiers during the Korean war, when black soldiers suffered far more frostbite than white soldiers.

One idea is that dark skin was more prone to frostbite in higher latitudes and was selected against

Juzeniene is not convinced by these alternatives. "The vitamin D hypothesis is the most likely hypothesis although there is still no consensus about it," she says.

Robins, on the other hand, is keen on the frostbite theory for the evolution of lighter skin. "If darker skin people are going to have frostbite, and babies and mothers' nipples are going to be frostbitten, then like sunburn, this is going to be a potent selective force," he says.

Geobiologists propose that the earliest complex organisms fed by absorbing ocean buffet

Blacksburg, Va. -- Research at Virginia Tech has shown that the oldest complex life forms -- living in nutrient-rich oceans more than 540 million years ago – likely fed by osmosis.

The researchers studied two groups of modular Ediacara organisms, the fern-shaped rangeomorphs and the air mattress-shaped erniettomorphs. These macroscopic organisms, typically several inches in size, absorbed nutrients through their outer membrane, much like modern microscopic bacteria, according to the cover story of the Aug. 25, 2009 issue of the Proceedings of the National Academy of Sciences (PNAS), "Osmotrophy in modular Ediacara organisms," by Marc Laflamme, Shuhai Xiao, and Michal Kowalewski. Laflamme, now a Postdoctoral Fellow in the Department of Geology and Geophysics at Yale University, did the research as a postdoc in Xiao's lab at Virginia Tech. Xiao and Kowalewski are professors of geobiology in the College of Science at Virginia Tech.

The rangeomorphs had a repeatedly branching system like fern leaves and the erniettomorphs had a folded surface like an inflated air mattress to make tubular modules. "These organisms are unlike any life forms since and so are poorly understood," said Laflamme.

Their feeding strategy has been a topic of controversy, with theories ranging from parasitism to symbiosis to photosynthesis. "Some hypotheses can be ruled out because the organisms lack feeding structures, such as tentacles or mouths, and because many of them lived in the deep ocean where there was no sunlight for photosynthesis" said Xiao.

The researchers decided to simulate various morphological changes in the overall construction of the organisms to test whether it would have been possible for them to attain surface area to volume ratios on the same order as modern bacteria that feed by osmosis. Theoretical models were constructed to explore the effects of length, width, thickness, number of modules, and presence of internal vacuoles, on the surface area of the Precambrian fossils. "Modeling efforts suggest that internal vacuoles – that is, voids filled with fluids or other biologically inert materials – are a particularly effective way of increasing surface-to-volume ratio of complex, macroscopic organisms," said Kowalewski.

They discovered that the two groups (the repeatedly branching rangeomorphs and the air-mattress like erniettomorphs) grew and constructed their bodies in different ways; however both groups attempted to maximize their surface-area to volume ratios in their own way. "The increase in size was clearly accomplished primarily by addition of modules for the erniettomorphs and repetitive branching and inflation of modules for the rangeomorphs," Laflamme said. "The repeated branching system in rangeomorphs was essential to allow for a high surface-area to volume ratio necessary for proper osmosis-based feeding."

Today, only microscopic bacteria find it efficient to us only osmosis to feed, although some animals, such as sponges and corals, use osmosis as a supplementary food source. But in the Ediacaran period, 635 to 541 million years ago, with nutrient-rich oceans, "a diffusion-based feeding strategy was more feasible," Laflamme said.

"We believe the Ediacarans were feeding on dissolved organic carbon, which can come in many forms," he said. "It represents the organic material originating from plants, fungi, animals -- you name it, which has dissolved into fats and proteins during natural organic decay. There is a growing body of evidence that in Ediacaran times, due mainly to the absence of animals with true guts capable of packaging organic matter into fecal pellets, there was a much greater pool of dissolved organic nutrients, especially in deeper waters. Without fecal pellets, organic substances would have remained in suspension and decomposed into fats and proteins capable of dissolution into marine waters," he said. "We believe these compounds were then absorbed via osmosis through Ediacaran "skin" due to the high surface-area to volume ratios."

The PNAS article concludes that today "giant sulfur bacteria, such as Thiomargarita, thrive along the coastal area of Namibia, where constant upwelling allows for greater access to (dissolved organic carbon) and nutrients. Such nutrient-rich areas may be modern-day analogs to Ediacaran deep oceans ... suggesting that it may be more than coincidental that the earliest rangeomorphs occurred in (dissolved organic carbon)-rich deep waters."

The research was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC) and Laflamme's Bateman Fellowship, the NASA Exobiology and Evolutionary Biology Program, and the National Science Foundation Sedimentary Geology and Paleobiology Program.

Find the article online at http://www.pnas.org/content/early/2009/08/13/0904836106.abstract

Not Exactly Rocket Science

Do lost people really go round in circles?

Posted on: August 20, 2009 12:00 PM, **by Ed Yong**

In 2007, Jan Souman dropped three volunteers into the Sahara desert and watched as they walked for several miles, in an attempt to walk in a straight line. Souman was interested in the widespread belief that lost travelers end up walking in circles, a belief that has never been properly tested but has nonetheless become firmly entrenched in the popular consciousness. Just think about Frodo and Sam's hike through Mordor or the three hapless teens in the Blair Witch Project.

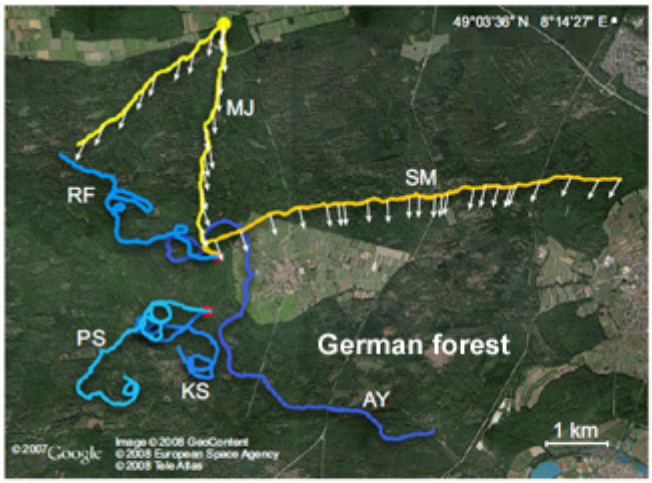
To see how non-fictional humans would fare, Souman tracked a group of volunteers using GPS as they walked through a thick German forest or a featureless Tunisian desert, as well as others who strolled through a large field blindfolded. The result: they did indeed go in circles but with no preference for any direction and only when they couldn't see or when the sun or moon weren't visible.

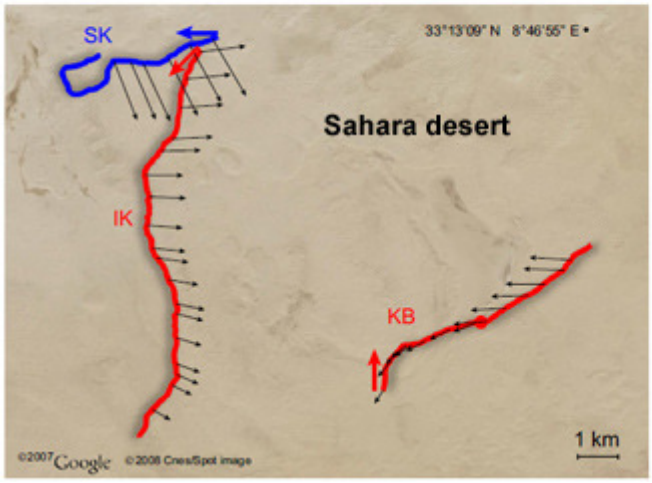
It seems that with some sort of reference point, we're entirely capable of walking in a straight line, even in a featureless desert where dunes obscure the horizon or a busy forest that's riddled with obstacles. The sun's good enough for these purposes, even though it's position changes as the hours pass. Without any such cues, we quickly veer off course.

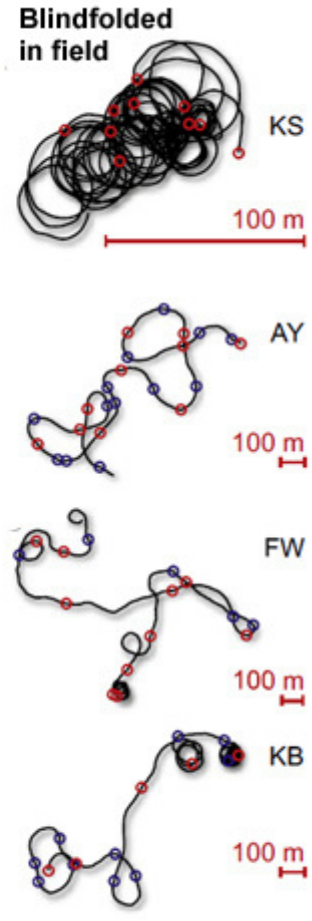
The two volunteers who walked through in the forest on a sunny day managed to keep to a perfectly straight line, wandering only in the first fifteen minutes when the sun was behind a cloud. The four people who walked on much cloudier days all ambled in circles, repeatedly crossing their own path without knowing it. The desert walkers fared about as well - those who walked during the heat of the day veered slightly but kept reasonably straight. A third man walked at night; he too kept a direct course when the moon was visible but when it vanished behind clouds, a couple of sharp turns sent him back in the direction he came from.

Scientists have put forward many explanations for the circular rambles of lost walkers. Some say that most people have one leg that's longer or stronger than the other and over time, these differences add up to a curving course. Others say that asymmetries in our very brains set up a tendency to turn in one direction. Without a guiding light or landmark, these small biases would make their presence felt.

But Souman thinks otherwise. He set a group of 15 blindfolded people loose in a large field, told them to walk straight ahead and watched them for 50 minutes. All of them walked in very random paths, including large flamboyant loops and, on occasion, surprisingly small circles of as little as 20 metres in diameter (little enough to fit within a basketball court).







Only three of the 15 people consistently veered in one direction and they did indeed go round in circles; the others walked more chaotic paths. On the whole, their meanderings had no consistent bias and they would turn one way as often as the other. Indeed, one of the volunteers, known only as KS, took part in both experiments and while he had the strongest directional bias while blindfolded, he actually veered in the opposite direction in the forest.

That strongly argues against the influence of asymmetric legs or brains. Souman certainly ruled out the leg hypothesis by showing that the relative strengths of his walkers' legs didn't relate to the average direction of their turns. He even X-rayed the legs of one of his recruits to measure their length

and then evened things up with shoes of varying soles. They made no difference to his path.

So without landmarks to guide them, the walkers were relying on feedback from their bodies (proprioception) and their sense of balance. These cues can help over short distances, but Souman says that they soon build up "sensory noise" that renders them inaccurate and causes the person's trajectory to drift both increasingly and randomly.

It's telling that the blindfolded walkers in the open field behaved in very similar ways to the ones in the cloudy forests - their jaunts included bouts of random direction interspersed with systematic circling. This may have been because of all sorts of obstacles or local landmarks in the forest, but not so in the field.

Instead, Souman suggests that people circle when their internal sense of "straight ahead" becomes corrupted by random errors in their sense of touch, balance or spatial awareness. Small errors lead to random walks, while larger errors cause circling. And that has a massive impact on their ability to get, well, anywhere.

Despite walking for 50 minutes, most of these people never made it very far. Within a few minutes, their average distance from the starting point levelled off so that they were usually around 100 metres of it. A visual cue, however, can do wonders for resetting our navigation. If Souman allowed his blindfolded bumblers to lift their blindfolds for a minute out of every five or ten, they managed to recalibrate their sense of "straight ahead" and started each block of time in a straight line again.

As Souman himself concludes, "Ironically, in the age of ubiquitous navigation systems in airplanes, cars, and even mobile phones, we are only beginning to understand how humans navigate through their environment, exploring uncharted terrain." His study shows that even the simple act of walking in a straight line is more complex than it might first appear. *Reference: Current Biology doi:10.1016/j.cub.2009.07.053*

Our nostrils share a rivalry too, study finds

Your nostrils may seem to be a happy pair, working together to pick up scents. However, a study published online on August 20th in Current Biology, a Cell Press publication, reveals that there can actually be a kind of rivalry between the two.

"The two nostrils of a person typically have similar olfactory experience at any given time," said Denise Chen of Rice University. "But in a laboratory setting in which each nostril simultaneously receives a different smell, subjects experience an olfactory illusion. Instead of perceiving a constant mixture of the two smells, they perceive one of the smells followed by the other in an alternating fashion, as if the nostrils were competing with one another."

Chen and her colleague Wen Zhou call this duel between nostrils binaral (meaning "two-nostril") rivalry.

In fact, this sort of rivalry of the senses has been observed before. Most of our sensory organs come in pairs: eyes, ears, and nostrils. Typically, the two eyes form slightly different retinal images of the same object, the researchers explained. There are likewise small differences in time and intensity between a sound arriving at one ear versus the other, as well as between a smell arriving at one nostril versus the other. Most of the time, our brain integrates these minor differences and generates one stable and accurate representation of the world around us.

But that kind of harmony can only go so far. "When the eyes simultaneously view two different visual images, one for each eye, we perceive the two images in alternation, one at a time," Chen said. Similarly, when alternating tones an octave apart are played out of phase to each ear, most listeners experience a single tone oscillating from ear to ear.

The new study shows that the same is true of our sense of smell. Chen says the finding tells us that although both smells are equally present, our brain primarily attends to them one at a time.

The strength of this effect came as something of a surprise to the researchers, especially given that the sense of smell is generally considered less prominent in human perception than our ability to see and hear. Chen says the discovery will undoubtedly stimulate new research on the workings of the olfactory system and olfactory awareness.

The researchers include Wen Zhou and Denise Chen, of the Department of Psychology, Rice University, Houston, TX.

Hello wearable kidney, goodbye dialysis machine

Researchers are developing a Wearable Artificial Kidney for dialysis patients, reports an upcoming paper in the Clinical Journal of the American Society of Nephrology (CJASN). "Our vision of a technological breakthrough has materialized in the form of a Wearable Artificial Kidney, which provides continuous dialysis 24 hours a day, seven days a week," comments Victor Gura, MD (David Geffen School of Medicine at UCLA).

The device - essentially a miniaturized dialysis machine, worn as a belt - weighs about 10 pounds and is powered by two nine-volt batteries. Because patients don't need to be hooked up to a full-size dialysis machine, they are free to walk, work, or sleep while undergoing continuous, gentle dialysis that more closely approximates normal kidney function.

Such a device could lead to a "paradigm change" in the treatment of dialysis patients. Despite enduring long hours on dialysis every week - with major limitations in activities, diet, and other areas of life - dialysis patients face high rates of hospitalization and death. The U.S. dialysis population currently exceeds 400,000, with costs of over $30 billion per year. "We believe that the Wearable Artificial Kidney will not only reduce the mortality and misery of dialysis patients, but will also result in significant reduction in the cost of providing viable health care," says Gura.

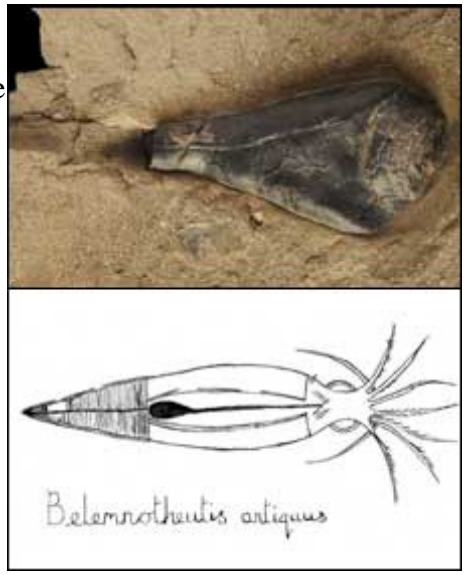
The Wearable Artificial Kidney is successful in preliminary tests, including two studies in dialysis patients. The new study provides important information on the technical details that made these promising results possible.

"However, the long-term effect of this technology on the well-being of dialysis patients must be demonstrated in much-needed clinical trials," adds Gura. "Although successful, this is but one additional step on a long road still ahead of us to bring about a much-needed change in the lives of this population."

Other authors were Alexandra S. Macy, Masoud Beizai, and Carlos Ezon (Xcorporeal, Inc); and Thomas A. Golper, MD (Vanderbilt University Medical Center). Dr. Gura receives a salary from Xcorporeal, Inc.
Additionally, significant contributions to the development of this new device were made by Hans Dietrich Polaschegg, PhD, Andrew Davenport, MD, Claudio Ronco MD, Andre Kaplan, MD, and Eli Friedman, MD.
The study entitled, "Technical Breakthroughs in the Wearable Artificial Kidney (WAK)," will appear online at http://cjasn.asnjournals.org/ on August 20, 2009, doi 10.2215/CJN.02790409.

Ink found in Jurassic-era squid

Palaeontologists have drawn with ink extracted from a preserved fossilised squid uncovered during a dig in Trowbridge, Wiltshire.



The specimen is now in the British Geological Survey collection

The fossil, thought to be 150 million years old, was found when a rock was cracked open, revealing the one-inch-long black ink sac. A picture of the creature and its Latin name was drawn using its ink.

Dr Phil Wilby of the British Geological Survey said it was an ancient creature similar to the modern-day squid.

"The structure is similar to ink from a modern squid so we can write with it," he said.

'Medusa effect'

The find was made at a site which was first excavated in Victorian times where thousands of Jurassic fossils with preserved soft tissues were found.

Dr Wilby, who led the excavation, said: "We think that these creatures were swimming around during the Jurassic period and were turned to stone soon after death. It's called the Medusa effect." Experts believe one possibility is that thousands of the creatures congregated in the area to mate before being poisoned by algae in the water.

Remains of a different species of squid have also been found, suggesting the carcasses attracted predators to feed on them and they in turn also died.

Dr Wilby said: "They can be dissected as if they are living animals, you can see the muscle fibres and cells.

"It is difficult to imagine how you can have something as soft and sloppy as an ink sac fossilised in three dimension, still black, and inside a rock that is 150 million years old."

The specimen is now in the British Geological Survey collection in Nottingham.

Part of the ink sac has been sent to Yale University in America for more in-depth chemical analysis.

Scientists discover bioluminescent 'green bombers' from the deep sea

Orbs lobbed by mysterious worms burst into brilliant light, thought to be a defensive measure

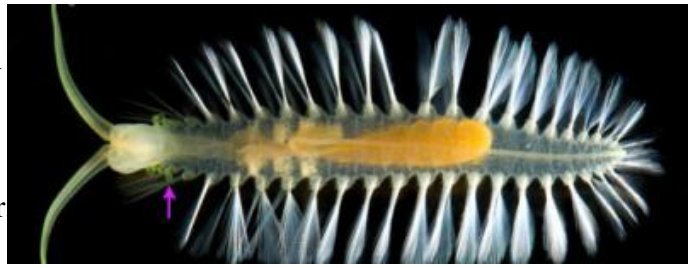
In the latest proof that the oceans continue to offer remarkable findings and much of their vastness remains to be explored, scientists at Scripps Institution of Oceanography at UC San Diego and their colleagues have discovered a unique group of worms that live in the depths of the ocean. The discoveries feature worms - nicknamed "green bombers" - that can release body parts that produce a brilliant green bioluminescent display.

The discovery is described in the August 21 issue of the journal Science and is led by Karen Osborn of Scripps Oceanography.

The researchers introduce seven previously unknown species of swimming worms in the annelid phylum ranging from 18 to 93 millimeters (.7 to 3.6 inches) in length. They were discovered by the scientists using remotely operated vehicles at depths between 1,800 and 3,700 meters (5,900 and 12,140 feet). The first species

described in the paper has been given the scientific name Swima bombiviridis, referring to its swimming ability and the green bombs.

Osborn says one key aspect of the discoveries is that the newly found worms are not rare. Opportunities to witness such animals and collect and study them, however have been extremely rare.



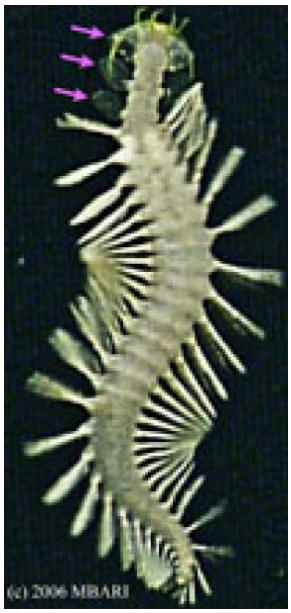
The transparent body of the worm Swima bombiviridisallows examination of internal anatomy without dissection. The purple arrow points to the several bioluminescent bombs still attached to the segments immediately behind the head.

Casey Dunn

"We found a whole new group of fairly large, extraordinary animals that we never knew anything about before," said Osborn, a post-doctoral researcher in the Marine Biology Research Division at Scripps. "These are not rare animals. Often when we see them they number in the hundreds. What's unique is that their habitat is really hard to sample."

Largely transparent except for the gut area, the worms propel themselves with fans of long bristles that form swimming paddles.

"The depths between 1,000 and 4,000 meters (3,280 and 13,120 feet) form the biggest habitat on Earth and also the least explored," said Scripps Professor Greg Rouse, a coauthor of the paper and curator of Scripps Benthic Invertebrate Collection. "With fairly limited time on submersible vehicles, mainly off California, we've picked up seven new species. It goes to show that we have much more exploration ahead and who knows what else we'll discover?"



Each of the species features a variety of elaborate head appendages. Five of them are equipped with luminescent structures, the "bombs," that are fluid-filled spheres that suddenly burst into light when released by the animal, glowing intensely for several seconds before slowly fading.

Due to the bright lights of the submersible, scientists were not able to witness bomb-casting in the worm's natural habitat, but rather on ships after the animals were captured. While the scientists speculate that the bombs are used as a defensive mechanism against potential predators, more studies are needed to fully understand the process.

This is a video image of a species of Swima (as yet undescribed) with arrows indicating the animal's large bombs.

Monterey Bay Aquarium Research Institute

Rouse says the green bombers in the newly discovered clade, (a common ancestor and all its descendant organisms), are fascinating from an evolutionary standpoint. Looking closely at their relatives that live on the seafloor, it appears the bombs were once gills that evolutionarily transformed over time.

"The relatives have gills that appear to be in exactly the same places as the bombs," said Rouse. "The gills can fall off very easily so there's a similarity of being detachable, but for some reason the gills have transformed to become these glowing little detachable spheres."

Osborn continues to probe many of the various adaptations the worms have made since evolving into swimming species. The challenges faced by animals living in a three-dimensional open water habitat above the seafloor are very different than those faced by animals living on the seafloor. These include locating new food sources, finding ways to maintain optimal depth and grappling with predators that come from various directions.

"I'm interested in how animals have evolved in the water column," said Osborn. "These worms are great examples. How does a worm transform into a wonderful glowing animal?"

In addition to Osborn and Rouse, coauthors of the Science paper include Steven Haddock of the Monterey Bay Aquarium Research Institute, Fredrik Pleijel of the University of Göteborg in Sweden and Laurence Madin of the Woods Hole Oceanographic Institution (WHOI).

The research was supported by Scripps Institution of Oceanography, a University of California President's Postdoctoral Fellowship, the David and Lucile Packard Foundation, NOAA, WHOI and the National Geographic Society.

Faster-growing flu vaccine could speed production

AS THE world awaits the next wave of the swine flu pandemic, delays plague vaccine production. Now new, faster-growing strains of the vaccine virus could speed up the process.

The first batches of pandemic vaccine were made in early August. After testing is completed, the rate of vaccination will depend on how fast the vaccine virus can be grown in chicken eggs. So far even the best strains have grown disappointingly slowly, at half the rate of ordinary flu vaccine strains. The US admitted late last week that it will have only 45 million doses of vaccine by mid-October, compared with the 120 million it originally forecast.

Now researchers at the New York Medical College in Valhalla have created improved strains by growing one sample of the virus repeatedly in chicken eggs until it adapted and grew faster. They will send two to vaccine manufacturers this week, says John Wood of the UK's National Institute for Biological Standards and Control (NIBSC). A vaccine made from these strains will still take time to roll out, warns Luc Hessel, head of public affairs at the biggest flu-vaccine maker, France's Sanofi Pasteur. The new strains must prove themselves under manufacturing conditions, and companies must make seed batches.

NIBSC has also created a faster-growing virus, which it sent to manufacturers earlier this month. It poses an extra problem, however: it was made using methods not used before for commercial vaccines.

Chinese culture at the crossroads

Prehistoric archaeological findings highlighted in Science

Recent archaeological discoveries from far-flung corners of China are forcing scientists to reconsider the origins of ancient Chinese civilization – and a new crop of young archaeologists are delving into the modern nation's roots. In the August 21 issue of the journal Science, a group of articles by Science news writer Andrew Lawler explore how, over several millennia, the most populous and economically vibrant nation in the world evolved from a much wider array of peoples and cultures than once imagined.

Lawler crisscrossed China recently for three weeks, traveling from the country's steamy southeastern plains to the rugged westernmost province of Xinjiang, interviewing dozens of archaeologists at a host of sites. This special news package puts a spotlight on how the various archaeological findings of the past decade are challenging what the Chinese people once thought about their country and themselves. As a construction boom continues to alter the physical face of the country – inadvertently uncovering vital clues to China's past, illuminating ancient trade routes and long-lost cultures – a new and more complex history of the Chinese people is emerging right before their very eyes.

The wealth of these recent archaeological discoveries demands a re-write of some history books – and young scholars are even now questioning the existence of a legendary Chinese dynasty, the Xia. Less willing to take ancient texts at face value than their predecessors, this new generation of Chinese researchers is relying on physical data – and more "Western" methods – in their attempts to accurately retrace Chinese history.

But looting and development threaten to destroy the country's heritage. In a land full of wealthy tombs and poor farmers, grave robbing has been an ancient tradition. China's current construction boom poses yet another threat to archaeological sites, though new laws are attempting to halt such damage. Those who destroy evidence of the country's rich history now face jail time and even the death penalty (though no one appears to have been executed for looting yet). Meanwhile, archaeologists are finding novel ways to work with developers and provincial governments to rescue at least some ancient sites from the destruction that comes with the country's economic growth.

“The exciting discoveries made recently across China, coupled with the country's fast-paced development, make this an opportune time to dig into new questions about China's origins, the state of its threatened ancient sites, and the increasing expertise of its archaeologists," says Andrew Lawler, author of the Science news package.

Lawler's special news package on Chinese archaeology covers the accidental discovery and later excavation of Jinsha, an ancient site located near downtown Chengdu in Sichuan, and about 600 miles (1000 kilometers) from the traditional center of Chinese civilization along the Yellow River. Long assumed to have been a cultural backwater, researchers have only recently gleaned the real history of Sichuan's surprisingly ancient and rich culture, which is thousands of years older than they had once believed. Now, thanks to a group of savvy archaeologists and their allies in the city government, Jinsha has become a museum, protected from looters and complete with adjacent land reserved for further archaeological digs in the future.

Another article by Lawler illuminates the earliest Silk Road which brought valued goods like bronze from the west and possibly the staple grain of ancient China, millet, to the west. These recent discoveries have led Chinese researchers to acknowledge significant outside influence on their ancient culture, breaking an old taboo put in place when China was largely closed to the outside world.

Parasites persuade immune cells to invite them in for dinner, says new research

The parasites that cause leishmaniasis use a quirky trick to convince the immune system to effectively invite them into cells for dinner, according to a new study published today in PLoS Pathogens. The researchers, from Imperial College London, say their findings improve understanding of the way Leishmania parasites establish an infection and could aid the search for a vaccine against this neglected tropical disease.

Leishmania parasites are transmitted by sand flies. After the parasites infect a sand fly, they make a sticky gel so that when the fly bites a human, it regurgitates this gel into the body. Today's research, which was funded

by the Wellcome Trust, shows that the gel persuades immune cells known as macrophages to feed the parasites, rather than killing them.

Leishmaniasis is an infection caused by Leishmania parasites that affects around 12 million people per year, mainly in tropical and sub-tropical countries. Symptoms include disfiguring and painful skin ulcers and in severe cases the infection can also spread to the internal organs. Patients with the infection often suffer from social exclusion because of their disfigurement. There is currently no vaccine to protect against infection and although treatments are available, they are not always effective and access to drugs is limited in many areas.

Leishmania-infected sand flies carry the parasites in their midgut. The parasites produce a gel that turns into a plug, stopping anything from passing in or out of the fly's gut. The fly must regurgitate the gel plug before it can feed on human blood. When the fly bites a person, its barbed mouth parts tear the skin so when it regurgitates parasites along with the gel plug, the skin becomes infected.

Today's study shows that the gel's work doesn't stop there - it also helps the parasites to establish an infection by enticing macrophages to the bite site. Macrophages usually kill invading pathogens by eating and digesting them. However, according to the new research, the gel persuades macrophages to engulf the parasites and feed them rather than digest them. This happens within the first few days following infection, enabling the parasites to establish themselves and infect the skin.

Previous research suggested that the sand fly's saliva could be involved in manipulating the immune system. Today's study suggests that the gel has an even bigger effect than the saliva on establishing infection.

Dr Matthew Rogers, lead author of the study from the Division of Investigative Science at Imperial College London, said: "Leishmaniasis is a very debilitating disease, yet we know comparatively little about the way the parasites are transmitted by sand flies. This is because when scientists study the disease they usually inject the parasite into tissues without including the gel or the sand fly's saliva. Our new research shows that we must consider the way the parasites enter the body - along with the gel and saliva - if we are to recreate infection and get an accurate picture of what is going on.

"Our new research shows that Leishmania parasites are very cunning - they make their own gel to control the human immune system so they can establish a skin infection. There is more work to be done here - our previous work in mice has suggested that injecting a synthetic version of the gel into people might provide them with some protection against infection and we would like to explore this further," added Dr Rogers.

The researchers looked at Leishmania infection in mice and found that the gel, called promastigote secretory gel (PSG) enticed macrophages to the site of entry. They compared the effect of PSG with the effects of saline and sand fly saliva on the number of macrophages recruited to a bite site, 4-72 hours after the bite. In the experiment, PSG recruited 108 times more macrophages to the bite than saline and five times more than sand fly saliva.

The researchers also found that PSG persuaded macrophages to feed, rather than kill, the parasites. When macrophages want to kill a pathogen, they produce nitric oxide. However, the researchers' experiments showed that PSG influences the immune cells to produce food, in the form of polyamines, for the parasites instead.

Finally, the researchers looked at the effect of PSG on parasite survival in vitro. They infected macrophage cells with Leishmania parasites with and without PSG. They found that more parasites survived in the first 48 hours following infection when PSG was added; both the proportion of infected cells and the number of parasites in the cells increased by up to 8-fold with PSG. The parasite infection declined after 48 hours in cells both with and without PSG, suggesting an early window of time in which PSG helps the parasites establish an infection.

This research was a collaboration between Imperial College London, Liverpool School of Tropical Medicine and the London School of Hygiene and Tropical Medicine, led by Imperial.

A clue to the elusive cause of type 1 diabetes: Ottawa researchers investigate immune response to wheat

Scientists at the Ottawa Hospital Research Institute and the University of Ottawa have discovered what may be an important clue to the cause of type 1 diabetes. Dr. Fraser Scott and his team tested 42 people with type 1 diabetes and found that nearly half had an abnormal immune response to wheat proteins. The study is published in the August 2009 issue of the journal Diabetes.

Early in life, the immune system is supposed to learn to attack foreign invaders such as viruses and bacteria, while leaving the body’s own tissues and harmless molecules in the environment alone (including food in the gut). When this process goes awry, autoimmune diseases and allergies can develop. Type 1 diabetes is an autoimmune disease that occurs when the immune system mistakenly attacks the pancreas, the organ that regulates blood sugar. Dr. Scott’s research is the first to clearly show that immune cells called T cells from

people with type 1 diabetes are also more likely to over-react to wheat. His research also shows that the over-reaction is linked to genes associated with type 1 diabetes.

"The immune system has to find the perfect balance to defend the body against foreign invaders without hurting itself or over-reacting to the environment and this can be particularly challenging in the gut, where there is an abundance of food and bacteria," said Dr. Scott, a Senior Scientist at the Ottawa Hospital Research Institute and Professor of Medicine at the University of Ottawa. "Our research suggests that people with certain genes may be more likely to develop an over-reaction to wheat and possibly other foods in the gut and this may tip the balance with the immune system and make the body more likely to develop other immune problems, such as type 1 diabetes."

In a commentary accompanying the paper, diabetes expert Dr. Mikael Knip of Finland said "These observations add to the accumulating concept that the gut is an active player in the diabetes disease process."

Dr. Scott's previous research has shown that a wheat-free diet can reduce the risk of developing diabetes in animal models, but he notes that more research will be required to confirm the link and determine possible effects of diet changes in humans. Research is also needed to investigate links with celiac disease, another autoimmune disease that has been linked to wheat.

This research was funded by the Juvenile Diabetes Research Foundation and the Canadian Institutes of Health Research. The authors include Dr. Majid Mojibian, Dr. Habiba Chakir, Dr. David E. Lefebvre, Jennifer A. Crookshank, Brigitte Sonier and Dr. Erin Keely, as well as Dr. Scott. Patients were enrolled at The Ottawa Hospital and the Children's Hospital of Eastern Ontario.

An estimated 246 million people have diabetes worldwide. Type 1 diabetes is the most severe form, representing about 10 per cent of all cases. Insulin injections can help control blood sugar levels in those affected but there is no cure.

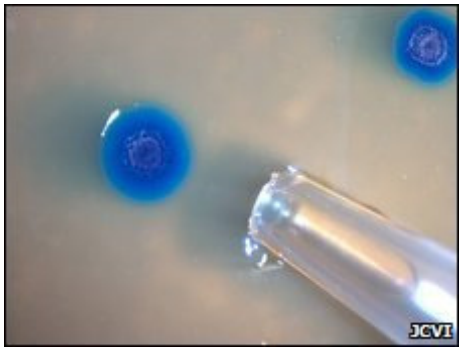
A step closer to 'synthetic life'

By Victoria Gill Science reporter, BBC News

In what has been described as a step towards the creation of a synthetic cell, scientists have created a new "engineered" strain of bacteria.

A team successfully transferred the genome of one type of bacteria into a yeast cell, modified it, and then transplanted into another bacterium. This paves the way to the creation of a synthetic organism - inserting a human-made genome into a bacterial cell. The team describe the work in the journal Science. This advance, the researchers say, overcomes the obstacle of making a new inserted genome work inside a recipient cell.

The experiment was carried out by a team that included scientist J Craig Venter, a leading figure in the controversial field of synthetic biology. Sanjay Vashee, a researcher at the J Craig Venter Institute in Rockville, Maryland, in the US, was one of the authors.



The cells replicated to produce a new strain of Mycoplasma mycoides

The resulting cell he and his team created went on to undertake multiple rounds of cell division, to produce a new strain of the modified bacteria.

Dr Vashee explained to BBC News that the work overcame a hurdle in the quest to create a fully synthetic organism. "Bacteria have 'immune' systems that protect them from foreign DNA such as those from viruses," he explained.

He and his colleagues managed to disable this immune system, which consists of proteins called restriction enzymes that home in on specific sections of DNA and chop up the genome at these points.

Bacteria can shield their own genomes from this process by attaching chemical units called methyl groups at the points which the restriction enzymes attack.

The scientists modified the original genome of the bacterium Mycoplasma mycoides, whilst it was inside the yeast cell. Then they either attached methyl groups to it, or inactivated the restriction enzyme of the recipient bacterium, before transplanting the genome into its new cell.

One of the team's ultimate aims is to transplant a fully synthetic genome into a bacterial cell - creating bacteria that can be programmed to carry out specific functions - for example, digesting biological material to produce fuel.

Race for life

Researchers at the same institute have already synthesised the complete genome of a bacterium they have called Mycoplasma genitalium . Dr Vashee described this work as a "logical extension" of that.

He told BBC News that attempts to create a synthetic bacterium by transplanting M. genitalium into a cell were "ongoing". "We have as of yet no conclusive proof that we have obtained M. genitalium cells after its genome has been put into various recipient cells," he said. "[But this] is a major advance in our effort to create a synthetic cell."

Dr Vashee continued: "We were very concerned that the differences between the modifications in... bacterial DNA and [yeast] DNA might be an insurmountable barrier, preventing transplantation into bacteria of genomes that were passed through yeast. "Now we know how to do this."

Critics have expressed reservations about synthetic biology, and the aim to create what has been widely referred to as artificial life.

Many are concerned that the technology to engineer organisms could end up in the wrong hands.

Dr Vashee concluded: "Dr Venter and the team at JCVI continue to work with bioethicists, outside policy groups, [politicians], and the public to encourage discussion and understanding about the societal implications of their work and the field of synthetic genomics."

Bizarre newt uses ribs as weapons

Matt Walker Editor, Earth News

One amphibian has evolved a bizarre and gruesome defence mechanism to protect itself against predators.

The ribs have burst through the skin, ready to sting any attacker

When attacked, the Spanish ribbed newt pushes out its ribs until they pierce through its body, exposing a row of bones that act like poisonous barbs. The newt has to force its bones through its skin every time it is attacked, say scientists who have described the form and function of the barbs in detail. Yet this bizarre behaviour appears not to cause the newt any ill effects.

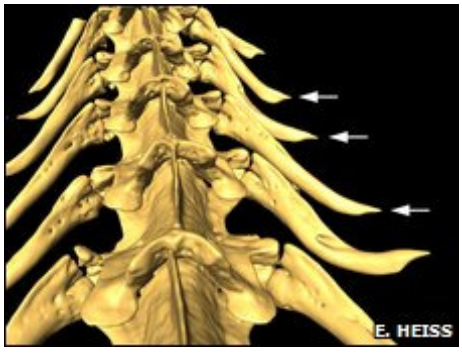
The ability of the Spanish ribbed newt to expose its rib bones was first noticed by a natural historian in 1879. But scientists have now used modern photographic and X-ray imaging techniques to reveal just how the animal does it. And what they discovered is even more gruesome than they imagined.

Arrows point to a poisonous secretion which coats the tips of protruding ribs

When the newt becomes agitated or perceives a threat, it swings its ribs forward, increasing their angle to the spine by up to 50 degrees. As it does this, the newt keeps the rest of its body still. "The forward movement of the ribs increases the body size and stretches the skin to the point of piercing it," says zoologist Egon Heiss of the University of Vienna in Austria. The tips of the newt's ribs then stick outside its body, like exposed spines.

But there is more to the newt's defence, Heiss and his Vienna-based colleagues report in the Journal of Zoology. "When teased or attacked by a predator, [the newt] secretes a poisonous milky substance onto the body surface. The combination of the poisonous secretion and the ribs as 'stinging' tools is highly effective," says Heiss.

The impact on any predator can be striking, particularly if they try to bite the newt or pick it up using their mouth. Then the poison in almost injected into the thin skin within the mouth, causing severe pain or possibly death to the attacker.



A computer tomograph shows the sharp rib points and vertebral column

As well as elucidating the spear-like shape of the ribs, and exactly how the ribs swing forward and protrude, the scientists have demonstrated that the bones must break through the newt's body wall every time the amphibian evokes the defence response. Initially, it was thought that the ribs may passively emerge through pores, rather than be actively driven through the body wall.

Surprisingly, the newt, which is related to other newts and salamanders, appears to suffer no major ill effects, despite repeatedly puncturing its own body and exposing its rib bones. "Newts, and amphibians in general, are known to have an extraordinary ability to repair their skin," says Heiss. "Anyway, if this newt can avoid being eaten in some cases, this surely has a positive influence."

It also seems that the newt is immune to its own poison, which is normally confined to glands in the newt's body. When the newt wounds itself by exposing its ribs, the poison can seep into its body tissue, again apparently with no ill effects. Heiss now hopes to investigate which compounds are in the poison.

Acupuncture may bring relief for a common condition in women

Polycystic ovary syndrome, a common condition among women, can be relieved by the use of acupuncture and exercise. This has been shown by a recent study at the Sahlgrenska Academy, University of Gothenburg, Sweden.

Nearly 10% of women of reproductive age have polycystic ovary syndrome (PCOS). The syndrome expresses itself as a large number of small immature cysts on the ovaries that cause a disturbance in the production of hormones and an increase in the secretion of the male sex hormone. This means that many women with the condition do not ovulate normally, and the syndrome may lead to infertility. The women run an increased risk of becoming obese, developing type 2 diabetes, or developing cardio-vascular disease.
“We do not know for certain what causes the condition, despite it being so common. We have seen that women with the syndrome often have high activity in that part of the nervous system that we cannot consciously control, known as the “sympathetic nervous system”. We believe that this may be an important underlying factor in the syndrome”, says Elisabet Stener-Victorin, who has led the research at the Sahlgrenska Academy.

During the study, one group of women with polycystic ovary syndrome received acupuncture regularly for four months. They received a type of acupuncture known as “electro-acupuncture”, in which the needles are stimulated with a weak low-frequency electric current, similar to that developed during muscular work. A second group of women were provided with heart rate monitors and instructed to exercise at least three times a week. A control group was informed about the importance of exercise and a healthy diet, but was given no other specific instructions.

The study showed that activity in the sympathetic nervous system was lower in the women who received acupuncture and in those who took regular exercise than it was in the control group. The acupuncture treatment brought further benefits. “Those who received acupuncture found that their menstruation became more normal. We could also see that their levels of testosterone became significantly lower, and this is an important observation, since elevated testosterone levels are closely connected with the increased activity in the sympathetic nervous system of women”, says Elisabet Stener-Victorin.

Journal: American Journal of Physiology - Regulatory, Integrative and Comparative Physiology
Title of the article: Low-frequency electro-acupuncture and physical exercise decrease high muscle sympathetic nerve activity in polycystic ovary syndrome
Authors: Elisabet Stener-Victorin, Elizabeth Jedel, Per Olof Jansson and Yrsa Bergmann Sverrisdottir

Study: Contrary to conventional wisdom, parents OK with homework load

Today's youngsters are buried under homework, which gobbles up free time that could be spent with family or friends. Parents, puzzled whether to help their children dig out from a pile of books or allow them to carry on alone, are frustrated by the take-home workload. And they're angry at the stress the immense amounts of homework can put on their whole family. Sound familiar?

That's the current conventional wisdom about homework, which is often perpetuated in the popular press through stories of stressed-out schoolchildren and perplexed parents.

But, a new study from University of Nebraska-Lincoln researchers actually shows parents see homework in a much more positive light.

While students are spending considerable time completing homework, parents are generally supportive of homework practices, the study shows. They're also involved in homework -- usually in minimal but supportive ways, said Ken Kiewra, UNL professor of educational psychology and an expert on learning strategies, homework, and study methods.

"Our findings should squelch the sentiments that homework is robbing children of free time and that parents are opposed to homework practices," Kiewra said. "Parents generally report that children spend ample time playing and socializing and report that homework workloads are reasonable."

Published in the latest issue of ScholarlyPartnershipsEdu, the study examined four key issues: how long it takes students to complete their daily homework, how parents feel about their child's amount of homework, how much parents are involved in it, and how well schools communicate with parents about homework levels and expectations.

The results of the study, which involved nearly 400 parents of middle schoolers, gave details to a number of contemporary questions about homework, Kiewra said. Among them:

Are students overburdened by too much homework and robbed of free time? No, the UNL study found. While most middle schoolers spend 60 to 90 minutes a day with homework -- slightly higher than what previous research in the area had shown -- parents in the study did not believe it interfered with their children's recreational or social activities.

Does daily homework create family stress and infringe on family life as a whole? No, the UNL study found. Most parents said they thought their kids' amount of daily homework was appropriate and did not encroach upon family activities. In fact, most parents surveyed were either indifferent about or thankful for homework.

Are parents unsure how to help their children with homework? No, the UNL study found: Most parents said they were involved in their child's homework, but in general their involvement was minimal but positive. They focused on motivating their children or checking their answers.

Do schools and parents communicate about homework levels and expectations? Not really - the UNL study confirmed prior research that there is scarcely any discussion about homework levels initiated by the school or parents.

Kiewra said the study unearths three main issues that merit further attention and repair.

"First, although findings cast a softer light on the homework battle that has raged between families and schools, it does not extinguish it," he said. "Twenty-five percent of parents still contend that excessive homework practices infringe on family life."

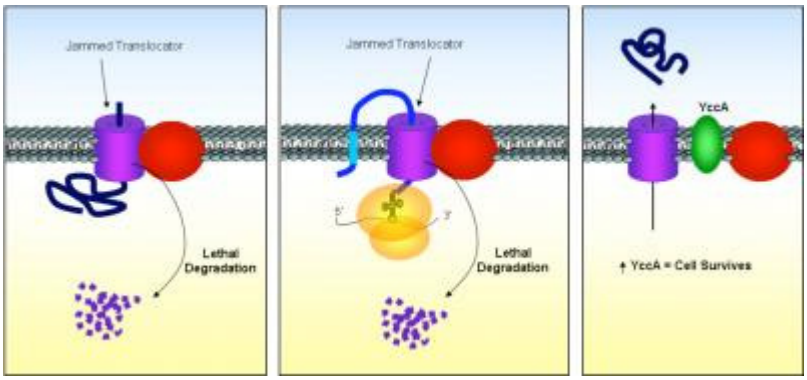
Second, although most parents help children with homework in positive ways, about one-quarter sometimes completes assignments for their children who are sometimes overburdened, he said.

Third, "homework communication between schools and parents is a dead-end street. With better communication, homework loads are more likely to be manageable and parental assistance more likely positive." *Involved in the study from UNL were Kiewra; Douglas Kaufmann, assistant professor of educational psychology; and several educators.*

Princeton team learns why some drugs pack such a punch

By studying the intricate mechanisms at work in protein production, a Princeton-led team has discovered why certain kinds of antibiotics are so effective. In doing so, they also have discovered how one protein protects against cell death, shedding light on a natural cancer-fighting process.

In a study appearing in the Aug. 7 edition of the journal Science, Thomas Silhavy, Princeton's Warner-Lambert Parke-Davis Professor of Molecular Biology, and Johna van Stelten, a graduate student, working with two Swiss researchers have uncovered how some antibiotics in common use for 50 years - tetracycline and chloramphenicol - can be so lethal against certain strains of bacteria. Simply put, these drugs plug things up.



A Princeton-led team has discovered new mechanisms at work in protein production. Here, a folded protein (the ribbon-like object) jams a translocator (purple cylinder on left). Once jammed, translocators emit a molecular signal that attracts a destructive enzyme, the protease FtsH (red sphere), which then starts shredding the translocator (chopped up bits at bottom). Similarly, when certain antibiotics are added to a bacterium's cytoplasm, the ribosome -- the cell's protein-producing machine (yellow area) -- stops midway through its process, causing partially constructed proteins to stick to the ribosome and jam the translocator. When scientists increase the amount of YccA (green ellipse), a protective protein, in the cell, the protein protects the translocator from the FtsH attacker. **Courtesy of Princeton University/Silhavy Laboratory**

Silhavy and van Stelten had been studying the mechanism by which proteins -- from antibodies to hormones -- are produced in bacteria's cytoplasm, the gooey substance that makes up the cell's interior, and then transported where they are needed. The spaghetti-like proteins exit the bacteria's cytoplasm through microscopic tubes known as translocators.

Sometimes, proteins fold up accidentally and jam the translocator. "Proteins go through the translocator, like a piece of spaghetti through a hole," Silhavy said. "But if you can imagine if you were to tie knots in the spaghetti, it wouldn't be able to get through; it gets stuck."

What happens then is ugly, according to Silhavy and van Stelten, who were the first ever to observe the event. The bacterial cell actually attacks the jammed translocator, decimating it.

The researchers wondered what might happen in a more complex scenario, such as if antibiotics were introduced into the cell cytoplasm to purposely thwart bacteria.

The scientists found that the antibiotics tetracycline and chloramphenicol cause the ribosomes, a cell's protein-producing machines, to stop midway through the process of making proteins, leaving partially constructed proteins stuck to the ribosome, jamming the translocator in the bacteria.

"This is very similar to plugging the translocator with a folded protein and, sure enough, this also causes translocator destruction," Silhavy said. "It's like putting an anchor on the spaghetti instead of a knot. They are stuck and dead forever."

Researchers had been confused as to why these antibiotics seemed to be so adept at killing some kinds of bacteria more quickly than others. These experiments provide an explanation. Translocators are essential for life and, if some bacteria have fewer translocators from the start, then they are more vulnerable to such an attack.

"While it has been known for many years that these antibiotics work by inhibiting bacterial protein synthesis, it was not clear why some bacteria in a population appeared more susceptible than others," van Stelten said. "Our work has identified a new reason why these antibiotics are lethal to bacteria that may help explain these earlier findings."

The researchers made their discovery not because of a new piece of equipment or a new technique. "Like the vast majority of advancements in science and medicine, we happened upon this remarkable answer through basic research," van Stelten said. The finding could have important implications for medicine.

"If we are to have any hope of outpacing the antibiotic resistance obtained by bacteria, it is paramount that we fully understand the mechanism of action of the antibiotics we currently use," van Stelten said. "Unfortunately, this is often very difficult as evidenced by the fact that, 50 years on, we are still learning new things about them."

Their work also produced another important result. When the translocators in bacteria became jammed by errant proteins, the researchers observed that the translocators emitted a molecular signal -- a stress response -- that called in a destructive enzyme known as the FtsH protease. Under normal circumstances, the FtsH protease chops up the jammed translocators, contributing to cell death.

The scientists found, however, that when they increased the amount of YccA, a protein that is present in the bacterial cell, YccA proteins protected the translocators from the FtsH attackers. YccA, it turns out, is very similar to a human protein known as Bax Inhibitor-1 (BI-1) that is of great interest to cancer researchers because cancer proliferates when it malfunctions.

"We have determined how YccA works in preventing stress-induced death in bacteria," van Stelten said. "We hope this new information will shed light on the mechanism of BI-1 in humans."

Other researchers on the paper included Filo Silva and Dominique Belin from the University of Geneva in Switzerland. The work was supported by the National Institute of General Medical Sciences of the National Institutes of Health, the New Jersey Commission on Cancer Research, the Canton de Geneve and the Swiss National Science Foundation.

Night home hemodialysis shown to be as good as transplant in treating kidney failure

For the first time, it has been shown that patients who receive night home hemodialysis live just as long as those who receive kidney transplants from deceased donors.

In a study entitled, "Survival among nocturnal home hemodialysis patients compared to kidney transplant recipients," published in the international September issue of Nephrology Dialysis Transplantation, a total of 1,239 patients were followed for up to 12 years. Night home hemodialysis patients were compared to patients who received either a deceased donor kidney transplant or a living donor kidney transplant. The study found that the survival between night home dialysis patients and those who received kidney transplants from deceased donors was comparable, while the survival of the patients who received a transplant from a living kidney donor was better than both the other groups.

These results suggest that night home hemodialysis, an intensive dialysis of six to eight hour sessions for up to seven times a week, may be a "bridge to transplant" or a "suitable alternative" to transplant should a patient be too high risk for a transplant or not be able to get a living or deceased donor as the organ shortage continues. Night home hemodialysis patients were from the Toronto General and Humber River Regional Hospitals, both hospitals together representing the largest and longest established group of such patients world-wide.

"This study allows me to actually answer what my patients have been asking me for over a decade: 'What does night home hemodialysis mean for my life span?' I can now tell them that this specific dialysis option is as good as getting a transplant from a deceased donor," says Dr. Christopher Chan, Medical Director of Home Hemodialysis at Toronto General Hospital, University Health Network, the R. Fraser Elliott Chair in Home Dialysis and Associate Professor, University of Toronto.

Until this study, there has been no long-term data on night home hemodialysis patient survival, or on how this type of treatment compares to transplantation. In the study, night home hemodialysis patients' data was carefully matched with deceased and living donor kidney transplantation mortality data from the U.S. Renal

Data System on characteristics such as age, race, diabetic status and duration of treatment with conventional in-centre dialysis prior to treatment.

The proportion of deaths in each group was then measured, with final figures of 14.7% for night home hemodialysis patients; 14.3% for patients with transplants from deceased donors; and 8.5% for patients with transplants from living donors.

These results diverge from the evidence to date that dialysis is inferior to transplantation, pointed out Dr. Chan, adding that there is much benefit to be gained by long, frequent dialysis.

Florence Tewogbade, 27, has been on home hemodialysis since April 2008, after trying conventional dialysis. "It has changed my life," she said. "I can now work, go to school, look forward to a future and be self-reliant." Florence was on the transplant waiting list in 2004, but her living donor was found to be ineligible.

Florence says that she would have had to wait about 10 years for a kidney from a deceased donor because of her specific risk factors for receiving a transplant. "I always thought that transplant was the only option, so I didn't consider home hemodialysis," she said. "I thought I couldn't do it. But here I am, doing it, and living a normal life."

Other researchers involved in the study include Robert Pauly, University of Alberta Hospital, John Gill and Caren Rose, St. Paul's Hospital, UBC, Reem Asad, TGH, Anne Cherry, UHN, Andreas Pierratos, Humber River Regional Hospital.
This study did not require any external funding.

Kidney Facts:

**** Shortage of organs and tissues remains a concern for Canada, and our national donation rates lag far behind many countries; in fact, we have one of the lowest donation rates among developed countries at 14 donors per million people, while Spain, for e.g., has a rate of 35 donors per million***

**** Of the 4,195 Canadians on the waiting list for a transplant as of December 31, 2007, 2,963 (71%) were waiting for a kidney***

**** At any point in time, there are more than 1,000 patients waiting for a kidney transplant in Ontario (more than any other organ)***

**** In the GTA, adults usually wait 4 – 10 years, depending on the blood group, for a kidney to become available, and about 2% of people on the waiting list die waiting for a kidney each year***

**** The number of patients being treated for end-stage kidney failure in Ontario climbed by nearly 20% in five years from 15.4 people per 100,000 in 1995 to 19.3 per 100,000 in 2000***

**** Each day, an average of three Ontarians learn that their kidneys have failed and their survival depends on dialysis treatments or a kidney transplant***

**** Currently, there are more than 10,000 Ontarians being treated for chronic kidney disease***

**** The number of new patients increases by 10-15%***

**** Reasons for this growth include an aging population and an increasing number of people with diabetes and diabetes complications***

Universal Influenza Vaccination May Reduce Antibiotic Use

We all know that influenza vaccination helps prevent disease, but a new study from Canada suggests it may also prevent another public health problem: inappropriate antibiotic use. The findings come from a new study in the September 1, 2009 issue of Clinical Infectious Disease, which is now available online.

Starting in 2000, the Canadian province of Ontario introduced a universal immunization program offering free influenza vaccines to anyone 6 months of age or older. Other provinces continued to target only high-risk groups and their contacts for vaccination. The authors compared prescription rates for influenza-associated respiratory antibiotics before and after the Ontario program began, and compared the Ontario prescription rates with those of other provinces.

The broader immunization effort in Ontario was associated with a 64 percent decline in these antibiotic prescriptions compared with the other provinces that maintained targeted vaccination programs. Additionally, influenza-associated mortality fell 39 percent. Flu-related hospitalizations, emergency department use, and doctors' office visits also fell an average of 52 percent.

Influenza and upper respiratory conditions account for a substantial number of antibiotic prescriptions, even though antibiotics don't work against viruses such as the flu. The overuse of antibiotics and the development of antibiotic-resistant bacteria continue to be serious public health problems. According to study author Fawziah Marra, PharmD, of the University of British Columbia, the study's findings suggest that "jurisdictions wishing to decrease antibiotic use might consider programs to increase influenza vaccination."

Evolution of the appendix: A biological 'remnant' no more

DURHAM, N.C. – The lowly appendix, long-regarded as a useless evolutionary artifact, won newfound respect two years ago when researchers at Duke University Medical Center proposed that it actually serves a critical function. The appendix, they said, is a safe haven where good bacteria could hang out until they were needed to repopulate the gut after a nasty case of diarrhea, for example.

Now, some of those same researchers are back, reporting on the first-ever study of the appendix through the ages. Writing in the Journal of Evolutionary Biology, Duke scientists and collaborators from the University of Arizona and Arizona State University conclude that Charles Darwin was wrong: The appendix is a whole lot more than an evolutionary remnant. Not only does it appear in nature much more frequently than previously acknowledged, but it has been around much longer than anyone had suspected.

"Maybe it's time to correct the textbooks," says William Parker, Ph.D., assistant professor of surgical sciences at Duke and the senior author of the study. "Many biology texts today still refer to the appendix as a 'vestigial organ.'"

Using a modern approach to evolutionary biology called cladistics, which utilizes genetic information in combination with a variety of other data to evaluate biological relationships that emerge over the ages, Parker and colleagues found that the appendix has evolved at least twice, once among Australian marsupials and another time among rats, lemmings and other rodents, selected primates and humans. "We also figure that the appendix has been around for at least 80 million years, much longer than we would estimate if Darwin's ideas about the appendix were correct."

Darwin theorized that the appendix in humans and other primates was the evolutionary remains of a larger structure, called a cecum, which was used by now- extinct ancestors for digesting food. The latest study demonstrates two major problems with that idea. First, several living species, including certain lemurs, several rodents and a type of flying squirrel, still have an appendix attached to a large cecum which is used in digestion. Second, Parker says the appendix is actually quite widespread in nature. "For example, when species are divided into groups called 'families', we find that more than 70 percent of all primate and rodent groups contain species with an appendix." Darwin had thought that appendices appeared in only a small handful of animals.

"Darwin simply didn't have access to the information we have," explains Parker. "If Darwin had been aware of the species that have an appendix attached to a large cecum, and if he had known about the widespread nature of the appendix, he probably would not have thought of the appendix as a vestige of evolution."

He also was not aware that appendicitis, or inflammation of the appendix, is not due to a faulty appendix, but rather due to cultural changes associated with industrialized society and improved sanitation. "Those changes left our immune systems with too little work and too much time their hands – a recipe for trouble," says Parker.

That notion wasn't proposed until the early 1900's, and "we didn't really have a good understanding of that principle until the mid 1980's," Parker said. "Even more importantly, Darwin had no way of knowing that the function of the appendix could be rendered obsolete by cultural changes that included widespread use of sewer systems and clean drinking water."

Parker says now that we understand the normal function of the appendix, a critical question to ask is whether we can do anything to prevent appendicitis. He thinks the answer may lie in devising ways to challenge our immune systems today in much the same manner that they were challenged back in the Stone Age. "If modern medicine could figure out a way to do that, we would see far fewer cases of allergies, autoimmune disease, and appendicitis."

Colleagues who contributed to the study include lead author Heather Smith, of the Arizona College of Osteopathic Medicine; Rebecca Fisher, of Arizona State University; and Mary Lou Everett, Anitra Thomas and R. Randal Bollinger from the Department of Surgery at Duke.