Brain Science

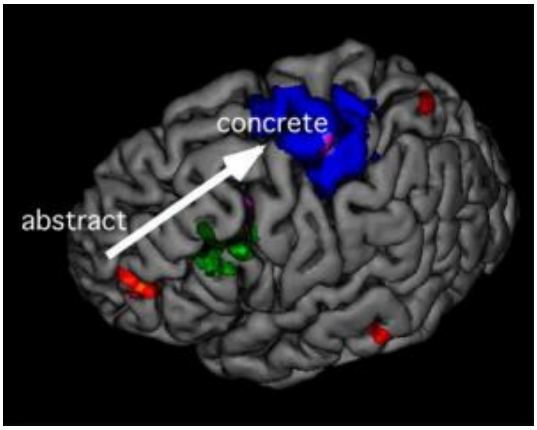
Evidence appears to show how and where frontal lobe works

Brown University's David Badre, an assistant professor of cognitive and linguistic sciences, and colleagues at the University of California–Berkeley mapped parts of the brain that control abstract or concrete decision making by studying stroke patients. Their findings are published March 1 in the journal Nature Neuroscience.

PROVIDENCE, R.I. [Brown University] — A new study of stroke victims has produced evidence that the frontal lobe of the human brain controls decision-making along a continuum from abstract to concrete, from front to back.

Lead author David Badre, assistant professor of cognitive and linguistic sciences at Brown University since 2007, conducted the study at the University of California–Berkeley as a postdoctoral fellow.

Abstract actions can be controlled at an abstract level, such as deciding to make a sandwich, or at more concrete and specific levels, such as choosing a sequence of movements that make the sandwich.



The neuroscience of decision-making By examining stroke victims, researchers determined that the brain's frontal lobe controls decision-making, with abstract decisions made closer to the front and concrete decisions farther back.
Credit: Journal of Cognitive Neuroscience

The scientific data supports preexisting theories that abstract decisions about action take place in the front of the frontal lobe, the back portion controls the capacity for concrete decisions, and the progression from front to back forms a gradient from abstract to concrete.

The study is among the first to show that specific areas of the frontal cortex are needed for different levels of abstract decision.

The finding, detailed March 1 in the journal Nature Neuroscience, represents a huge leap in comprehending how the brain supports higher level cognition and intelligent behavior. It could lead to advances in everything from the treatment of strokes to understanding how humans develop thought. "It is among the strongest evidence to date for a systemic organization of the frontal cortex," Badre said.

The frontal cortex of brain has been long known to affect the internal control of behavior. It controls the capacity to plan, reason, conduct higher-level thinking and connect what we know about the world to how we behave.

Badre and his collaborators at Berkeley came to their conclusion by studying stroke victims who suffered damage to different parts of the frontal lobe. The patients all suffered a stroke at least six months prior to testing. All were screened with an MRI or CT scan to determine where any lesions existed in the brain post-stroke.

The scientists recruited 11 patients — seven men and four women, ranging from age 45 to 73. A 12th patient was recruited but could not perform any of the tests involved.

Researchers gave the patients four different tests that ultimately required selecting a finger-press response. For example, the first test would show a color such as red, which required an index finger push. Blue would trigger the middle finger. The test would then become more difficult by adding more alternate finger presses.

Patients faced greater challenges in selecting a response as subsequent, progressive tests became more complex, with more abstract options.

Badre and colleagues found that damage at a given location affected more abstract decisions but left intact the capacity for more concrete decisions. "If there is damage in a given spot, it will affect all higher (decision-making) functions but not lower functions," Badre said.

The National Institutes of Health, Veterans Administration Research Service and a National Research Service Award supported the research.

Names turn preschoolers into vegetable lovers

Do you have a picky preschooler who's avoiding their vegetables? A new Cornell University study shows that giving vegetables catchy new names – like X-Ray Vision Carrots and Tomato Bursts – left preschoolers asking for more.

When 186 four-year olds were given carrots called "X-ray Vision Carrots" ate nearly twice as much as they did on the lunch days when they were simply labeled as "carrots." The Robert Wood Johnson-funded study also showed the influence of these names might persist. Children continued to eat about 50% more carrots even on

the days when they were no longer labeled. The new findings were presented on Monday at the annual meeting of the School Nutrition Association in Washington DC.

"Cool names can make for cool foods," says lead author Brian Wansink. "Whether it be 'power peas' or 'dinosaur broccoli trees,' giving a food a fun name makes kids think it will be more fun to eat. And it seems to keep working – even the next day," said Wansink.

Similar results have been found with adults. A restaurant study showed that when the Seafood Filet was changed to "Succulent Italian Seafood Filet," sales increased by 28% and taste rating increased by 12%. "Same food, but different expectations, and a different experience," said Wansink, author of "Mindless Eating: Why We Eat More Than We Eat More Than We Think."

Although the study was conducted in pre-schools, the researchers believe the same naming tricks can work with children. "I've been using this with my kids," said researcher Collin Payne, "Whatever sparks their imagination seems to spark their appetite."

The research was funded by Healthy Eating Research grant funded by the Robert Wood Johnson Foundation. Further details on the study are available at www.SmarterLunchrooms.org.

Human vaccine against bird flu a reality with new discovery

A vaccine to protect humans from a bird flu pandemic is within reach after a new discovery by researchers at the University of Melbourne, Australia

The discovery, published today in the prestigious Proceedings of the National Academy of Sciences, reveals how boosting T cell immunity could better protect humans from a bird flu pandemic.

The continued spread of the highly virulent "bird flu" virus has experts worried that we are facing a new potential influenza pandemic which could transfer between humans. Furthermore, given the bird flu is new, there is no pre-existing immunity in the population and current vaccine formulations would be useless.

"The 'Killer T cell' is the hit-man of the immune system. It is able to locate and destroy virus-infected cells in our body helping rid us of infection," said A/Prof Stephen Turner, from the Department of Microbiology and Immunology at the University of Melbourne who is a lead author on the paper.

"Unfortunately, current influenza vaccines are poor at inducing killer T cell immunity. Therefore, we wanted to see if we could improve the current vaccine formulation to induce killer T cells after vaccination," he said. "We added a compound, known to increase immunity, to the flu vaccine in an animal model. The addition of this compound promoted significant generation of potent killer T cell immunity and provided protection from infection.

"The significance of these findings is that rather than having to design a new vaccine altogether, we can improve current flu vaccines by adding this potent immune modulator.

"With appropriate clinical testing, we could see improvements to current vaccines within the next five years."

Dr Turner said the key to vaccine effectiveness was ensuring a match between the vaccine and the current circulating flu strain. However, the spike proteins varied over the course of a flu season rendering the current vaccine ineffective. As such, the vaccine needs to be updated every year to match the likely strain for that winter.

"It is a different situation for influenza pandemics. Pandemics arise due to the introduction of a new influenza virus into human circulation. As such, there is little or no pre-existing immunity to the bird flu virus enabling it to spread rapidly."

"'Killer' T cells recognise components that are conserved between different influenza viruses. Therefore, a vaccine strategy that induced killer T cells pre-emptively would provide protection from a potential pandemic."

1 drug may help people both lay down the drink and put out the cigarette

A popular smoking cessation drug dramatically reduced the amount a heavy drinker will consume, a new Yale School of Medicine study has found. Heavy-drinking smokers in a laboratory setting were much less likely to drink after taking the drug varenicline compared to those taking a placebo, according to a study published online in the journal Biological Psychiatry.

The group taking varenicline, sold as a stop-smoking aid under the name Chantix, reported feeling fewer cravings for alcohol and less intoxicated when they did drink. They were also much more likely to remain abstinent after being offered drinks than those who received a placebo, the study found.

Additionally, there were no adverse effects associated with combining varenicline with alcohol in the doses studied. When combined with low doses of alcohol, varenicline did not change blood pressure or heart rate, nor did it seem to induce nausea or dizziness.

"We anticipate that the results of this preliminary study will trigger clinical trials of varenicline as a primary treatment for alcohol use disorders, and as a potential dual treatment for alcohol and tobacco use disorders,"

said Sherry McKee, associate professor of psychiatry at the Yale School of Medicine and lead author of the study.

Smokers are more likely to drink alcohol and to consume greater quantities of alcohol, and they are four times more likely to meet criteria for alcohol use disorders. Diseases related to tobacco use are the leading causes of death in alcoholics.

"A medication such as varenicline, which may target shared biological systems in alcohol and nicotine use, holds promise as a treatment for individuals with both disorders" according to McKee.

McKee said that 80% of participants receiving varenicline did not take a drink at all, compared to 30% of the placebo group. The findings suggest that varenicline has the potential to be at least as effective in reducing drinking as naltrexone, another drug found to reduce alcohol consumption in heavy drinkers. Unlike naltrexone, varenicline is not metabolized by the liver and may be safe to use by those with impaired liver function, a frequent consequence of heavy alcohol use, McKee said.

Other Yale authors of the study are; Emily L.R. Harrison, Stephanie S. O'Malley, Suchitra Krishnan-Sarin, Julia Shi, Jeanette M. Tetrault, Marina R. Picciotto, Ismene L. Petrakis, Naralys Estevez, and Erika Balchunas.

The study was funded by the National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health.

Technique may help stem cells generate solid organs, Stanford study shows

STANFORD, Calif. — Stem cells can thrive in segments of well-vascularized tissue temporarily removed from laboratory animals, say researchers at the Stanford University School of Medicine. Once the cells have nestled into the tissue's nooks and crannies, the so-called "bioscaffold" can then be seamlessly reconnected to the animal's circulatory system.

The new technique neatly sidesteps a fundamental stumbling block in tissue engineering: the inability to generate solid organs from stem cells in the absence of a reliable supply of blood to the interior of the developing structure.

"Efforts to use tissue engineering to generate whole organs have largely failed," said Geoffrey Gurtner, MD, associate professor of surgery, "primarily due to the lack of available blood vessels. Now we've essentially hijacked an existing structure to overcome this problem." The key, the researchers discovered, is to keep the tissue adequately supplied with oxygen and nutrients while outside of the body.

In the near future, the researchers believe that the stem cells in the tissue could be induced to become an internal, living factory of healthy, specialized cells churning out proteins missing in people with conditions such as hemophilia or diabetes. In the long run, they hope to encourage the cells to become entire transplantable organs such as livers or pancreases.

Gurtner, who is also a member of Stanford's Cancer Center, is the senior author of the study, which is featured in the March issue of the FASEB Journal.

The technique devised by Gurtner and his colleagues does more than provide the versatile stem cells with a readily accessible blood supply and a pre-formed cellular framework within which to begin differentiating. It also eliminates the chance of rejection or complications caused by the use of artificial or donor scaffolding materials by utilizing the animal's own tissue.

The researchers capitalized on a portion of the circulatory system shared by animals and humans called microcirculatory beds. To understand what they are, spread the fingers of each of your hands apart and then touch your fingertips together. One wrist represents the inflow of blood, and the other, the outflow. The fingers are the tiny capillaries that supply oxygen and nutrients to the surrounding tissue wrapping itself invisibly around your hands.

In many cases these beds create a flap of expendable tissue that can be easily removed. (With your fingertips still touching, bring your elbows together. Now imagine lopping off your hands midway down the forearm. Your fingers and wrists now represent a free microcirculatory bed.)

Gurtner and his colleagues removed microcirculatory beds about the size of a half-dollar coin from the groin of laboratory rats and attached the ends of the two main blood vessels to a modified piece of equipment called a bioreactor designed to keep livers and kidneys healthy outside the body. The modified bioreactor pumps an oxygenated soup of nutrients into one vessel and recovers it from the other; Gurtner referred to it as a "kind of life support, or cardiopulmonary bypass, machine for tissue."

The scientists showed that, once the appropriate blood pressure and nutrient balance was achieved, the bioreactor could keep the tissue healthy enough for reimplantation into a second, genetically identical animal for up to 24 hours. In many cases, the tissue became nearly indistinguishable from surrounding skin within 28 days of transplant, although the success rate of the procedure decreased as time spent on the bioreactor increased. In contrast, control tissue not connected to the bioreactor after removal died within six hours of transplantation.

The team then used the bioreactor to pump multipotent stem cells from a variety of sources, including bone marrow and fat tissue, through the tissue. Unlike embryonic stem cells, which can become any type of cell in the body, multipotent cells are more restricted in their potential. The researchers found that the cells could migrate out of the vascular spaces and into the surrounding tissue. Once there, they set up shop and began to form colonies. Unlike stem cells injected directly into the tissue, the stem cells that had been seeded into the tissue continued to thrive even eight weeks after reimplantation.

"This is an incredible opportunity to bulk-deliver cells that don't just die," said Gurtner. "Conceivably, we could use this technique at least to supply the synthetic function of an organ by stimulating the cells to form insulin-producing pancreas cells or albumin-producing liver cells."

Members of Gurtner's team are now trying to use the technique to deliver Factor VIII and Factor IX — crucial blood-clotting components that are missing in people with hemophilia. The researchers concede, however, that much remains to be done before the technique could be used to generate whole organs. Indeed, Gurtner readily agrees that other methods might be developed that could be more effective. But for now, they've overcome a major hurdle in tissue engineering.

"Eventually science will find a way to fabricate an organ in all its complexity," said Gurtner. "But in the short term we need to find more options for patients who are dying while waiting for transplants."

Stanford collaborators on the research include postdoctoral scholars Edward Chang, MD, Robert Bonillas, MD, Eric Chang, MD, and Denise Chan, PhD; and medical students Samyra El-ftesi and Ivan Vial. The research was supported by grants from the National Institutes of Health and the National Institute of Biomedical Imaging and Bioengineering.

Scripps research scientists engineer new type of vaccination that provides instant immunity

The experiments, thus far performed only in mice, appear to overcome a major drawback of vaccinations – the lag time of days, or even weeks, that it normally takes for immunity to build against a pathogen. This new method of vaccination could potentially be used to provide instantaneous protection against diseases caused by viruses and bacteria, cancers, and even virulent toxins.

The work is being published in the Early Edition of the Proceedings of the National Academy of Sciences (PNAS) the week of March 2, 2009.

The team, led by Scripps Professor Carlos Barbas, III, Ph.D., tested the vaccination method – called covalent immunization – on mice with either melanoma or colon cancer.

The scientists injected these mice with chemicals specifically designed to trigger a programmable and "universal" immune reaction. They developed other chemicals, "adapter" molecules," that recognized the specific cancer cells. Once injected into the animal, the adapter molecules self-assembled with the antibodies to create covalent antibody-adapter complexes.

"The antibodies in our vaccine are designed to circulate inertly until they receive instructions from tailor-made small molecules to become active against a specific target," Barbas says. "The advantage of this method is that it opens up the possibility of having antibodies primed and ready to go in the time it takes to receive an injection or swallow a pill. This would apply whether the target is a cancer cell, flu virus, or a toxin like anthrax that soldiers or even civilian populations might have to face during a bioterrorism attack."

Only those mice that received both the vaccine and the adapter compound generated an immediate immune attack on the cancer cells that led to significant inhibition of tumor growth. This is the first time that such a covalent vaccine has been successfully designed and tested – typically, antibodies do not bind to chemicals in this covalent fashion.

The current breakthrough builds on work the Barbas laboratory has been engaged in for the past few years on chemically programmed monoclonal antibodies, a new class of therapeutics that the group invented. In this type of therapy, small, cell-targeting molecules and non-targeting catalytic monoclonal antibodies self-assemble to target pathogens. Monoclonal antibodies are produced in the laboratory from a single cloned B-cell – the immune system cell that makes antibodies – to bind to a specific substance. Three clinical trials are now under way by Pfizer to test the therapeutic effectiveness of this new type of therapy in cancer and diabetes. The antibodies in the antibody-adapter complex are monoclonal antibodies engineered to link themselves to adapter molecules.

The Search for the Ideal Vaccination

The practice of vaccination has been extraordinarily successful in controlling certain diseases, but there are drawbacks. Vaccine development can be an educated guessing game – in the case of the flu, for example, scientists must study worldwide outbreak patterns to anticipate which type of flu might strike a particular area. In addition, the most common vaccination strategies use whole proteins, viruses, or other complex immunogens – not just the specific part of the macromolecule that is recognized by the immune system – to elicit an immune

response, which makes for wasted immune activity. Then there is the body's own kinetics – the time it takes to mount a disease-relevant immune response to immunogens limits the speed with which immunity can be achieved. Finally, age-related declines in the ability to mount strong immune responses to biological-based vaccines present another challenge to the effectiveness of such vaccines.

Barbas's chemical-based – rather than biological based – approach to vaccine development addresses many of these challenges.

"Our approach differs from the traditional vaccine approach in the sense that when we design an antibody-adapter compound we know exactly what that compound will react with," Barbas says. "The importance of this is best exemplified with HIV. In current vaccines, many antibodies are generated against HIV, but most are not able to target the active part of the virus."

In the near term, Barbas will apply his covalent vaccination approach to HIV, cancer, and infectious diseases for which no vaccines currently exist. A particular focus will be creating adapter molecules specific to these diseases.

"We believe that chemistry-based vaccine approaches have been underexplored and may provide opportunities to make inroads into intractable areas of vaccinology," Barbas says.

In addition to Barbas, co-authors of the paper, "Instant immunity through chemically programmable vaccination and covalent self-assembly," are Mikhail Popkov (who is first author), Beatriz Gonzalez, and Subhash C. Sinha, all of The Scripps Research Institute.

The study was funded by the Skaggs Institute for Chemical Biology and the National Institutes of Health.

Epstein-Barr Virus May Be Associated with Progression of MS

BUFFALO, N.Y. -- Epstein-Barr virus (EBV), the pathogen that causes mononucleosis, appears to play a role in the neurodegeneration that occurs in persons with multiple sclerosis, researchers at the University at Buffalo and the University of Trieste, Italy, have shown.

Multiple sclerosis (MS) is an autoimmune disease that can cause major disability. There currently is no cure.

"This study is one of the first to provide evidence that a viral agent may be related to the severity of MS disease process, as measured by MRI," said Robert Zivadinov, M.D., Ph.D., associate professor of neurology in UB's Jacobs Neurological Institute (JNI) and first author on the study.

The research appears in the Online First section of the Journal of Neurology, Neurosurgery and Psychiatry and is available at http://jnnp.bmj.com/cgi/rapidpdf/jnnp.2008.154906v1.

"A growing body of experimental evidence indicates that past infection with EBV may play a role in MS," said Zivadinov, "but the relationship of EBV and the brain damage that can be seen on MRI scans had not been explored."

The study involved 135 consecutive patients diagnosed with MS at the Multiple Sclerosis Center of the University of Trieste. Evaluations of the MRI scans were carried out at the University of Trieste and at the JNI's Buffalo Neuroimaging Analysis Center (BNAC), which Zivadinov directs.

The Buffalo researchers measured total brain volume, as well as the decrease in gray matter, at baseline and three years later.

Results showed that higher levels of anti-EBV antibody measured at the beginning of the study were associated with an increased loss of gray matter and total brain volume over the three-year follow-up.

The researchers now are carrying out prospective longitudinal studies in patients who experienced a condition called "clinically isolated syndrome," a first neurologic episode that lasts at least 24 hours, and is caused by inflammation/demyelination in one or more sites in the central nervous system. If a second episode occurs, the patient is diagnosed with MS.

The study will investigate the relationship of anti-EBV antibody levels to development of gray matter atrophy, neurocognitive function and disability progression over time.

UB and Trieste researchers also are investigating interactions between environment, certain genes and EBV antibodies and the association with MRI injury in MS. A paper on this work is "in press" in the Journal of Neuroimmunology.

Marino Zorzon, M.D., from the University of Trieste, is second author on the Journal of Neurology, Neurosurgery and Psychiatry study. Murali Ramanathan, Ph.D., from the UB School of Pharmacy and Pharmaceutical Sciences and the JNI, is co-corresponding author with Zivadinov. The BNAC and JNI are located in Kaleida Health's Buffalo General Hospital. Additional contributors to the study are Bianca Weinstock-Guttman, M.D., from UB; Maurizia Serafin, M.D., from Cattinara Hospital in Trieste; and Antonio Bosco, M.D., Ph.D., Alessio Bratina, M.D., Cosimo Maggiore, M.D., Attilio Grop, Maria Antonietta Tommasi, M.D., all from the University of Trieste, and Bhooma Srinivasaraghavan, from the BNAC.

The study was supported in part by the Consortium for International Development of the University of Trieste, Italy. The researchers also gratefully acknowledge additional support from the National Multiple Sclerosis Society and a Pediatric MS Center of Excellence Center Grant.

Certain combined medications following heart attack may increase risk of death

Following an acute coronary syndrome such as a heart attack or unstable angina, patients who receive a medication to reduce the risk of gastrointestinal bleeding that may be associated with the use of the antiplatelet drug clopidogrel and aspirin have an increased risk of subsequent hospitalization for acute coronary syndrome or death, according to a study in the March 4 issue of JAMA.

Treatment with clopidogrel in addition to aspirin reduces recurrent cardiovascular events following hospitalization for acute coronary syndrome (ACS) for patients treated either medically or with angioplasty or stent placement. Proton pump inhibitor (PPI) medications are often prescribed at the start of treatment with clopidogrel, with the goal of reducing the risk of gastrointestinal tract bleeding while patients are taking dual-antiplatelet therapy. Recent studies, however, suggest that PPIs may reduce the effectiveness of clopidogrel, but the clinical significance of these findings to patients is not clear, according to background information in the article.

P. Michael Ho, M.D., Ph.D., of the Denver VA Medical Center, and colleagues evaluated the use of clopidogrel plus PPI following hospital discharge for ACS and compared rates of all-cause death and rehospitalization for ACS, between patients taking clopidogrel plus PPI vs. clopidogrel without PPI. The study included patients from 127 Veterans Affairs hospitals. Vital status information was available for all patients through September 30, 2006.

Of 8,205 patients with ACS taking clopidogrel after hospital discharge, 63.9 percent (n = 5,244) were prescribed PPI at discharge or during follow-up. Death or rehospitalization for ACS occurred in 29.8 percent of patients prescribed clopidogrel plus PPI and 20.8 percent of patients prescribed clopidogrel without PPI . Use of clopidogrel plus PPI at any point in time was associated with a 25 percent increased odds of death or rehospitalization for ACS compared with use of clopidogrel without PPI.

For the individual outcomes, the rates of recurrent hospitalization for ACS (14.6 percent vs. 6.9 percent) and revascularization procedures (15.5 percent vs. 11.9 percent) were higher among patients taking clopidogrel plus PPI compared with those taking clopidogrel without PPI. However, the risk of death was similar between the two groups.

"When patients were not taking clopidogrel after hospital discharge, a prescription for PPI was not associated with death or rehospitalization for ACS, supporting the hypothesis that the interaction of PPI and clopidogrel, rather than PPI itself, was associated with increased adverse outcomes," the authors write. "… this study raises some concern about concomitant [accompanying] use of PPI medications and clopidogrel following hospitalization for ACS. While the risk estimates associated with clopidogrel plus PPI vs. clopidogrel without PPI were modest, the absolute number of adverse events attributable to this potential drug interaction is considerable when extrapolated to a population level, given how frequently PPI medications are prescribed to patients receiving dual-antiplatelet therapy," the researchers write. "Pending additional evidence, however, the results of this study may suggest that PPIs should be used for patients with a clear indication for the medication, such as history of gastrointestinal tract bleeding, consistent with current guideline recommendations, rather than routine prophylactic prescription. Alternative gastrointestinal tract medication regimens also may be considered until additional data regarding concomitant use of PPI and clopidogrel becomes available."

(JAMA. 2009;301[9]:937-944. Available pre-embargo to the media at www.jamamedia.org)

Lack of ability does not explain women's decisions to opt out of math-intensive science careers

WASHINGTON – Women don't choose careers in math-intensive fields, such as computer science, physics, technology, engineering, chemistry, and higher mathematics, because they want the flexibility to raise children, or because they prefer other fields of science that are less math-intensive--not because they lack mathematical ability, according to a new study.

The study, an integrative analysis of 35 years of research on sex differences in math, offers explanations for why women are underrepresented in math-intensive science careers. The findings appear in the March issue of Psychological Bulletin, published by the American Psychological Association.

Researchers from Cornell University reviewed more than 400 articles and book chapters to reconcile conflicting evidence on why math-proficient women are underrepresented in math-intensive fields such as engineering, why they choose less math-intensive fields (such as biology, medicine, dentistry and veterinary medicine), and why when they do choose math-intensive careers, they are more likely to drop out as they advance.

"Career preferences and lifestyle needs largely dictate why women aren't choosing physics or engineering as their profession," said lead author Stephen J. Ceci, PhD. Women with advanced math abilities choose non-math fields more often than men with advanced math abilities. They also drop out of scientific fields--especially math and physical science--at higher rates than do men, particularly as they advance, said Ceci.

"A major reason explaining why women are underrepresented not only in math-intensive fields but also in senior leadership positions in most fields is that many women choose to have children, and the timing of childrearing coincides with the most demanding periods of their career, such as trying to get tenure or working exorbitant hours to get promoted," Ceci said.

Further, if women enter these fields, they are more likely to drop out before they advance very far due to the need for greater flexibility and the demands of parenting and caregiving, said co-author Wendy M. Williams, PhD. "These are choices that all women, but almost no men, are forced to make."

Women today compose approximately 50 percent of medical school classes; however, despite these gains, women who enter academic medicine are less likely than men to be promoted or serve in leadership posts, the authors said. As of 2005, only 15 percent of full professors and 11 percent of department chairs were women. Non-math fields are also affected: for example, only 19 percent of the tenure track faculty in the top 20 philosophy departments are women.

"Hormonal, brain and other biological sex differences did not emerge as primary factors explaining why women were underrepresented in science careers," said co-author Susan Barnett, PhD. And the authors found studies on social and cultural effects to be inconsistent and inconclusive.

Much of the evidence on discrimination was dated or anecdotal, the authors said, and the effects were not strong enough to explain women's current low numbers in math-intensive fields. "Even though institutional barriers and discrimination exist, these influences still cannot explain why women are not entering or staying in STEM careers," said Ceci. "The evidence did not show that removal of these barriers would equalize the sexes in these fields, especially given that women's career preferences and lifestyle choices tilt them towards other careers such as medicine and biology over mathematics, computer science, physics, and engineering."

Men did outscore women on spatial ability tests, a measure that predicts later mathematics achievement but, said the authors, this still doesn't account for the low numbers of women in the STEM fields. Moreover, studies showing that men's scoring in the top 1 to 0.1 percent on the SAT-M and GRE-Q exams more frequently than women cannot account for the low numbers of women in math-intensive careers.

The evidence shows that if math ability were solely a function of sex, there would be roughly double the number of women in math-intensive careers compared to what exists now, assuming a 2:1 male-female ratio at the top 1 percent in math ability, Ceci said. "Women would comprise 33 percent of the professorships in math-intensive fields if it was based solely on being in the top 1 percent of math ability, but they currently comprise less than 10 percent."

Several large surveys examined in the analysis found that lifestyle choice had the largest influence on career preferences. In a survey of 2,000 33-year-old academic professionals in science careers who were in the top 1 percent of their high school math classes, the men devoted more time to their current job and said they would devote even more time in their dream job compared to the women, suggesting that this could lead to more productivity and promotions.

Another survey of almost 5,000 tenure-track faculty at nine California universities revealed that family issues affected women's success and satisfaction more than it affected men's. And a National Science Foundation survey of doctoral recipients in scientific and engineering fields found that women with children under 18 worked and published less than the men.

Science, technology, engineering and math are not the only professions affected by women's career choices, said the authors. Several studies showed that while women are well-represented in less math-intensive fields, such as medicine, law, biology, psychology, dentistry, and veterinary science, they are still underrepresented in the top positions of these fields. They are either not on tenure track, drop off tenure track or opt for part-time positions until their children get older, the researchers found.

"It appears that the family-career trade-offs constitute a major factor in the dearth of women in fields such as engineering, physics, computer science and in higher-level positions in non math-related fields," said Ceci. "Women who are good in math seem to have more career options. Those who are highly competent in math are more likely than men to have high verbal competence, too, thus opening up the option of going into the humanities or law, which may offer more flexibility in their career tracks."

There are ways to remedy the situation, the authors said. They suggest that universities, other institutions and companies create options for women with math talents who want to pursue math-intensive careers. These could include deferred start-up of tenure-track positions and part-time work that segues to full-time tenure-track work for women who are raising children, and courtesy appointments for women unable to work full-time but who would benefit from use of university resources (e-mail, library resources, grant support) to continue their research from home.

Article: "Women's Underrepresentation in Science: Sociocultural and Biological Considerations," Stephen J. Ceci, PhD, Wendy M. Williams, PhD, and Susan M. Barnett, PhD, Cornell University; Psychological Bulletin, Vol. 135, No. 2. (Full text of the article is available from the APA Public Affairs Office and at http://www.apa.org/journals/releases/bul1352218.pdf)

Schizophrenia linked to signaling problems in new brain study

Schizophrenia could be caused by faulty signaling in the brain, according to new research published today

Schizophrenia could be caused by faulty signalling in the brain, according to new research published today in the journal Molecular Psychiatry. In the biggest study of its kind, scientists looking in detail at brain samples donated by people with the condition have identified 49 genes that work differently in the brains of schizophrenia patients compared to controls.

Many of these genes are involved in controlling cell-to-cell signalling in the brain. The study, which was carried out by researchers at Imperial College London and GlaxoSmithKline, supports the theory that abnormalities in the way in which cells 'talk' to each other are involved in the disease.

Schizophrenia is thought to affect around one in 100 people. Symptoms vary but can include hallucinations, lack of motivation and impaired social functioning. The disorder has little physical effect on the brain and its causes are largely unknown.

Some scientists believe that schizophrenia could be caused by the brain producing too much dopamine, partly because drugs that block dopamine action provide an effective treatment for the condition. Another theory is that the coat surrounding nerve cells, which is made of myelin, is damaged in people with schizophrenia. However, the new study found that the genes for dopamine and for myelin were not acting any differently in schizophrenia patients compared with controls.

Professor Jackie de Belleroche, the corresponding author of the paper from Imperial College London said: "The first step towards better treatments for schizophrenia is to really understand what is going on, to find out what genes are involved and what they are doing. Our new study has narrowed the search for potential targets for treatment."

As well as pointing towards signalling as the cause of schizophrenia, the new findings could also lead to new ways of diagnosing the condition. At the moment, patients are diagnosed on the basis of their behaviour.

"Most patients are diagnosed as teenagers or in their early 20s, but if they could be diagnosed earlier, they could be treated more effectively and they could have a better quality of life. To have the possibility of transforming someone's life early on instead of having to take drugs indefinitely would be wonderful," added Professor de Belleroche.

The researchers reached their conclusions after analysing brain tissue from 23 controls and 28 schizophrenia patients, selected from brains donated by UK patients being treated for schizophrenia and comparing the data to an equivalent study in the USA. The changes described in this study were common to both studies. This is the biggest cohort of schizophrenia patients used for this type of study to date.

This is part of a larger study looking at proteins and DNA as well as mRNA in the samples, which were taken from two brain regions associated with schizophrenia: the frontal cortical area and the temporal cortex. mRNA are copies of small sections of our DNA that cells use to build proteins. Unlike DNA, mRNA varies in different parts of the body, where different proteins are needed.

The research was possible due to a successful collaboration between Imperial College and GlaxoSmithKline.

Gutsy bloodworms pump out laughing gas

* 22:00 02 March 2009 **by Catherine Brahic**

They may be no match for methane-burping cows, but bloodworms are doing their best to make a name for themselves with climate scientists. New research shows that their guts leak "laughing gas" - a powerful greenhouse gas - albeit in amounts too small to significantly affect the climate. Previously, no water-dwelling animal was known to produce the gas, more properly known as nitrous oxide (N_20).

Some land invertebrates such as earthworms are known to produce nitrous oxide, so to see if water invertebrates are also a source, Peter Stief and his colleagues at Aarhus University in Denmark surveyed seven aquatic sites including freshwater creeks, lakes and the seashore.

They collected a wide range of worms, larvae and bugs, placed them in closed vials, and analysed what came off. They found not only that N20 is produced, but that the amount increased with time.

Bloodworms are just one type of water-dwelling animal that produces laughing gas **(Image: Christian Lott / MPI Bremen / HYDRA)**

The researchers suspected that microbial "bioreactors" in the animals' guts might produce the gas. To test their hypothesis, they took a closer look at the bloodworm (Chironomus plumosus), a ruby-red midge larva that is a favourite food of trout.

Mud munchers

Bloodworm larvae live in U-shaped burrows in sediment at the bottom of lakes and rivers. They wriggle within these tubes in order to draw in oxygen- and nutrient-rich water through one opening and pump it out through the other. For food, they munch on organic material from the sediment.

Along with their food, the larvae also ingest bacteria that live in the mud. These bacteria are not digested, however, and can survive in the larvae's guts by metabolising nitrates, producing N20 as a by-product.

The team dissected bloodworms, placed the guts in vials, and then looked for changes in gas concentrations.

They found that in the absence of oxygen, bloodworm gut produces the same amount of laughing gas as the whole larva, demonstrating that processes within the gut are solely responsible for the leak. Adding nitrate to the vials boosted the amount of N20 that leaked out of the guts; adding oxygen decreased it.

By tracking the movement of nitrous oxide in the dissected guts, the researchers showed that the gas leaks through the gut wall, then through the skin and out into the environment.

No laughing matter

Steif's experiments suggest that the presence of bloodworm larvae and other animals contribute less than 1% of the N20 in the atmosphere. The bulk of it is emitted by fossil-fuel burning.

Maija Repo of the University of Kuopio in Finland says the finding adds to our understanding of how aquatic systems respond to certain chemical changes in the environment, such as nitrate pollution.

Sadly, Steif was unable to determine if the laughing gas made the larvae happier than they otherwise would have been. "I tried to see if they smiled when they were all crowded into sealed test-tubes," he jokes.

Journal reference: Proceedings of the National Academy of Sciences (DOI: 10.1073/pnas.0808228106)

Really?

The Claim: Morning Is the Best Time to Exercise

By ANAHAD O'CONNOR

Leif Parsons

THE FACTS Without a doubt, exercise at any time of the day beats no exercise at all. But are there physiological advantages to working out in the morning versus evening, or vice versa?

In various studies, scientists have found that subjects tend to do slightly better on measures of physical performance — including endurance, strength output, reaction time and aerobic capacity — between 4 and 7 p.m. The explanations are numerous: the body's temperature and hormone levels peak in late afternoon, making muscles more flexible and producing the best ratio of testosterone (the muscle-building hormone) to cortisol (the hormone that does the reverse).

But these variations have only small effects. And much as one can adjust to waking up at the same time daily, studies have shown that the body can adapt to the time of day that you train. In several long-term studies, for example, scientists randomly split people into groups and instructed them to train only in the morning or only in the early evening. In the end, the morning exercisers generally did better on tests of physical performance early in the day, while the evening exercisers did better when tested later.

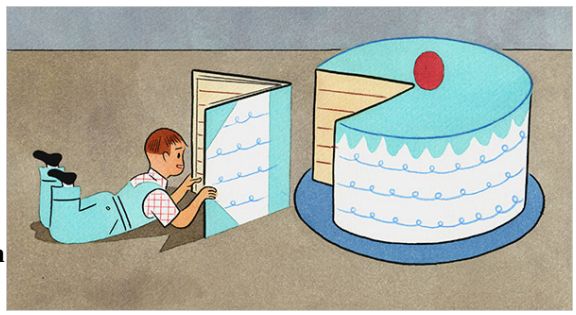
On a practical level, that means that if you plan to run a marathon that starts in the morning, it may be best to schedule your training runs early in the day.

THE BOTTOM LINE In general, research suggests that the ideal time to exercise is late afternoon, though the advantages are slight.

Rewards for Students Under a Microscope

By LISA GUERNSEY

For decades, psychologists have warned against giving children prizes or money for their performance in school. "Extrinsic" rewards, they say - a stuffed animal for a 4-year-old who learns her alphabet, cash for a good report card in middle or high school - can undermine the joy of learning for its own sake and can even lead to cheating.



But many economists and businesspeople disagree, and their views often prevail in the educational marketplace. Reward programs that pay students are under way in many cities.

Michael Klein

In some places, students can bring home hundreds of dollars for, say, taking an Advanced Placement course and scoring well on the exam.

Whether such efforts work or backfire "continues to be a raging debate," said Barbara A. Marinak, an assistant professor of education at Penn State, who opposes using prizes as incentives. Among parents, the issue often stirs intense discussion. And in public education, a new focus on school reform has led researchers on both sides of the debate to intensify efforts to gather data that may provide insights on when and if rewards work.

"We have to get beyond our biases," said Roland Fryer, an economist at Harvard University who is designing and testing several reward programs. "Fortunately, the scientific method allows us to get to most of those biases and let the data do the talking."

What is clear is that reward programs are proliferating, especially in high-poverty areas. In New York City and Dallas, high school students are paid for doing well on Advanced Placement tests. In New York, the payouts come from an education reform group called Rewarding Achievement (Reach for short), financed by the Pershing Square Foundation, a charity founded by the hedge fund manager Bill Ackman. The Dallas program is run by Advanced Placement Strategies, a Texas nonprofit group whose chairman is the philanthropist Peter O'Donnell.

Another experiment was started last fall in 14 public schools in Washington that are distributing checks for good grades, attendance and behavior. That program, Capital Gains, is being financed by a partnership with SunTrust Bank, Borders and Ed Labs at Harvard, which is run by Dr. Fryer. Another program by Ed Labs is getting started in Chicago.

Other systems are about stuff more than money, and most are not evaluated scientifically. At 80 tutoring centers in eight states run by Score! Educational Centers, a national for-profit company run by Kaplan Inc., students are encouraged to rack up points for good work and redeem them for prizes like jump-ropes.

An increasing number of online educational games entice children to keep playing by giving them online currency to buy, say, virtual pets. And around the country, elementary school children get tokens to redeem at gift shops in schools when they behave well.

In the cash programs being studied, economists compare the academic performance of groups of students who are paid and students who are not. Results from the first year of the A.P. program in New York showed that test scores were flat but that more students were taking the tests, said Edward Rodriguez, the program's executive director.

In Dallas, where teachers are also paid for students' high A.P. scores, students who are rewarded score higher on the SAT and enroll in college at a higher rate than those who are not, according to Kirabo Jackson, an assistant professor of economics at Cornell who has written about the program for the journal Education Next.

Still, many psychologists warn that early data can be deceiving. Research suggests that rewards may work in the short term but have damaging effects in the long term.

One of the first such studies was published in 1971 by Edward L. Deci, a psychologist at the University of Rochester, who reported that once the incentives stopped coming, students showed less interest in the task at hand than those who received no reward.

This kind of psychological research was popularized by the writer Alfie Kohn, whose 1993 book "Punished by Rewards: The Trouble With Gold Stars, Incentive Plans, A's, Praise and Other Bribes" is still often cited by educators and parents. Mr. Kohn says he sees "social amnesia" in the renewed interest in incentive programs.

"If we're using gimmicks like rewards to try to improve achievement without regard to how they affect kids' desire to learn," he said, "we kill the goose that laid the golden egg."

Dr. Marinak, of Penn State, and Linda B. Gambrell, a professor of education at Clemson University, published a study last year in the journal Literacy Research and Instruction showing that rewarding third graders with so-called tokens, like toys and candy, diminished the time they spent reading.

"A number of the kids who received tokens didn't even return to reading at all," Dr. Marinak said.

Why does motivation seem to fall away? Some researchers theorize that even at an early age, children can sense that someone is trying to control their behavior. Their reaction is to resist. "One of the central questions is to consider how children think about this," said Mark R. Lepper, a psychologist at Stanford whose 1973 study of 50 preschool-age children came to a conclusion similar to Dr. Deci's. "Are they saying, 'Oh, I see, they are just bribing me'?"

More than 100 academic studies have explored how and when rewards work on people of all ages, and researchers have offered competing analyses of what the studies, taken together, really mean.

Judith Cameron, an emeritus professor of psychology at the University of Alberta, found positive traits in some types of reward systems. But in keeping with the work of other psychologists, her studies show that some

students, once reward systems are over, will choose not to do the activity if the system provides subpar performers with a smaller prize than the reward for achievers.

Many cash-based programs being tested today, however, are designed to do just that. Dr. Deci asks educators to consider the effect of monetary rewards on students with learning disabilities. When they go home with a smaller payout while seeing other students receive checks for $500, Dr. Deci said, they may feel unfairly punished and even less excited to go to school.

"There are suggestions of students making in the thousands of dollars," he said. "The stress of that, for kids from homes with no money, I frankly think it's unconscionable."

Economists, on the other hand, argue that with students who are failing, everything should be tried, including rewards. While students may be simply attracted by financial incentives at first, couldn't that evolve into a love of learning?

"They may work a little harder and may find that they aren't so bad at it," said Dr. Jackson, of Cornell. "And they may learn study methods that last over time."

In examining rewards, the trick is untangling the impact of the monetary prizes from the impact of other factors, like the strength of teaching or the growing recognition among educators of the importance of A.P. tests. Dr. Jackson said his latest analyses, not yet published, would seek to answer the questions.

He also pointed out that with children in elementary school, who typically show more motivation to learn than teenagers do, the outcomes may be different.

Questions about how rewards are administered, to whom and at what age are likely to drive future research. Can incentives — praise, grades, pizza parties, cash — be added up to show that the more, the better? Or will some of them detract from the whole?

Dr. Deci says school systems are trying to lump incentives together as if they had a simple additive effect. He emphasizes that there is a difference between being motivated by something tangible and being motivated by something that is felt or sensed. "We' ve taken motivation and put it in categories," Dr. Deci said of his fellow psychologists. "Economics is 40 years behind with respect to that."

Some researchers suggest tweaking reward systems to cause less harm. Dr. Lepper says that the more arbitrary the reward — like giving bubble gum for passing a test — the more likely it is to backfire. Dr. Gambrell, of Clemson, posits a "proximity hypothesis," holding that rewards related to the activity — like getting to read more books if one book is read successfully — are less harmful. And Dr. Deci and Richard M. Ryan report that praise — which some consider a verbal reward — does not have a negative effect.

In fact, praise itself has categories. Carol Dweck, a Stanford psychologist, has found problems with praise that labels a child as having a particular quality ("You're so smart"), while praise for actions ("You're working hard") is more motivating.

Psychologists have also found that it helps to isolate differences in how children perceive tasks. Are they highly interested in what they are doing? Or does it feel like drudgery? "The same reward system might have a different effect on those two types of students," Dr. Lepper said. The higher the interest, he said, the more harmful the reward.

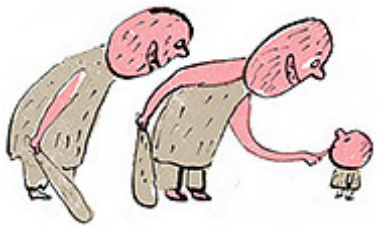
Meanwhile, Dr. Fryer of Ed Labs urges patience in awaiting the economists' take on reward systems. He wants to look at what happens over many years by tracking subjects after incentives end and trying to discern whether the incentives have an impact on high school graduation rates.

With the money being used to pay for the incentive programs and research, "every dollar has value," he said. "We either get social science or social change, and we need both."

Basics

In a Helpless Baby, the Roots of Our Social Glue

By NATALIE ANGIER



Serge Bloch

In seeking bipartisan support for his economic policies, President Obama has tried every tip on the standard hospitality crib sheet: beer and football, milk and cookies, Earth, Wind and Fire.

Maybe the president needs to borrow a new crib sheet - the kind with a genuine baby wrapped inside.

A baby may look helpless. It can't walk, talk, think symbolically or overhaul the nation's banking system. Yet as social emulsifiers go, nothing can beat a happily babbling baby. A baby is born knowing how to work the crowd. A toothless smile here, a musical squeal there, and even hard-nosed cynics grow soft in the head and weak in the knees.

In the view of the primatologist Sarah Blaffer Hrdy, the extraordinary social skills of an infant are at the heart of what makes us human. Through its ability to solicit and secure the attentive care not just of its mother

but of many others in its sensory purview, a baby promotes many of the behaviors and emotions that we prize in ourselves and that often distinguish us from other animals, including a willingness to share, to cooperate with strangers, to relax one's guard, uncurl one's lip and widen one's pronoun circle beyond the stifling confines of me, myself and mine.

As Dr. Hrdy argues in her latest book, "Mothers and Others: The Evolutionary Origins of Mutual Understanding," which will be published by Harvard University Press in April, human babies are so outrageously dependent on their elders for such a long time that humanity would never have made it without a break from the great ape model of child-rearing. Chimpanzee and gorilla mothers are capable of rearing their offspring pretty much through their own powers, but human mothers are not.

Human beings evolved as cooperative breeders, says Dr. Hrdy, a reproductive strategy in which mothers are assisted by as-if mothers, or "allomothers," individuals of either sex who help care for and feed the young. Most biologists would concur that humans have evolved the need for shared child care, but Dr. Hrdy takes it a step further, arguing that our status as cooperative breeders, rather than our exceptionally complex brains, helps explain many aspects of our temperament. Our relative pacifism, for example, or the expectation that we can fly from New York to Los Angeles without fear of personal dismemberment. Chimpanzees are pretty smart, but were you to board an airplane filled with chimpanzees, you "would be lucky to disembark with all 10 fingers and toes still attached," Dr. Hrdy writes.

Our capacity to cooperate in groups, to empathize with others and to wonder what others are thinking and feeling — all these traits, Dr. Hrdy argues, probably arose in response to the selective pressures of being in a cooperatively breeding social group, and the need to trust and rely on others and be deemed trustworthy and reliable in turn. Babies became adorable and keen to make connections with every passing adult gaze. Mothers became willing to play pass the baby. Dr. Hrdy points out that mother chimpanzees and gorillas jealously hold on to their infants for the first six months or more of life. Other females may express real interest in the newborn, but the mother does not let go: you never know when one of those females will turn infanticidal, or be unwilling or unable to defend the young ape against an infanticidal male.

By contrast, human mothers in virtually every culture studied allow others to hold their babies from birth onward, to a greater or lesser extent depending on tradition. Among the !Kung foragers of the Kalahari, babies are held by a father, grandmother, older sibling or some other allomother maybe 25 percent of the time. Among the Efe foragers of Central Africa, babies spend 60 percent of their daylight hours being toted around by somebody other than their mother. In 87 percent of foraging societies, mothers sometimes suckle each other's children, another remarkable display of social trust.

Dr. Hrdy wrote her book in part to counter what she sees as the reigning dogma among evolutionary scholars that humans evolved their extreme sociality and cooperative behavior to better compete with other humans. "I'm not comfortable accepting this idea that the origins of hypersociality can be found in warfare, or that in-group amity arose in the interest of out-group enmity," she said in a telephone interview. Sure, humans have been notably violent and militaristic for the last 12,000 or so years, she said, when hunter-gatherers started settling down and defending territories, and populations started getting seriously dense. But before then? There weren't enough people around to wage wars. By the latest estimates, the average population size during the hundreds of thousands of years of human evolution that preceded the Neolithic Age may have been around 2,000 breeding adults. "What would humans have been fighting over?" Dr. Hrdy said. "They were too busy trying to keep themselves and their children alive."

Dr. Hrdy also argues that our human ancestors became emotionally modern long before the human brain had reached its current average volume of 1,300 cubic centimeters, which is about three times the size of a chimpanzee brain - in other words, that we became the nicest apes before becoming the smartest. You don't need a bulging brain to evolve cooperative breeding. Many species of birds breed cooperatively, as do lions, rats, meerkats, wolves and marmosets, among others. But to become a cooperatively breeding ape, and to persuade a bunch of smart, hot-tempered, suspicious, politically cunning primates to start sharing child care and provisionings, now that took a novel evolutionary development, the advent of this thing called trust.

To explain the rise of cooperative breeding among our forebears, Dr. Hrdy synthesizes an array of new research in anthropology, genetics, infant development, comparative biology. She notes that recent research has overturned the longstanding insistence that humans are a patrilocal species, that is, with women moving away from their birth families to join their husbands. Instead, it seems that young mothers in many traditional societies have their own mothers and other female relatives close at hand, and who better to trust with baby care than your mom or your aunt? New studies have also shown the importance of postmenopausal women to gathering roots and tubers, the sort of unsexy foods that are difficult to disinter and lack the succulent status of, say, a freshly killed oryx, but that just may help feed the kids in hard times. Other anthropologists have made

the startling discovery that children have entertainment value, and that among traditional cultures without television or Internet access, a bobble-headed baby is the best show in town.

However cooperative breeding got started, its impact on human evolution was profound. With helpers in the nest, women could give birth to offspring with ever longer childhoods - the better to build big brains and stout immune systems - and, paradoxically, at ever shrinking intervals. The average time between births for a chimpanzee mother is about six years; for a human mother, it's two or three years. As a result of our combined braininess and fecundity, humans have managed to colonize the planet; exploit, marginalize or exterminate all competing forms of life; build a vast military-industrial complex all under the auspices of Bernard Madoff and with one yeti of a carbon footprint, and will somebody please hand me that baby before it's too late.

Obesity linked to hormone imbalance that impacts sexual quality of life

Weight loss through gastric bypass surgery can reverse hormonal changes

Hormonal changes and diminished sexual quality of life among obese men are related to the degree of obesity, and both are improved after gastric bypass surgery according to a new study accepted for publication in The Endocrine Society's Journal of Clinical Endocrinology & Metabolism (JCEM).

"Previous studies have found that obesity is correlated to lower sperm count and can be associated with infertility, but we wanted to know if obesity was biologically associated with an unsatisfying sex life, and if so, could it be reversible," said Dr. Ahmad Hammoud, MD, of the University of Utah and lead author of the study. "Our results show that the answer to both questions may be yes."

For this study, researchers followed 64 men over two years who participated in the Utah Obesity Study, which investigated the two-year morbidity of severely obese men undergoing Roux-en-Y gastric bypass surgery compared to controls. Researchers measured weight, BMI (body mass index) and reproductive hormone levels of participants at the beginning of the study and once more two years later. Similarly subjects completed a questionnaire designed to assess the impact of weight on quality of life in obese individuals at the onset of the study and again two years later.

"In our study population, we found that lower testosterone levels and diminished ratings for sexual quality of life were correlated with increased BMI," said Dr. Hammoud. "Subjects who lost weight through bariatric surgery experienced a reduction in estradiol levels, an increase in testosterone levels and an increase in ratings of sexual quality of life."

Dr. Hammoud points out that results from this study highlight an association between sexual quality of life and hormonal measures independent from weight. Because this relationship is confounded by biopsychosocial aspects of obesity, further studies are required to determine a cause and effect relationship.

Other researchers working on the study include Mark Gibson, Stephen Hunt, Ted Adams, and Douglass Carrell of the University of Utah; Ronette Kolotkin of Obesity and Quality of Life Consulting in Durham, NC; and A. Wayne Meikle of the ARUP Institute for Clinical and Experimental Pathology at the University of Utah.

The article "Effect of Roux-en-Y Gastric Bypass Surgery on the Sex Steroids and Quality of Life in Obese Men," will appear in the April 2009 issue of JCEM.

New study reveals: Gifted children shape their personalities according to social stigma

They know from a young age what they want to be when they grow up; they usually choose to study applied sciences; but they cannot explain why they made those choices

Gifted youths already know what they want to be when they grow up. They usually choose to study applied sciences, but when they are asked why they made their choices, they are not able to explain.

"Society identifies the gifted child with high intelligence and is often hasty to identify this intelligence with specific subjects, especially exact or prestigious sciences. The maturing children are quick to adopt this identity, renouncing the process of building self-identity," said Dr. Inbal Shani of the University of Haifa, who carried out this study under the supervision of Prof. Moshe Zeidner.

The study surveyed 800 gifted and non-gifted high-school students and examined the differences in self-concept and other psychological variables between the two groups. The study also observed the ways in which maturing gifted students form their identity. The results showed that while gifted youths have higher self-esteem in their educational achievements, they have lower self-esteem in social and physical aspects.

The researchers pointed out that as soon as students are defined as gifted, they are entered into special educational programs. This process causes them to feel that they excel in the academic field and therefore they strive to meet the expectations set for them in the programs built specially for them. This is particularly prominent in those classes that participate in intensive daily programs fostering gifted children.

"Maturing gifted students know from a very young age what their life's course will be – usually in the applied sciences. Most of them demonstrate neither deliberation nor interest in other fields, and they speak of

studying in academic or military-academic tracks . . . which is of much significance in the process of self-exploration," Dr. Shani noted.

She added that it is likely that applied science tracks are adjusted for the maturing gifted, and it could be that many of these youths would have chosen them regardless of the social labeling; but the problem is that they do primarily tend to choose their professional identity based on the social expectations. "It is a paradox: It is the gifted - who are often multi-talented - who tend to limit the realization of those very talents into specific fields. Instead of selecting from many options open to them, they limit themselves to applied or prestigious subjects," she said.

Dr. Shani added that gifted youths frequently report social difficulties and the feeling that other children keep distant from them because of the gifted label, and therefore it is important to enable them – in the process of forming an identity – to relate to emotional and social characteristics, such as motivation, self-concept, and external pressures, and not only to those characteristics related to cognitive aptitude.

Fowl soil additive breaks down crude oil

It is an unlikely application, but researchers in China have discovered that chicken manure can be used to biodegrade crude oil in contaminated soil. Writing in the International Journal of Environment and Pollution the team explains how bacteria in chicken manure break down 50% more crude oil than soil lacking the guano.

Bello Yakubu, Huiwen Ma, and ChuYu Zhang of Wuhan University, China, point out that contamination of soil by crude oil occurs around the world because of equipment failure, natural disasters, deliberate acts, and human error. However, conventional approaches to clean-up come with additional environmental costs. Detergents, for instance, become pollutants themselves and can persist in the environment long after any remediation exercise is complete.

A more environmentally benign approach is to bioremediation, which uses natural or engineered microbes that can metabolize the organic components of crude oil. Stimulating such microbial degradation in contaminated soil often involves the use of expensive fertilizers containing nitrogen and phosphorus, and again may come with an additional environmental price tag despite the bio label. Soil hardening and a loss of soil quality often accompany this approach.

Ma and colleagues suggest that animal waste, and in particular chicken manure, may provide the necessary chemical and microbial initiators to trigger biodegradation of crude oil if applied to contaminated soil. One important factor is that chicken manure raises the pH of soil to the range 6.3 to 7.4 which is optimal for the growth of known oil-utilizing bacteria.

In tests, the team added chicken manure to soil contaminated with 10 percent volume to weight of crude to soil. They found that the almost 75% of the oil was broken down in soil with the fowl additive after about two weeks. Whereas additive-free soil was naturally remediated to just over 50%.

The team carried out a microbial analysis of their samples and identified 21 different microbial species known as aerobic heterotrophs. The team explains that Bacillus species and Pseudomonas aeruginosa were the best oil-munching microbes but of the 21 isolates 12 were capable of metabolizing components of crude oil. Other microbes included Proteus, Enterobacter, and Micrococcus species. Bacillus represented the most prevalent species.

"The use of chicken manure to stimulate crude oil biodegradation in the soil could be one of the several sought-after environmentally friendly ways of abating petroleum hydrocarbon pollution in the natural ecosystem," the team concludes.

"Biodegradation of crude oil in soil using chicken manure", by Bello M. Yakubu, Huiwen Ma, and ChuYu Zhang in International Journal of Environment and Pollution, 2009, 36, 400-410

Moderate alcohol intake associated with bone protection

Epidemiological study examines effects of beer, wine and liquor on BMD

BOSTON - (March 3, 2009) In an epidemiological study of men and post-menopausal women primarily over 60 years of age, regular moderate alcohol intake was associated with greater bone mineral density (BMD). Researchers at the Jean Mayer USDA Human Nutrition Research Center on Aging (USDA HNRCA) at Tufts University found associations were strongest for beer and wine and, importantly, BMD was significantly lower in men drinking more than two servings of liquor per day. The results suggest that regular moderate consumption of beer or wine may have protective effects on bone, but that heavy drinking may contribute to bone loss.

"Previous research suggests that moderate alcohol consumption in older men and post-menopausal women may protect against BMD loss, a major risk factor for osteoporosis," said Katherine L. Tucker, PhD, corresponding author and director of the Dietary Assessment and Epidemiology Research Program at the USDA HNRCA. The 2005 Dietary Guidelines issued by the federal government defines moderate alcohol consumption as one drink per day for women and two drinks per day for men.

"Our study also looks at the possible effects of the three alcohol classes, beer, wine and liquor on BMD," Tucker continued. "We saw stronger associations between higher BMD and beer drinkers, who were mostly men, and wine drinkers, who were mostly women, compared to liquor drinkers." The results were published online February 25 by the American Journal of Clinical Nutrition.

Tucker, who is also a professor at the Friedman School of Nutrition Science and Policy at Tufts, and colleagues analyzed BMD measurements taken at three hip sites and the lumbar spine in 1,182 men, 1,289 post-menopausal women, and 248 pre-menopausal women whose parents or in-laws participated in the original Framingham Heart Study. There was not enough data to determine the effects of more than two servings of alcohol per day in post-menopausal women or the effects of daily alcohol consumption on BMD in pre-menopausal women. Participants self-reported their alcohol intake on dietary questionnaires. One serving of beer equaled a glass, bottle or can (356 mL), one serving of wine equaled a 4-oz. glass (118 mL), and one serving of liquor equaled one mixed drink or shot (42 mL).

After adjusting for several other factors that may have accounted for the higher BMD, such as silicon intake, calcium intake and smoking history, the authors still saw an association between higher BMD and moderate alcohol consumption. One of the strongest associations was seen in men who reported consuming one or two servings of total alcohol (a combination of beer, wine and liquor) or one or two servings of beer per day. Hip BMD in this group was significantly greater compared to non-drinkers.

In contrast, the authors observed significantly lower BMD at the hip and spine in men who consumed more than two servings of liquor per day compared to men who consumed one or two servings of liquor per day. "There is a body of research showing alcoholism is devastating to bones," Tucker said. "It's a major risk factor for osteoporosis. No one should depend solely on alcohol to maintain bone health."

The authors hypothesize that the silicon found in beer is contributing to the higher BMD scores in the men who reported consuming one or two servings of total alcohol or beer per day, citing previous studies finding silicon has greater bioavailability as a liquid. It is less clear why liquor and wine might protect BMD.

"We cannot say definitively what component of these alcoholic drinks might be beneficial to bone health because our findings are from an observational study, as opposed to a clinical trial," Tucker said. "Future studies might dig deeper into patterns of alcohol consumption, as we relied on a self-reported dietary questionnaire. Another component of data worthy of exploration is whether the antioxidants found in wine, such as revesterol or polyphenols, have a protective effect on bone in addition to other health benefits."

The study was supported by a USDA contract and grants from the National Institutes of Health (NIH). Co-authors Ravin Jugdaohsingh and Jonathan J. Powell, at the Rayne Institute, St. Thomas' Hospital, London, UK, have an active grant from the charitable foundation of the Institute of Brewing and Distilling. Co-author Supannee Sripanyakorn is sponsored by a studentship from the Government of Thailand and Jugdaohsingh is sponsored by a fellowship from The Frances and Augustus Newman Foundation.

Tucker KL, Jugdaohsingh R, Powell JJ, Qiao N, Hannan MT, Sripanyakorn S, Cupples LA, Kiel DP. American Journal of Clinical Nutrition. February 25, 2009 (online) "Effects of beer, wine and liquor intakes on bone mineral density in older men and women."

Earth's highest known microbial systems fueled by volcanic gases

University of Colorado scientists detect microscopic life near 19,850 feet

Gases rising from deep within the Earth are fueling the world's highest-known microbial ecosystems, which have been detected near the rim of the 19,850-foot-high Socompa volcano in the Andes by a University of Colorado at Boulder research team.

The new study shows the emission of water, carbon dioxide and methane from small volcanic vents near the summit of Socompa sustains complex microbial ecosystems new to science in the barren, sky-high landscape, said CU-Boulder Professor Steve Schmidt. He likened the physical environment of the Socompa volcano summit -- including the thin atmosphere, intense ultraviolet radiation and harsh climate -- to the physical characteristics of Mars, where the hunt for microbial life is under way by NASA.

CU-Boulder researchers have discovered that volcanic gases are fueling microbial life near summit of 19,500-foot-tall Socompa volcano in the high Andes. **Steve Schmidt, University of Colorado**

The microbial communities atop Socompa -- which straddles Argentina and Chile high in the Atacama Desert -- are in a more extreme environment and not as well understood as microbes living in hydrothermal vents in deep oceans, he said. The Socompa microbial communities are located adjacent to several patches of

green, carpet-like plant communities -- primarily mosses and liverworts -- discovered in the 1980s by Stephan Halloy of Conservation International in La Paz, Bolivia, a co-author on the new CU-Boulder study.

"These sites are unique little oases in the vast, barren landscape of the Atacama Desert and are supported by gases from deep within the Earth," said Schmidt, a professor in the ecology and evolutionary biology department. "Scientists just haven't been looking for microorganisms at these elevations, and when we did we discovered some strange types found nowhere else on Earth."

A paper on the subject by Schmidt and his colleagues was published in the February 2009 issue of the journal Applied and Environmental Microbiology. Co-authors on the study included CU-Boulder's Elizabeth Costello and Sasha Reed, Preston Sowell of Boulder's Stratus Consulting Inc., and Halloy.

The team used a sophisticated technique that involves extracting DNA from the soil to pinpoint new groups of microbes, using polymerase chain reaction, or PCR, to amplify and identify them, providing a snapshot of the microbial diversity on Socompa.

The new paper is based on an ongoing analysis of soil samples collected during an expedition to Socompa several years ago. The research team also reported a new variety of microscopic mite in the bacterial colonies near Socompa's rim, which appears to be the highest elevation that mites have ever been recorded on Earth, Schmidt said.

Costello, a research associate in CU-Boulder's chemistry and biochemistry department, said small amounts of sunlight, water, methane and CO2 work in concert in the barren soils to fuel microbial life near the small volcanic vents, or fumaroles. Such conditions "relieve the stress" on the high-elevation, arid soils enough to allow extreme life to get a toehold, Costello said. "It's as if these bacterial communities are living in tiny, volcanic greenhouses."

The CU-Boulder team also discovered unique colonies of bacteria living on the slopes of Socompa in extremely dry soils not associated with fumaroles. The bacteria detected in such dry soils may be transient life transported and deposited by wind in the extreme environment of Socompa, with some organisms surviving to bloom during periodic pulses of water and nutrients, said Schmidt.

"These sites are significantly less diverse," said Costello. "But the thing that really stands out is just how tough these microbes are and how little it takes for them to become established."

Schmidt, who likened the high Andes to the harsh Dry Valleys of Antarctica under study by researchers from NASA's Astrobiology Institute because of their hostile, arid conditions, said the new research also provides information on how the cold regions of Earth function and how they may respond to future climate change. Research in such extreme environments could lead to the discovery of new antibiotics and other products.

A return expedition to Socompa in February 2009 by Schmidt included a Chilean scientist, an Argentinean microbiologist, a Boulder spectral-imaging expert and an Argentinean archaeologist. There is archaeological evidence that ancient Incans once roamed over Socompa, and the remains of three, 500-year-old mummified Inca children were discovered in 1999 atop the nearby Llullaillaco volcano, apparent sacrifice victims.

Although reaching the summit of Socompa requires two days in a four-wheel drive vehicle and two more days of hiking, recent footpaths near the summit apparently made by adventurers may have damaged some of the mat-like plant communities, Costello said.

The 2009 and 2005 expeditions to Socompa were funded by grants from the National Geographic Society and the Microbial Observatory Program of the National Science Foundation. For more information visit CU's Alpine Microbial Observatory site at http://amo.colorado.edu/.

Half in US see another country emerging as world's technological leader

New national survey

DURHAM, N.C. -- Half of all Americans expect another country to emerge this century as the world's leader in addressing technological challenges that range from the economy to global warming, according to a survey of U.S. public opinion released Tuesday by Duke University.

Although only 34 percent of Americans gave themselves a grade of A or B for understanding "the world of engineers and what they do," 72 percent nonetheless expect the technological advancements of the 21st century to surpass those of the previous century. However, only 49 percent predict the United States will lead the way in producing these advances, according to the survey of 808 adults carried out Jan. 22-25 by Hart Research Associates.

Duke's Pratt School of Engineering commissioned the survey, "Americans' Attitudes Toward Engineering and Engineering Challenges," for a national summit on engineering "grand challenges" it is co-hosting March 2-3 in Durham.

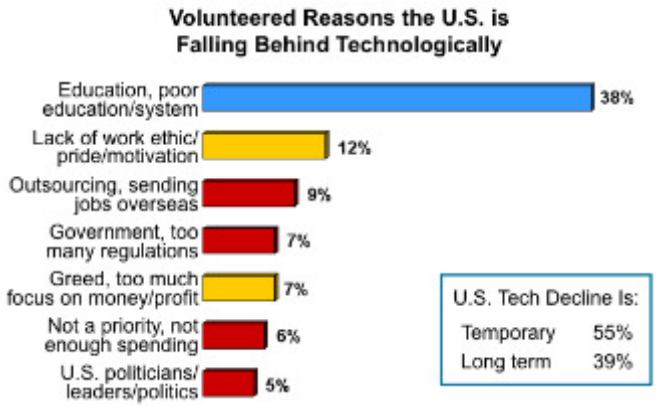
Americans with more education are even less optimistic about the likelihood the United States will be the world's technological leader in the 21st century. China was cited by 20 percent of all the respondents as being

most likely to assume this position, followed by Japan and Europe at 10 percent each, and India at 4 percent. Americans were just as likely to say their country's ability to compete technologically over the past century has worsened as to say it has improved.

Among those who see a decline in America's ability to compete technologically, 55 percent say the situation is temporary and 39 percent say it is long term.

"Americans understand that innovation is critical to their future, but also recognize that our country's continued leadership isn't assured just because we invented everything from the airplane to the personal computer," said Thomas Katsouleas, dean of the Pratt School. "The survey shows that when Americans focus on how central engineers are to solving our biggest problems, they come to view the discipline as essential and want to attract more talented young people to it."

Education is the main reason given for a loss of U.S. competitiveness.



In response to a list of major engineering challenges facing the world, those surveyed gave highest priority to developing better medicines, providing clean water around the world and developing environmentally friendly power sources. They gave less priority to securing cyberspace against attacks or to restoring and improving deteriorating urban infrastructures.

The respondents said the best ways to improve U.S. global competitiveness are with more training for workers, improved K-12 math and science teaching, and tougher standards for public school teachers and students. They were much less likely to endorse tax breaks for business and investment, or new immigration policies to attract foreign engineers and other technical experts.

A majority of the respondents -- 58 percent -- said engineering is losing out to other professions when it comes to young people choosing careers. They said this is happening because engineering does not pay as much as other fields, requires extensive schooling and is seen as being difficult. "Not as glamorous" was cited least often among seven possible answers in explaining why engineering has been a less attractive career choice.

Katsouleas released the survey results Tuesday morning during the two-day summit Duke is hosting with the University of Southern California Viterbi School of Engineering and Olin College. More than 1,000 people registered for the event, which is bringing together "leading engineering, science, humanities and social science scholars from across the nation" to discuss a series of societal "grand challenges" laid out by the National Academy of Engineering. *The complete survey results are available online at http://tinyurl.com/nsr33.*

Musicians' Brains 'Fine-Tuned' to Identify Emotion

EVANSTON, Ill. - Looking for a mate who in everyday conversation can pick up even your most subtle emotional cues? Find a musician, Northwestern University researchers suggest.

In a study in the latest issue of European Journal of Neuroscience, an interdisciplinary Northwestern research team for the first time provides biological evidence that musical training enhances an individual's ability to recognize emotion in sound.

"Quickly and accurately identifying emotion in sound is a skill that translates across all arenas, whether in the predator-infested jungle or in the classroom, boardroom or bedroom," says Dana Strait, primary author of the study.

A doctoral student in the Henry and Leigh Bienen School of Music, Strait does research in the Auditory Neuroscience Laboratory directed by neuroscientist Nina Kraus. The laboratory has done pioneering work on the neurobiology underlying speech and music perception and learning-associated brain plasticity.

Kraus, Northwestern's Hugh Knowles Professor of Communication Sciences and Neurobiology; Richard Ashley, associate professor of music cognition; and Auditory Neuroscience Laboratory manager Erika Skoe co-authored the study titled "Musical Experience and Neural Efficiency: Effects of Training on Subcortical Processing of Vocal Expressions in Emotion."

The study, funded by the National Science Foundation, found that the more years of musical experience musicians possessed and the earlier the age they began their music studies also increased their nervous systems' abilities to process emotion in sound.

"Scientists already know that emotion is carried less by the linguistic meaning of a word than by the way in which the sound is communicated," says Strait. A child's cry of "Mommy!" -- or even his or her wordless utterance -- can mean very different things depending on the acoustic properties of the sound.

The Northwestern researchers measured brainstem processing of three acoustic correlates (pitch, timing and timbre) in musicians and non-musicians to a scientifically validated emotion sound. The musicians, who learn to use all their senses to practice and perform a musical piece, were found to have "finely tuned" auditory systems.

This fine-tuning appears to lend broad perceptual advantages to musicians. "Previous research has indicated that musicians demonstrate greater sensitivity to the nuances of emotion in speech," says Ashley, who explores the link between emotion perception and musical experience. One of his recent studies indicated that musicians might even be able to sense emotion in sounds after hearing them for only 50 milliseconds.

The 30 right-handed men and women with and without music training in the European Journal of Neuroscience study were between the ages of 19 and 35. Subjects with music training were grouped using two criteria -- years of musical experience and onset age of training (before or after age 7).

Study participants were asked to watch a subtitled nature film to keep them entertained while they were hearing, through earphones, a 250-millisecond fragment of a distressed baby's cry. Sensitivity to the sound, and in particular to the more complicated part of the sound that contributes most to its emotional content, was measured through scalp electrodes.

The results were not exactly what the researchers expected. They found that musicians' brainstems lock onto the complex part of the sound known to carry more emotional elements but de-emphasize the simpler (less emotion conveying) part of the sound. This was not the case in non-musicians.

In essence, musicians more economically and more quickly focus their neural resources on the important - in this case emotional - aspect of sound. "That their brains respond more quickly and accurately than the brains of non-musicians is something we'd expect to translate into the perception of emotion in other settings," Strait says.

The authors of the study also note that the acoustic elements that musicians process more efficiently are the very same ones that children with language disorders, such as dyslexia and autism, have problems encoding. "It would not be a leap to suggest that children with language processing disorders may benefit from musical experience," says Kraus.

Strait, a pianist and oboe player who formerly worked as a therapist with autistic children, goes a step further. Noting that impaired emotional perception is a hallmark of autism and Asberger's syndromes, she suggests that musical training might promote emotion processing in these populations.

To learn more about the link between music, the brain and language processing, visit Northwestern's Auditory Neuroscience Laboratory at http://www.brainvolts.northwestern.edu.

New study shows how spikes in nitrite can have a lasting impact on the heart

BOSTON - A new study provides insight into how a short burst in nitrite can exert lasting beneficial effects on the heart, protecting it from stress and assaults such as heart attacks. In this study, just published in Circulation Research, researchers at Boston University School of Medicine have demonstrated for the first time that short elevations in circulating levels of this simple anion are sufficient to have a lasting impact on the heart by modulating its oxidation status and its protein machinery.

Nitrite, an oxidation product of the ubiquitous short-lived cell signaling molecule, nitric oxide (NO), was until recently thought to be biologically inert at the relatively low levels found in the body. Traces of nitrite are present in our diet and significant amounts are continuously produced from nitrate, another oxidation product of NO and a constituent of green, leafy vegetables. The suspicion that high levels of nitrite and nitrate may cause cancer, as well as concerns about their risk to compromise the ability of red blood cells to deliver oxygen to tissues, have led to strict regulations aimed at limiting our exposure to these substances through drinking water and food products.

In the past few years, however, multiple research groups have shown that low concentrations of nitrite exert numerous beneficial effects, ranging from anti-bacterial activities to increases in local blood flow, and that they can somehow protect tissues from damage when oxygen is suddenly cut off and then rapidly restored, as occurs during heart attacks and strokes.

To study the molecular underpinnings of this protective effect of nitrite, the researchers at Boston University School of Medicine used a rat model in which they administered nitrite only once, causing a short spike in circulating levels, as a way to simulate the types of naturally occurring increases in nitrite that follow exercise or consumption of a meal rich in nitrate.

The researchers used a systems-biology approach in which changes in multiple biological and biochemical systems (e.g., the composition of a large number of proteins, the concentration of several small molecule metabolites, and functional outcomes) are simultaneously monitored and then integrated to produce one final picture in order to provide a broader view of the impact of this treatment on the heart. They tested their theory

that following these changes over time and at different doses of nitrite might help to explain the protective effects of nitrite on the heart.

"What we found was that a single brief nitrite treatment elicited persisting changes in the heart's oxidation status together with lasting alterations to numerous proteins involved in the heart's energy metabolism, redox regulation, and signaling," said David H. Perlman, a post-doctoral research associate in the Cardiovascular Proteomics Center at Boston University School of Medicine, and lead author of the study. "These alterations were particularly striking because they persisted at least 24 hours after the actual nitrite levels had returned back to normal, and they were correlated strongly with the improvements in heart function observed at the same time."

He noted that this type of protection, called 'cardiac preconditioning', is a recently discovered phenomenon shown to be caused by numerous pharmacological agents.

"The proteins we have implicated include some key proteins, such as mitochondrial aldehyde dehydrogenase, that have been shown by others to be critical to cardiac protection afforded by other agents and triggers," added Perlman. "This is exciting because it ties nitrite-triggered cardioprotection into the broader preconditioning field. Our study complements and extends other work, and identifies new players of potential importance for protection of the heart."

Perlman explained that nitrite levels in our bodies change under a number of circumstances, such as when we run up a flight of stairs or eat a big serving of salad.

"For years, the resulting bursts in nitrite were considered to be of little if any physiological relevance. Now we have good reason to believe that even small spikes in nitrite concentration can alter protein function in the heart in ways that afford protection," noted Perlman.

"We are intrigued by the breadth and magnitude of the proteomic changes in heart mitochondria elicited by a single, short-lasting elevation in nitrite concentration and believe that our findings will have broad implications for mitochondrial signalling and cardiac energetics," commented Martin Feelisch, senior author of the study. "It looks as though nitrite is triggering an ancient program aimed at fine-tuning mitochondrial function. Although the present study focussed on the heart, our observations may extend to other tissues and translate into relevant changes in muscle function elsewhere. If true, this may help explain, for example, the training effects of very short periods of exercise, which are known to be associated with elevations in circulating nitrite concentrations."

Interestingly, only low and high doses of nitrite, but not those in-between, were found to be protective. Although further studies will be needed to fully delineate the mechanisms of nitrite-induced cardioprotection, this study informs ongoing basic and translational studies by highlighting the importance of the dose-effect relationship for nitrite and the broad array of downstream targets possibly involv ed in its cardioprotective efficacy, the researchers concluded.

The study, "Mechanistic Insights into Nitrite-Induced Cardioprotection Using an Integrated Metabonomic/Proteomic Approach," was carried out as a collaboration between researchers at the Cardiovascular Proteomics Center at Boston University School of Medicine under the direction of Prof. Catherine E. Costello and core lab director Prof. Mark E. McComb, Prof. Martin Feelisch and his lab members of the Whitaker Cardiovascular Institute at Boston University School of Medicine, and Prof. Houman Ashrafian of Oxford University's Department of Cardiovascular Medicine. It was supported by grants and a contract from the National Institutes of Health, National Heart Lung and Blood Institute and National Center for Research Resources, as well as a Medical Research Council Strategic Appointment Award. It is available in the February 19th online edition of Circulation Research.

Mind

Liked the Show? Maybe It Was the Commercials

By BENEDICT CAREY

People eat chocolate bars in pieces, waiting and savoring. They space their cigarettes through the day, their gossip sessions, their calls to friends. They like their sports with timeouts, and practice their religion with fasts and periods of self-denial, like Lent.

So why is it that commercial interruptions always ruin TV programs?

Maybe they don't. In two new studies, researchers who study consumer behavior argue that interrupting an experience, whether dreary or pleasant, can make it significantly more intense.

"The punch line is that commercials make TV programs more enjoyable to watch. Even bad commercials," said Leif Nelson, an assistant professor of marketing at the University of California, San Diego, and a co-author

of the new research. “When I tell people this, they just kind of stare at me, in disbelief. The findings are simultaneously implausible and empirically coherent.”

Over the years, psychological research has found that people are not always so clear on what makes them happy. When reporting on their own well-being, they exhibit a kind of equilibrium: After a loss (divorce, say) or a gain (a promotion), they typically return in time to about the same happiness level as before. Humans habituate quickly, to hardship and prosperity, to war and peace.

Yet even modest pleasures — a cup of coffee in the morning, an afternoon walk, a Scotch before bed — seem to follow a law of diminishing returns. “Alcohol is like love,” says a roué in Raymond Chandler’s “The Long Goodbye.” “The first kiss is magic. The second is intimate. The third is routine.”

To Sonja Lyubomirsky, a psychologist at the University of California, Riverside, and the author of the book “The How of Happiness,” this raises a provocative question: “If you adapt so quickly to pleasurable activities, and the pleasure decreases, how do you sustain a level of happiness or ever move up on the scale?”

One way people do this, research suggests, is to favor novel experiences over material goodies. The smell of a new car may go to a person’s head for months. But the memory of a mind-bending trek through the Australian outback — or the Amsterdam museums — seems to provide longer-lasting psychological sustenance, some researchers argue. In some studies, couples report greater satisfaction in their relationship after trying new things together.

The new consumer research analyzed similar dynamics at a moment-to-moment level. In one experiment, Dr. Nelson, along with Tom Meyvis and Jeff Galak of New York University, had 87 undergraduates watch an episode of the sitcom “Taxi.” Half watched it as it was originally broadcast, with commercials for the Jewelry Factory Store and the law office of Michael Brownstein, among other ads. The other half watched the show straight through, without commercials.

After the show was over, the students rated how much they enjoyed it, using an 11-point scale and comparing it with the sitcom “Happy Days,” which they were all familiar with.. Those who saw “Taxi” without commercials preferred “Happy Days”, but those who saw the original show, Jewelry Factory Store and all, preferred “Taxi” by a significant margin.

In similar experiments, using other video clips and a variety of interruptions, the results were the same: people rated their experiences as more enjoyable with commercials , no matter their content, or other disruptions.. The effect wasn’t limited to watching TV; interrupting a massage also heightened people’s enjoyment, one experiment found.

The opposite was true for irritating experiences, like listening to vacuum cleaner noise: a break only made it seem worse, they found.

“The reason this happens, we argue, is that we tend to adapt to a variety of experiences, as they’re happening,” Dr. Nelson said. “Listening to a song, watching a TV program, having a massage: these all start out very enjoyable, and within a few minutes we get used to it. Interruptions break that up.”

In one of their papers, the authors even propose that commercial television evolved culturally to maximize enjoyment. The millions of Americans who record their favorite shows on TV may scoff; but they, too, often stop the shows to get a drink, make a call or talk. This kind of controlled interruption may represent a kind of ideal, Dr. Nelson said.

Gal Zauberman, an associate professor of marketing at the Wharton School at the University of Pennsylvania, said the findings were solid, and added: “To me, the most interesting part is that almost everyone says, ‘I just wish I never had to watch a commercial.’

“It’s all a part of this phenomenon that we have found in other work,” he continued, “that people are not fully aware of what makes them happy, especially when there’s a temporal component, when one experience affects another in time.”

Interruption hardly improves all pleasurable activities. Dr. Nelson and his colleagues have found that people often do not habituate to shows or stories that are particularly demanding — with unexpected plot twists — and that interruptions can snap the thread, souring the experience. When artists, tradesmen, musicians and others lose themselves in their work, the selfless pleasure some psychologists call flow, the lunchtime whistle can be a hazard.

But life’s more common pleasures may have more in common with spending a morning in the hotel hot tub. Pretty wonderful; all the more so if you can slip out and dip in the pool every few minutes.

Lazy spider steals from the mouths of ants

* 13:45 04 March 2009 **by Jessica Griggs**

Forget stealing from the mouths of babes, zoologists have observed a similarly heinous crime - spiders stealing food from the mouths of ants.

At Mbita Point on the shores of Lake Victoria in Kenya, the walls of the buildings and other surfaces are covered with insects, including thousands of tiny lake flies. Within the throng lurks Menemerus, one of the jumping spiders or salticids.

These predatory spiders adopt an approach similar to the big cats when hunting. They move very slowly, with their body close to the ground, before leaping on their prey.

Stalking is helped by extremely good vision: there are eight eyes in total and importantly, two that face forward. These anterio-medial eyes have a visual acuity about one sixth as good as humans and let them "see like a primate and hunt like a lion," says Simon Pollard from the University of Canterbury in Christchurch, New Zealand, who led the study.

Jumping spiders are also are known to be capable of solving cognitively complex tasks.

Menemerus bivittatus is one of three species of jumping spider that steal food from ant columns **(Image: Simon Pollard)**

Rare behaviour

Now Pollard and colleague Robert Jackson, have filmed three species of Menemerus adopting an alternative feeding strategy: stealing recently killed lake flies from ants and carrying their loot back to the nest. This is a behaviour not seen since 1936, when it was first documented in India.

The jumping spiders - ranging from 2 to 6 millimetres in length - lurk about 10 centimetres from a column of ants on the wall. After about 5 seconds, the spider scuttles in and uses its mouthparts to snatch the object from the ant's jaws, before returning to its home to feed. This process may be repeated for as many as four times in one feeding session.

Pollard says that the snatching method may offer a less energetic way of ensuring a meal compared with the usual stalking and leaping technique - live prey do sometimes manage to avoid the spiders' attacks.

Stealing might also be a way of getting the ants to do the hard work, picking out fresh and nutritious flies from those that have dried up, he says.

"Menemerus will often spend the time and energy stalking and leaping on a dead lake fly," says Pollard. "Like macabre puppets, the corpses of lake flies trapped by a strand of silk [from various other species of spider] can dance in the wind just like live flies."

But long-dead flies are no use to the spiders as they won't be moist enough to produce the soupy mix of saliva and bodily fluids necessary for digestion. Without ants to do the sorting, the spiders might waste energy.

Learned behaviour?

Eileen Hebets from the University of Nebraska in Lincoln told New Scientist: "I think one of the most intriguing aspects is the possibility of learning being involved in this foraging strategy. I would love to know if exposure to another individual foraging in this way increases the likelihood of attempting it on one's own."

Jérôme Casas from the University of Tours in France suggests that it might also be interesting to look at the behaviour of robbed ants. "It might change according to the 'value' of the lost prey," he says.

Journal reference: Journal of Arachnology (DOI: 10.1636/ST07-55.1)

Jellyfish sushi: Seafood's slimy future

* 04 March 2009 **by Caroline Williams**

It's a Friday night in 2050. It's been a long week at work and even if you could be bothered to cook, there's nothing in the fridge. So what fast food will you pick up on your way home? How about some squid and chips? Perhaps an algae burger? And don't forget the crunchy fried jellyfish rings on the side.

One thing's for sure: unless something changes soon, familiar favourites such as cod, haddock, hake and plaice will be off the menu. In fact, if we're not careful, an assortment of exotic alternatives will be all the ocean has left to offer us.

This may seem an extreme vision of the future, but marine biologists are alarmed by the imbalances that are appearing in marine ecosystems. The ocean is changing fast - too fast, it seems, for us to reliably predict the combined effects of overfishing, pollution and climate change. What is clear is that the changes, by and large, are not good news for our bellies. "We are entering a time of great uncertainty," says Boris Worm, of Dalhousie University in Halifax, Nova Scotia, Canada, and the Census of Marine Life project. "If we continue as we have been, in 50 years there may not be much left to take from the ocean."

Worm and an international team of ecologists have taken a comprehensive look at the state of the world's fisheries. Their results, published in the journal Science in 2006 (vol 314, p 787), make grim reading. In short, catches of wild fish are plummeting and the researchers predict that without steps to protect biodiversity, all current commercial fish and seafood species will collapse by 2050 (see graph).

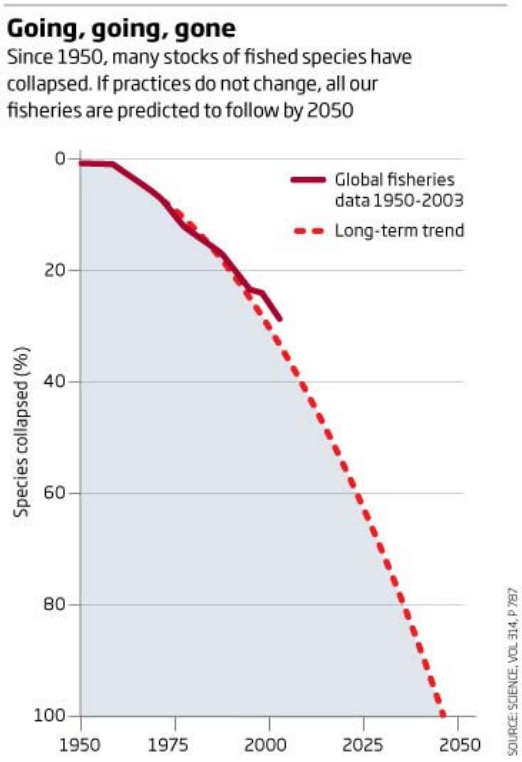
If we do empty the oceans of fish, it will leave a gaping hole in our diet. Fish provide around 20 per cent of our intake of animal proteins, according to a 2007 estimate of the UN's Food and Agriculture Organization (FAO). That means each of us wolfs down an average of 16.4 kilograms of fish per year. National figures vary widely, from virtually none in some landlocked nations like Afghanistan, to about 20 kilograms per person per year in the UK and US and a whopping 180 kilograms in the Maldives.

This demand is increasing rapidly, as a result of the rising global population and increasing prosperity in the developing world. Maintaining catches at current levels is becoming difficult, let alone increasing them. According to the FAO, more than 75 per cent of the world's fish stocks are either fully exploited, over-exploited, or recovering from past depletion.

Overfishing is not only affecting those whose diets depend on fish, of course. It is also creating huge gaps in marine ecosystems that are quickly exploited by opportunistic species. The shrimp and crab fisheries off the coast of Nova Scotia and Newfoundland are the direct result of the removal of large cod and haddock stocks through fishing.

While replacing one tasty marine food may not seem like much of a hardship, not all of the replacements for fish will be as delicious. In recent years, the fishing industry has shifted its focus down the food chain, taking larger numbers of small, plankton-eating fish like sardine and anchovy. This could be a dangerous strategy. Small fish are not only crucial to the survival of larger predatory fish such as hake, as well as birds and marine mammals - they also help to maintain balance in the species below them in the food chain. "If you remove small fish there is every possibility that other species in the food chain, like jellyfish, will have a good time of it," says Tom Anderson, a marine ecologist at the National Oceanography Centre in Southampton, UK.

This is already happening in one of the world's most productive fisheries, the Benguela current off the coast of Namibia in southern Africa. When Christopher Lynam of the University of St Andrews in the UK and his colleagues surveyed the area in 2003, they found that the ecosystem, which once supported large populations of sardines and anchovies, had been taken over by two species of jellyfish. The study estimated the biomass of jellyfish in the region at 12.2 million tonnes, more than three times that of mackerel, hake, sardine and anchovies combined (Current Biology, vol 16, p R492).



The reasons for these changes are complex. Shifts in climate, currents and sea temperature will have played a part, but a major factor is the collapse of the once abundant sardine and anchovy fisheries. In the late 1970s, the total fish catch was around 17 million tonnes per year. Now it is closer to 1 million tonnes. And since jellyfish eat fish eggs and larvae, as well as compete with young fish for food, the shift to a jellyfish-dominated ecosystem rather than a fish-dominated one may be irreversible, say the team.

Blooms of jellyfish have also appeared in the overfished waters of the Black Sea, Alaska, the Mediterranean and the Gulf of Mexico. In the Sea of Japan, overfishing of sardines and anchovies, plus blooms of phytoplankton caused by nutrient-rich coastal run-off, have led to a jellyfish problem of epic proportions: autumn blooms of the giant jellyfish Nemopilema nomurai, which can grow to more than 2 metres in diameter. In 2003 alone this jellyfish cost the Japanese fishing industry over $100 million, "clogging and bursting nets, causing high mortality of the catch due to venom, increasing the risk of capsizing trawlers and giving fishermen painful stings", says Masato Kawahara, a marine ecologist at Hiroshima University in Japan.

Removing fish from an ecosystem may also have other consequences. In the Benguela current, the crash in phytoplankton-eating fish has also been linked to more frequent phytoplankton blooms (Ecology Letters, vol 7, p 1015). That can spell bad news: when the blooms die off, bacteria gobble them up, along with most of the oxygen in the water.

Even overfishing large predatory fish could encourage these blooms. Zooplankton-eating fish thrive once their predators are gone, leading to a decline in their own prey. With fewer zooplankton to feed on phytoplankton, the latter can bloom unchecked.

The collapse of cod, haddock, hake, pollock, plaice and flounder fisheries off Nova Scotia have all coincided with an increase in phytoplankton. So has a reduction in the number of salmon in the north Pacific. And last year, Michele Casini of the Swedish Board of Fisheries in Lysekil, and colleagues, found a strong link between the collapse of cod stocks in the Baltic Sea in the early 1980s and phytoplankton blooms.

Squid, too, are increasingly thriving throughout the oceans. While changes in water temperatures may play a part, the main reason is the removal of their predators. "Almost everything eats squid in the ocean - tuna, marlin and swordfish hardly eat anything else - so if you remove the squid's predators, how can it not have an impact?" says George Jackson of the University of Tasmania in Hobart, Australia. And as squid grow quickly and live for less than a year, their numbers can rise rapidly if the conditions are right. "They're the weeds of the sea," he says.

The best-documented example is the Gulf of Thailand, which has been heavily overfished in recent decades. Here the Indo-Pacific squid Sepioteuthis lessoniana has moved in to fill the gaps in the ecosystem, forcing the fishing industry to adapt. "You see fishermen walking down the beach in Thailand with baskets of squid," says Jackson.

Off the US coast, the Humboldt squid, Dosidicus gigas, has begun to expand its territory north from the east Pacific equatorial waters to the seas off central California. This has happened before, during El Niño years, when the water warmed enough for them to spread their range. The last time this happened, in 1997-98, predation and competition from tuna and billfish sent most of them back south when the waters cooled. In the past five years, though, they have stayed put despite cooler seas, and seem to be thriving. Now they even threaten the Californian Pacific hake fishery.

If the outlook for today's fisheries is as bleak as some suggest, we can expect to see growing numbers of gelatinous, rubbery and slimy creatures swimming or drifting through the oceans. So what will that leave us to eat with our fries?

Shrimp and crab aside, squid are likely to be the most palatable bet since they are already well established on menus worldwide. Larger species like the Humboldt squid are also commercially fished in Mexico, Peru and northern Chile. They yield a decent-sized steak and, as long as they are tenderised with lemon juice and not overcooked, they need not be tough or rubbery (see recipe online*).

Nutritionally, squid are high in protein - about 16 per cent - low in fat and a good source of zinc, vitamins B2, B3 and B12, as well as some trace elements such as phosphorus, copper and selenium. On the downside, they are very high in cholesterol.

Future foods

If current seafood stocks collapse, other species such as squid and jellyfish may dominate the oceans. But how would they stack up nutritionally against fish such as cod?

	Amount per 100g portion	As a % of the FDA's recommended daily intake based on a 2000 kilocalorie diet	Amount per 100g portion	As a % of the FDA's recommended daily intake based on a 2000 kilocalorie diet	Amount per 100g portion	As a % of the FDA's recommended daily intake based on a 2000 kilocalorie diet	Amount per 100g portion	As a % of the FDA's recommended daily intake based on a 2000 kilocalorie diet
	Cod raw, fresh		Jellyfish dried, salted		Squid raw, fresh		Kelp raw, fresh	
Kilocalories	82		36		92		43	
Fat (g)	0.7	1	1.4	2	1.4	2	0.7	1
Sodium (g)	0.05	2	9.7	404	0.04	2	0.2	8
Carbohydrates (g)	0	0	0	0	3.1	1	9.3	3
Protein (g)	18	36	5.5	11	16	31	1.7	3
Vitamin A (mg)	10	1	2	<1	10	1	35	3
Vitamin C (mg)	1	2	0	0	4.7	9	3	6
Calcium (mg)	16	2	2	<1	32	4	168	20
Iron (mg)	0.4	2	2.3	12	0.7	4	2.8	14
	• Low in saturated fat • Good source of vitamins, potassium and protein • High in cholesterol		• High in potassium and copper • Very good source of iron and selenium • Low in protein • Often served salted, so very high in sodium		• Low in saturated fat • Good source of protein, vitamin B_3 and zinc • Very high in cholesterol		• Good source of fibre, vitamin C, vitamin K, and minerals including calcium and zinc • Very high in sodium	

SOURCE: NUTRITIONDATA.COM

Jellyfish crunch

Compared to jellyfish, though, squid are positively nutritious and delicious. A common ingredient in Asian cuisine, jellyfish have been eaten for more than 1000 years in China, where they are often added to salads (Hydrobiologia, vol 451, p 11). In Japan they are served as sushi and in Thailand they are turned into a kind of crunchy noodle (see recipe online*) For those with a western palate, though, the taste and texture may take some getting used to. "I wouldn't describe it as a sensation that would sweep the globe," says Kevin Raskoff of Monterey Peninsula College in California. "It's reminiscent of slightly tough strips of cucumber."

Jellyfish are low in fat and high in copper, iron and selenium, but they are only about 5 per cent protein. Furthermore, they are typically prepared by being dried and salted so, unless a new approach is taken, jellyfish products could end up too high in sodium to become dietary staples (see table).

Each year, around a quarter of a million tonnes of jellyfish are landed worldwide. As well as China and Japan, there are small fisheries in Australia, India and the US. Cost remains a challenge: once caught, jellyfish have to go through a multistage treatment to reduce water content, decrease pH and firm the flesh - a process

that can take up to 40 days. This, together with its unpredictable population and low nutritional value, makes further commercialisation a challenge.

So while inventive locals in Obama, Japan, coped with a bloom of giant jellyfish in 2006by turning them into sushi, soup and even novelty cookies, it is unlikely that they will replace fish as a major food source for the world. "If it's a question of could we eat jellyfish, then yes we could, but the nutritional value is quite low," say Raskoff. "I'd be concerned if they were the last things left on the menu."

This leaves plankton as a possible fish replacement. The idea is not as odd as it first seems. After all, the Aztecs are said to have eaten a kind of "cake" made from the dried froth of blue-green algae, probably spirulina, that grew on the surface of Lake Texcoco. According to the accounts of Spanish conquistadores, it was highly nutritious and tasted like cheese. It is still eaten in a number of countries, including several in central Africa, where it is harvested from Lake Chad.

The Aztecs are said to have eaten a kind of 'cake' made from the dried froth of blue-green algae

Marine phytoplankton, too, are packed with omega-3 fatty acids and trace minerals. Since their blooms tend to consist of mostly one species they could, in theory, be scooped up and turned into food. Even so, converting fishing trawlers to fish for algae would be unlikely to work in practice, says Peter Franks, a plankton ecologist at Scripps Institution of Oceanography in La Jolla, California. "Plankton blooms are dense - with up to a million cells in a litre of water. But a million cells would hardly make a phytoplankton cracker," he says.

Besides, adds Franks, the practicalities of predicting where a bloom will occur and ensuring that the catch is not contaminated by the handful of species that are toxic would make it financially unfeasible. "I would not want to be running a business based on filtering plankton from the ocean as human food. You would be better off growing spinach," he says.

Even squid, which look like a good option on paper, could be a risky bet as a major fishery, warns Jackson. "Squid are very much boom and bust," he says, a characteristic that makes fisheries tricky to manage. "If there is a lot of food, they grow fast and reproduce early. But if conditions change, the population crashes." He adds that "if you put pressure on squid populations, you'll just create the same problem as we have with fish".

Worm, though, dismisses talk of converting the global fishing fleet to seek out alternatives to fish. He points out that our fisheries are not quite finished, and says there are several instances where creating "no take" zones next to fisheries has allowed them to recover, making them more profitable than others where no such measures have been taken.

And, he says, we are beginning to learn from our mistakes. Proposals to fish for krill off Nova Scotia have not yet been acted on because krill is such an important food source for other organisms, says Worm. "I think people are drawing a line in the sand. Doing this to a predator is one thing, but taking away the foundation of the ecosystem? That's too risky."

Worm is so confident we can turn the situation around that he is willing to bet on the oceans of the future having more fish than we have today. "In 2048 I'll be 80 years old and I hope I'll be able to host a fish supper to celebrate," he says. It is certainly not impossible, but it will take a seismic shift in the way we manage the oceans. Without some serious changes, Worm's seafood supper could be nutritious, it might even be delicious, but it probably won't be fish.

Bibliography

*1. *See recipes and add your comments at www.newscientist.com/article/dn16654*

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Heart hazards of woeful wives

Depression ties marital strain to cardiovascular risks in women, not men

SALT LAKE CITY – Women in strained marriages are more likely to feel depressed and suffer high blood pressure, obesity and other signs of "metabolic syndrome," a group of risk factors for heart disease, stroke and diabetes, University of Utah psychologists found.

The same study found men in strained marriages also are more likely to feel depressed, yet - unlike women - do not face an increased risk of metabolic syndrome, which is characterized by five symptoms: hypertension, obesity around the waistline, high blood sugar, high triglycerides and low levels of HDL, which is "good cholesterol."

"We hypothesized that negative aspects of marriages like arguing and being angry would be associated with higher levels of metabolic syndrome," says the study's first author, Nancy Henry, a doctoral student in psychology. "We further anticipated that this relationship would be at least partly due to depressive symptoms."

"In other words, those who reported experiencing more conflict, hostility and disagreement with their spouses would more depressed, which in turn would be associated with a higher risk of heart disease due to metabolic syndrome," she adds

"We found this was true for wives in this study, but not for husbands," says Henry, who was scheduled to present the findings Thursday, March 5 in Chicago during the American Psychosomatic Society's annual meeting.

"The gender difference is important because heart disease is the number-one killer of women as well as men, and we are still learning a lot about how relationship factors and emotional distress are related to heart disease," she says.

Putting Your Heart into Your Marriage

Does the study suggest women should avoid men to reduce heart disease risks?

"We know they should," jokes Tim Smith, a psychology professor and study co-author who heads a larger University of Utah study of the role of marriage quality in heart disease. The new study is part of the larger effort.

Smith, turning serious, says: "The reason you have to be careful about 'what does it mean?' is that this study is a simple, preliminary test of what might be unhealthy about relationships for women."

"There is good evidence they [women] should modify some of the things that affect metabolic syndrome – like diet and exercise – but it's a little premature to say they would lower their risk of heart disease if they improved the tone and quality of their marriages – or dumped their husbands," he says.

Other data from the larger study indicate "that a history of divorce is associated with coronary disease," he adds, noting the researchers are pursuing the hypothesis that improving marriage might improve health.

"The immediate implication is that if you are interested in your cardiovascular risk – and we all should be because it is the leading killer for both genders – we should be concerned about not just traditional risk factors [such as blood pressure and cholesterol] but the quality of our emotional and family lives," Smith says.

In addition to possible health benefits, more immediate benefits include "getting along better and enjoying each other more, improving your mood," he says.

Some critics have questioned the concept and clinical usefulness of metabolic syndrome – also known as syndrome X or insulin resistance syndrome – and have asserted that it is nothing more than the sum of its parts, namely, a group of five risk factors for heart disease, stroke and diabetes.

"It is defined as a syndrome, but there still is controversy in the medical community – what should be included, how the different factors should be measured, whether all the factors hang together as a distinct syndrome or are they just separate things," Henry says.

She says she chose to study metabolic syndrome because there is no question its components are risk factors for cardiovascular disease and because the syndrome was a possible explanation for how "psychosocial risk factors" in marriage are related to cardiovascular disease.

"Strained marriages can increase your risk of heart disease, and that may in part be because strained marriages increase the risk of metabolic syndrome and thus heart disease," Smith says. "The reason strained marriages might be related to metabolic syndrome is that strained marriages can be depressing, and depression is then the link to metabolic syndrome."

Smith says the endocrinology of depression's psychological stress may explain why the five risk factors that comprise metabolic syndrome fit together.

He hypothesizes that perhaps "the hormonal effects of stress are why you are depositing fat [around the waist], why your insulin resistance goes up, why your lipids and blood pressure get out of whack. Part of the reason these things may be clumping together is because they are part of an unhealthy body response to stress."

How the Study Was Performed

Henry and Smith conducted the new study with University of Utah psychologists Jonathan Butner, an associate professor; Bert Uchino, a professor; and Cynthia Berg, a professor and chair of the university's Department of Psychology.

For their wider study, the psychologists used the Dan Jones & Associates polling firm and newspaper ads during 2001-2005 to recruit 276 couples, who were married an average of 20 years and from ages 40 to 70.

Each couple filled out several questionnaires for both the encompassing study and for Henry's study. The questionnaires included 10 scales: three to assess positive aspects of marriage quality, such as mutual support, emotional warmth and friendliness, and confiding in each other; three scales to measure negative aspects of marital quality such as arguments, feelings of hostility and extent of disagreement over various topics such as kids, sex, money and in-laws; and four scales to gauge symptoms of depression (not necessarily full-blown clinical depression).

Each couple also went to a university clinic, where their waists and blood pressure were measured and they were given lab tests for "good" cholesterol, fasting glucose and triglycerides. Together, those data determined if

a study participant had metabolic syndrome. They also underwent a screening test designed to exclude any couple that already had cardiovascular disease.

The findings:

* Women who reported more marital strain were more likely to also report depressive symptoms, Henry says.
* "Women who reported more marital strain had more metabolic syndrome symptoms, and that association can be explained by the fact they also reported more depressive symptoms," says Smith.
* "Men in bad marriages also reported more depression, but neither marital strain nor depression was related to their levels of metabolic syndrome," he adds.

"We know from previous research that women are more sensitive and responsive to relationship problems than men," Henry says. "The results of this study suggest those problems could harm their health. Understanding the emotional and relationship health of couples can be an important overall factor in understanding physical health. Improving aspects of intimate relationships might help your emotional and physical well-being."

Antibody key to treating variant CJD, scientists find

Scientists at the University of Liverpool have determined the atomic structure of the 'binding' between a brain protein and an antibody that could be key to treating patients with diseases such as variant CJD.

Variant Creutzfeldt-Jakob Disease (vCJD) is part of a family of rare progressive neurodegenerative disorders, called prion diseases, which affect both animals and humans. It is thought that those who have developed vCJD became infected through the consumption of cattle products contaminated with Bovine Spongiform Encephalopathy (BSE) – a brain disorder in cows, commonly known as Mad Cow Disease.

Prion diseases can develop when a naturally occurring brain prion protein called, PrP, comes into contact with infectious prions. This converts PrP into a form that has a different shape, and eventually leads to a build-up of protein in the brain, causing brain cells to die. It is thought that immunisation with antibodies that can 'stick' to PrP could treat and even prevent the development of the disease.

To understand the 'connection' between the antibody and the protein, scientists at Liverpool used X-ray crystallography technology to build a three-dimensional picture of the binding between an antibody called ICSM18 – designed to 'stick' effectively to prion proteins – and PrP cells.

Samar Hasnain, Professor of Molecular Biophysics at the University, explains: "To pin-point where the antibody 'sticks' to the protein we used X-ray crystallography, pioneered by Nobel Prize winner Max Perutz. Significantly we found that the point at which the protein and antibody came together was also where scientists at the Medical Research Council (MRC) Prion Unit had identified a single amino acid, which we now know has a significant impact on a patient's susceptibility to prion disease."

Scientists at the MRC Prion Unit, University College London, who collaborated on the research, have found that ICSM18 could help prevent brain cells from becoming infected as well as reverse early damage caused by the disease.

Professor John Collinge, Director of the MRC Prion Unit, added: "We have shown that ICSM18 has the highest therapeutic potential in animal and cell based studies, but we have yet to establish its impact on people who have vCJD or other prion diseases. We are currently working, however, to make human versions of the antibodies for future trials in people."

The research is funded by the Medical Research Council and is published in Proceedings of the National Academy of Sciences (PNAS.)

Mountain on Mars may answer big question

Rice study hints at water – and life – under Olympus Mons

The Martian volcano Olympus Mons is about three times the height of Mount Everest, but it's the small details that Rice University professors Patrick McGovern and Julia Morgan are looking at in thinking about whether the Red Planet ever had – or still supports – life.

Using a computer modeling system to figure out how Olympus Mons came to be, McGovern and Morgan reached the surprising conclusion that pockets of ancient water may still be trapped under the mountain. Their research is published in February's issue of the journal Geology.

The scientists explained that their finding is more implication than revelation. "What we were analyzing was the structure of Olympus Mons, why it's shaped the way it is," said McGovern, an adjunct assistant professor of Earth science and staff scientist at the NASA-affiliated Lunar and Planetary Institute. "What we found has implications for life – but implications are what go at the end of a paper."

Co-author Morgan is an associate professor of Earth science.

In modeling the formation of Olympus Mons with an algorithm known as particle dynamics simulation, McGovern and Morgan determined that only the presence of ancient clay sediments could account for the volcano's asymmetric shape. The presence of sediment indicates water was or is involved.

Olympus Mons is tall, standing almost 15 miles high, and slopes gently from the foothills to the caldera, a distance of more than 150 miles. That shallow slope is a clue to what lies beneath, said the researchers. They suspect if they were able to stand on the northwest side of Olympus Mons and start digging, they'd eventually find clay sediment deposited there billions of years ago, before the mountain was even a molehill.

The European Space Agency's Mars Express spacecraft has in recent years found abundant evidence of clay on Mars. This supports a previous theory that where Olympus Mons now stands, a layer of sediment once rested that may have been hundreds of meters thick.

Morgan and McGovern show in their computer models that volcanic material was able to spread to Olympus-sized proportions because of the clay's friction-reducing effect, a phenomenon also seen at volcanoes in Hawaii.

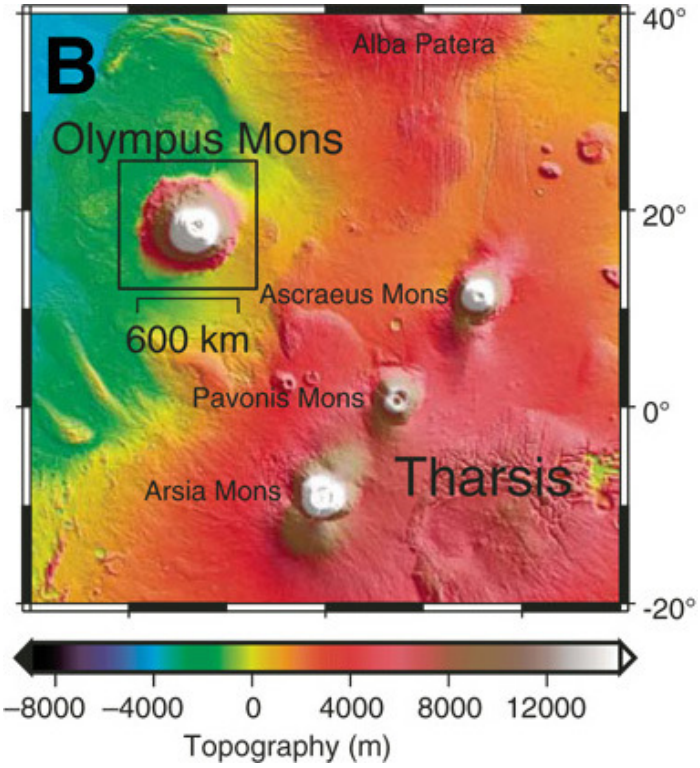


Image: wikipedia.com

What may be trapped underneath is of great interest, said the researchers. Fluids embedded in an impermeable, pressurized layer of clay sediment would allow the kind of slipping motion that would account for Olympus Mons' spread-out northeast flank – and they may still be there.

Thanks to NASA's Phoenix lander, which scratched through the surface to find ice underneath the red dust last year, scientists now know there's water on Mars. So Morgan and McGovern feel it's reasonable to suspect water may be trapped in pores in the sediment underneath the mountain.

"This deep reservoir, warmed by geothermal gradients and magmatic heat and protected from adverse surface conditions, would be a favored environment for the development and maintenance of thermophilic organisms," they wrote. This brings to mind the primal life forms found deep in Earth's oceans, thriving near geothermal vents.

Finding a source of heat will be a challenge, they admitted. "We'd love to have the answer to that question," said McGovern, noting evidence of methane on Mars is considered by some to be another marker for life. "Spacecraft up there have the capability to detect a thermal anomaly, like a magma flow or a volcano, and they haven't.

"What we need is 'ground truth' – something reporting from the surface saying, 'Hey, there's a Marsquake,' or 'Hey, there's unusual emissions of gas.' Ultimately, we'd like to see a series of seismic stations so we can see what's moving around the planet."

The paper appears online in Geology at: http://geology.gsapubs.org/cgi/content/abstract/37/2/139

Is one diet as good as another? U of I study says no and tells you why

Any diet will do? Not if you want to lose fat instead of muscle. Not if you want to lower your triglyceride levels so you'll be less likely to develop diabetes and heart disease. Not if you want to avoid cravings that tempt you to cheat on your diet. And not if you want to keep the weight off long-term.

"Our latest study shows you have a better chance of achieving all these goals if you follow a diet that is moderately high in protein," said Donald Layman, a University of Illinois professor emeritus of nutrition. The research was published in the March Journal of Nutrition.

Layman's new study followed the weight-loss efforts of 130 persons at two sites, the U of I and Penn State University, during 4 months of active weight loss and 8 months of maintenance.

Two previous studies had looked at short-term weight loss; this one was designed to look at long-term effects, he said.

Although both plans were equal in calories, half the group followed a moderate-protein diet (40% carbohydrates, 30% protein, 30% fat) while the other followed a diet based on USDA's food-guide pyramid (55% carbohydrates, 15% protein, 15% fat).

"Persons in the first group ate twice the amount of protein as the second group," said Layman.

And the difference in protein made all the difference in improved body composition and body lipids, he said.

Although the amount of weight lost in both groups was similar, at 4 months participants in the protein group had lost 22 percent more body fat than members of the food-pyramid group. At 12 months, the moderate-protein dieters had lost 38 percent more body fat.

"The additional protein helped dieters preserve muscle. That's important for long-term weight loss because muscle burns calories—if you lose muscle, and you used to be able to consume 2,000 calories without gaining weight, you'll find that now you can only eat, say, 1,800 calories without weight gain," he said.

What were the effects on lipids? Although at 4 months the food-guide pyramid appeared to be more effective in lowering LDL and total cholesterol levels, at 12 months LDL levels came back up until both diets were equally effective, Layman said.

"This is the first study to show that short-term changes in LDL cholesterol are not maintained with long-term weight loss. Most scientists believe that high cholesterol is more a factor of genetics than of diet," he said.

But the moderate-protein diet had by far the bigger effect on lowering triglycerides, and that lasted as long as individuals remained on the diet, he said.

"Of the two types of lipid problems, high triglycerides pose a greater risk for heart disease. Approximately twice as many people have high triglycerides, and people with this condition are approximately four times more likely to die from heart disease," the scientist said.

To ensure compliance, participants met every week for weigh-ins and nutrition instruction. "We taught participants how to follow their diet, how to grocery shop, and how to prepare the meals. They also measured everything they ate three days a week," he said.

"Studies that report there is no difference among diets also report that subjects were not carefully following the diets," said Layman. "It's very important to realize the difference between diet compliance and diet effectiveness."

The protein diet was easier to follow and maintain long-term, with 64 percent of the moderate-protein dieters completing the study compared to 45 percent of dieters using the high-carbohydrate diet, Layman said.

"Subjects on the moderate-protein diet reported that they weren't as interested in snacks or desserts, and they didn't have food cravings. When you eat protein, you feel full longer," he said.

Average weight loss for the protein group was 23 percent higher than the food-pyramid group, with 31 percent of "completers" in the protein group losing more of than 10 percent of their initial body weight versus 21 percent of the food-pyramid group.

Co-authors of the study are Ellen Evans of the U of I Department of Kinesiology and Public Health; Donna Erickson, Jennifer Seyler, and Judy Weber of the U of I Department of Food Science and Human Nutrition; and Deborah Bagshaw, Amy Griel, Tricia Psota, and Penny Kris-Etherton of The Pennsylvania State University Department of Nutritional Sciences.

It was funded by the National Cattlemen's Beef Association, The Beef Checkoff, and Kraft Foods.

Mortality Risk Greater for Elderly Women Who Nap Daily

San Francisco, Calif. - March 04, 2009 – A new study appearing in Journal of the American Geriatrics Society has found that older women who reported taking daily naps had a significantly greater risk of dying. The results of the study are in contrast to a number of prior studies which have indicated that daily napping improves health.

Four communities consisting of 8,101 Caucasian women aged 69 and older were studied over a 7-year period. Women who reported napping daily were 44 percent more likely to die from any cause, 58 percent more likely to die from cardiovascular causes and 59 percent more likely to die from non-cardiovascular, non-cancer causes. This relationship remained significant among relatively healthy women.

The findings also showed that older women who reported sleeping between 9-10 hours per 24-hour period also had a greater risk of mortality compared to those who slept between 8-9 hours. The association was strongest for cardiovascular-related mortality.

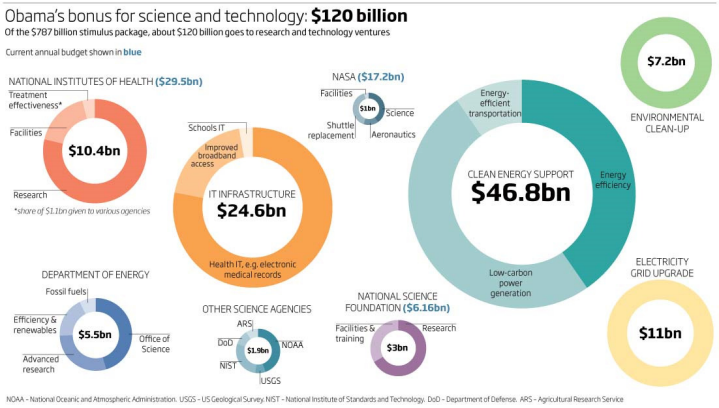
The results of this study should not be interpreted to mean that napping causes poor health outcomes, and it is not recommended that older adults avoid napping. Napping and long sleep duration may be caused by sleepiness due to underlying sleep disorders or other medical conditions. “Since excessive sleep suggests that night time sleep is disrupted, interventions to treat sleep disorders and improve sleep quality in older women may reduce mortality risk,” says Katie L. Stone, co-author of the study. Additional studies are needed to explain why napping is linked with increased risk of death.

Noted in the study, however, was that elderly women who napped less than 3 hours per week were not at increased risk of mortality compared to women who did not nap at all. “Shorter and less frequent naps do not appear to be related to any increase in risk of death,” says Stone.

*To view the abstract for this article, please **click here.***

Obama goes 'all in' for science

* 04 March 2009 **by Peter Aldhous, San Francisco**



NEVER has so much money been pumped into science so quickly and with so much hanging on a successful outcome. The full scope of President Barack Obama's agenda to revitalise the ailing US economy has now been revealed, and it is arguably the biggest bet on science and technology in history.

The Obama administration's latest attempt to tackle the problems facing the US is a record $3.6 trillion budget request for 2010. This has come hard on the heels of a $787 billion "stimulus package" designed to give the US economy a shot in the arm. Both are packed with funding for science and technology ventures, from healthcare research to an electricity supergrid. The stimulus alone hands out more than $20 billion for basic research and about $50 billion to support renewable power and energy efficiency (see charts).

The stimulus bill calls for the funds to be spent in two years, though in some areas it may take longer. In terms of dollars per year, it is arguably the most cash that has ever been pumped into scientific research. Even the Apollo programme and the Manhattan project - which cost over $200 billion and $35 billion at today's value - were spread over 11 and five years, respectively. It seems Obama is delivering on his promise to restore science to its rightful place. "He is committed to putting his money where his mouth is - or putting our money where his mouth is," says Lesley Stone of the lobby group Scientists and Engineers for America.

Yet in the light of US budget plans for 2010, it is clear that Obama's goal is about more than giving the economy a kick-start by spending on scientists' salaries and test tubes. In the detail of the stimulus are key components of a wider agenda, aspects of which might have triggered a fight if they had not been hurried through.

Take healthcare: the stimulus includes $1.1 billion for research into the comparative effectiveness of treatments. This is a bold move, given the powerful organisations that profit from the status quo, such as big pharma. It is crucial to Obama's wider plan to save big, by cracking down on ineffective treatments, and to spend big, to extend healthcare insurance coverage to tens of millions of people who don't have it.

Obama's plans for healthcare exemplify the risks inherent in his agenda. Delivering the promised efficiency will require a shake-up of a system that currently rewards doctors and hospitals according to the quantity of the care they provide, not its quality.

The stimulus package and budget for 2010 also include windfalls for the main agencies that fund basic research. Officials are scrambling to work out how to spend their allocations effectively. The National Institutes of Health, which is the biggest winner, is combing through its backlog of unmet grant proposals. This dash to allocate cash has some observers worried. "I don't believe it is possible to spend that much money, that fast, that wisely," says Gail Wilensky of the international health foundation Project HOPE in Millwood, Virginia.

Having made such a huge gamble, Obama's political future rides on that bet coming in. So, too, may the fortunes of the scientists and engineers who will benefit from his largesse - and who will be held to account if things go awry. "It will be important for scientists to understand that it's an opportunity that cannot be wasted," says Rita Colwell at the University of Maryland at College Park, a former director of the US National Science Foundation.

Yet given the scale of the global economic crisis, most science leaders back Obama's decision to go "all in" rather than tackle one issue at a time. "I think we only get one real shot at this," says Glenn Ruskin of the American Chemical Society. "It's unprecedented, but it has to be done."

Editorial: The pitfalls of Obama's science bonanza

A REVOLUTION is under way in the US that will affect the entire world. It is orchestrated by a president and Congress who are convinced that the future of the economy lies in science and technology. Under normal circumstances, this might lead to modest budget increases for research, and a supportive environment for high-tech business - warm glows all round. But with the economy in a state of collapse, and long-neglected problems with energy, climate, health and infrastructure coming home to roost, these are extraordinary times, and they have prompted extraordinary action.

President Barack Obama has decided to deluge research and high-tech projects with unprecedented levels of funding (see "Obama makes biggest gamble on science in history"). It is a thrilling prospect for anyone who recognises science as a force for progress. But there are perils. The American public is notoriously impatient. If

the scientists can't quickly demonstrate the benefits of all the tax dollars they will be getting, they had better watch out - witness the ire directed at bank executives perceived to have squandered multibillion-dollar bail-outs. Merely promising that the fruits of innovation will be harvested years down the line won't cut it.

The trickle-down effect of high-wage, high-tech jobs into spending in malls and restaurants is just the start. There is in fact good evidence that spending on science can be as effective an economic stimulus as spending on conventional infrastructure. According to one report this year, $20 billion spent on research and scientific infrastructure should create and retain 402,000 jobs. Another analysis suggests that broadband networks are almost as effective as roads and bridges at creating short-term jobs, and probably better in the long run. Scientists must also understand that unprecedented funding brings unprecedented accountability. They really do need to deliver clean energy, cheap and effective medicines, and so on.

Obama's agenda is so audacious that it is inevitable that some aspects will misfire. Plans to use research into evidence-based medicine to cut wasteful treatments will be particularly hard to deliver. That brings a real danger that the science boom will dissolve into a bust. If the stimulus isn't backed by sustained investment, scientists will join the unemployment lines.

Other leading economies face pitfalls too. In the UK, for example, the prime minister, Gordon Brown, has matched Obama in terms of pro-science rhetoric, but there is no sign of a flood of new funding for British science. If Obama's gamble pays off, then the UK and other nations will wish they had made a similar bet. America's brain gain will become their brain drain.

Immune reaction to metal debris leads to early failure of joint implants

Debris triggers danger signals that lead to inflammation

Researchers at Rush University Medical Center have identified a key immunological defense reaction to the metals in joint replacement devices, leading to loosening of the components and early failure.

The study, funded by the National Institutes of Health, won the annual William H. Harris, MD Award for scientific merit from the Orthopaedic Research Society. Currently posted online, it is expected to be published in the June issue of the Journal of Orthopaedic Research.

Over 600,000 total joint replacements are performed in the United States each year. The vast majority are successful and last well over 10 years. But in up to 10 percent of patients, the metal components loosen, requiring the patient to undergo a second surgery.

The loosening is often caused by localized inflammation, an immune reaction to tiny particles of debris from the components themselves as they rub against one another. No infection is involved.

"As soon as joint replacement devices are implanted, they begin to corrode and wear away, releasing particles and ions that ultimately signal danger to the body's immune system," said Nadim Hallab, associate professor at Rush University Medical Center and the study author.

There are two different types of inflammatory pathways: one that reacts to foreign bodies like bacteria and viruses, which cause an infection, and another that reacts to "sterile" or non-living danger signals, including ultraviolet light and oxidative stress. This is the first time that researchers have shown that debris and ions from implants trigger this danger-signaling pathway.

According to Hallab, when specialized cells of the immune system, called macrophages, encounter this metallic debris, they "engulf it in sacs called lysosomes and try to get rid of the debris by digesting it with enzymes." But the particles damage the lysosomes, Hallab said, "and the cells start screaming 'danger.'"

These danger signals are detected by large complexes of proteins, called inflammasomes. The inflammasomes mobilize, precipitating a chain of chemical events that cause inflammation.

The researchers are hopeful that identification of this molecular pathway that triggers inflammation without infection could lead to new and specific therapeutic strategies to avoid the early failure of joint replacements.

Other researchers at Rush involved in the study were Marco Caicedo, Ronak Desai, Kyron McAllister, Dr. Anand Reddy, and Dr. Joshua Jacobs.

Depression increases risk for heart disease more than genetics or environment

By Jim Dryden March 3, 2009

A history of major depression increases the risk of heart disease over and above any genetic risks common to depression and heart disease, according to researchers at Washington University School of Medicine in St. Louis and the VA. The findings are reported this week at the annual meeting of the American Psychosomatic Society this week in Chicago.

The researchers analyzed data gathered from more than 1,200 male twins who served in the U.S. military during the Vietnam War. The men were surveyed on a variety of health issues in 1992, including depression, and were assessed again in 2005.

In the study, investigators looked at the onset of heart disease in depressed study participants between 1993 and 2005. Men with depression in 1992 were twice as likely to develop heart disease in the ensuing years, compared to men with no history of depression.

"Based on our findings, we can say that after adjusting for other risk factors, depression remains a significant predictor of heart disease," says first author Jeffrey F. Scherrer, Ph.D., research assistant professor of psychiatry at Washington University School of Medicine and the St. Louis Veterans Affairs Medical Center. "In this study, we have demonstrated that exposure to depression is contributing to heart disease only in twins who have high genetic risk and who actually develop clinical depression. In twins with high genetic risk common to depression and heart disease, but who never develop depression itself, there was no increased risk for heart disease. The findings strongly suggest that depression itself independently contributes to risk for heart disease."

The investigators were looking for evidence of what they call incident heart disease, an event such as a heart attack, heart surgery, stent placement or medical treatment for angina. Those who had evidence of heart disease prior to the original survey in 1992 were excluded from this study.

Because twins were studied, the researchers could divide participants into risk groups: twins with high genetic and environmental risk for depression, those with moderate risk and those with a low risk. The risk groups then were compared for incident heart disease adjusting for other influences on heart disease such as smoking, obesity, hypertension and diabetes.

"By separating the twins into these groups based on their genetic and environmental risks, we are able differentiate the genetic risks common to depression and heart disease and the risks for heart disease from exposure to depression," says co-investigator Hong Xian, Ph.D., associate professor of mathematics in medicine at Washington University and health science specialist at the VA.

Twins automatically are matched by age. They normally grow up in the same family environment, and in the case of identical twins, they share identical DNA.

"If one twin has depression, but his twin brother does not, both twins will share genetic vulnerability for depression, but it turns out the twin who was not depressed has less risk for heart disease," says Scherrer. "In sum, depression itself remains a significant contributor to incident heart disease after controlling for genes, environment and mental and physical risk factors."

Scherrer and Xian plan to follow these twins as they age. They also plan to study the effects of successful depression treatment on heart disease risk.

Scherrer JF, Xian H, Franz CD, Lyons MJ, Jacobson KC. Eisen SA, Kremen WS. Depression is a risk factor for incident heart disease in a genetically informative twin design. Presented at the Annual Meeting of the American Psychosomatic Society, March 4-7, 2009: Chicago, Ill.

This research was supported by grants from the National Institute of Health and the Veterans Administration.

Horses tamed earlier than thought

Horses were domesticated much earlier than previously thought, according to a team of researchers. They found evidence suggesting that the animals were used by a culture in northern Kazakhstan 5,500 years ago.

Until now, the earliest evidence of horse riding was metal parts from harnesses dating from the Bronze Age.

Writing in Science, a team from the UK's Exeter University suggested that the community in Kazakhstan rode their horses 1,000 years earlier. They also ate them and drank their milk, possibly as an alcoholic brew.

The researchers traced the origins of horse domestication to the Botai culture of Kazakhstan. Analysis of ancient bones showed that the horses were a similar shape to domesticated horses from the Bronze Age.

The UK team studied the remains for evidence of damage to their mouths and teeth caused by the riding bits used to harness the animals.

The scientists also analysed the remains of food and drink in pottery and traces of horse meat and milk. Horse milk is still drunk in Kazakhstan, usually fermented into an alcoholic drink known as koumiss.

The site has only recently been opened to researchers

Lead researcher Dr Alan Outram from Exeter University, said horse domestication was an important indication of the state of human civilisation.

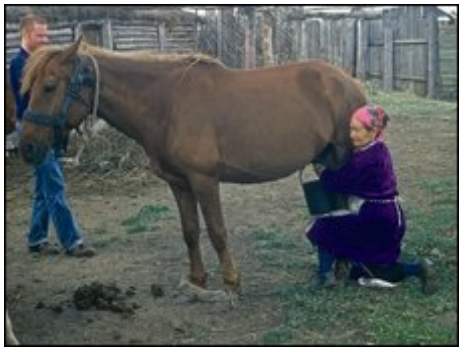
"The domestication of the horse does have implications for human culture globally," he said. "It increases people's ability to trade and it has great advantages in warfare.

"So if we are moving the origins of horse domestication much further back, we are going to have to think about the impact on the development of human culture at the time."

Some researchers associate the domestication of the horse with the spread of bronze working across Eurasia thousands of years ago.

It may also be linked to the ancient expansion of the Indo-European languages - a widespread language group which today includes English, German, Hindi and Persian.

Listen to Dr Outram on the current edition of Science In Action on the BBC World Service. You can also download the programme



Communities in Kazakhstan have been milking horses for thousands of years

Ecologists propose first prevention for white-nose syndrome death in bats

Localized heating of caves during hibernation may reduce bat mortality

White-nose syndrome (WNS) is a poorly understood condition that, in the two years since its discovery, has spread to at least seven northeastern states and killed as many as half a million bats. Now researchers have suggested the first step toward a measure that may help save the affected bats: providing localized heat sources to the hibernating animals.

"We have no idea why it's spreading so rapidly," says Justin Boyles, a graduate student in biology at Indiana State University and the first author of the paper, published this week in Frontiers in Ecology and the Environment e-View.

The syndrome has baffled scientists since its discovery in the winter of 2006 in upstate New York, where hibernating bats were found with a mysterious white fungus growing on their faces and wing membranes. Hundreds of emaciated bats were found dead in and around their caves, suggesting that they had starved to death during their hibernating months, and affected populations commonly suffer 75 to 100 percent mortality.

The origins of WNS are virtually unknown – scientists just identified the fungus species last month. But they are still mystified by its relationship to such unprecedented bat mortality.

Boyles and his coauthor Craig Willis of the University of Winnipeg tested the idea, suspected by many in the bat research community, that the fungus causes bats to spend more time out of hibernation during the winter. Mammals must rouse from hibernation periodically, but doing so too often or for long periods of time is energetically costly. When they rouse, the bats must use body energy to keep warm; spending too much time out of hibernation may deplete their fat reserves and cause them to starve to death, say the authors.

Because of the rapid spread of the fungus and the fact that field experiments can take months to years to complete, Boyles and Willis instead created a mathematical simulation to test the idea that the fungus is causing bats to spend more time out of hibernation. Their model took into account the patterns of arousal, body mass and percentage body fat of a particular species, called little brown bats, which are affected by the fungus.

The simulation showed that the patterns and proportion – about 82 percent – of bat mortality observed in affected populations in the wild are consistent with a large increase in the amount of time spent out of hibernation during the winter months. Their results, they say, provide evidence that the fungus is likely affecting bat hibernation patterns.

The researchers then took the simulation one step further. They reasoned that one way to help affected bats save their energy reserves and survive the winter is to provide them with a heat source, so they don't have to create as much body heat when they rouse. Bats often fly to the warmest parts of their cave during bouts of arousal.

"They already do this in the wild," Boyles says. "What we're suggesting is accentuating that behavior."

When the authors altered the simulation to include localized heat sources the bats could gather in during arousals, the model showed that mortality levels dropped to as little as 8 percent.

These results could be used in the short-term to prevent bat populations from crashing below sustainable levels, the authors say. They are currently developing a system, using wooden boxes and heating coils, to create warm pockets in bat caves. The plan holds no guarantees: the overall temperature in the cave needs to stay cold enough so that bats can still lower their body temperatures during hibernation. But the researchers are optimistic. "By insulating the bat boxes and carefully selecting where we will place them, we think we can solve this issue," says Willis.

Further, saving afflicted animals may not be sustainable in the long term, say the authors. If WNS is transmitted in spring and summer by surviving bats, saving its carriers will also save the disease, they write. At present, the search for a remedy for this mysterious fungus continues to stymie scientists. "I can't even guess what the cure or the solution to this is going to be," says Boyles. "This isn't a cure. We're going for a stopgap."

Researchers' new goal: Drug-free remission for HIV infection

A group including leading academic and industry scientists has issued a challenge to researchers in the field of HIV/AIDS: find a way to effectively purge latent HIV infection and eliminate the need for chronic, suppressive therapy to control this disease. "The Challenge of a Cure for HIV Infection," to be published in the March 6 issue of Science, calls for a coordinated initiative involving academia, industry, patient advocates and government to accelerate the search for a cure.

Highly active antiretroviral therapy (HAART) for the chronic suppression of HIV replication has been the major accomplishment in HIV/AIDS medicine, a therapy now being used by more than four million people around the world to keep the latent HIV virus in check, according to lead author Douglas Richman, Professor of Pathology and Medicine at the University of California San Diego and the Florence Seeley Riford Chair in AIDS Research. He is Director of the Center for AIDS Research at UC San Diego and staff physician at the VA San Diego Healthcare System.

While HAART therapy has allowed many patients to assume a relatively healthy life, unencumbered by symptoms or side effects of the once-daily treatment, HAART is no panacea, according to the authors which include David M. Margolis of the University of North Carolina, Chapel Hill, Warner C. Greene of the Gladstone Institute of Virology and Immunology and UC San Francisco, Daria Hazuda of Merck and Co., Roger Pomerantz, of Tibotec Pharmaceuticals Inc. and Johnson & Johnson Corporation and the late Martin Delaney of "Project Inform."

The team states that combination therapy for HIV infection represents a triumph for modern medicine. However, they add that HAART's success is limited by its cost, the requirements of lifelong adherence required to contain persistent HIV infection – meaning that interruption of treatment can result in a rapid rebound of replicating HIV virus – and the unknown effects of such long-term treatment. There is already growing concern about increased rates of heart disease, diabetes, liver disease and many forms of cancer in aging HIV-infected patients on treatment, according to the paper.

"If we could purge the latent reservoir of HIV infection, we could withdraw chronic suppressive therapy – with great potential impact on cost, toxicity, convenience and transmission," Richman said, adding that the scientific challenges to achieving this goal are substantial but "considering the payoff, the effort is well worth it."

The goal of HIV therapeutics, they propose, should be a drug-free remission. Such a goal requires understanding of the persistence of HIV infection or low-level viremia – the presence of the virus in the bloodstream. Persistent infection is maintained in reservoirs like latently infected lymphocytes or macrophage cells of the immune system. There may be other, as yet unrecognized, reservoirs as well. As multiple mechanisms may contribute to maintenance of this viral latency, combination approaches would likely be required to eradicate infection. Such therapeutic approaches would also affect host cell function, says Richman, so global immune activation must be avoided.

The scientists agree that a major clinical and ethical challenge will be how to safely test future drug development in humans since current antiretroviral therapy is so effective and relatively safe. However, such studies would be required in order to cure HIV. The difficulty of developing a preventive vaccine or microbicide for HIV puts even great pressure on other methods in order to contain the ongoing pandemic of HIV.

"Without a vaccine, we are left with the substantial financial burden of lifelong treatment for tens of millions of people," said Richman. "Acknowledging and addressing the challenges outlined in this paper is the first step toward progress."

"Success – if achieved – will not occur quickly," Richman added. "But, bear in mind, the dramatic success of combination antiretroviral therapy which has transformed HIV/AIDS in the developed world and is beginning to impact the developing world required 15 years of substantial effort."

Breakthrough produces Parkinson's patient-specific stem cells free of harmful reprogramming genes

FINDINGS: Deploying a method that removes potentially cancer-causing genes, Whitehead Institute researchers have "reprogrammed" human skin cells from Parkinson's disease patients into an embryonic-stem-cell-like state. Whitehead scientists then used these so-called induced pluripotent stem (iPS) cells to create dopamine-producing neurons, the cell type that degenerates in Parkinson's disease patients.

RELEVANCE: This marks first time researchers have generated human iPS cells, successfully removed the potentially problematic reprogramming genes, and seen the cells maintain their embryonic stem-cell-like state. Previous methods to reprogram mature cells into iPS cells inserted cancer-causing genes into the cells' DNA. Because the current method removes the cancer-causing genes, the resulting iPS cells' DNA is virtually

identical to the DNA of the original adult cells. These iPS cells can be matured into any cell type, allowing for screens of potential drug therapies and study of patient-specific disease at the cellular level.

CAMBRIDGE, Mass. (March 5, 2009) – Whitehead Institute researchers have developed a novel method to remove potential cancer-causing genes during the reprogramming of skin cells from Parkinson's disease patients into an embryonic-stem-cell-like state. Scientists then used the resulting induced pluripotent stem (iPS) cells to derive dopamine-producing neurons, the cell type that degenerates in Parkinson's disease patients.

This marks the first time researchers have generated human iPS cells that have maintained their embryonic stem-cell-like properties after the removal of reprogramming genes. The findings are published in the March 6 edition of the journal Cell.

"Until this point, it was not completely clear that when you take out the reprogramming genes from human cells, the reprogrammed cells would actually maintain the iPS state and be self-perpetuating," says Frank Soldner, a postdoctoral researcher in Whitehead Member Rudolf Jaenisch's laboratory and co-author of the article.

Since August 2006, researchers have been reprogramming adult cells into iPS cells by using viruses to transfer four genes (Oct4, Sox2, c-Myc and Klf4) into the cells' DNA. Although necessary for reprogramming cells, these genes, the known oncogene c-Myc in particular, also have the potential to cause cancer. In addition, the four genes interact with approximately 3000 other genes in the cell, which may change how the cell functions. Therefore, leaving the genes behind in successfully reprogrammed cells may cause unintended alterations that limit the cells' applicability for therapeutic use, for drug screens or to study disease in cell culture.

In the current method, Whitehead researchers used viruses to transfer the four reprogramming genes and a gene coding for the enzyme Cre into skin cells from Parkinson's disease patients. The reprogramming genes were bracketed by short DNA sequences, called loxP, which are recognized by the enzyme Cre.

After the skin cells were reprogrammed to iPS cells, the researchers introduced the Cre enzyme into the cells, which removed the DNA between the two loxP sites, thereby deleting the reprogramming genes from the cells. The result is a collection of iPS cells with genomes virtually identical to those of the Parkinson's disease patients from whom original skin cells came.

Removing the reprogramming genes is also important because of those genes' effect on an iPS cell's gene expression (a measure of which genes the cell is using and how much it's using those genes). When the researchers compared the gene expressions of human embryonic stem cells to iPS cells with and without the reprogramming factors, iPS cells without the reprogramming genes had a gene expression closer to human embryonic stem cells than to the same iPS cells that still contained the reprogramming genes.

"The reprogramming factors are known to bind to and affect the expression of 3,000 genes in the entire genome, so having artificial expression of those genes will change the cell's overall gene expression," Dirk Hockemeyer, who is also a co-author of the Cell article. "That's why the four reprogramming genes can mess up the system so much. From now on, it will be tough for researchers to leave the reprogramming genes in iPS cells."

Jaenisch says that the process to remove the reprogramming genes is very successful, when compared with earlier experiments. "Other labs have reprogrammed mouse cells and removed the reprogramming genes, but it was incredibly inefficient, and they couldn't get it to work in human cells," he says. "We have done it much more efficiently, in human cells, and made reprogrammed, gene-free cells."

After removing the reprogramming genes, the Jaenisch researchers differentiated the cells from the Parkinson's disease patients into dopamine-producing nerve cells. In Parkinson's disease patients, these cells in the brain die or become impaired, causing such classic Parkinson's symptoms as tremors, slowed movement, and balance problems.

Because the cells reside in the patients' brains, researchers cannot easily access them to investigate how the disease progresses at the cellular level, what kills the cells, or what might prevent cellular damage. Therefore, the ability to create patient-specific iPS cells, derive the dopamine-producing cells, and study those patient-specific cells in the lab could be a great advantage for Parkinson's disease researchers.

Although the initial results are extremely promising, Jaenisch acknowledges that the process is far from over. "The next step is to use these iPS-derived cells as disease models, and that's a high bar, a real challenge. I think a lot of work has to go into that."

Written by Nicole Giese.

Rudolf Jaenisch's primary affiliation is with Whitehead Institute for Biomedical Research, where his laboratory is located and all his research is conducted. He is also a professor of biology at Massachusetts Institute of Technology.

Full Citation: "Parkinson's disease patient-derived induced pluripotent stem cells free of viral reprogramming factors" Cell, March 5, 2009

Frank Soldner (1, 4), Dirk Hockemeyer (1, 4), Caroline Beard (1), Qing Gao (1), George W. Bell (1), Elizabeth G. Cook (1), Gunnar Hargus (3), Alexandra Blak (3), Oliver Cooper (3), Maisam Mitalipova (1), Ole Isacson (3), Rudolf Jaenisch (1,2).

Viral infection may prime some people for diabetes

* 19:00 05 March 2009 **by Celeste Biever**

Viruses that cause diarrhoea and vomiting may also trigger diabetes in children with a particular genetic make-up. The finding could one day lead to "diabetes" vaccines that might be targeted at children with certain genes.

Some children are genetically predisposed to develop type-1 diabetes, but studies of identical twins show that if one twin gets the disease, the other has only a 40% chance of developing it too, suggesting that an environmental trigger is also at work.

One suspect is a family of viruses called Coxsackie B enteroviruses (CVBs). In type-1 diabetes, the body attacks and destroys insulin-producing pancreatic cells called beta cells. It is thought that when CVBs infect beta cells, they may trigger this "autoimmunity", but only in children with a particular genetic make-up.

This would make sense as the genes that are linked to type-1 diabetes code for proteins involved in the immune response. However, evidence supporting the theory has relied on a small number of samples. For example, in 2007, evidence of CVB infection was reported in two of five patients with type-1 diabetes, but not in 26 non-diabetic controls.

Tell-tale protein

To test the CVB theory in a much larger group, a team led by Noel Morgan at the Peninsula Medical School in Plymouth, UK, analysed tissue taken from the pancreases of 72 children who had died of type-1 diabetes shortly after becoming ill. In more than 60% of the pancreases, they found a protein that makes up CBV's viral coating, in the beta cells. There was almost no evidence of infection in control tissue samples taken from children who had not had diabetes.

"This is the first time that scientists have been able to provide such extensive evidence for the relationship between enteroviral infection of the beta cells and the development of type 1 diabetes," says Morgan.

'Conservative estimate'

Although 40% of the samples did not show evidence of CBV, Adrian Bone of the University of Brighton, UK, says the people that provided these samples may still have been infected with CBV - evidence of it just didn't show up in the protein test. "The protein isn't completely stable, so 60% is a conservative estimate," he says.

The next step will be working out which strains of CBV trigger type-1 diabetes, and testing whether these can be used in a vaccine that prevents the disease, says Bone.

"The study is hugely significant because for the first time we have a large enough study of pancreas post mortem samples from patients who died near to diagnosis - this has been lacking and therefore we have had to rely on the odd case report," says Mark Peakman at King's College London School of Medicine.

Journal reference: Diabetologia (DOI: 10.1007/s00125-009-1276-0, in press)

CU-Boulder research team identifies stem cells that repair injured muscles

Research effort may have important implications for muscular dystrophy

A University of Colorado at Boulder research team has identified a type of skeletal muscle stem cell that contributes to the repair of damaged muscles in mice, which could have important implications in the treatment of injured, diseased or aging muscle tissue in humans, including the ravages of muscular dystrophy.

The newly identified stem cells are found within populations of satellite cells located between muscle fibers and the surrounding connective tissue that are responsible for the repair and maintenance of skeletal muscles, said Professor Bradley Olwin of CU-Boulder's molecular, cellular and developmental biology department.

When muscle fibers are stressed or traumatized, satellite cells divide to make more specialized muscle cells and repair the muscle, said Olwin. The stem cell population identified by the CU team within the satellite cells -- dubbed "satellite-SP" cells -- were shown to renew the satellite cell population after injection into injured muscle cells, contributing to recovery of muscle tissue in the laboratory mice.

"This research shows how satellite cells can maintain their populations within injured tissues," said Olwin. "The hope is this new method will allow us to repair damaged or diseased skeletal muscle tissue."

A paper on the subject was published in the March 5 issue of the journal Cell Stem Cell. Co-authors on the study included the MCD biology department's Kathleen Tanaka, John Hall and Andrew Troy, as well as Dawn Cornelison from the University of Missouri and Susan Majka from the University of Colorado Denver.

Stem cells are distinguished by their ability to renew themselves through cell division and differentiate into specialized cell types. In healthy skeletal muscle tissue, the population of satellite cells is constantly maintained, leading the CU-Boulder team to believe that at least some of the satellite cell population in the mouse study included stem cells.

For the study, the researchers injected 2,500 satellite-SP cells into a population of satellite cells within injured mouse muscle tissue. They found that 75 percent of the satellite cells that reproduced were derived from

the previous satellite-SP cells injected into the tissue. The results demonstrated the injected satellite-SP cells were renewing the satellite cell pool, Olwin said.

"The key point here is we are not just repairing the tissue," said Olwin. "We injected a permanent, self-renewing population of stem cells. One advantage of using this technology is that we can use a relatively small number of stem cells and do the job with a small number of injections -- in this case, only one."

The research has implications for a number of human diseases, he said. In muscular dystrophy, the loss of a protein called dystrophin causes the muscle to literally tear itself apart, a process that cannot be repaired without cell-based intervention. Although injected cells will repair the muscle fibers, maintaining the muscle fibers requires additional cell injections.

The research was funded in part by the National Institutes of Health and the Muscular Dystrophy Association.

Olwin is now collaborating with a group at the University of Washington and the Fred Hutchinson Cancer Research Center in Seattle to extend the research.

Sunlight turns carbon dioxide to methane

Dual catalysts may be the key to efficiently turning carbon dioxide and water vapor into methane and other hydrocarbons using titania nanotubes and solar power, according to Penn State researchers.

Burning fossil fuels like oil, gas and coal release large amounts of carbon dioxide, a greenhouse gas, into the atmosphere. Rather than contribute to global climate change, producers could convert carbon dioxide to a wide variety of hydrocarbons, but this makes sense to do only when using solar energy.

"Recycling of carbon dioxide via conversion into a high energy-content fuel, suitable for use in the existing hydrocarbon-based energy infrastructure, is an attractive option, however the process is energy intense and useful only if a renewable energy source can be used for the purpose," the researchers note in a recent issue of Nano Letters.

Craig A. Grimes, professor of electrical engineering and his team used titanium dioxide nanotubes doped with nitrogen and coated with a thin layer of both copper and platinum to convert a mixture of carbon dioxide and water vapor to methane. Using outdoor, visible light, they reported a 20-times higher yield of methane than previously published attempts conducted in laboratory conditions using intense ultraviolet exposures.

The chemical conversion of water and carbon dioxide to methane is simple on paper -- one carbon dioxide molecule and two water molecules become one methane molecule and two oxygen molecules. However, for the reaction to occur, at least eight photons are required for each molecule.

"Converting carbon dioxide and water to methane using photocatalysis is an appealing idea, but historically, attempts have had very low conversion rates," said Grimes who is also a member of Penn State's Materials Research Institute. "To get significant hydrocarbon reaction yields requires an efficient photocatalyst that uses the maximum energy available in sunlight."

The team, which also included Oomman K. Varghese and Maggie Paulose, Materials Research Institute research scientists and Thomas J. LaTempa, graduate student in electrical engineering, used natural sunlight to test their nanotubes in a chamber containing a mix of water vapor and carbon dioxide. They exposed the co-catalyst sensitized nanotubes to sunlight for 2.5 to 3.5 hours when the sun produced between 102 and 75 milliwatts for each square centimeter exposed.

The researchers found that nanotubes annealed at 600 degrees Celsius and coated with copper yielded the highest amounts of hydrocarbons and that the same nanotubes coated with platinum actually yielded more hydrogen, while the copper coated nanotubes produced more carbon monoxide. Both hydrogen and carbon monoxide are normal intermediate steps in the process and as the building blocks of syngas, can be used to make liquid hydrocarbon fuels.

When the team used a nanotube array with about half the surface coated in copper and the other half in platinum, they enhanced the hydrocarbon production and eliminated carbon monoxide. The yield for these dual catalyst nanotubes was 163 parts per million hydrocarbons an hour for each square centimeter. The yield from titania nanotubes without either copper or platinum catalysts is only about 10 parts per million.

"If we uniformly coated the surface of the nanotube arrays with copper oxide, I think we could greatly improve the yield," said Grimes.

Grimes also found that lengthening the titanium dioxide tubes, which for other applications increases yield, does not improve results. "We think that distribution of the sputtered catalyst nanoparticles is at the top surface of the nanotubes and not inside and that is why increased length does not improve the reaction," says Grimes.

Although all these experiments were done with nitrogen-doped titanium dioxide nanotubes, the researchers conclude that the nitrogen did not enhance the conversion of carbon dioxide to hydrocarbons. The catalysts, however, did shift the reaction from one that used only the energy in ultraviolet light to one that used other wavelengths of visible light and therefore more of the sun's energy.

The researchers are now working on converting their batch reactor into a continuous flow-through design that they believe will significantly increase yields. The researchers have filed a provisional patent on this work.

Not so sweet: Over-consumption of sugar linked to aging

University of Montreal scientists explain how sugar shortens lifespan in PLoS Genetics

Montreal – We know that lifespan can be extended in animals by restricting calories such as sugar intake. Now, according to a study published in the journal PLoS Genetics, Université de Montréal scientists have discovered that it's not sugar itself that is important in this process but the ability of cells to sense its presence.

Aging is a complex phenomenon and the mechanisms underlying aging are yet to be explained. What researchers do know is that there is a clear relationship between aging and calorie intake. For example, mice fed with half the calories they usually eat can live 40 percent longer. How does this work?

As part of the PLoS Genetics study, Université de Montréal Biochemistry Professor Luis Rokeach and his student Antoine Roux discovered to their surprise that if they removed the gene for a glucose sensor from yeast cells, they lived just as long as those living on a glucose-restricted diet. In short, the fate of these cells doesn't depend on what they eat but what they think they're eating.

There are two obvious aspects of calorie intake: tasting and digestion. By the time nutrients get to our cells there is an analogous process: sensors on the surface of the cell detect the presence of, for example, the sugar glucose and molecules inside the cell break down the glucose, converting it to energy. Of these processes, it is widely thought that the by-products of broken down sugars are the culprits in aging. The study by Rokeach and Roux suggests otherwise.

To understand aging, Rokeach and Roux in collaboration with Université de Montréal Biochemistry Professors Pascal Chartrand and Gerardo Ferbeyre used yeast as a model organism. At a basic level, yeast cells are surprisingly similar and age much like human cells, as well as being easy to study.

The research team found that the lifespan of yeast cells increased when glucose was decreased from their diet. They then asked whether the increase in lifespan was due to cells decreasing their ability to produce energy or to the decrease in signal to the cells by the glucose sensor.

The scientists found that cells unable to consume glucose as energy source are still sensitive to the pro-aging effects of glucose. Conversely, obliterating the sensor that measures the levels of glucose significantly increased lifespan. "Thanks to this study, the link between the rise in age-related diseases and the over-consumption of sugar in today's diet is clearer. Our research opens a door to new therapeutic strategies for fighting age-related diseases," says Professor Rokeach.

Partners in research: *Professor Rokeach's research is supported by the Canadian Institutes of Health Research (www.cihr-irsc.gc.ca) and by the National Science and Engineering Research Council (www.nserc-crsng.gc.ca). Professor Ferbeyre's and Professor Chartrand's research are funded by the Canadian Institutes of Health Research (www.cihr-irsc.gc.ca)*

Support for adjunctive vitamin C treatment in cancer

New Rochelle, NY, March 5, 2009—Serious flaws in a recent study, which concluded that high doses of vitamin C reduce the effectiveness of chemotherapeutic drugs in the treatment of cancer, are revealed in the current issue of Alternative and Complementary Therapies, a journal published by Mary Ann Liebert, Inc. (www.liebertpub.com). This report is available free online at www.liebertpub.com/act

In the Medical Journal Watch column of the latest issue, Jack Challem, a personal nutrition coach and nutrition author from Tucson, Arizona, and a regular contributor to the Journal, challenges the findings of a study published in Cancer Research (2008;68:8031-8038), in which the authors conclude that vitamin C given to mice or cultured cells treated with common anti-cancer drugs reduces the antitumor effects of the chemotherapeutic agents.

Challem points out two main problems with the study: the oxidized form of vitamin C (dehydroascorbic acid) and not actual vitamin C (ascorbic acid) was used; and in the mouse experiments, the animals were given toxic doses of dehydroascorbic acid, a compound that is not used as a dietary supplement in humans.

"This study and the subsequent headlines [it generated] were a grievous disservice to physicians and patients with cancer," says Challem. He adds that "considerable positive research…has shown striking benefits from high-dose vitamin C (ascorbic acid) in cancer cells and animals—and in actual human beings."

High-dose intravenous vitamin C is a common form of alternative and complementary therapy for patients receiving chemotherapeutic drugs and is believed to help bring about tumor cell death. In addition, it may promote postsurgical healing by enhancing collagen formation, and increase tissue resistance to tumor spread.

Challem suggests that, "The ideal therapeutic approach would be to tailor individual treatment, including IV vitamin C, from a menu of options."

Alternative and Complementary Therapies is a bimonthly journal that publishes original research articles, reviews, and commentaries evaluating alternative therapies and how they can be integrated into clinical practice. Topics include botanical

medicine, vitamins and supplements, nutrition and diet, mind-body medicine, acupuncture and Traditional Chinese Medicine, ayurveda, indigenous medicine systems, homeopathy, naturopathy, yoga and meditation, manual therapies, energy medicine, and spirituality and health. A complete table of contents and free sample issue may be viewed online at www.liebertpub.com/act

Japanese pioneer developed first general anaesthetic

* 06 March 2009 **by Stephanie Pain**

"When the dreadful steel was plunged into my breast... I began a scream that lasted unintermittingly during the whole time of the incision. I almost marvel that it rings not in my ears still, so excruciating was the agony." When English writer Fanny Burney had surgery for breast cancer in 1811, she felt every move of the knife as the surgeon cut through her all too resistant flesh. The introduction of ether and chloroform as general anaesthetics was still 35 years away. Yet, unknown to doctors in the west, Japanese surgeon Seishu Hanaoka had performed the same operation several years earlier - and his patient hadn't felt a thing.

IT WAS nine months before Fanny Burney could bring herself to write about the operation to remove her breast. In a letter to her sister Esther, she described in harrowing detail what she had felt as the surgeon cut and scraped and cut some more. By the early 19th century, Europe's surgeons had the knowledge and skills to perform major operations. What they didn't have was an effective anaesthetic. Opium or copious amounts of cognac could help dull the pain, but no one had yet found a reliable way to render a patient unconscious during surgery - or so European surgeons thought.

Pioneering Japanese surgeon Seishu Hanaoka, with his mother (left) and wife **(Image: International Museum of Surgical Science)**

Unknown to the rest of the world, on 13 October 1804, Japanese surgeon Seishu Hanaoka had put 60-year-old Kan Aiya under with a general anaesthetic in order to remove her cancerous breast. While Hanaoka's surgical technique owed much to western medicine, his anaesthetic was rooted firmly in the tradition of Chinese medicine that prevailed in Japan at the time. By combining the two, Hanaoka was able to perform surgery other Japanese doctors dared not try - and Europe's surgeons could perform only after tying down the patient and blocking out their screams.

Hanaoka was born in the small town of Hirayama in 1760, possibly the perfect time for a pioneering doctor. Worried by the spread of Christianity and angered by the activities of Portugal's Jesuit priests, Japan had expelled all Europeans in 1639. An exception was made for the Dutch, who were tolerated because they stuck to business and kept their religion to themselves. Even so, Dutch traders were confined to the tiny walled settlement of Dejima, an artificial island in Nagasaki Bay. Their activities were strictly controlled and their movements closely watched. All communication was through official Japanese interpreters, who ensured that foreign ideas did not slip in among the Dutch imports, but here too there was an exception.

Japan's doctors had always been curious about the medicine practised by the Jesuits. After they were expelled, the one window onto western medicine was at Dejima, and Dutch medical books were allowed to trickle into the country. Better still, the Dutch East India Company sent a succession of surgeons to Dejima. The interpreters watched them at work, took notes, and reported what they had seen. A few even took lessons. Soon, Japanese doctors began to try some of the simple surgery picked up from the Dutch, and schools of "Dutch-style surgery" began to spring up.

Despite its name, Dutch-style surgery bore only a passing resemblance to that practised in Europe. It was based on a handful of badly translated books and sketchy accounts of operations performed by a string of Dutch surgeons, some no more than ship's doctors. Japan's doctors were also highly selective in what they chose to adopt. One of the main tenets of Chinese medicine was to avoid harming the body, so while Japan's doctors followed Dutch advice on treating wounds and fractures, they rejected invasive surgical procedures. European doctors routinely amputated limbs, removed cataracts and extracted bladder stones. In Japan, even bloodletting was regarded as abhorrent.

In the 1740s, however, there was a big push to find out more about western science and medicine. The authorities actively encouraged "Dutch learning", and while earlier interpreters had learned just enough Dutch to do business, scholars were now exhorted to learn the language fluently enough to read and translate Dutch books.

By the time Hanaoka was beginning his medical studies in the 1780s, attitudes towards surgery were changing. What prompted the change was a book of anatomy. In Europe, anatomy was the foundation stone of medicine and its medical students pored over anatomy texts and dissected bodies. In Japan, students learned about the body from stylised drawings in ancient Chinese texts. Dissection of human bodies was forbidden.

In 1771, the revered doctor Genpaku Sugita, a proponent of Dutch learning, acquired a Dutch edition of Johann Kulmus's Anatomical Plates. Curious to find out how Kulmus's drawings compared with Chinese ideas of the body, Sugita and fellow doctor Ryotaku Maeno bribed an executioner to allow them to watch the dissection of a criminal - and took the book along with them. They were so impressed by the book's accuracy they spent the next four years translating it. Its appearance marked a turning point in Japanese medicine. No one could deny that Dutch surgery was based on sound knowledge of the body.

Following in his father's footsteps, Hanaoka left Hirayama in 1782 to study medicine in Kyoto. After studying traditional Chinese medicine, he took lessons in Dutch-style surgery, which by then was far more advanced than in his father's day. At 25 he took over his father's practice in Hirayama and immediately began work on his anaesthetic.

Hanaoka's great ambition was to save women from breast cancer by surgically removing their tumours, an operation he had seen in "a foreign book". But he also considered it his duty to prevent pain, and there the Dutch were no help at all. He could find no mention of anaesthesia in their books. Chinese medicine, by contrast, was well endowed with drugs that deadened pain, numbed sensation and induced sleep. Hanaoka wanted something that did all these things without killing the patient in the process.

That was a tall order. All these drugs came from extremely poisonous plants, and while some could safely be smeared onto skin to numb a small area before minor surgery, for more serious operations the drug would have to work on the whole body, which meant it would have to be swallowed.

It took 20 years of experiment before Hanaoka found the right formula. He started by combining different herbs at different doses, testing his draughts on cats and dogs. The difficulties were all too evident: if the drug wasn't powerful enough, the animals still felt pain; if it was too strong they suffered nerve damage or died. When he thought he had arrived at a safe dose, he tried it on his wife. She went blind, transforming a story of wifely devotion into one of medical heroism.

It took almost 20 years of experiment before Hanaoka found the right formula

Hanaoka persisted and eventually found a formula that worked without inflicting terrible after-effects. He called it tsusensan. The key ingredients were Angel's trumpet (Datura metel) and monkshood (Aconitum japonicum). The first contains scopolamine, hyoscyamine and atropine, which are still used as sedatives and muscle relaxants, while monkshood contains aconitine, a powerful neurotoxin. To bolster the analgesic and sedative effects he added angelica, Szechuan lovage (Ligusticum wallichii) and the arum Arisaema serratum.

News of the experiments spread, and in 1804 Hanaoka finally achieved his ambition of performing cancer surgery under anaesthetic. Aiya, his first patient, had a large tumour in her left breast and had turned to Hanaoka in desperation. The anaesthetic worked, the operation was a success and Aiya went home. Sadly it came too late. Her cancer had spread and she died six months later.

Hanaoka went on to perform more than 150 similar operations and other procedures deemed too difficult by his contemporaries. Patients and students eager to learn his techniques flocked to Hirayama, and Hanaoka's place in Japanese history was assured. Yet Japan's policy of isolation meant the world outside remained ignorant of Hanaoka's anaesthetic. By the time Japan reopened its doors to foreigners, in 1853, they had no interest in it: they had finally found anaesthetics of their own.

Bibliography

1. Find out more about the history of surgery and anaesthesia at www.sciencemuseum.org/uk/broughttolife, the London Science Museum's new multimedia website. Brought to Life explores centuries of medical history through 2500 objects from the Wellcome Trust collection held at the museum, many of which are on display for the first time.

'Vampire' discovered in mass grave

A SKELETON exhumed from a grave in Venice is being claimed as the first known example of the "vampires" widely referred to in contemporary documents.

Matteo Borrini of the University of Florence in Italy found the skeleton of a woman with a small brick in her mouth (see right) while excavating mass graves of plague victims from the Middle Ages on Lazzaretto Nuovo Island in Venice.

At the time the woman died, many people believed that the plague was spread by "vampires" which, rather than drinking people's blood, spread disease by chewing on their shrouds after dying. Grave-diggers put bricks in the mouths of suspected vampires to stop them doing this, Borrini says.

The belief in vampires probably arose because blood is sometimes expelled from the mouths of the dead, causing the shroud to sink inwards and tear. Borrini, who presented his findings at a meeting of the American Academy of Forensic Sciences in Denver, Colorado, last week, claims this might be the first such vampire to have been forensically examined. The skeleton was removed from a mass grave of victims of the Venetian plague of 1576.

However, Peer Moore-Jansen of Wichita State University in Kansas says he has found similar skeletons in Poland and that while Borrini's finding is exciting, "claiming it as the first vampire is a little ridiculous".

Borrini says his study details the earliest grave to show archaeological "exorcism evidence against vampires".

To stop the "vampires" supposedly chewing shrouds and spreading disease, grave-diggers put bricks in the mouths of plague victims **(Image: Matteo Borrini)**

Kill the inflammation, kill the HIV?

* 08 March 2009 **by Debora MacKenzie**

WE don't yet know why HIV spreads to women so much more readily in Africa than elsewhere, but African women desperately need protection from the virus during sex. Now a cheap and relatively safe chemical that damps down vaginal inflammation may do just that.

Ashley Haase and colleagues at the University of Minnesota in Minneapolis have discovered that a few epithelial cells on the cervix of female macaques are the first point of entry for SIV, the monkey equivalent of HIV. Nearby immune cells respond by emitting molecules that trigger inflammation and summon T-cells to the cervix. These would normally destroy invaders but T-cells happen to be the very cells SIV (and HIV) use to infect their new host.

Studies of toxic shock syndrome, a life-threatening bacterial infection that can affect women using tampons, had already identified chemicals that can suppress vaginal inflammation, including glycerol monolaurate, a constituent of vegetable oils used widely in food and deodorants.

When Haase's team mixed glycerol monolaurate with vaginal lubricant, and applied it to the vaginas of five macaques, they found that the animals resisted infection even after repeated exposure to SIV. It seems the chemical blocked the immune reaction that summons the T-cells to the cervix (Nature, DOI: 10.1038/nature07831).

It is not yet clear whether glycerol monolaurate would block HIV in a woman's cervix already inflamed by other infections, or whether blocking cervical immune responses might leave her less protected from other infections. But the team argues that even if the gel - which costs less than a cent a dose - is only 60 per cent effective, it would prevent nearly a million infections a year, and might slow the heterosexual transmission of HIV in Africa.

Survey: Few physicians support private banking of umbilical cord blood

BOSTON—A survey of physicians has found broad support for the position that parents should not bank their newborns' umbilical cord blood in a private blood bank unless another member of the family is at risk for a blood disease that will require a stem cell transplant.

The results of the survey are reported by researchers at Dana-Farber Cancer Institute and their colleagues in the March issue of the journal Pediatrics. Their findings are in general accord with the recommendations of medical organizations that have previously weighed in on the issue.

"Physicians who perform hematopoietic cell transplants in children are well positioned to judge the advisability of private cord blood banking, but their views had never been systematically sought and collected," says the study's senior author, Steven Joffe, MD, MPH, of Dana-Farber. "We found that these physicians have performed relatively few transplants involving privately banked cord blood, and that their position on such banking is generally in line with that of larger medical organizations."

Cord blood is a source of "hematopoietic" (blood forming) cells that can be used in stem cell transplants to treat a range of diseases and disorders. Expanding the collection of cord blood for use in public cord blood banks increases the chance that more people are eligible for transplant, because stem cells culled from cord blood do not have to match a patient's tissue type as closely as donated bone marrow does. Cord blood stored in public banks is made available to unrelated children and adults in need of a stem cell transplant.

Private cord blood banks are for-profit companies that, unlike public banks, store umbilical cord blood for personal or family use. Private cord blood banks typically charge a $1,500 - $2,000 collection fee and an annual $100 - $200 storage fee. Families may decide to store cord blood privately if a relative has, or is at risk for, a disease such as leukemia or aplastic anemia that can be treated by a stem cell transplant. Families without such

at-risk members may choose to have the blood stored as a form of "biological insurance," in case the child or another family member unexpectedly develops a disease that can be treated by stem cell transplant.

For the current study, surveys were sent to 152 pediatric hematopoietic cell transplant physicians in the United States and Canada, 93 of whom responded. Questions addressed the number of transplants physicians had performed using privately banked cord blood, their willingness to use such blood in specific situations, and their recommendations to parents regarding private cord blood banking.

The respondents reported that of the thousands of stem cell transplants they had performed, only 50 involved privately banked cord blood. Forty one of those cases were "allogeneic" transplants, in which blood from one individual was used to treat another member of the family. And in 36 of those cases, families already knew of a member who was a candidate for a transplant prior to banking the cord blood. The researchers identified only four or five cases in which cord blood that had been privately banked "just in case" it would someday be needed was actually used to treat a sibling of the donor. They also identified only nine cases in which children whose cord blood had been banked subsequently underwent transplants using their own stem cells (known as autologous transplantation), despite the fact that this is the primary use for which private cord blood banks market their services.

Few of the respondents said they would choose a patient's own cord blood over other alternatives as a source of stem cells for treatment of acute lymphoblastic leukemia. By contrast, more than half said they would use an individual's own cord blood to treat high-risk neuroblastoma, or to treat severe aplastic anemia in the absence of an available sibling donor.

In addition, few would recommend banking of cord blood in families without a member known to have, or be at risk for, a disease that can be treated by transplantation.

"In the absence of a family member known to be a candidate for stem cell transplantation, the chances that privately banked cord blood will be used are quite small," Joffe says. "Families need to balance the high cost of banking such blood against the remote odds of its ever being needed. Pediatricians, family physicians, obstetricians, nurse midwives, and other professionals who work with families should educate parents about the medical community's consensus view on this issue."

The lead author of the study is Ian Thornley, MD, of North Shore Medical Center in Salem, Mass. Co-authors are Mary Eapen, MD, of the Medical College of Wisconsin, Milwaukee; Lillian Sung, MD, PhD, of the Hospital for Sick Children in Toronto; Stephanie Lee, MD, MPH, of the Fred Hutchinson Cancer Research Center, Seattle; and Stella Davies, MD, PhD of Cincinnati Children's Hospital Medical Center.

'Holy powder' ingredient makes membranes behave for better health

ANN ARBOR, Mich.---Revered in India as "holy powder," the marigold-colored spice known as turmeric has been used for centuries to treat wounds, infections and other health problems. In recent years, research into the healing powers of turmeric's main ingredient, curcumin, has burgeoned, as its astonishing array of antioxidant, anti-cancer, antibiotic, antiviral and other properties has been revealed.

Yet little has been known about exactly how curcumin works inside the body.

Now, University of Michigan researchers led by Ayyalusamy Ramamoorthy have discovered that curcumin acts as a disciplinarian, inserting itself into cell membranes and making them more orderly, a move that improves cells' resistance to infection and malignancy.

"The membrane goes from being crazy and floppy to being more disciplined and ordered, so that information flow through it can be controlled," said Ramamoorthy, a professor of chemistry and biophysics. The findings were published online March 3 in the Journal of the American Chemical Society.

The research project melds Ramamoorthy's past with his current scientific interests. As a child in India, he was given turmeric-laced milk to drink when he had a cold, and he breathed steam infused with turmeric to relieve congestion. Now as researcher he is fascinated with proteins that are associated with biological membranes, and he uses a technique called solid-state NMR spectroscopy to reveal atom-level details of these important molecules and the membranous milieu in which they operate.

"Probing high-resolution intermolecular interactions in the messy membrane environment has been a major challenge to commonly-used biophysical techniques," Ramamoorthy said. His research group recently developed the two-dimensional solid-state NMR technique that they used to probe curcumin-membrane communication in this study.

Scientists have speculated that curcumin does its health-promoting work by interacting directly with membrane proteins, but the U-M findings challenge that notion. Instead, the researchers found that curcumin regulates the action of membrane proteins indirectly, by changing the physical properties of the membrane.

Ramamoorthy's group now is collaborating with chemistry professor Masato Koreeda and U-M Life Sciences Institute researcher Jason Gestwicki to study a variety of curcumin derivatives, some of which have

enhanced potency. "We want to see how these various derivatives interact with the membrane, to see if the interactions are the same as what we have observed in the current study," Ramamoorthy said. "Such a comparative study could lead to the development of potent compounds to treat infection and other diseases."

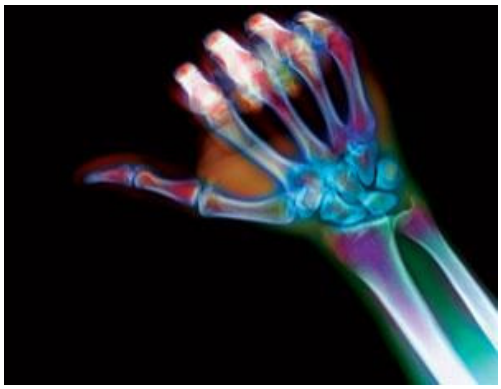
In a related line of research, Ramamoorthy's team is using the same methods to investigate the effects of curcumin on the formation of amyloids---clumps of fibrous protein believed to be involved in type 2 diabetes, Alzheimer's disease, Parkinson's disease, and many other maladies. In addition, the researchers are looking to see whether other natural products, such as polyphenols (compounds found in many plant foods that are known to have antioxidant properties) and capsaicin (a pain reliever derived from hot peppers), interact with membranes in the same way as curcumin.

Along with Ramamoorthy, the paper's authors are undergraduates Jeffrey Barry and Michelle Fritz, post-doctoral fellow Jeffrey Brender, graduate student Pieter Smith and a visiting professor from South Korea, Dong-Kuk Lee.
This research was supported by funding from the National Institutes of Health.
For more information on Ramamoorthy, visit: http://www.ns.umich.edu/htdocs/public/experts/ExpDisplay.php?ExpID=1170
Journal of the American Chemical Society: http://pubs.acs.org/journal/jacsat

Thumbs up for 3D bone printer

* 07 March 2009 **by Andy Coghlan**

EXACT replicas of a man's thumb bones have been made for the first time using a 3D printer. The breakthrough paves the way for surgeons to replace damaged or diseased bones with identical copies built from the patients' own cells.



"In theory, you could do any bone," says Christian Weinand of the Insel Hospital in Berne, Switzerland, head of the team that copied his thumb bones. "Now I can put spares in my pocket if I want," he says.

Weinand "grew" his replacement bones on the backs of laboratory mice, in the same way that Jay Vacanti of Massachusetts General Hospital famously grew a human ear from human cartilage cells back in 1997.

Exact replicas of a man's thumb bones have been made for the first time using a printer that uses natural materials for ink **(Image: Gustoimages / SPL)**

However, a surrogate mouse would normally be unnecessary, says Weinand. For example, if someone had lost a thumb, the replacement bones could be grown in situ. For now, the only options are to replace the thumb with the patient's own toe, or with bone fragments from elsewhere.

There are several steps in the new process. Firstly, you need a 3D image of the bone you want to copy. If the bone has been lost or destroyed, you can make a mirror image of its surviving twin.

This image is then fed into a 3D inkjet printer, which deposits thin layers of a pre-selected material on top of one another until a 3D object materialises.

Weinand loaded the printer with tricalcium phosphate and a type of polylactic acid - natural structural materials found in the human body. The resulting bone "scaffolds" contained thousands of tiny pores into which bone cells could settle, grow and eventually displace the biodegradable scaffold altogether.

A 3D printer deposits thin layers of a natural material that builds into a scaffold for bone cells

The team extracted CD117 cells from bone marrow left over after hip-replacement operations. CD117 cells grow into primordial bone cells called osteoblasts, which the team syringed onto the bone scaffolds in a gel designed to support and nourish them. Finally, the scaffolds were sewn under the skin on the backs of mice where they grew for up to 15 weeks, until the scaffold had changed into human bone (Tissue Engineering Part A, DOI: 10.1089/ten.tea.2008.0467).

Anthony Hollander, a stem cell researcher at the University of Bristol in the UK, says that the work capitalises on a breakthrough a year ago, in which a Finnish team headed by Riitta Suuronen at the University of Tampere reconstructed a man's jawbone on a "scaffold" left for nine months in his abdomen. In that case, the stem cells came from the patient's own fat cells.

"The nice aspect of this new work is that a method was used to make sure the bones grew to the exact dimensions of a particular thumb," Hollander says. "The next stage will be to demonstrate that such implants are functional and that they acquire blood vessels when implanted."

Weinand says there were "hints" that blood vessels were nourishing the implants in the mice, so he is hopeful the same thing will happen in people. He hopes to apply to try out the procedure in the clinic in the near future.