First compound for receptors in schizophrenia and Alzheimer's holds promise

Effective drugs without side effects

For almost 20 years, pharmacological companies have known that certain compounds that activate two specific CNS receptors, causing them to release the neurotransmitter acetylcholine, are effective in treating the cognitive and motor problems related to both schizophrenia and Alzheimer's disease (AD).

But because the compounds are "dirty" – scientific lingo for a lack of selectivity – they activate not only the essential M1 and M 4 muscarinic receptors but also the other three members of the family, designated M2, M3 and M5, resulting in unacceptable gastrointestinal and other side effects.

That may soon change, thanks to the discovery of a truly selective agonist that targets only the M1 receptor, known to be central to cognition and thus implicated in diseases like AD and schizophrenia.

On April 20, speaking at the Experimental Biology 2009 meeting in New Orleans, Vanderbilt graduate student Evan Lebois in the laboratories of Dr. David Weaver and Dr. Craig Lindsley describes the complex, labor-intensive screening and discovery process that allowed Vanderbilt scientists to pinpoint what big pharma's computers and robots could not, and the process now underway to move the compound toward becoming an effective drug to treat AD and schizophrenia. The presentation is part of the scientific program of the American Society for Pharmacology and Experimental Therapeutics.

In stage one, the search for the appropriate molecule, Dr. David Weaver, director of the Vanderbilt Chemical Biology's High-Throughput Screening facility and co-director of the Molecular Library Screening Center, painstakingly ran high-throughput screens of every compound in the molecular library to see which ones activated the M1 receptor. Most such studies are done on computers with robots and automatic scoring mechanisms. By looking with his own eyes at the waveform reactions of every compound in the library, including those already rejected by the robotic systems, Dr. Weaver identified the molecule the scientists dubbed VU019467.

It was now time for stage two, and therefore the turn of Dr. Craig Lindsley, head of Medicinal Chemistry and Director of the Vanderbilt Specialized Chemistry Center for Accelerated Probe Development. His task was to create an effective probe compound.

"There is no point optimizing a molecule's potency in vitro if it turns out not to work in vivo," says Lindsley. His probe works in both. The team now is trying the compound in mouse and rat models of Alzheimer's and schizophrenia to determine what dose range restores the appropriate level of signaling through the targeted receptor. In addition, this compound provides a tool of unprecedented selectivity that will allow the researchers to tease apart the basic role of the M1 and M4 receptors in CNS function and disease states to degree that has never before been possible.

The team hopes that within a year they will have a compound ready to license to a pharmacological company that can continue with preclinical development and then onward to human trials.

Co-authors on the study are Mr. Lebois, who carried out chemical syntheses and conducted the assays; Dr. Weaver and Dr. Lindsley; graduate students Thomas Bridges and Phillip Kennedy; Dr. Zixiu Xiang; Dr. Satyawan Jadhav; Dr. Huiyong Yin; Dr. Carrie Jones; and Dr. Jeffrey Conn, Global Director of the Vanderbilt program in drug discovery. Funding for the research comes from the National institutes of Health, National Institute of Mental Health, and the Molecular Libraries Probe Production Centers Network.

Human lung tumors destroy anti-cancer hormone vitamin D, Pitt researchers find

DENVER, Colo., April 20 – Human lung tumors have the ability to eliminate Vitamin D, a hormone with anti-cancer activity, a new study from the University of Pittsburgh Cancer Institute (UPCI) suggests. Results of the study, Abstract Number 2402, are being presented at the 100th annual meeting of the American Association for Cancer Research (AACR), April 18 to 22, in Denver.

"High levels of Vitamin D help the body produce proteins with anti-tumor activity," explained principal investigator Pamela Hershberger, Ph.D., a research assistant professor in UPCI's Department of Pharmacology and Chemical Biology. "We've discovered that lung cancer cells make an enzyme called CYP24, which counteracts the positive effects of Vitamin D. To better study it, we developed the first radioactive-free assay that measures the amount of Vitamin D in tissues and blood."

According to Dr. Hershberger, this test is sensitive enough to have clinical potential. "We hope this new assay will help identify the best approaches to maintain therapeutic levels of Vitamin D in tissues," she said.

Lung cancer is the leading cause of cancer death in the United States in both men and women, killing 160,000 people annually, and remains one of the most difficult cancers to treat. The five-year survival rate remains low, and better treatments are much needed. According to Dr. Hershberger, it is possible that one day Vitamin D could be used as a chemopreventive agent to improve patient outcomes.

This study was supported by UPCI's Lung Cancer Specialized Program of Research Excellence.

Pregnancy hormone hCG protects against breast cancer even in short-term treatments

In an animal model of breast cancer, Fox Chase Cancer Center researcher shows how smaller doses of hCG could offer some of the same benefits of longer doses

One of the most effective ways to prevent breast cancer is through a full-term pregnancy at an early age. Studies out of Fox Chase Cancer Center have linked this protective effect to the presence of human chorionic gonadotropin (hCG), a hormone produced by the placenta to maintain the early stages of pregnancy. Their findings in an animal model of breast cancer showed that rats exposed to hCG over a 21 day period (the length of rat pregnancy), are far less likely to develop breast cancer when exposed to a known carcinogen.

Today, at the 100th Annual Meeting of the American Association for Cancer Research. Johana Vanegas, M.D., a research associate at Fox Chase, presents findings suggesting that even a much shorter exposure to hCG can prevent breast cancer in rats.

Venegas is a member of the laboratory of Jose Russo, M.D. and Irma Russo, M.D., who were the first scientists to propose hCG as an anti-cancer agent. Their studies have shown that hCG offers lasting, protective changes within breast tissue. Clinical trials of hCG in women, based on their work, are currently under way at three locations, nationally, including Fox Chase Cancer Center, and in one European country. The hCG hormone is an FDA-approved agent frequently used for fertility treatments.

"The ability to replicate the naturally protective effects of pregnancy against breast cancer will hold a significant public health value," says Vanegas. "In order to translate our finding into humans, a clinical trial with hCG as a preventive agent against breast cancer, is already ongoing in pre-menopausal women with no previous pregnancy."

Vanegas and her colleagues studied virgin female rats, which had been divided into four groups: a control group, which did not receive hCG, and three groups that received hCG for five, ten or fifteen consecutive days. Following the treatment, each rat received a single dose of a breast cancer-inducing agent.

According to Vanegas, 90.9 percent of the rats in the control group developed breast tumors, compared to 71.4 percent, 57.1 percent, and 15.4 percent in the five, ten and fifteen day-treated animals, respectively. In addition, the average tumor size was also smaller in all the animals that received any of the three hCG treatments.

"The animals that received hCG, but still developed breast cancer did so much later than the control group, which further demonstrates the protective effects of hCG," Vanegas says. "While we don't foresee side effects among humans in using hCG, it is helpful to know that even smaller doses confer benefits on breast tissue."

Funding for this research comes from grants from the National Institutes of Health and the National Cancer Institute.

New imaging technology reveals prevalence of 'silent' heart attacks

DURHAM, N.C. – So-called "silent" heart attacks may be much more common than previously believed, according to researchers at Duke University Medical Center.

Studies show that each year, nearly 200,000 people in the U.S suffer a heart attack but may not realize it. These "silent" heart attacks aren't noted because they don't cause any pain – or at least any pain that patients believe is related to their heart – and they don't leave behind any telltale irregularities on electrocardiograms (ECGs).

New imaging research from Duke University Medical Center appearing in PLoS Medicine suggests that these heart attacks (now called unrecognized myocardial infarctions, or UMIs) may be happening much more frequently than physicians had suspected. Duke investigators also found that these attacks were associated with a surprisingly high risk of untimely death.

"No one has fully understood how often these heart attacks occur and what they mean, in terms of prognosis," says Han Kim, M.D., a cardiologist at Duke and the lead author of the study. "With this study, we can now say that this subset of heart attacks, known as non-Q wave UMIs, is fairly common, at least among people with suspected coronary artery disease."

Physicians can usually tell when a heart attack has recently occurred by signature changes on ECGs and in certain blood enzyme levels. But if a heart attack happened in the distant past, physicians rely on the appearance of a specific alteration on an ECG called a Q-wave, which signals the presence of damaged tissue.

"The problem is, not all UMIs result in Q-waves on the electrocardiogram. Those that don't are called non-Q-wave myocardial infarctions. Those are the ones we haven't been able to count because we've never had a good way to document them," says Kim.

Kim believed that using delayed enhancement cardiovascular magnetic resonance, or DE-CMR, might be good way to get an idea about how frequently non-Q-wave myocardial infarctions occur. Previous studies had shown that DE-CMR was particularly adept in discerning damaged tissue from healthy tissue.

Researchers used DE-CMR to examine185 patients suspected of having coronary artery disease but who had no record of any heart attacks. All of them were scheduled to undergo angiography to find out if excess plaque had narrowed or blocked any of their arteries. Investigators followed the patients for two years to see if the presence of any unrecognized non-Q-wave heart attacks were associated with a higher risk of death.

They found that 35 percent of the patients had evidence of a heart attack and that non-Q-wave attacks were three times more common than Q-wave UMIs. Non-Q-wave attacks were also more common among those with more severe coronary artery disease. In addition, researchers discovered that those who suffered non-Q-wave UMIs had an 11-fold higher risk of death from any cause and a 17-fold higher risk of death due to heart problems, when compared to patients who did not have any heart damage.

"Right now, there are no specific guidelines about how patients with UMIs should be treated," says Kim. "If patients with UMIs happen to be identified, they are usually treated similarly to those patients where heart disease has already been documented. Future studies will likely examine how common unrecognized non-Q-wave heart attacks are in other patient groups and how these UMIs should be treated."

The National Institutes of Health supported the study.

Duke researchers who contributed to the study include Igor Klem, Dipan Shah, Michele Parker, Anna Lisa Crowley, Robert Judd and senior author Raymond J. Kim. Additional co-authors include Edwin Wu, Sheridan Meyers and Robert Bonow, from the Feinberg Cardiovascular Research Institute at Northwestern University.

Drs. Judd and Raymond Kim are named on a U.S. patent for DE-CMR technology, which is owned by Northwestern University. Raymond Kim and Han Kim are not related.

Grapefruit juice boosts drug's anti-cancer effects

In a small, early clinical trial, researchers at the University of Chicago Medical Center have found that combining eight ounces of grapefruit juice with the drug rapamycin can increase drug levels, allowing lower doses of the drug to be given. They also showed that the combination can be effective in treating various types of cancer.

For two decades, pharmacists have pasted DO-NOT-TAKE-WITH-GRAPEFRUIT-JUICE stickers on various pill bottles because it can interfere with the enzymes that break down and eliminate certain drugs. This interference makes the drugs more potent. In data presented at the AACR 100th Annual Meeting 2009, the Chicago researchers examine ways to exploit this fruit's medication-altering properties.

"Grapefruit juice can increase blood levels of certain drugs three to five times," said study director Ezra Cohen, MD, a cancer specialist at the University of Chicago Medical Center. "This has always been considered a hazard. We wanted to see if, and how much, it could amplify the availability, and perhaps the efficacy of rapamycin, a drug with promise for cancer treatment."

This trial was designed to test "whether we could use this to boost rapamycin's bioavailability to the patient's advantage, to determine how much the juice altered drug levels, and to assess its impact on anti-cancer activity and side effects," he said.

The study followed 28 patients with advanced solid tumors, for which there is no effective treatment. The dose of the drug increased with each group of five patients, from 15 milligrams up to 35. Patients took the drug by mouth, as a liquid, once a week.

Beginning in week two, they washed it down with a glass of grapefruit juice (Citius paradisi), taken immediately after the rapamycin and then once a day for the rest of the week.

Twenty-five participants remained in the study long enough to be evaluated. Seven of those 25 (28%) had stable disease, with little or no tumor growth. One patient (4%) had a partial response, with the tumor shrinking by about 30 percent. That patient is still doing well more than a year after beginning the trial.

"My first cancer doctor gave me five years to live," said that patient, Albina Duggan of Bourbonnais, IL. "That time runs out next July."

Duggan, mother of four, has a rare cancer, an epitheliod hemangioendothelioma that originated in the liver and subsequently spread to two vertebrae in the neck and to the lymph nodes. She had surgery and radiation therapy and was evaluated for a liver transplant, but evidence of cancer beyond the liver made her ineligible for a transplant. She "shopped around" for other therapies and was able to keep the disease in check for a year with sorafenib, a drug approved for kidney and liver cancers.

After a year of stable disease, however, her tumor began growing again and she had to look for an alternative therapy. Her doctors at the University of Chicago offered three clinical trials. The most appealing to her was the rapamycin plus grapefruit juice study. She took her first dose March 11, 2008, and is still on the drug-juice combination. "My tumor is smaller and it's no longer growing. I feel fine. I can do whatever I like and I have no real side effects," she said. "What's not to like?"

Trial subjects do not like the taste of rapamycin. "It's not pleasant," Duggan admitted. She has also tired of grapefruit juice. Many patients in the study did report side effects. More than half experienced elevated blood sugar levels, diarrhea, low white blood cell counts or fatigue.

Duggan, more fortunate than most, has had milder side effects, including fragile toe and finger nails and curly hair. "I now have very curly hair," she said, "seriously curly. I have to adjust to it."

Rapamycin, also known as sirolimus, was originally developed to suppress the immune system, preventing rejection in patients receiving a transplanted kidney. Cancer specialists became interested in the drug when they learned that it disrupted a biochemical pathway involved in the development of the new blood vessels that tumors need to grow. But the drug is expensive and poorly absorbed. Less than 15 percent of rapamycin is absorbed when taken by mouth.

This study showed that substances known a furanocoumarins, plentiful in some forms of grapefruit juice, can decrease the breakdown of rapamycin. This makes the drug reach higher levels in the bloodstream, two to four times the levels seen without a juice boost, and thus increases the amount of the drug that reaches its targets.

"That means more of the drug hits the target, so we need less of the drug," said Cohen.

Many of the newer cancer medications, precisely focused on specific targets, are now taken as pills rather than intravenously. Some of these drugs, including rapamycin, can cost thousands of dollars a month. Hence, "this is an opportunity for real savings," Cohen said. "A daily glass of juice could lower the cost by 50 percent."

Wanted: Science advisor for British spy agency

* 17:40 20 April 2009 **by Linda Geddes**

If it hadn't been for Q, James Bond would have been dead long ago. But can any of New Scientist's readers fill the boots of the real-life Q?

While Bond and Q work for Britain's secret intelligence service MI6, the security service, MI5, wants in on the act. It is currently recruiting a chief scientific adviser to co-ordinate how science and technology are used across its branches.

The job is being advertised on MI5's website, and specifies that the candidate should be of a high academic standing – probably an FRS or FREng – have demonstrated management skills at a senior level in a medium-to-large organisation, and ideally have experience of working within a complex government environment.

The post will take up two or three days a week, and will last 3-5 years.

"It could be a scientist or an engineer, and they're open-minded about what areas of scientific expertise a person has," says a spokesman for the UK Department of Innovation, Universities and Skills, which supports evidence-based policy making across government.

Listening in

However, recruitment consultants Egon Zehnder International, who are advertising the role, say that expertise in at least one of: physics, chemistry, acoustics, optics, materials science, radiofrequency technologies, communications, telephony and data mining would be an advantage – suggesting that developing cutting-edge of surveillance technology is one of MI5's goals.

"I think it's unlikely the candidate will be required to create a new weapons system for the latest Aston Martin," John Beddington, the government's chief scientific adviser told the BBC. "Nevertheless there is a really important role in providing scientific and technological advice that agents working in the field will address."

As for the type of person that will fit in at MI5, Egon Zehnder International offers the following advice: "To get things done in the Security Service, individuals need to be pragmatic and results oriented – credibility comes through delivery and an ability to build good working relationships. The incumbent will be looked on as a role model for thought leadership and integrity and will live by the values of the Security Service."

Discretion is also essential, as applicants are told they should only discuss their application with a close partner or immediate family. Applications close on 24 April.

Snatched From the Air

Carbon dioxide as a carbon source—a carbene catalyst opens new perspectives

It’s the reason why chemists envy green plants: by using photosynthesis, plants can easily fix the carbon dioxide that is so plentiful in air to make biomass, or organic compounds. Chemists would also like to be able to simply produce carbon compounds out of CO2 from air. In contrast to the usual sources of carbon used today—fossil fuels and natural gas—carbon dioxide is a renewable resource and an environmentally friendly chemical reagent. Unfortunately, its carbon–oxygen bonds are too strong to be broken easily. Researchers working with Yugen Zhang and Jackie Y. Ying at the Institute of Bioengineering and Nanotechnology in Singapore have now developed a novel reaction scheme by which CO2 can be efficiently converted into methanol under very mild conditions. As reported in the journal Angewandte Chemie, it is based on an N-heterocyclic carbene catalyst and a silent as the reducing agent.

The basic framework of an N-heterocyclic carbene is a five-membered ring made of two nitrogen and three carbon atoms. Instead of having the usual four bonds, one of these carbon atoms only has two. The two electrons left over in the form of a lone pair, which makes this species highly reactive - reactive enough to attack CO2.

The researchers in Singapore produced the carbene catalyst used in the reaction in situ from a precursor. The carbene activates the CO2, but is then split off again to end the reaction cycle in its original state. The formal reaction partner is a hydrosilane, an organosilicon compound that acts as a reducing agent. The reaction product into which the CO2 is converted can easily be collected in the form of methanol in the last step of the reaction series. Methanol is an important starting material for many chemical syntheses and serves as an alternative fuel and as a raw material for the production of energy in methanol fuel cells.

The big advantage: unlike prior reaction mechanisms using metal-containing catalysts, air can be used as the source of the CO2 because the carbene catalyst is not sensitive to oxygen. The carbene is more efficient than the metal-containing catalysts as well, and the reaction can be carried out under very mild conditions.

Yeast and bacterium turned into gasoline factory

* 20:07 20 April 2009 **by Peter Aldhous,** San Francisco

Take brewer's yeast, add a gene from a salt marsh plant, grow it with an obscure bacterium found in a French landfill, and what have you got? A cheap, renewable way to fuel our cars, claims Christopher Voigt, a synthetic biologist at the University of California, San Francisco.

While biofuels derived from plants can theoretically be a carbon-neutral energy source, many also displace food-producing crops. Making them from cellulose – structural material abundant in crop waste and grasses – can sidestep that problem.

But efficient processes to do so are lacking. Voigt's team was looking for a way to get microbes to do the hard work, converting cellulose from crop waste or grasses into chemicals called methyl halides, which can in turn be turned into regular gasoline in a simple catalytic reaction.

Enzyme hunt

A variety of plants and microorganisms naturally make methyl halides in small amounts using methyl halide transferase enzymes (MHTs). But only a handful of such enzymes were known, so Voigt's team set out on a detective hunt to find more.

They scoured DNA sequence databases for genes that would produce proteins 18% or more similar to the known MHTs. Then they asked a DNA synthesis company to make the 89 matching genes found, and spliced them into the genome of E. coli bacteria, to see which of them produced methyl halides most efficiently. “We were essentially mining the sequence databases for function," Voigt explains.

The clear winner was one of the previously known MHT genes, from Batis maritima, known as turtleweed or saltwort, a plant found on the salt marshes of the southeastern US and California.

Bug buddies

Voigt's team spliced the gene into yeast to produce a strain able to make methyl halides in large amounts. But the puzzle was not over yet. They still needed to find an organism that would digest cellulose into smaller molecules that the yeast could readily convert into the substrate for the MHT enzyme.

Most cellulose-digesting microbes grow slowly, and become efficient only at relatively high temperatures. The researchers needed an organism that could grow at about the same rate as yeast at the same temperature it favours – around 30 °C.

After an extensive search through the scientific literature, they found the ideal candidate: a bacterium called Actinotalea fermentans, isolated in the 1980s from a landfill dump in France.

That bacterium excretes acetate: if it is cultured alone, it soon poisons itself with this waste product. But yeast can happily use acetate as a food source.

Voigt and colleagues had assembled the perfect microbial team – A. fermentans converts cellulose into acetate, which is in turn made into methyl halides by the engineered yeast. It is a low-temperature, cheap process that produces the methyl halides that are readily converted into fuel.

Cheaper than oil

The researchers are now working to make the process more efficient, altering their yeast's genes to tune its metabolism to produce more substrate for the MHT enzyme from the available acetate. Assuming their system could be made to work as efficiently as yeast converts sugars to ethanol, they calculate that it could produce gasoline more cheaply than from oil.

Voigt's novel co-culture is one of several attempts to make microbes produce advanced biofuels. For instance, James Liao's team at the University of California, Los Angeles, has engineered E. coli to produce long-chain alcohols, which pack more energy than the plant-derived ethanol that is the main biofuel used today.

Meanwhile, South San Francisco company LS9 is tinkering with bacterial biochemical pathways that turn sugars into fatty acids – which can be converted to biodiesel.
"It's valuable to have as many approaches on the table as possible," says Jay Keasling of the University of California, Berkeley, who heads the US Department of Energy's Joint BioEnergy Institute in Emeryville, California.
Journal reference: Journal of the American Chemical Society (DOI: 10.1021.ja8094611u)

Our brains make their own marijuana: We're all pot heads deep inside

New study in the FASEB Journal shows that our brains make proteins that act directly on the marijuana receptors in our head

U.S. and Brazilian scientists have just proven that one of Bob Dylan's most famous lines—"everybody must get stoned"— is correct. That's because they've discovered that the brain manufactures proteins that act like marijuana at specific receptors in the brain itself. This discovery, published online in The FASEB Journal (http://www.fasebj.org), may lead to new marijuana-like drugs for managing pain, stimulating appetite, and preventing marijuana abuse.

"Ideally, this development will lead to drugs that bind to and activate the THC receptor, but are devoid of the side effects that limit the usefulness of marijuana," said Lakshmi A. Devi of the Department of Pharmacology and Systems Therapeutics at Mount Sinai School of Medicine in New York and one of the senior researchers involved in the study. "It would be helpful to have a drug that activated or blocked the THC receptor, and our findings raise the possibility that this will lead to effective drugs with fewer side effects."

Scientists made their discovery by first extracting several small proteins, called peptides, from the brains of mice and determining their amino acid sequence. The extracted proteins were then compared with another peptide previously known to bind to, but not activate, the receptor (THC) affected by marijuana. Out of the extracted proteins, several not only bound to the brain's THC receptors, but activated them as well.

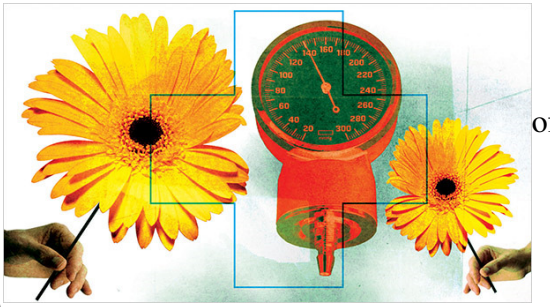
"The War on Drugs has hit very close to home," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "Last year, scientists found that our skin makes its own marijuana-like substance. Now, we see that our brain has been making proteins that act directly on the marijuana receptors in our head. The next step is for scientists to come up with new medicines that eliminate the nasty side of pot—a better joint, so to speak."

Well

What Are Friends For? A Longer Life

By TARA PARKER-POPE

In the quest for better health, many people turn to doctors, self-help books or herbal supplements. But they overlook a powerful weapon that could help them fight illness and depression, speed recovery, slow aging and prolong life: their friends.



Stuart Bradford

Researchers are only now starting to pay attention to the importance of friendship and social networks in overall health. A 10-year Australian study found that older people with a large circle of friends were 22 percent less likely to die during the study period than those with fewer friends. A large 2007 study showed an increase of nearly 60 percent in the risk for obesity among people whose friends gained weight. And last year, Harvard researchers reported that strong social ties could promote brain health as we age.

“In general, the role of friendship in our lives isn’t terribly well appreciated,” said Rebecca G. Adams, a professor of sociology at the University of North Carolina, Greensboro. “There is just scads of stuff on families and marriage, but very little on friendship. It baffles me. Friendship has a bigger impact on our psychological well-being than family relationships.”

In a new book, “The Girls From Ames: A Story of Women and a 40-Year Friendship” (Gotham), Jeffrey Zaslow tells the story of 11 childhood friends who scattered from Iowa to eight different states. Despite the distance, their friendships endured through college and marriage, divorce and other crises, including the death of one of the women in her 20s.

Using scrapbooks, photo albums and the women’s own memories, Mr. Zaslow chronicles how their close friendships have shaped their lives and continue to sustain them. The role of friendship in their health and well-being is evident in almost every chapter.

Two of the friends have recently learned they have breast cancer. Kelly Zwagerman, now a high school teacher who lives in Northfield, Minn., said that when she got her diagnosis in September 2007, her doctor told

her to surround herself with loved ones. Instead, she reached out to her childhood friends, even though they lived far away.

"The first people I told were the women from Ames," she said in an interview. "I e-mailed them. I immediately had e-mails and phone calls and messages of support. It was instant that the love poured in from all of them."

When she complained that her treatment led to painful sores in her throat, an Ames girl sent a smoothie maker and recipes. Another, who had lost a daughter to leukemia, sent Ms. Zwagerman a hand-knitted hat, knowing her head would be cold without hair; still another sent pajamas made of special fabric to help cope with night sweats.

Ms. Zwagerman said she was often more comfortable discussing her illness with her girlfriends than with her doctor. "We go so far back that these women will talk about anything," she said.

Ms. Zwagerman says her friends from Ames have been an essential factor in her treatment and recovery, and research bears her out. In 2006, a study of nearly 3,000 nurses with breast cancer found that women without close friends were four times as likely to die from the disease as women with 10 or more friends. And notably, proximity and the amount of contact with a friend wasn't associated with survival. Just having friends was protective.

Bella DePaulo, a visiting psychology professor at the University of California, Santa Barbara, whose work focuses on single people and friendships, notes that in many studies, friendship has an even greater effect on health than a spouse or family member. In the study of nurses with breast cancer, having a spouse wasn't associated with survival.

While many friendship studies focus on the intense relationships of women, some research shows that men can benefit, too. In a six-year study of 736 middle-age Swedish men, attachment to a single person didn't appear to affect the risk of heart attack and fatal coronary heart disease, but having friendships did. Only smoking was as important a risk factor as lack of social support.

Exactly why friendship has such a big effect isn't entirely clear. While friends can run errands and pick up medicine for a sick person, the benefits go well beyond physical assistance; indeed, proximity does not seem to be a factor.

It may be that people with strong social ties also have better access to health services and care. Beyond that, however, friendship clearly has a profound psychological effect. People with strong friendships are less likely than others to get colds, perhaps because they have lower stress levels.

Last year, researchers studied 34 students at the University of Virginia, taking them to the base of a steep hill and fitting them with a weighted backpack. They were then asked to estimate the steepness of the hill. Some participants stood next to friends during the exercise, while others were alone.

The students who stood with friends gave lower estimates of the steepness of the hill. And the longer the friends had known each other, the less steep the hill appeared.

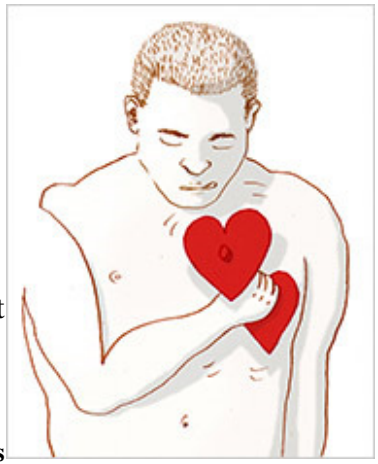
"People with stronger friendship networks feel like there is someone they can turn to," said Karen A. Roberto, director of the center for gerontology at Virginia Tech. "Friendship is an undervalued resource. The consistent message of these studies is that friends make your life better."

Really?

The Claim: Weight Training Is Bad for Blood Pressure

By ANAHAD O'CONNOR

THE FACTS It's well known that regular aerobic exercise can improve circulation and reduce blood pressure. But what about weight lifting?



Leif Parsons

For years, people with hypertension were warned against it, because doctors feared that spikes in blood pressure during strenuous lifting might cause dangerous problems and, in the long term, raise blood pressure. But studies had not provided much evidence. And in recent years, large studies have found the opposite: that ultimately weight lifting reduces resting blood pressure, because with stronger muscles, there is less demand on the heart during everyday activities.

For example, an analysis in the journal Hypertension examined 11 clinical trials comparing 182 adults who lifted weights several times a week and 138 who did not Over all, it found that weight training lowered resting systolic blood pressure (the top number in a pressure reading) by 2 percent, and diastolic pressure by about 4 percent — small gains that can greatly improve cardiovascular health.

Another report by the American Heart Association, published in the journal Circulation, found that just two or three bouts of weight training a week — with exercises like curls and presses — were enough to lower blood pressure.

The association says that resistance training can benefit heart patients as well but recommends consulting with a doctor first for guidance.

THE BOTTOM LINE Weight training can actually lower resting blood pressure.

Avian Flu Cases in Egypt Raise Alarms

By DONALD G. McNEIL Jr.

An unusual pattern of avian flu cases in Egypt — almost all are in toddlers, all of whom have survived — has led some flu-tracking Web sites to speculate that dozens of silent cases are circulating there.

That would be an alarming development, but other experts, including those at the World Health Organization, say such fears are exaggerated. Although thousands of Egyptians have rushed their children to hospitals this flu season, there is no evidence yet of asymptomatic avian flu cases or any significant mutation in the H5N1 virus.

"Right now, it's all hot air," said Dr. Robert G. Webster, a flu expert at St. Jude Children's Research Hospital in Memphis. "I hope to hell it's not happening, because it would mean the virus is adapting to humans. But there's not a shred of data."

Bird flu has faded from world headlines because it has not caused a pandemic. But the disease is still circulating in poultry in Egypt, Indonesia, China, Vietnam and along the India-Bangladesh border. It has mutated into at least 10 strains and occasionally infects humans.

An April 8 Reuters article from Cairo quoted a visiting W.H.O. expert saying his agency feared "something strange happening in Egypt" and would help the government test the blood of healthy people for antibodies this summer.

Antibodies to the flu would indicate they had recovered from silent infections.

But a W.H.O. spokesman said privately that the agency was just helping the Egyptians with a long-planned study and the article had "jumped the gun."

Translations of Egyptian media reports posted on flu-tracking sites say dozens of suspected cases have been hospitalized, but some seem to confuse avian flu with seasonal flu and even confirmed poultry cases. The Egyptian health ministry, which works closely with a United States Navy laboratory based in Cairo, has confirmed 15 human cases this year, with no deaths; almost all were in young children.

Dr. Nikki Shindo, a W.H.O. medical officer who works in Egypt, said the surge in toddler cases and survivals had a possible explanation. The government has loudly warned its citizens to avoid sick poultry and has trained doctors in remote clinics to give Tamiflu quickly and move cases to state hospitals, where treatment is free. In a country where chickens are both kept as pets and eaten, toddlers still touch dying birds but poultry workers would not.

Egypt's outbreak response contrasts sharply to Indonesia's, where the sick often take herbal medicine first and where rural clinics lack Tamiflu, she said.

Dr. Arnold S. Monto, a flu expert at the University of Michigan School of Public Health who also teaches in Egypt, said even geography helps. All cases are along the Nile and easily moved to Cairo, while travel among Indonesia's thousands of islands is slower.

Also, he said, the government has been more aggressive since it was criticized by opposition parties for not wiping out the poultry epidemic that began in 2006.

Henry L. Niman, a biochemist who tracks flu mutations, has speculated that a mild strain of H5N1 is more common in Egypt than has been found because nasal swabs for flu are inaccurate. He noted that mild cases were found in Qena, Egypt, in 2007, and has called for more testing and for releasing the genetic sequences of strains found in both poultry and people.

Dr. Tim Uyeki, a flu specialist at the Centers for Disease Control and Prevention in Atlanta, said there had been mild cases of H5N1 among children in several countries. There have also, he said, been studies in Indonesia, Thailand, Cambodia and Nigeria similar to the one proposed for Egypt in which the blood of cullers, poultry workers and relatives of sick people has been tested.

"Those are the ideal people to look at," he said. "And there was zero or extremely low prevalence of antibodies," meaning silent infections were very uncommon.

More Wii Warriors Are Playing Hurt

By ANDREW DAS

In the moments after I felt the pop in my left shoulder, the sensation I felt was not pain. It was panic. How exactly does a 40-year-old man explain to his wife that he might have torn his rotator cuff during a midnight game of Wii tennis? Dr. Charles Young made me feel better without even examining me.

Late last year, Dr. Young, an orthopedic surgeon, spent about an hour experimenting with the balance games and strength-training exercises on his new Wii Fit. Running on a virtual trail. Slalom skiing. Walking on a tightrope. “They have this hula-hoop one where you’re supposed to spin yourself in a circle and try to get a high score,” said Dr. Young, who is completing a sports medicine fellowship at the Cleveland Clinic. “I was really hurting.”

In the operating room the next day he commiserated with several nurses who confessed that they had, at least figuratively, already felt his pain.

To say that Wii injuries are an epidemic would be an overstatement, but they are proliferating along with the popular video-game system. Interviews with orthopedists and sports medicine physicians revealed few serious injuries, but rather a phenomenon more closely resembling a spreading national ache: patients of all ages complaining of strains and swelling related to their use — and overuse — of the Wii.

Call it Wii Shoulder. Or Wii Knee. If there is an epidemic of anything, it probably falls under a broader label: Nintendinitis.

“Skateboarding, snowboarding, you name it,” said Dr. William N. Levine, the director of sports medicine at NewYork-Presbyterian Hospital/Columbia University Medical Center. “Take the newest fad, and there’s always a slew of specific orthopedic injuries associated with it.”

The difference now is that the surging sales of the Wii system mean that misery gets more company every day. Nintendo, which introduced the Wii in November 2006, sold more than 10 million of the game systems in the United States last year, including a record 2.1 million in December. The complementary Wii Fit exercise program has been nearly as popular, with more than 6.5 million sold since its introduction last May.

Consumers who avoided sedentary video-game systems have flocked to the Wii, which lures users off the couch with a handheld, wireless remote and a selection of familiar, free-swinging games like tennis, boxing and bowling. For some parents, and even grandparents, the games are a way to connect with children on their own turf. The fact that everyone gets a little exercise along the way is an added plus.

“It’s great in the concept that it gets people active and involved,” said Dr. Brian Halpern, a sports medicine physician at the Hospital for Special Surgery in Manhattan. “It’s not great in that you get lost in that and are overloading areas that you haven’ t worked out in a long time, if ever.”

Dr. Halpern said he had treated two types of injuries: traumatic injuries like twisted knees and sprained ankles from playing the games in confined spaces, and repetitive stress problems from playing too long. A common problem is the realization by players that a full swing is not required; a flick of the wrist is often enough to return a serve or bowl a strike. As several doctors pointed out, that is the exact motion — concentrating the force of a swing in the muscles of the forearm — that can cause tennis elbow.

The Wii system was built with warnings about prolonged use, and electronic prompts interrupt players regularly to urge them to take a break.

Denise Kaigler, a vice president for marketing and corporate affairs at Nintendo of America, said in an e-mail message that “as consumers adapt to this new style of play, there have been a few reports of minor incidents during overly enthusiastic game play,” but that more health and safety warnings — about playing in an area free of obstructions, for example — had been added.

“As with any new activity, people playing the Wii system should pace themselves and not overdo it,” Ms. Kaigler said.

Dr. John Sperling, a physician at the Mayo Clinic in Rochester, Minn., called the aches and pains a sign of the times. “It’s a syndrome of injuries and people presenting with complaints that we couldn’t have imagined three years ago,” he said.

Dr. Levine said the youngest patient he had treated was 12. Dr. Young, who overworked his core muscles using the Wii Fit, is 32. Dr. Sperling’s patients have included a 22-year-old whose arm swelled to twice its size after a marathon Wii session, and a man in his 60s.

“I was asking him what happened,” Dr. Sperling said of the older patient, “and he said, ‘Well, we bought a Wii system for the grandkids. Next thing I know, my shoulder’s killing me.’ ”

Dr. Halpern, a former assistant team physician for the Mets, compared some Wii injuries to those sustained by professional athletes.

"It's like if you have a pitcher who has gone to spring training and hasn't worked hard in the off-season and starts throwing too much and kind of overloads his shoulder or elbow," he said.

And just as that pitcher might have to take several days off, a person experiencing pain from a session of Wii games should do the same. While "the rush of beating kids a fraction of your age in Wii Sports far outweighs the discomforts of getting older," Ms. Kaigler said, moderation is just as important. That may be especially true for older players.

My shoulder recovered with time away from the Wii, not a problem in a household with three children who were all eager to play and who are apparently more durable than their father. The lasting image of Christmas at my family's home was that of my 5-year-old daughter in a velvet dress, blond hair tucked behind one ear, raining punches on a hulking man with a goatee. She knocked him out, but quickly moved on to baseball and bowling and golf.

Dr. Halpern said the shorter attention spans of younger children were probably preventing them from developing overuse injuries, describing their exposure to a variety of Wii games as "cross-training without even thinking about it." Sore-shouldered and gimpy-kneed adults could be victims of their better focus, but also of their innate competitiveness.

"It's good to be a kid at heart," said Dr. Susan Joy, the director of the Cleveland Clinic's women's sports health program. "But sometimes when you start a new exercise program, it's good to remember that you're not a kid."

A Conversation With Richard Wrangham

From Studying Chimps, a Theory on Cooking

By CLAUDIA DREIFUS

Richard Wrangham, a primatologist and anthropologist, has spent four decades observing wild chimpanzees in Africa to see what their behavior might tell us about prehistoric humans. Dr. Wrangham, 60, was born in Britain and since 1989 has been at Harvard, where he is a professor of biological anthropology. His book, "Catching Fire: How Cooking Made Us Human," will be published in late May. He was interviewed over a vegetarian lunch at last winter's American Association for the Advancement of Science meeting in Chicago and again later by telephone. An edited version of the two conversations follows.

Q. In your new book, you suggest that cooking was what facilitated our evolution from ape to human. Until now scientists have theorized that tool making and meat eating set the conditions for the ascent of man. Why do you argue that cooking was the main factor?

A. All that you mention were drivers of the evolution of our species. However, our large brain and the shape of our bodies are the product of a rich diet that was only available to us after we began cooking our foods. It was cooking that provided our bodies with more energy than we'd previously obtained as foraging animals eating raw food.

I have followed wild chimpanzees and studied what, and how, they eat. Modern chimps are likely to take the same kinds of foods as our early ancestors. In the wild, they'll be lucky to find a fruit as delicious as a raspberry. More often they locate a patch of fruits as dry and strong-tasting as rose hips, which they'll masticate for a full hour. Chimps spend most of their day finding and chewing extremely fibrous foods. Their diet is very unsatisfying to humans. But once our ancestors began eating cooked foods — approximately 1.8 million years ago — their diet became softer, safer and far more nutritious.

And that's what fueled the development of the upright body and large brain that we associate with modern humans. Earlier ancestors had a relatively big gut and apelike proportions. Homo erectus, our more immediate ancestor, has long legs and a lean, striding body. In fact, he could walk into a Fifth Avenue shop today and buy a suit right off a peg.

Our ancestors were able to evolve because cooked foods were richer, healthier and required less eating time.

Q. To cook, you need fire. How did early humans get it?

A. The australopithicines, the predecessors of our prehuman ancestors, lived in savannahs with dry uplands. They would often have encountered natural fires and food improved by those fires. Moreover, we know from cut marks on old bones that our distant ancestor Homo habilis ate meat. They certainly made hammers from stones, which they may have used to tenderize it. We know that sparks fly when you hammer stone. It's reasonable to imagine that our ancestors ate food warmed by the fires they ignited when they prepared their meat.

Now, once you had communal fires and cooking and a higher-calorie diet, the social world of our ancestors changed, too. Once individuals were drawn to a specific attractive location that had a fire, they spent a lot of time around it together. This was clearly a very different system from wandering around chimpanzee-style, sleeping wherever you wanted, always able to leave a group if there was any kind of social conflict.

We had to be able to look each other in the eye. We couldn't react with impulsivity. Once you are sitting around the fire, you need to suppress reactive emotions that would otherwise lead to social chaos. Around that fire, we became tamer.

Q. Your critics say you have a nice theory, but no proof. They say that there's no evidence of fireplaces 1.8 million years ago. How do you answer them?

A. Yes, there are those who say we need archaeological proof that we made fires 1.8 million years ago. And yes, thus far, none have been found. There is evidence from Israel showing the control of fire at about 800,000 years ago. I'd love to see older archaeological signals. At some point, we'll get them.

But for the meanwhile, we have strong biological evidence. Our teeth and our gut became small at 1.8 million years. This change can only be explained by the fact that our ancestors were getting more nutrition and softer foods. And this could only have happened because they were cooking. The foraging diet that we see in modern chimps just wasn't enough to fuel it.

Q. I understand that you once embarked on a chimpanzee diet. What was that like?

A. In 1972, when I was studying chimpanzee behaviors in Tanzania, I thought it would be interesting to see how well I could survive on what chimps ate. I asked Jane Goodall, the director of the project, if it I could live like a chimp for a bit. She said O.K. Now I wanted to be really natural and truly be a part of the bush and so I added, "I'd like to do it naked." There, she put her foot down: "You'll wear at least a loincloth!"

In the end, I never did the full experiment. However, there were times when I went off without eating in the mornings and tried living off whatever I found. It left me extremely hungry.

Q. What do you usually eat?

A. Oh, ordinary Western industrialized food. I won't eat an animal I'm not prepared to kill myself. I haven't eaten a mammal in about 30 years, except a couple of times during the 1990s, when I ate some raw monkey the chimps had killed and left behind.

I wanted to see what it tasted like. The black and white Colobus monkey is very tough and unpleasant. The red Colobus is sweeter. The chimps prefer it for good reason.

Q. You ate raw monkey for science?

A. Yes. I feel that by getting under the skin of a chimpanzee, you get insights that you don't otherwise get. That's how I came to this understanding about the role of cooking.

Q. Since you believe that the raw fare of prehistory would leave a modern person starving, does that mean we are adapted to the foods that we currently eat — McDonald's, pizza?

A. I think we're adapted to our diet. It's that our lifestyle is not. We're adapted in the sense that our bodies are designed to maximize the amount of energy we get from our foods. So we are very good at selecting the foods that produce a lot of energy. However, we take in far more than we need. That's not adaptive.

Sibling worlds may be wettest and lightest known

* 15:49 21 April 2009 **by Stephen Battersby**, Hatfield

A planet orbiting a red dwarf star 20 light years away could be the first known water world, entirely covered by a deep ocean

The planet, named Gliese 581d, is not a new discovery, but astronomers have now revised its orbit inwards, putting it within the "habitable zone" where liquid water could exist on the surface. "It is the only low-mass planet known inside the habitable zone", says Michel Mayor of Geneva Observatory.

Mayor and his team used the European Southern Observatory's 3.6-metre telescope in Chile to observe the low-mass star Gliese 581, and a precise spectrometer called HARPS to analyse its light.

That turned up the faint footprints of four planets, since the orbiting planets make the star wobble slightly, giving its light a slight Doppler shift. Three of the planets had been identified previously.

Video: ***Water world discovered***

The outermost planet had been thought to have a period of 83 days, putting it too far away from the small star's gentle heat to bear liquid water. But that was a mistake. "We only had a limited number of observations", Mayor told New Scientist. Now with three times as much data, he finds an orbital period of 66 days, putting the planet closer to its star – about a quarter of the Earth-Sun distance – and just inside the red dwarf's habitable zone.

New class

Gliese 581d is about seven times as massive as Earth, so it is much too small to be a gas giant like Jupiter, but probably too big to be a rocky world like our own. "Around such a small star, it is very difficult to have so much rocky material at such a [large] distance," says Mayor. Instead, the planet is likely to have a makeup similar to Neptune or Uranus, which are dominated by ices of water, ammonia and methane.

In the warmth of the habitable zone, these substances should form a sea thousands of kilometres deep. "Maybe this is the first of a new class of ocean planets. That is my favourite interpretation," says Mayor. "Whether there is life or not, I don't know."

The same set of observations also revealed a new world, Gliese 581e, with only 1.9 times the mass of Earth. That is the lowest published mass of any exoplanet around a normal star – although preliminary results have hinted that another exoplanet may weigh just 1.4 Earth masses. Gliese 581e is very close to the star, however, and probably far too hot for liquid water.

The results were announced on Tuesday at the European Week of Astronomy and Space Science meeting in Hatfield, UK.

Lightest exoplanet is discovered

By Paul Rincon and Jonathan Amos Science reporters, BBC News

Astronomers have announced the discovery of the lightest planet ever detected outside our Solar System.

Situated in the constellation Libra, it is only about twice as massive as the Earth, whereas most other exoplanets identified have been far bigger.

The scientists say the planet's orbit takes it far too close to its star Gliese 581 for life to be possible.

The detection was made by an international team of researchers using a 3.6m telescope at La Silla, Chile.

"This is by far the smallest planet that's ever been detected," said group member Michel Mayor, from the Geneva Observatory, Switzerland. This is just one more step in the search for the twin of the Earth."

"At the beginning, we discovered Jupiter-like planets several hundred times the mass of the Earth; and now we have the sensitivity with new instruments to detect very small planets very close to that of the Earth," he told BBC News.

THE GLIESE 581 SOLAR SYSTEM
From closest in to furthest out
Planet e is 1.9 Earth masses
Planet b is 16 Earth masses
Planet c is 5 Earth masses
Planet d is 7 Earth masses
The first planet to be found is always given the 'b' designation

Habitable zone

The planet joins three others previously detected around its star and takes the designation Gliese 581 e.

As with the previous discoveries, its presence was picked up using the so-called wobble technique. This is an indirect method of detection that infers the existence of orbiting planets from the way their gravity makes a parent star appear to twitch in its motion across the sky.

Astronomy is working right at the limits of the current technology capable of detecting exoplanets and most of those found so far are Jupiter scale and bigger. To discover one so small is a major coup. The previous record holder was about four times as massive as the Earth.

Because Gliese 581 e takes just 3.15 days to orbit its host star, it lies beyond what scientists call the habitable, or "Goldilocks", zone, where it is neither too hot nor too cold for liquid water to exist.

But one of the other planets in this system does appear to be. Gliese 581 d was first discovered in 2007. The latest research has allowed scientists to refine details of its orbit.

The team now believes planet d (which is about seven Earth-masses in size) circles Gliese 581 in 66.8 days.

"This planet is probably not just rocky; it's very probably an icy planet - but relatively close to the star so at the surface, we should have some big ocean," said Professor Mayor.

"Maybe, it's the first candidate in a new class of planet called an 'ocean planet'."

The exoplanet discovery was announced at the JENAM conference during the European Week of Astronomy & Space Science, which is taking place at the University of Hertfordshire, UK.

A scientific paper detailing the research has been submitted for publication in the journal Astronomy & Astrophysics.

Upcoming challenge

The US space agency (Nasa) recently launched its Kepler telescope dedicated to finding Earth-size planets. It will use a different approach to the HARPS/La Silla set-up.

Kepler will look for the tiny dip in light coming from a star as a planet crosses its face as viewed from Earth.

Michel Mayor commented: "The challenge in coming years will be to find Earth-mass planets in the habitable zones of stars." He added: "I'm absolutely confident that in one year or two years, we will arrive at [a planet with] the mass of the Earth."

In the future, some of these planets could be imaged in some detail by the next generation of ground telescopes.

One of these projects, the European Extremely Large Telescope (E-ELT) is currently coming to the end of its design process.

"One of the interesting things about today's announcement is that some of the planets in this system would actually be imageable with the next generation of telescopes," said Isobel Hook, from Oxford University and the UK project scientist on the E-ELT.

"The type of technology coming along, such as extreme adaptive optics, will allow you to produce very sharp images. The seven-Earth-mass planet we think could be imaged directly. You would be able to see it go around its star and see what it was made of," she told BBC News.

Tim de Zeeuw, director-general of the European Southern Observatory (Eso) organisation, which will operate the E-ELT, told BBC News: "The E-ELT will make it possible to take images of (Earth-mass planets) and indeed find evidence for many of them.

"This then leads to very interesting questions: do we find many Solar Systems like our own? Or is there only one like us?" He added: "I don't follow this field daily... (but) the number of cases we have is steadily growing to a size where we can start asking this question and there are some indications that perhaps our Solar System is a little unusual."

The 42m E-ELT comprises five large mirrors. Its adaptive optics system will compensate for the distortions to images of the sky caused by turbulence in the Earth's atmosphere.

Construction of the ground observatory could begin in 2011 if all goes to plan. Eso intends to select a location for the telescope by the end of this year.

Six sites have been shortlisted: three in Chile; one in the Canary Islands, Spain; one in Morocco; and one in Argentina.

Drinking wine may increase survival among non-Hodgkin's lymphoma patients

DENVER – Pre-diagnostic wine consumption may reduce the risk of death and relapse among non-Hodgkin's lymphoma patients, according to an epidemiology study presented at the American Association for Cancer Research 100th Annual Meeting 2009.

Xuesong Han, the first author of the abstract and a doctoral candidate at the Yale School of Public Health, said their findings would need to be replicated before any public health recommendations are made, but the evidence is becoming clearer that moderate consumption of wine has numerous benefits.

"This conclusion is controversial, because excessive drinking has a negative social and health impact, and it is difficult to define what is moderate and what is excessive," said Han. "However, we are continually seeing a link between wine and positive outcomes in many cancers."

This study was the first to examine the link among patients with non-Hodgkin's lymphoma. Han and her colleagues analyzed data about 546 women with non-Hodgkin's lymphoma.

They found that those who drank wine had a 76 percent five-year survival compared with 68 percent for non-wine drinkers. Further research found five-year, disease-free survival was 70 percent among those who drank wine compared with 65 percent among non-wine drinkers.

Beer and/or liquor consumption did not show a benefit.

The study team at Yale also looked at subgroups of lymphoma patients, and found the strongest link between wine consumption and favorable outcomes among patients with diffuse large B-cell lymphoma. These patients had a 40 to 50 percent reduced risk of death, relapse or secondary cancer.

Researchers then conducted an analysis to examine the effect of wine consumption among those who had drunk wine for at least the previous 25 years before diagnosis. Non-Hodgkin's lymphoma patients who had been drinking wine for at least this long had a 25 to 35 percent reduced risk of death, relapse or secondary cancer.

Those patients with large B-cell lymphoma had about 60 percent reduced risk of death, relapse or secondary cancer if they had been drinking wine for at least the previous 25 years before diagnosis.

"It is clear that lifestyle factors like alcohol can affect outcome," said Han.

Charred meat may increase risk of pancreatic cancer

DENVER – Meat cooked at high temperatures to the point of burning and charring may increase the risk of pancreatic cancer, according to data presented at the American Association for Cancer Research 100th Annual Meeting 2009.

Kristin Anderson, Ph.D., associate professor at the University of Minnesota School of Public Health, said the finding was linked to consumption of well and very well done meats cooked by frying, grilling or barbecuing. Cooking in this way can form carcinogens, which do not form when meat is baked or stewed.

Anderson and colleagues conducted a prospective analysis that included 62,581 participants. "My research has been focused on pancreatic cancer for some time, and we want to identify ways to prevent this cancer because treatments are very limited and the cancer is often rapidly fatal," she said.

Anderson and colleagues used information from surveys that were a part of the PLCO (Prostate, Lung, Colorectal and Ovarian) Multi-center Screening Trial. Participants provided information about their meat intake, preferred cooking methods and doneness preferences.

Over the course of nine years, researchers identified 208 cases of pancreatic cancer. Preferences for high temperature cooked meat were generally linked with an increased risk; subjects who preferred very well done steak were almost 60 percent as likely to get pancreatic cancer as compared to those who ate steak less well done or did not eat steak. When overall consumption and doneness preferences were used to estimate the meat-derived carcinogen intake for subjects, those with highest intake had 70 percent higher risk than those with the lowest intake.

"We cannot say with absolute certainty that the risk is increased due to carcinogens formed in burned meat," said Anderson. "However, those who enjoy either fried or barbecued meat should consider turning down the heat or cutting off burned portions when it's finished; cook meat sufficiently to kill bacteria without excess charring. In addition, the precursors of cancer-causing compounds can be reduced by microwaving the meat for a few minutes and pouring off the juices before cooking it on the grill."

'Fraction cells' found in human brain

FRACTIONS may be written as the ratio of two whole numbers, but that's not how our brains process them. Instead it seems we respond to fractions directly, without processing whole numbers along the way. This suggests that kids, who often dread fractions, could be taught them more intuitively.

Previous tests have shown that specific groups of neurons respond to different whole numbers, with the number one altering the firing patterns of different neurons than the number three. Now Simon Jacob and Andreas Nieder of the University of Tübingen in Germany have shown that we have fraction-specific neurons too.

The pair scanned the brains of adults as they were shown a variety of different fractions - either as numerical ratios or in words. In both cases, specific groups of neurons altered their firing patterns. Crucially, control experiments showed that the volunteers weren't responding first to whole numbers, and then calculating the ratio, but were reacting to the fraction itself (The Journal of Neuroscience, DOI: 10.1523/jneurosci.0651-09.2009).

Fractions tend to be taught as ratios of whole numbers, but Nieder says this may not tap our neural machinery in the most constructive way, making fractions harder to grasp than they need to be.

Power steering for your hearing

Study: Ears have tiny 'flexoelectric' motors to amplify sound

SALT LAKE CITY – Utah and Texas researchers have learned how quiet sounds are magnified by bundles of tiny, hair-like tubes atop "hair cells" in the ear: when the tubes dance back and forth, they act as "flexoelectric motors" that amplify sound mechanically.

"We are reporting discovery of a new nanoscale motor in the ear," says Richard Rabbitt, the study's principal author and a professor and chair of bioengineering at the University of Utah College of Engineering. "The ear has a mechanical amplifier in it that uses electrical power to do mechanical amplification."

"It's like a car's power steering system," he adds. "You turn the wheel and mechanical power is added. Here, the incoming sound is like your hand turning the wheel, but to drive, you need to add power to it. These hair bundles add power to the sound. If you did not have this mechanism, you would need a powerful hearing aid."

The new study is scheduled for publication Wednesday, April 22 in PLoS ONE, a journal published by the Public Library of Science. The first author is Katie Breneman, a bioengineering doctoral student at the University of Utah. The study was coauthored by William Brownell, a professor of otolaryngology (ear, nose and throat medicine) at Baylor College of Medicine in Houston.

The researchers speculate flexoelectrical conversion of electricity into mechanical work also might be involved in processes such as memory formation and food digestion.

Dancing Cells and Hair-like Tubes in Your Ears

Previous research elsewhere indicated that hair cells within the cochlea of the inner ear can "dance" – elongate and contract – to help amplify sounds.

The new study shows sounds also may be amplified by the back-and-forth flexing or "dancing" of "stereocilia," which are the 50 to 300 hair-like nanotubes projecting from the top of each hair cell.

Such flexing converts an electric signal generated by incoming sound into mechanical work – namely, more flexing of the stereocilia – thereby amplifying the sound by what is known as a flexoelectric effect.

"Dancing hairs help you hear," says Breneman. The study "suggests sensory cells in the ear are compelled to move when they hear sounds, just like a music aficionado might dance at a concert. In this case, however, they'll dance in response to sounds as miniscule as the sound of your own blood flow pulsating in your ear."

In a yet-unpublished upcoming study, Rabbitt, Breneman and Brownell find evidence the hair cells themselves – like the stereocilia bundles atop those cells – also amplify sound by getting longer and shorter due to flexoelectricity.

Rabbitt and Brownell estimate the combined flexoelectric amplification – by both hair cells and the hair-like stereocilia atop hair cells – makes it possible for humans to hear the quietest 35 to 40 decibels of their range of hearing. Rabbitt says the flexoelectric amplifiers are needed to hear sounds quieter than the level of comfortable conversation.

"The beauty of the amplifier is that it allows you to hear very quiet sounds," Brownell says. Rabbit says that because hair cells die as people age, older people often "need a hearing aid because amplification by the hair cells is not working."

Because hair-like stereocilia also are involved in our sense of balance, the flexing of stereocilia not only contributes to hearing, but "also likely is involved in our sense of gravity, motion and orientation – all the things needed to have balance," Rabbitt says.

The new study is part of an effort by researchers to understand the amazing sensitivity of human hearing. Rabbitt says the hair cells are so sensitive they can detect sounds almost as small as those caused by Brownian motion, which is the irregular movement of particles suspended in gas or liquid and bombarded by molecules or atoms.

An Amplifier for All Sorts of Ears

Hair cells are inside the inner ears of many animals. They are within the ear's cochlea, which is the spiral, snail-shell-shaped cavity where incoming sound vibrations are converted into nerve impulses and sent to the brain. Incoming sounds must be amplified because incoming sound waves are "damped" by fluid that fills the inner ear.

Hair cells are about 10 microns wide, and 30 to 100 microns long. By comparison, a human hair is roughly 100 microns wide. A micron is one-millionth of a meter. The hair-like stereocilia tubes poking out the top of a hair cell are each a mere 1 to 10 microns long and about 200 nanometers wide, or 200 billionths of a meter wide.

Brownell says the new study shows how the flexoelectric effect "can account for the amplification of sound in the cochlea."

Stereocilia essentially are membranes that have been rolled into tiny tubes, so "the fact that a membrane can generate acoustic [mechanical] energy is novel," says Brownell. "Imagine hearing a soap bubble talk." Flexoelectricity in a membrane was noted a few decades ago when a researcher in Europe showed that flexing or bending a simple membrane in a laboratory generated an electrical field. Then, in 1983, Brownell showed that a hair cell from a guinea pig's ear changed in length when an electric field was applied to it in a lab dish.

The length of stereocilia changes along the coiled length of the cochlea. Different lengths are sensitive to different frequencies of sound. And different animals have different ranges of stereocilia lengths.

Breneman and colleagues devised math formulas and used computer simulations to arrive at the new study's key finding: The flexoelectric amplifier can explain why varying lengths of stereocilia predict which sound frequencies are heard most easily by a variety of animals, from humans to bats, mice, turtles, chickens and lizards. "They found that a longer stereocilium was more efficient if it was receiving low-frequency sounds," while shorter stereocilia most efficiently amplified high-frequency sound, Brownell says.

Breneman says scientists now know of five ways the ears amplify sound, and "what makes this one unique is that it would be present in the stereocilia bundles of all hair cells, not only outer hair cells."

The cochleae of humans and other mammals have "inner hair cells" that sense sound passively and active "outer hair cells" that amplify sounds. Other higher animals have hair cells, without a distinction between inner and outer.

Because the new study shows the dancing hair-like stereocilia act like an amplifier on any hair cell, "it explains how this amplifier may work in all higher animals like birds and reptiles, not just humans," Rabbitt says.

How the Amplifier Works in the Inner Ear – and Perhaps Elsewhere

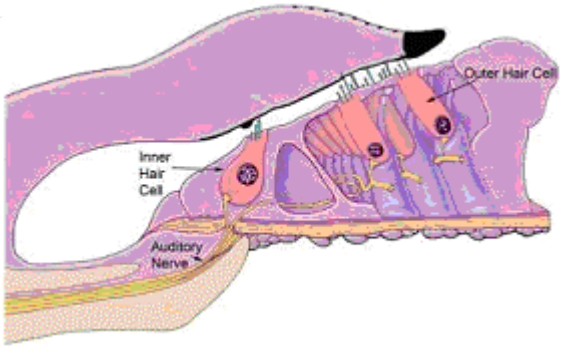
When sound enters the cochlea and reaches the hair cells, sound pressure makes the hair-like stereocilia tubes "pivot left or right similar to the way a signpost bends in heavy wind," Breneman says.

The tops of the tubes are connected to each other by protein filaments. Where each filament comes in contact with the top end of a stereocilium tube, there is an "ion channel" that opens and closes as the bundle of stereocilia sway back and forth.

When the channel opens, electrically charged calcium and potassium ions flow into the tubes. That changes the electric voltage across the membrane encasing each stereocilium making the tubes flex and dance even more.

Such flexoelectricity amplifies the sound and ultimately releases neurotransmitter chemicals from the bottom of the hair cells, sending the sound's nerve signal to the brain, Breneman says.

"We've got these nanotubes – stereocilia – moving left and right and converting electrical power [from ions] into mechanical amplification of sound-induced vibrations in the ear," Rabbitt says. He says the "flexoelectric motor" is the collective movement of the stereocilia in response to sound.



The illustration shows a cross-section of part of the cochlea, the fluid-filled part of the inner ear that converts vibrations from incoming sounds into nerve signals that travel to the brain via the auditory nerve. University of Utah and Baylor College of Medicine researchers found evidence that stereocilia -- bundles of tiny hair-like tubes atop "hair cells" in the cochlea -- dance back and forth to mechanically amplify incoming sounds via what is known as the "flexoelectric effect." **William Brownell, Baylor College of Medicine.**

Brownell says the new study – showing that sound is amplified by "dancing" membrane tubes atop hair cells – adds to growing evidence that membranes do not "just sit there," but instead are "dynamic structures capable of doing work using a mechanism called flexoelectricity."

Brownell and Rabbitt note that stereocilia involved in amplifying hearing have similarities with other tube-like structures in the human body, such as villi in the gut, dendritic spines on the signal-receiving ends of nerve cells and growth cones on the signal-transmitting axon ends of growing nerve cells.

So they speculate flexoelectricity may play a role in how villi in the intestines help absorb food and how nerves grow and repair themselves.

"There is some evidence that dendrites and axons change their diameter during intracellular voltage changes, and that could well have flexoelectric origins," says Rabbitt. "Any time you have a membrane with small diameter – like in axons, dendrites and synaptic vesicles [located between nerve cells], there will be large flexoelectric forces and effects. Therefore, the flexoelectric effect may be at work in things like learning and memory. But that's pretty speculative."

Lip-reading computers can detect different languages

Scientists at the University of East Anglia (UEA) have created lip-reading computers that can distinguish between different languages.

Computers that can read lips are already in development but this is the first time they have been 'taught' to recognise different languages. The discovery could have practical uses for deaf people, for law enforcement agencies, and in noisy environments.

Led by Stephen Cox and Jake Newman of UEA's School of Computing Sciences, the groundbreaking research will be presented at a major conference in Taiwan on Wednesday April 22.

The technology was developed by statistical modelling of the lip motions made by a group of 23 bilingual and trilingual speakers. The system was able to identify which language was spoken by an individual speaker with very high accuracy. These languages included English, French, German, Arabic, Mandarin, Cantonese, Italian, Polish and Russian.

"This is an exciting advance in automatic lip-reading technology and the first scientific confirmation of something we already intuitively suspected -¬ that when people speak different languages, they use different mouth shapes in different sequences," said Prof Cox.

"For example, we found frequent 'lip-rounding' among French speakers and more prominent tongue movements among Arabic speakers."

Funded by the EPSRC, the research is part of a wider UEA project on automatic lip-reading. The next step will be to make the system more robust to an individual's physiology and his or her way of speaking.

The IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP) 2009 takes place at the Taipei International Convention Centre in Taipei, Taiwan from April 19-24. For more details, visit www.icassp09.com.

Evidence mounts that short or poor sleep can lead to increased eating and risk of diabetes

Laboratory and epidemiological studies continue to show that sleep curtailment and/or decreased sleep quality can disturb neuroendocrine control of appetite, leading to overeating, and can decrease insulin and/or increase insulin resistance, both steps on the road to Type 2 diabetes.

On April 22, at the Experimental Biology 2009 meeting in New Orleans, a panel of leading sleep researchers describes recent and new studies in this fast growing field. The session is part of the scientific program of the American Association of Anatomists (AAA).

Short sleep, poor sleep: novel risk factors for obesity and for type 2 diabetes.

Dr. Eve Van Cauter, University of Chicago, is a specialist in the effect of circadian rhythms on the endocrine system and has conducted several studies in which short-term sleep restriction damaged the body's ability to regulate eating by lowering levels of leptin, the hormone that tells the body when it has had enough. In the AAA symposium, Dr. Van Cauter describes other recently published studies from her group, one showing that only three days sleep disruption is sufficient to increase insulin resistance in humans (thus causing the body to need higher levels of insulin) and a large epidemiological study showing that short sleep over a five year period causes an increase in systolic blood pressure.

Dr. Van Cauter also describes work in other laboratories, such as a multi-center study, headed by Dr. Sanjay Patel, Case Western Reserve Medical School, in which thousands of older patients wore wrist monitors 24 hours a day, allowing researchers to objectively document how long and well they slept instead of relying on self reports. Some scientists and clinicians had believed that the relationship of short/poor sleep and obesity was important in children and adults but waned with age. Dr. Van Cauter says this study found that short/poor sleep was associated with obesity regardless of age.

Energy metabolism during chronic sleep deprivation: sleep less, eat more, don't gain weight, yet show signs of progression toward diabetes.

Panel member Dr. Michael Koban, Morgan State University, reports a new study in which sleep restriction in rats led to glucose intolerance, a prediabetic state in which the blood glucose remains higher than normal after glucose challenge. Significantly, this is the first rodent study of sleep deprivation in which there was no association between glucose dysregulation and weight gain.

For 13 days, the rats were kept awake 20 of every 24 hours, then returned to their cages where they could sleep. As in a number of other studies of sleep deprivation or poor sleep in humans and rats, the sleep restricted rats greatly increased their consumption of food, in this case a human food supplement laced with chocolate, which rats love and which allowed for a more precise measure of consumption than rat chow, which often gets strewn around like bird seed in a feeder. Control rats allowed to sleep as much as they wanted also had access to the same treat, but ate less.

Significantly, while the sleep-deprived rats ate substantially more than well-rested rats, they did not gain weight. This was due, says Dr. Koban, to an increase in energy metabolism. The resting metabolism of the sleep-deprived rats rose sharply, coupled with rapid mobilization of hepatic and muscle glycogen followed by reduction in abdominal white adipose tissue.

Further studies are now underway in the Koban laboratory that more closely mimics chronic sleep deprivation in humans. The researchers believe that extending sleep restriction will produce more pronounced glucose intolerance in which glucose levels do not return to normal levels for a longer period, thus providing more evidence that not sleeping enough could lead to diabetes in humans. The researchers also are looking for mechanisms to explain the change in metabolism related to sleep deprivation and the dissociation between weight gain and glucose dysregulation and insulin resistance.

Stress-related behaviors and hormone changes after prolonged sleep deprivation – and environmental factors that appear to modify them

Dr. Deborah Suchecki, Universidade Federal de Sao Paulo, describes how prolonged sleep deprivation activates the neuroendocrine stress response, as measured by increased blood levels of the stress-related hormones adrenaline, adrenocorticotropic hormone (ACTH), and corticosterone. Earlier studies have shown that sleep restriction in animals can gradually change brain and neuroendocrine systems in ways similar to those seen in stress-related disorders such as depression, while epidemiological studies suggest that sleep restriction may be an important risk factor for cardiovascular and other diseases linked to stress.

In the sleep panel at Experimental Biology 2009, Dr. Suchecki reports from two new studies in her laboratory that suggest how environmental factors can modulate the stress response to sleep deprivation. In the first, group support (rats were sleep deprived in groups of 10) reduced both anxiety-like behavior and the blood levels of stress hormones.

In the second, having access to water sweetened with saccharin or sucrose lowered the levels of stress hormones in sleep-deprived animals, although the levels still remained higher than animals with sufficient sleep. Despite the fact that sleep-deprived animals consumed a large amount of the sucrose solution, they still consumed more chow than their control counterparts and lost just as much weight as the water-only group, indicating an intense metabolic change. The reason, discovered Dr. Suchecki, was that insulin levels were

greatly reduced after sleep deprivation and remained low after four days of sleep recovery, whereas corticosterone levels remained high even after the 96 hours of recovery. The loss of body weight appeared related to elevated corticosterone levels. Stimulation of feeding behavior results from, among other factors, increased activity of orexin (hypocretin) neurons in the hypothalamus, the brain center that controls motivated behaviors and the stress response.

CNS changes after chronic sleep deprivation have role in both food intake and metabolism.

Symposium chair Dr. Gloria Hoffman, also of Morgan State University, presents studies that explain the role of the central nervous system pathways in stimulating feeding and causing metabolic changes associated with progression to diabetes. Specifically, increased production of the neurotransmitter neuropeptide Y and decreased production of proopiomelanocortiini products in the hypothalamus explain the hyperphagic response.

Although the CNS's role in regulating metabolic rate is not well understood, she believes that histamine might be involved. Histamine neurons not only affect the maintenance of wakefulness but also are regulators of peripheral metabolism. In sleep deprived rats, elevations in the glucose to insulin ratio were positively correlated with an increase in histamine expression that raises the possibility that a dysregulation of histamine function during impaired sleep might serve to trigger metabolic and other changes leading to diabetes.

The scientists agree that as sleep curtailment becomes more common in industrialized countries it becomes increasingly important to understand how limited or poor quality sleep produces changes that can lead to obesity and diabetes, both epidemic in the developed world. More and more scientists are jumping on board with these lines of investigation, says Dr. Hoffman, and there is an increased demand for information on the part of health professionals and members of the general public, many of whom consider themselves sleep deprived.

Changing the way organ donation requests are made could prevent relatives denying consent

Research: Modifiable factors influencing relatives' decision to offer organ donation: Systematic review

Timing and whether a transplant coordinator makes the request are key factors in whether relatives consent to organ donation, according to a study published on bmj.com today.

Demand for organs far exceeds supply and in the UK this results in one patient on the transplant waiting list dying every day. One of the biggest barriers to increased donor rates is the refusal of consent by relatives.

A recent audit of 341 deaths in intensive care units in the UK revealed that 41% of relatives of potential donors denied consent. In an interview study a third of relatives who had refused donation said that they would not refuse again, whereas only a few of people who had given consent regretted their decision.

Lead author Dr Duncan Young, from John Radcliffe Hospital in Oxford, believes that given the refusal from relatives blocks so many transplants from going ahead, it is important to find out what factors would help them uphold the wishes of their next of kin.

The authors carried out a review of 20 studies on organ donation to investigate what factors either encouraged or discouraged relatives to consent. Two issues had the strongest effect on relatives: timing and the person making request. It is essential that a request for organ donation does not take place when notification of death is communicated to relatives or when brain stem death testing takes place – it is very important that there is a gap between 'bad news' and a request for donation, say the authors.

The person making the request is also key and the study concludes that in an ideal situation a donor transplant coordinator together with hospital staff would make the request.

The following issues were also significantly linked to relatives denying or allowing donation to go ahead: the level of information they were given, how they perceived the quality of care given to their loved one, understanding what brain stem death actually means, the setting for the request (a private location is best), the approach and expertise of the individual and giving families enough time to consider the request.

The authors conclude that although their findings may be "unsurprising," implementing them may increase donation rates and ultimately save lives. They argue that "organ donation may be of sufficient benefit to society generally, and to organ recipients specifically, to justify the study and modification of organ donation requests to maximize consent."

In an accompanying editorial, Teresa Shafer from the LifeGift Organ Donation Center in Texas, says that requesting consent for donation is not simply "popping the question" but rather "a dynamic process consisting of observation, collaboration, planning, and action that is based on family and hospital dynamics."

She argues that hospitals and organ procurement organisations need to work together to increase the number of organs available and that "the donation request is too important to delegate to those who are not expert, prepared and focused on a successful outcome."

Mayo Clinic researchers find agents that speed up destruction of proteins linked to Alzheimer's

JACKSONVILLE, Fla. — Taking a new approach to the treatment and prevention of Alzheimer's disease, a research team led by investigators at the Mayo Clinic campus in Florida has shown that druglike compounds can speed up destruction of the amyloid beta (A-beta) proteins that form plaque in the brains of patients with the disorder.

Researchers say their study, published in the April 22 online issue of PLoS ONE, demonstrates that this strategy is a viable and exciting alternative to the approach most drug designers have taken to date.

"Historically, a lot of effort has been made at stopping initial production of A-beta in order to halt development of Alzheimer's disease, but we are interested in what happens to A-beta after it is produced," says the study's lead researcher, Malcolm Leissring, Ph.D., from Mayo's Department of Neuroscience.

The researchers found two chemicals that could speed up activity of a molecule, insulin-degrading enzyme (IDE), which helps chew up A-beta proteins produced in the brain.

In laboratory experiments, they found that one agent, dubbed Ia1, increased the activity of IDE by about 700 percent, while the second compound, Ia2, increased it by almost 400 percent.

"This study describes the first examples of synthetic small-molecule activators of IDE, showing that activation of this important enzyme with druglike compounds is achievable," Dr. Leissring says.

"If it is possible to generate drugs for human use that stimulate the activity of IDE, these agents might offer therapeutic benefit for treating and preventing Alzheimer's disease," he says.

Since IDE also chews up excess insulin in the body, the role for which it is primarily known, small molecule activators might also be useful in controlling diabetes, he says.

A-beta is produced when a larger protein, known as the amyloid precursor protein (APP), is cut into smaller pieces by other enzymes known as beta-secretase and gamma-secretase.

Not much is known about what happens to A-beta after it is produced, says Dr. Leissring. What is known is that A-beta proteins, especially those of a certain length, are found sticking to each other in clumps of plaque in the brains of patients with Alzheimer's disease. Because of this, drug designers have taken the tack of trying to inhibit the cutting of APP by beta-secretase and gamma-secretase, reasoning that if A-beta isn't produced, plaques won't form. But, to date, this and other approaches have not yet resulted in clearly beneficial therapies. This group of researchers is focused, instead, on what ultimately happens to A-beta produced in a normal brain, and have found that, surprisingly, more than 99 percent of all A-beta is destroyed immediately, Dr. Leissring says. "Normally, there is a balance between production and elimination of A-beta in the brain," he says. "We don't know why that balance is skewed in individuals that develop Alzheimer's disease, but one hypothesis is that, as we age, activity of the enzymes that destroy A-beta goes down."

IDE was the first degrading enzyme, or protease, implicated in this imbalance, Dr. Leissring says. The enzyme is shaped like a clamshell that opens and shuts, like the well-known video game protagonist, Pac-Man, he says. A-beta fits inside the open enzyme, which then closes and gobbles up the protein inside.

In this study, the research team screened tens of thousands of chemicals looking for ones that could bind to IDE and modulate its activity. That led to discovery and testing of Ia1 and Ia2.

Dr. Leissring says that the findings don't suggest that these compounds should be tested in humans. Rather, he says they have shown that activating IDE in a test tube is possible and that further work is needed on this new approach.

“The story that is emerging now is that the level of activity of A-beta degrading enzymes may play a significant role in the development of Alzheimer's disease," he says. "We are actively pursuing the next chapter."

The study was funded by grants from the National Institutes of Health. The first author of the study, Christelle Cabrol, participated as a summer intern at Mayo Clinic Florida, from the University of Paris. Her internship was supported by a donation from The Unforgettable Fund, a Florida charity.

Co-authors of the study include researchers at The Scripps Research Institute and Harvard Medical School. Dr. Leissring conducted research at those institutions before joining Mayo Clinic in 2007.

Increasing levels of rare element found worldwide

Dartmouth researchers link it to catalytic converters

HANOVER, NH – Dartmouth researchers have determined that the presence of the rare element osmium is on the rise globally. They trace this increase to the consumption of refined platinum, the primary ingredient in catalytic converters, the equipment commonly installed in cars to reduce smog. A volatile form of osmium is generated during platinum refinement and also during the normal operation of cars, and it gets dispersed globally through the atmosphere.

While osmium is found naturally, the researchers were surprised to discover that most of the osmium in rain and snow, and in the surface waters of rivers and oceans, is produced during the refining of platinum. "It's

interesting, maybe ironic, that we stopped adding lead to gasoline in the 70s so that catalytic converters could be introduced to remove smog from car exhaust," says Dartmouth Associate Professor of Earth Sciences Mukul Sharma. "Now we learn that using platinum in the converters is responsible for an increase in osmium. Fortunately, unlike lead, the concentration of osmium in water is extremely small and may not adversely affect biology."

Sharma worked with Dartmouth Ph.D. student Cynthia Chen and Peter Sedwick at Old Dominion University. Their study will be published in the online edition of the Proceedings of the National Academy of Sciences during the week of April 20, 2009.

The research team measured osmium in precipitation in North America, Europe, Asia, and Antarctica, and in both surface water and deep water from the North Atlantic, Pacific, Indian, and Antarctic (or Southern) Oceans. Human-made osmium also comes from chromium smelters, hospital incinerators, and the normal operation of cars, but it's primarily the industrial extraction and refining of platinum that produces the bulk of the osmium found in rain and snow.

Sharma explains that about 95 percent of the world's platinum comes from South Africa and Russia where it is roasted at extremely high temperatures during the extraction and refinement process. The process removes sulfur present in the ore as sulfur dioxide and, at the same time, releases osmium, which is abundant in the ore.

"Neither South Africa nor Russia has implemented environmental laws regulating this, but if steps are taken to minimize these emissions, the incidence of osmium will certainly subside," says Sharma. "It's surprising that we are seeing this measurable increase in osmium on a global scale, and we can virtually blame it on one thing: our insatiable demand for platinum-based catalytic converters."

Think memory worsens with age? Then yours probably will

Thinking your memory will get worse as you get older may actually be a self-fulfilling prophecy. Researchers at North Carolina State University have found that senior citizens who think older people should perform poorly on tests of memory actually score much worse than seniors who do not buy in to negative stereotypes about aging and memory loss.

In a study published earlier this month, psychology professor Dr. Tom Hess and a team of researchers from NC State show that older adults' ability to remember suffers when negative stereotypes are "activated" in a given situation. "For example, older adults will perform more poorly on a memory test if they are told that older folks do poorly on that particular type of memory test," Hess says. Memory also suffers if senior citizens believe they are being "stigmatized," meaning that others are looking down on them because of their age.

"Such situations may be a part of older adults' everyday experience," Hess says, "such as being concerned about what others think of them at work having a negative effect on their performance – and thus potentially reinforcing the negative stereotypes." However, Hess adds, "The positive flip side of this is that those who do not feel stigmatized, or those in situations where more positive views of aging are activated, exhibit significantly higher levels of memory performance." In other words, if you are confident that aging will not ravage your memory, you are more likely to perform well on memory-related tasks.

The study also found a couple of factors that influenced the extent to which negative stereotypes influence older adults. For example, the researchers found that adults between the ages of 60 and 70 suffered more when these negative stereotypes were activated than seniors who were between the ages of 71 and 82. However, the 71-82 age group performed worse when they felt stigmatized.

Finally, the study found that negative effects were strongest for those older adults with the highest levels of education. "We interpret this as being consistent with the idea that those who value their ability to remember things most are the most likely to be sensitive to the negative implications of stereotypes, and thus are most likely to exhibit the problems associated with the stereotype."

"The take-home message," Hess says, "is that social factors may have a negative effect on older adults' memory performance."

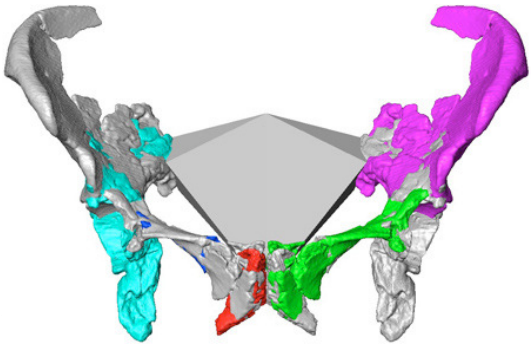
Hess is the lead author on the study, "Moderators of and Mechanisms Underlying Stereotype Threat Effects on Older Adults' Memory Performance." Co-authors on the study are former NC State students Joey T. Hinson and Elizabeth A. Hodges. The study was published online April 1 by Experimental Aging Research.

Neandertals Babies Didn't Do the Twist

By Ann Gibbons ScienceNOW Daily News

Giving birth is more difficult--and dangerous--for modern humans than for any other primate. Not only do human mothers have to push out babies with unusually big heads, but infants also have to rotate to fit their heads through the narrow birth canal. Now, a new virtual reconstruction of the pelvis of a Neandertal woman suggests that Neandertal mothers also had a tough time giving birth to their big-headed infants--but the babies, at least, didn't have to rotate to get out.

Once upon a time, a major shift took place in the evolution of childbirth. Fossil female pelvises of a 1.2-million-year-old Homo erectus, a 3.1-million-year-old australopithecine, and a 500,000-year-old archaic modern human all contain oval birth canals that are widest transversely--from side to side--when viewed from the top. But modern women's birth canals, though also oval, change shape halfway down the birth canal so that they are widest from front to back at the bottom, near the pelvic outlet. This means that the baby has to rotate its head to fit as it moves through the birth canal. If a baby fails to rotate, another part of its body, such as its shoulders, hands, or feet, may obstruct the birth canal which is painful and dangerous for the mother and infant.



Twist and shout. This virtual reconstruction of a Neandertal pelvis suggests that Neandertal babies didn't rotate during birth. **Timothy Weaver and Jean-Jacques Hublin**

Like many other researchers, paleoanthropologist Timothy Weaver of the University of California, Davis, thought the shift to this more complicated rotational birth predated the split between modern humans and Neandertals. That's because Neandertals, which lived until 30,000 years ago in Europe, also had big heads and, presumably, used the same evolutionary strategy to deliver their big-brained babies. But it has been difficult to test this idea. The only known female pelvis of a Neandertal, discovered in 1929 near Tabun, Israel, is fragmentary. Two earlier reconstructions of this partial pelvis suggested that Neandertals also had rotational birth, but the fossil is missing its sacrum and, hence, the birth canal.

Now, new tools have given Weaver a way to work around that problem. Collaborating with Jean-Jacques Hublin at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, Weaver got permission to make computed tomography-scans of the pelvis, which is kept at the British Museum in London. The two researchers were able to refit the pieces of the pubis, ischium, and ilium together in a three-dimensional, virtual reconstruction. They also used landmarks on the pelvic fragments to compare the pelvis to those of modern humans - and to predict the size and shape of the missing pieces, such as the sacrum and dimensions of the pelvic outlet.

The reconstruction suggests that the pelvis of the Tabun Neandertal was widest from side to side all the way down the birth canal, more like that of Homo erectus or australopithecines than modern humans. And that means that although Neandertal mothers still had difficult births because of their babies' large heads, their babies did not rotate in the womb, the team reports online today in the Proceedings of the National Academy of Sciences.

So why would our ancestors evolve such a complicated birth in the first place? Other research shows that they had to balance pressures to adapt to the hot climate in equatorial Africa--and tall, slender-hipped humans thermoregulate in the heat better than short, stocky humans (whose physiology retains heat better in the frigid latitudes). By evolving a birth canal that is wide front to back, our ancestors were able to accommodate both narrower pelvises and the delivery of big-brained babies, suggests Weaver.

But it will take more than a virtual pelvis to convince other researchers. "I don't know if I believe the reconstruction," says paleoanthropologist Karen Rosenberg of the University of Delaware, Newark. She and others have questions about the accuracy of the reconstruction of the missing parts of the pelvis, which are critical for proving there was no rotation. "Given the poor preservation of the Tabun pelvis, ... this is a bold claim," says anthropologist Marcia Ponce de León of the University of Zurich in Switzerland. She does agree, however, with one conclusion: "Birth was equally difficult in Neandertals as in modern humans," with or without a twist.

Straw house beats the shakes in earthquake test

* 22 April 2009 **by Jeff Hecht**

CHEAP houses built from straw bales could dramatically improve building safety in earthquake zones. That's the conclusion from tests in the US in which a simple straw bale house withstood shaking equivalent to a major earthquake.

Originally developed a century ago in Nebraska, homes with straw-bale walls are enjoying a revival in the US and Europe because they use green materials and provide excellent insulation. But the technology could also provide protection in quakes.

Civil engineer Darcey Donovan was designing straw-bale houses in Truckee, California, when she heard of the quake that had just killed more than 75,000 people in the Kashmir region of northern Pakistan in October 2005. Most died when their homes collapsed. She volunteered to help with the recovery, and in May 2006 spent a month in the devastated area building a women's community centre made of straw bales. She was struck by

the number of people who were homeless or living in tents yet who were afraid to return to or rebuild traditional stone-and-mud homes. "I had helped build one building, but I needed to do more," she says.

Realising that straw-bale houses might help, Donovan came up with a design that could be built cheaply with local materials. The foundations are made with sacks of gravel, while the building's base uses clay and sand mixed with cement. Straw bales form the walls, which can then be covered with a plaster made from clay, sand and chopped straw. The roof is made of corrugated sheet metal. In western designs, the bales serve as insulation while a wooden frame supports the load, but Donovan was able to use the straw walls for structural support by keeping the houses to a single storey. Not only are the buildings sturdier than stone, they are much lighter, so a collapse is less likely to kill anyone inside.

Donovan has since founded the Pakistan Straw Bale and Appropriate Building organisation to promote the idea. PAKSBAB has already helped local workers build nine homes in Kashmir, all of which are now occupied.

To test how the houses would fare in an earthquake, Donovan built one on a quake simulation table at the University of Nevada in Reno. In tests late last month, it stood through a series of eight quakes of increasing intensity. The plaster cracked and flakes crumbled off in the final run, when the accelerations reached 0.82 times the force of gravity - stronger than the 7.6-magnitude Kashmir quake - but the house survived.
In the final test, which was stronger than the Kashmir quake, the plaster cracked but the house survived

"The structure did exceptionally well," says Ian Buckle, who runs the Reno test lab. Given refinements to speed up construction, he thinks the design has a great future in quake zones around the world.

'Missing link' fossil seal walked

By Richard Black Environment correspondent, BBC News website

Reconstructing the skeleton of the "walking seal"

It may look like a cross between a seal and an otter; but an Arctic fossil could, scientists say, hold the secret of seal evolution in its feet. A skeleton unearthed in northern Canada shows a creature with feet that were probably webbed, but were not flippers.

Writing in the journal Nature, scientists suggest the 23 million-year-old proto-seal would have walked on land and swum in fresh water. It is the oldest seal ancestor found so far and has been named Puijila darwini.

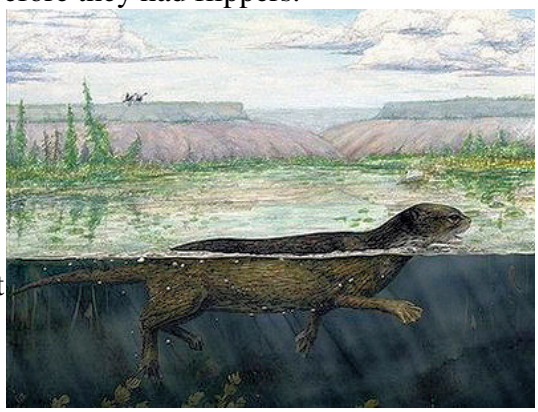
Pujilla is the term for "young sea mammal" in the Inuktitut language, spoken by Inuit groups in Devon Island where the fossil was found.

And the reference to Charles Darwin honours the famous biologist's contention that land mammals would naturally move into the marine environment via a fresh water stage, just as pinnipeds - seals, sealions and walruses - have apparently done.

"The find suggests that pinnipeds went through a fresh water phase in their evolution," said Natalia Rybczynski from the Canadian Museum of Nature (CMN) in Ottawa, who led the fieldwork.

"It also provides us with a glimpse of what pinnipeds looked like before they had flippers."

Flip side



The skeleton was about 65% complete, which enabled the researchers to reconstruct what the animal would have looked like in remarkable detail.

The legs suggest it would have walked upright on land; but the foot bones hint strongly at webbed feet. The fact that the remains were found in a former crater lake that has also yielded fossil fish from the same period was additional evidence for a semi-aquatic past.

"The remarkably preserved skeleton of Puijila had heavy limbs, indicative of well developed muscles, and flattened phalanges (finger or toe bones) which suggest that the feet were webbed - but not flippers," said Mary Dawson from the Carnegie Museum of Natural History in Pittsburgh, US, another of the scientists involved. This animal was likely adept at both swimming and walking on land. Puijila is the evolutionary evidence we have been lacking for so long."

Until now, the most primitive fossil pinniped was a creature called Enaliarctos that dates from about the same period and appears to have lived in the sea along the northwestern coasts of North America.

Enaliarctos had flippers, but may have had to bring its prey to the shore for eating, whereas modern pinnipeds manage it at sea.

Intriguingly, different species of present-day seal swim in different ways - either rotating their flippers, or waving their hind-quarters from side to side, using the hind limbs for propulsion.

Enaliarctos appears to have been capable of both modes of swimming - and as a four-legged animal with four webbed feet, Puijila is a logical fore-runner of this creature which could swim with all four limbs.

The new discovery also shows, the scientists say, that seals, sealions and walruses very likely had their origins in the Arctic.

Darwin forecast the transition from land to sea via fresh water in his seminal work On the Origin of Species, published 150 years ago this year. "A strictly terrestrial animal, by occasionally hunting for food in shallow water, then in streams or lakes, might at last be converted in an animal so thoroughly aquatic as to brave the open ocean," he wrote.

Pain relievers ibuprofen and naproxen may delay -- not prevent -- Alzheimer's disease

ST. PAUL, Minn. – A new study shows that nonsteroidal anti-inflammatory drugs (NSAIDs) such as the pain relievers ibuprofen and naproxen do not prevent Alzheimer's disease, but they may instead delay its onset. The study suggests a need for re-interpretation of earlier findings that suggested NSAIDs can prevent the disease. The research is published in the April 22, 2009, online issue of Neurology®, the medical journal of the American Academy of Neurology.

Researchers identified 2,736 members of Group Health, an integrated healthcare delivery system, who did not have dementia when they enrolled in the study at an average age of 75. The investigators followed these people for 12 years to see if they developed Alzheimer's or dementia. They checked Group Health pharmacy records for NSAID prescriptions and also asked participants about their use of NSAIDs.

Of the participants, 351 people had a history of heavy use of NSAIDs at the start of the study, and another 107 people became heavy NSAID users during the follow-up period. Heavy use was defined as having prescriptions for NSAIDs 68 percent of the time or more over a two-year period.

During the study, 476 people developed Alzheimer's disease or dementia. The risk of developing dementia among heavy NSAID users was 66 percent higher than among people with little or no NSAID use.

"A key difference between this study and most of those done earlier is that our participants were older," said study author John C. S. Breitner, MD, MPH, of the Department of Veterans Affairs and the University of Washington School of Medicine in Seattle. "It has been argued for some time that NSAID use delays the onset of Alzheimer's disease. It would follow that studies looking at younger people who use NSAIDs would show fewer cases of Alzheimer's, while in groups of older people there might be more cases, including those that would have occurred earlier if they had not been delayed."

"This is one interpretation of the results, but other explanations are possible," cautioned Breitner, who added, "We must not ignore the fundamental finding, which is an increase in the risk of dementia in the NSAID users. We need further research to understand that result more clearly."

The study was supported by the U.S. Department of Veterans Affairs, the National Institutes of Health, and the Paul B. Beeson Career Development Awards in Aging Research Program.

New study shows chewing gum can lead to better academic performance in teenagers

Higher math scores seen in classroom setting

WHAT: New research from Baylor College of Medicine indicates a positive effect of chewing gum on academic performance in teenagers.[i] The study examined whether chewing Wrigley sugar-free gum can lead to better academic performance in a "real life" classroom setting. Major findings include:

* The researchers found that students who chewed gum **showed an increase in standardized math test scores and their final grades were better** compared to those who didn't chew gum.

* Students who chewed gum had a significantly greater increase in their standardized math test scores after 14 weeks of chewing gum in math class and while doing homework compared to those who did not chew gum. Chewing gum was associated with a three percent increase in standardized math test scores, a small but statistically significant change.

* Students who chewed gum had final grades that were significantly better than those who didn't chew gum.

Today's competitive testing environment has parents and students looking for approaches to improve academic performance, particularly as standardized test scores have become a mandatory requirement for assessing academic achievement. Together, these findings can be meaningful when related to small steps that can lead to better academic performance.

Previous research conducted in a laboratory setting has shown that gum chewing can help reduce stress, improve alertness and relieve anxiety. The current study builds on this previous research and for the first time, provides a possible role for chewing gum in helping to improve academic performance in a "real life" classroom setting. A Research Summary with additional information on methodology is available upon request.

[i] *Johnston C A, Tyler C, Stansberry SA, Palcic JL, Foreyt JP: Gum chewing affects academic performance in adolescents. ASN Scientific Sessions and Annual Meeting at Experimental Biology 2009, "Late breaking abstract" New Orleans, LA, April 2009.*

Double-lung transplants work better than single for long-term survival

Immune system matching and college education also important

Having both lungs replaced instead of just one is the single most important feature determining who lives longest after having a lung transplant, more than doubling an organ recipient's chances of extending their life by over a decade, a study by a team of transplant surgeons at Johns Hopkins shows.

The finding is potentially controversial, researchers say, because there is already a shortage of organ donors, and more widespread use of bilateral lung transplants could nearly halve the potential number of beneficiaries. Though more than 1,400 lung transplants occurred in the United States in 2008, another 2,000 Americans remain on lung waiting lists, while 80 more are waiting for both a heart and lung.

"Our results suggest that double-lung transplants have a long-term advantage, and surgeons should consider bilateral lung transplants whenever possible," says study senior investigator and transplant surgeon Ashish Shah, M.D. But, he notes, "Not all lung recipients necessarily need a bilateral transplant. Many people with chronic obstructive pulmonary disease, including emphysema and different kinds of pulmonary fibrosis, can survive with just one lung being replaced, while other lung diseases, such as cystic fibrosis, usually require transplantation of both lungs. But double-lung transplants clearly perform better over time.

"What we're really after here is to find as many factors as possible that support long-term survival, so that we maximize the gains in average lifespan for all our patients," says Shah. Among the team's other key findings, to be presented April 22 in Paris at the 29th annual meeting of the International Society for Heart & Lung Transplantation, are that a perfect or near perfect match between the donor's immune-activating protein antigens with a recipient's and having a college education increases chances for long-term survival by 38 percent and 40 percent, respectively.

The study, believed to be the most widespread search ever conducted for factors that may extend the life of lung transplant recipients, are among the first to emerge from an analysis of 836 so-called long-term survivors of lung transplants, men and women who have lived at least a decade after transplant surgery between 1987 and 1997, an extended period for which detailed medical histories are now available.

Seventeen percent of all lung transplant recipients survive this long or longer with their new lungs, a figure that Shah, an associate professor at the Johns Hopkins University School of Medicine and its Heart and Vascular Institute, says is "pretty good, but not good enough" and the result of advances made in the last two decades with immune-suppressing drugs that prevent the recipient's body from rejecting the transplant. "Until now, we knew how best to ensure that transplant recipients survive for the first few months after surgery, avoiding infection of the transplanted lung, and then staying healthy for the next two years to five years. But we never really knew what factors distinguished the long-term survivors from those who succumbed earlier, to either organ rejection or death," says Shah, who has performed over 100 lung transplants in the past decade.

Lead study investigator Eric Weiss, M.D., says that a patient's education, though key, is more likely a cover or surrogate, masking some other factor or combination of factors that are accounting for the increased longevity. Possible explanations, he says, are that better educated people may have better health insurance and access to care than those with less formal schooling, or that people with degrees are better at keeping their physician appointments on schedule, taking their medications as prescribed and sooner alerting their physicians to problems.

"Our results are a reminder to both patients and physicians that we still have a lot to learn about how best to prolong lung transplant survival, and that we need to be constantly evaluating our procedures to determine what is in the patient's best, long-term interests," says Weiss, a postdoctoral research fellow in cardiac surgery at Hopkins.

Indeed, he points out that a key advantage in double-lung transplants over single-lung transplants is that residual disease is not left behind in the spared lung. Moreover, when both lungs are replaced, the new lungs, which must breathe together as a pair, are already adapted to each other.

The vast majority of the lung transplants performed by Shah's team at The Johns Hopkins Hospital involve the fully paired organs, including 15 of 17 in 2008, 20 of 22 in 2007 and 20 of 23 in 2006.

In the latest study, long-term survival for lung recipients was also upped when they had "highly compatible" immune systems with their donor, with at least five of six so-called human leukocyte antigens (or HLA) the same as the donors. HLA antigens are proteins that sit on the cell surface and act like a secret passcode among the body's cells, triggering the body's immune system to reject anything that's not recognizable as its own. The better the match, Weiss says, the better are chances for immunosuppressive drugs to work over the long term at preventing organ rejection.

The study analysis involved a detailed review of the patient records for all single-lung and double-lung transplants performed in the United States and Canada from 1987 to 1997. The data came from the United Network for Organ Sharing (UNOS), a national network that allocates donated organs across the country.

Weiss says the team next plans to evaluate what aspects of education make the difference in long-term survival, with the goal of identifying independent factors that can influence better adherence to drug treatment plans or that could potentially be altered in people to extend the amount of time they can potentially live with their new organ.

Funding for the study was supplied in part by the U.S. Health Resources and Services Administration, the U.S. National Institutes of Health, and the Joyce Koons Family Fund for Cardiac Surgery Research.

In addition to Shah and Weiss, other Johns Hopkins researchers involved in this study were Jeremiah G. Allen, M.D.; Christian Merlo, M.D., M.P.H.; and John Conte, M.D.

(Presentation title: Factors indicative of long-term survival after lung transplantation, a review of 890 10-year survivors.)

Self-healing concrete for safer, more durable infrastructure

ANN ARBOR, Mich.— A concrete material developed at the University of Michigan can heal itself when it cracks. No human intervention is necessary—just water and carbon dioxide.

A handful of drizzly days would be enough to mend a damaged bridge made of the new substance. Self-healing is possible because the material is designed to bend and crack in narrow hairlines rather than break and split in wide gaps, as traditional concrete behaves.

"It's like if you get a small cut on your hand, your body can heal itself. But if you have a large wound, your body needs help. You might need stitches. We've created a material with such tiny crack widths that it takes care of the healing by itself. Even if you overload it, the cracks stay small," said Victor Li, the E. Benjamin Wylie Collegiate Professor of Civil Engineering and a professor of Materials Science and Engineering.

A paper about the material is published online in Cement and Concrete Research. It will be printed in a forthcoming edition of the journal.

In Li's lab, self-healed specimens recovered most if not all of their original strength after researchers subjected them to a 3 percent tensile strain. That means they stretched the specimens to 3 percent beyond their initial size. It's the equivalent of stretching a 100-foot piece an extra three feet—enough strain to severely deform metal or catastrophically fracture traditional concrete.

"We found, to our happy surprise, that when we load it again after it heals, it behaves just like new, with practically the same stiffness and strength," Li said. "Self-healing of crack damage recovers any stiffness lost when the material was damaged and returns it to its pristine state. The material can be damaged and still remain safe to load."

The engineers found that cracks must be kept below 150 micrometers, and preferably below 50, for full healing. To accomplish this, Li and his team improved the bendable engineered cement composite, or ECC, they've been developing for the past 15 years.

More flexible than traditional concrete, ECC acts more like metal than glass. Traditional concrete is considered a ceramic. Brittle and rigid, it can suffer catastrophic failure when strained in an earthquake or by routine overuse, Li said. But flexible ECC bends without breaking. It is studded with specially-coated reinforcing fibers that hold it together. ECC remains intact and safe to use at tensile strains up to 5 percent. Traditional concrete fractures and can't carry a load at .01 percent tensile strain.

The average crack width in Li's self-healing concrete is below 60 micrometers. That's about half the width of a human hair. His recipe ensures that extra dry cement in the concrete exposed on the crack surfaces can react with water and carbon dioxide to heal and form a thin white scar of calcium carbonate. Calcium carbonate is a strong compound found naturally in seashells. In the lab, the material requires between one and five cycles of wetting and drying to heal.

Self-healing concrete works because it can bend. When it's strained, many microcracks form instead of one large crack that causes it to fail. Here, a specimen is bending as a force of five percent tensile strain is being applied. Regular concrete would fail at .01 percent tensile strain. **Video Here**

To test the healed concrete, the researchers used resonant frequency measurements to determine the stiffness and strength before and after inducing the cracks. These tests send sound waves through the material to detect changes in its structure.

Today, builders reinforce concrete structures with steel bars to keep cracks as small as possible. But they're not small enough to heal, so water and deicing salts can penetrate to the steel, causing corrosion that further

weakens the structure. Li's self-healing concrete needs no steel reinforcement to keep crack width tight, so it eliminates corrosion.

The professor says this new substance could make infrastructure safer and more durable. By reversing the typical deterioration process, the concrete could reduce the cost and environmental impacts of making new structures. And repairs would last longer. The American Society of Civil Engineers recently gave the country's roads, bridges, water systems and other infrastructure a "D" grade for health. The federal stimulus package includes more than $100 billion for public works projects.

"Our hope is that when we rebuild our roads and bridges, we do it right, so that this transportation infrastructure does not have to undergo the expensive repair and rebuilding process again in another five to 10 years," Li said. "Also, rebuilding with self-healing bendable concrete would allow a more harmonious relationship between the built and natural environments by reducing the energy and carbon footprints of these infrastructure. As civil and environmental engineers, we are stewards of these mega-systems. Advanced materials technology is one means to keep them healthy."

The paper is called "Autogenous healing of engineered cementitous composites under wet-dry cycles." This research is funded by the National Science Foundation and a China National Scholarship. Li will give a keynote address on self-healing concrete at the International Conference on Self-Healing Materials in Chicago in June 2009. The University is pursuing patent protection for the intellectual property, and is seeking commercialization partners to help bring the technology to market.

Scholars at odds over mysterious Indus script

* 19:00 23 April 2009 **by Ewen Callaway**

An as yet undeciphered script found on relics from the Indus valley constitutes a genuine written language, a new mathematical analysis suggests.

The finding is the latest chapter in a bitter dispute over the interpretation of "Indus script". This is the name given to a collection of symbols found on artefacts from the Indus valley civilisation, which flourished in what is now eastern Pakistan and western India between 2500 and 1900 BC. In 2002, a team of linguists and historians argued that the script did not represent language at all, but religious or political imagery.

Ordered or random?

From an analysis of the frequency and distribution of the script's characters, the team concluded that it showed few of the hallmarks of language. Most of the inscriptions contain fewer than five characters, few of the characters repeat, and many of the symbols occur very infrequently.

Examples of the Indus script. The four square artifacts with animal and human iconography are stamp seals that measure one or two inches per side. On the top right are three elongated seals that have no iconography, as well as three miniature tablets (one twisted). The tablets measure about 1.25" long by 0.5" wide. J. M. Kenoyer / Harappa.com

The new analysis by computer scientist Rajesh Rao and his team at the University of Washington in Seattle comes to the opposite conclusion.

Rao's team assessed the script samples using what is called "conditional entropy". When aimed at language, this statistical technique comes up with a measure for the "orderedness" of words, letters or characters – from totally ordered to utterly random.

"If you look at strings that contain words, then you should see that for any particular word in the string there is going to be some amount of flexibility in choosing the next word, but they're not randomly ordered," Rao says.

Which word next?

For instance, in English text, if you find the fragment "The boy went to the", there is some flexibility in what follows. Nouns like "park" and "circus" make sense, but a verb such as "eat" does not.

Rao's team applied this analysis to Indus script, Sanskrit, an ancient south Indian language called Old Tamil, and English. They also tested the conditional entropy of the Fortran computer programming language and non-languages, including DNA and protein sequences.

Indus script characters turned out to be about as randomly ordered as the other languages. Unsurprisingly, they proved less random than DNA or protein sequences and more random than the computer language, where unambiguity is essential.

Grammatical structure

"Now we can say, based on this evidence, that they probably were literate, so the big question becomes: Can you get at the underlying grammar?" Rao says. He hopes to refine his team's technique to determine the grammatical structure of Indus script and, potentially, the language family it belongs to.

"I think we are going to need more archival data, and if we are lucky enough we might stumble on a Rosetta Stone-like artefact," Rao says.

Rao's paper has already drawn a strong response from the researchers who proposed that Indus script represents religious and political symbols, not language.

"There's zero chance the Indus valley is literate. Zero," says Steve Farmer, an independent scholar in Palo Alto, California who authored a 2004 paper with two academics with the goading title "The Collapse of the Indus Script Thesis: The myth of a literate Harappan civilization."

Simulated language

As well as comparing the conditional entropy of Indus script to that of known languages, they compared it with two simulated character sets – one totally random, one totally ordered.

Farmer and colleagues Michael Witzel of Harvard University and Richard Sproat of Oregon Health and Sciences University in Portland contend that the comparison with artificially created data sets is meaningless, as are the resulting conclusions. "As they say: garbage in, garbage out," Witzel says.

Unlocking history

Farmer says that the debate over Indus script is more than academic chest thumping. If Indus script is not a language, a close analysis of its symbols could offer unique insight into the Indus Valley civilisation. Some symbols are more common in some geographical locations than others, and symbol usage seems to have changed over time. "You suddenly have a new key for unlocking how that civilisation functioned and what its history was like," he says.

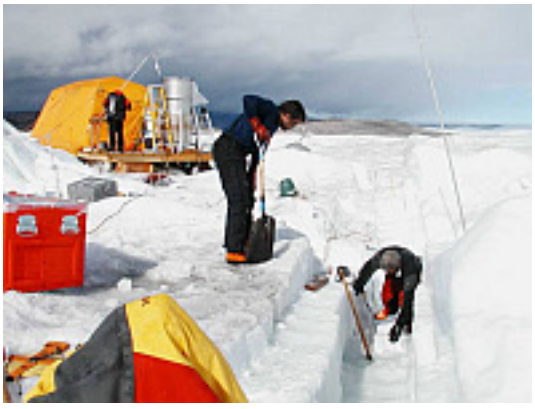
J. Mark Kenoyer, a linguist at the University of Wisconsin-Madison, says Rao's paper is worth publishing, but time will tell if the technique sheds light on the nature of Indus script.

"At present they are lumping more than 700 years of writing into one data set," he says. "I am actually going to be working with them on the revised analysis, and we will see how similar or different it is from the current results." Journal reference: Science, DOI: 10.1126/science.1170391 (in press)

Study rules out ancient bursts of seafloor methane emissions

CORVALLIS, Ore. – Measurements made from the largest Greenland ice sample ever analyzed have confirmed that an unusual rise in atmospheric methane levels about 12,000 years ago was not the result of a catastrophic release of seafloor "hydrate deposits," as some scientists had feared.

The findings, to be published Friday in the journal Science, are good news for those who have worried that this unusual mechanism of releasing methane into the atmosphere might provide a serious reinforcement to global warming at some point in the future. The five-year project was funded by the National Science Foundation, American Chemical Society and other agencies.



It now appears almost certain that the major methane increases that occurred near the end of the last Ice Age were due to the growth of wetlands and the methane releases associated with that, which occurred shortly after some significant warming in the Northern Hemisphere. They did not come from sudden bursts of methane trapped in deep seafloor deposits.

Researchers from OSU and other institutions did field work in the summer of 2003 at Pakitsoq, on the west side of the Greenland ice sheet

The newest conclusions were made possible by identification of some ancient ice exposed at the edge of a Greenland ice sheet, and samples of it cut with chain saws that totaled thousands of pounds.

"To get enough air trapped in ice to do the types of measurements we needed, it took some of the largest ice samples ever worked on," said Edward Brook, a professor of geosciences at Oregon State University, and international expert on using ice samples to explore ancient climate.

"The test results were unequivocal, but it was a lot of heavy lifting," Brook said. "It was like working in a quarry. We could have used some help from the OSU football team."

Methane, and the possible sources of it, is a significant concern to scientists because it is a potent greenhouse gas. It has natural sources in places like wetlands and permafrost, and its concentration has more than doubled

since the Industrial Revolution from human activities such as natural gas exploration, landfills and agriculture. Natural gas used for home heating is composed mostly of methane.

But more hidden, and potentially of much greater concern, are massive deposits of methane buried beneath the sea in solid hydrate deposits, where cold temperatures and pressure supposedly keep it stable and unable to enter the atmosphere in large amounts. There have been concerns that this methane might be released suddenly by warming of ocean waters or other causes. These huge deposits of methane hold more carbon in them than all the known oil and gas fields on Earth.

If only 10 percent of that seafloor methane were to be released in a few years, it could be the equivalent of a 10-fold increase in the level of atmospheric carbon dioxide, the researchers said in their report. And 12,000 years ago, methane levels went up 50 percent in less than 200 years, according to studies by Brook and others. Researchers wanted to know why. "There are hundreds to thousands of times more methane trapped in seafloor deposits than there is in the atmosphere, and it's important that we know whether it's stable and is going to stay there or not," Brook said. "That's a pretty serious issue."

To test whether the seafloor deposits had been the source of the large methane increase thousands of years ago researchers measured levels of carbon 14, an isotope of carbon, from the Greenland ice samples. The seafloor deposits are old and have very little carbon 14 in them. Based on the results of those measurements, the scientists were able to determine whether the methane increases 12,000 years ago were linked to seafloor deposits or not.

"The data made it pretty clear that seafloor methane hydrates had little to do with the increase in methane thousands of years ago," Brook said. "This largely rules out these deposits either as a cause of the warming then or a feedback mechanism to it, and it indicates the deposits were stable at that point in time. The increased methane must have come from larger or more productive wetlands that occurred when the climate warmed."

Researchers now hope to do similar experiments in Antarctica to verify the results of this study, Brook said.

This research was a collaboration of scientists from Oregon State University, the Scripps Institution of Oceanography, Australian Nuclear Science and Technology Organisation, National Institute of Water and Atmospheric Research in New Zealand, National Space Institute in Denmark, and the Commonwealth Scientific and Industrial Research Organisation in Australia.

Stem cells from fat tissue offer hope for MS treatment

A preliminary study on the use of stem cells obtained from a patient's own adipose tissue in the treatment of multiple sclerosis (MS) has shown promising results. The three case studies, described in BioMed Central's open access Journal of Translational Medicine support further clinical evaluation of stromal vascular fraction (SVF) cells in MS and other autoimmune conditions.

Thomas Ichim, from Medistem Inc., and Dr. Boris Minev, from the Division of Neurosurgery, University of California San Diego, worked with a team of researchers to demonstrate the possible effectiveness of SVF cells in MS treatment. Minev said, "All three patients in our study showed dramatic improvement in their condition after the course of SVF therapy. While obviously no conclusions in terms of therapeutic efficacy can be drawn from these reports, this first clinical use of fat stem cells for treatment of MS supports further investigations into this very simple and easily-implementable treatment methodology".

MS is an autoimmune condition, in which the body's own defences attack nerve cells, resulting in loss of their fatty myelin sheath. The first symptoms usually occur in young adults, most commonly in women. It is believed that SVF cells, and other stem cells, may be able to treat the condition by limiting the immune reaction and promoting the growth of new myelin. According to Minev, "None of the presently available MS treatments selectively inhibit the immune attack against the nervous system, nor do they stimulate regeneration of previously damaged tissue. We've shown that SVF cells may fill this therapeutic gap".

Minev and his colleagues provided the SVF treatment to three patients with MS. The first had suffered frequent painful seizures for the previous three years; after treatment he reported that the seizures had stopped completely and that he had seen significant improvements in his cognition and a reduction of spasticity in his arms and legs. The second patient reported improvements in his sense of balance and coordination, as well as an improved energy level and mood. The final patient had been diagnosed with MS in 1993. After SVF treatment in 2008, his gait, balance and coordination improved dramatically over a period of several weeks. According to Minev, "His condition continued to improve over the next few months and he is currently reporting a continuing improvement and ability to jog, run and even bicycle".

Notes to Editors *1. Non-Expanded Adipose Stromal Vascular Fraction Cell Therapy for Multiple Sclerosis*
Neil H Riordan, Thomas E Ichim, Wei-Ping Min, Hao Wang, Fabio Solano, Fabian Lara, Miguel Alfaro, Jeorge P Rodriguez, Robert J Harman, Amit N Patel, Michael P Murphy and Boris Minev
Journal of Translational Medicine (in press)

Poor treatment for common vertebral compression fractures

The advice and treatment given to patients with vertebral compression fractures is not satisfactory. A thesis presented at the Sahlgrenska Academy shows that the majority of patients still have severe pain one year after the fracture.

Vertebral compression fracture describes the pressing together of a vertebra in the spine such that its height is decreased. Approximately 15,000 patients suffer from vertebral compression fractures in Sweden each year, most of these caused by osteoporosis. The fracture that arises is treated with analgesics, and the patients are advised about exercise.

− The patients are told that the prognosis is good and that most people get better after a few months, but no-one has actually investigated the prognosis and course of such acute compression fractures, says Professor Tommy Hansson who was supervisor for the thesis.

The author of the thesis, research student Nobuyi Suzuki, returned to Japan immediately after the disputation.

The thesis shows that reality is quite different for patients with vertebral compression. The study followed 107 men and women in Gothenburg for one year after they had been admitted to hospital with a vertebral compression fracture. Once the initial period of acute pain had passed, the patients' condition improved somewhat, but many subsequently deteriorated. Over two thirds had intense pain or very intense pain one year after the injury. This degree of pain is fully comparable with that experienced by patients with lumbar disc herniation immediately before undergoing surgery.

− The thesis shows clearly that the treatment and advice that is given to patients with an acute vertebral compression fracture is far from satisfactory. We must develop new methods for l investigating and treating these patients, says Tommy Hansson.

Osteoporosis In Brief *Osteoporosis causes a reduction in the strength of the skeleton making it much easier for a person with osteoporosis to suffer from fractures. The most common fractures occur in the vertebrae, hip and wrist. Osteoporosis is more than twice as common in women than it is in men, and a middle-aged woman has a 50% risk of suffering a fracture caused by osteoporosis in her remaining years.*

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Scientists give a hand(edness) to the search for alien life

Visiting aliens may be the stuff of legend, but if a scientific team working at the National Institute of Standards and Technology (NIST) is right, we may be able to find extraterrestrial life even before it leaves its home planet—by looking for left- (or right-) handed light.

The technique the team has developed* for detecting life elsewhere in the universe will not spot aliens directly. Rather, it could allow spaceborne instruments to see a telltale sign that life may have influenced a landscape: a preponderance of molecules that have a certain "chirality," or handedness. A right-handed molecule has the same composition as its left-handed cousin, but their chemical behavior differs. Because many substances critical to life favor a particular handedness, Thom Germer and his colleagues think chirality might reveal life's presence at great distances, and have built a device to detect it.

"You don't want to limit yourself to looking for specific materials like oxygen that Earth creatures use, because that makes assumptions about what life is," says Germer, a physicist at NIST. "But amino acids, sugars, DNA - each of these substances is either right- or left-handed in every living thing."

Many molecules not associated with life exhibit handedness as well. But when organisms reproduce, their offspring possess chiral molecules that have the same handedness as those in their parents' bodies. As life spreads, the team theorizes, the landscape will eventually have a large amount of molecules that favor one handedness.

"If the surface had just a collection of random chiral molecules, half would go left, half right," Germer says. "But life's self-assembly means they all would go one way. It's hard to imagine a planet's surface exhibiting handedness without the presence of self assembly, which is an essential component of life."

Because chiral molecules reflect light in a way that indicates their handedness, the research team built a device to shine light on plant leaves and bacteria, and then detect the polarized reflections from the organisms' chlorophyll from a short distance away. The device detected chirality from both sources.

The team intends to improve its detector so it can look at pond surfaces and then landscape-sized regions on Earth. Provided the team continues to get good results, Germer says, they will propose that it be built into a large telescope or mounted on a space probe.

"We need to be sure we get a signal from our own planet before we can look at others," he says. "But what's neat about the concept is that it is sensitive to something that comes from the process behind organic self-assembly, but not necessarily life as we know it."

Funding for this research was provided by STSI and the European Space Agency.
** W.B. Sparks, J. Hough, T.A. Germer, F. Chen, S. DasSarma, P. DasSarma, F.T. Robb, N. Manset, L. Kolokolova, N. Reid, F.D. Macchetto and W. Martin. Detection of circular polarization in light scattered from photosynthetic microbes. Proceedings of the National Academy of Sciences, April 20, 2009*

Living outside the box: New evidence shows going abroad linked to creativity

WASHINGTON – Living in another country can be a cherished experience, but new research suggests it might also help expand minds. This research, published by the American Psychological Association, is the first of its kind to look at the link between living abroad and creativity.

"Gaining experience in foreign cultures has long been a classic prescription for artists interested in stimulating their imaginations or honing their crafts. But does living abroad actually make people more creative?" asks the study's lead author, William Maddux, PhD, an assistant professor of organizational behavior at INSEAD, a business school with campuses in France and Singapore. "It's a longstanding question that we feel we've been able to begin answering through this research"

Maddux and Adam Galinsky, PhD, from the Kellogg School of Management at Northwestern University, conducted five studies to test the idea that living abroad and creativity are linked. The findings appear in the May issue of the Journal of Personality and Social Psychology, published by the American Psychological Association.

In one study, master of business administration students at the Kellogg School were asked to solve the Duncker candle problem, a classic test of creative insight. In this problem, individuals are presented with three objects on a table placed next to a cardboard wall: a candle, a pack of matches and a box of tacks. The task is to attach the candle to the wall so that the candle burns properly and does not drip wax on the table or the floor. The correct solution involves using the box of tacks as a candleholder – one should empty the box of tacks and then tack it to the wall placing the candle inside.

The solution is considered a measure of creative insight because it involves the ability to see objects as performing different functions from what is typical (i.e., the box is not just for the tacks but can also be used as a stand). The results showed that the longer students had spent living abroad, the more likely they were to come up with the creative solution.

In another study, also involving Kellogg School MBA students, the researchers used a mock negotiation test involving the sale of a gas station. In this negotiation, a deal based solely on sale price was impossible because the minimum price the seller was willing to accept was higher than the buyer's maximum. However, because the two parties' underlying interests were compatible, a deal could be reached only through a creative agreement that satisfied both parties' interests.
Here again, negotiators with experience living abroad were more likely to reach a deal that demanded creative insight. In both studies, time spent traveling abroad did not matter; only living abroad was related to creativity.

Maddux and Galinsky then ran a follow-up study to see why living abroad was related to creativity. With a group of MBA students at INSEAD in France, they found that the more students had adapted themselves to the foreign cultures when they lived abroad, the more likely they were to solve the Duncker candle task.

"This shows us that there is some sort of psychological transformation that needs to occur when people are living in a foreign country in order to enhance creativity. This may happen when people work to adapt themselves to a new culture," said Galinsky.

Although these studies show a strong relationship between living abroad and creativity, they do not prove that living abroad and adapting to a new culture actually cause people to be more creative. "We just couldn't randomly assign people to live abroad while others stay in their own country," said Maddux.

To help get at this question of what causes someone to be creative, the authors tried a technique called "priming." In two experiments, they asked groups of undergraduate students at the Sorbonne in Paris to recall and write about a time they had lived abroad or adapted to a new culture; other groups were asked to write about other experiences, such as going to the supermarket, learning a new sport or simply observing but not adapting to a new culture.

The results showed that priming students to mentally recreate their past experiences living abroad or adapting to a new culture caused students, at least temporarily, to be more creative. For example, these students drew space aliens and solved word games more creatively than students primed to recall other experiences.

"This research may have something to say about the increasing impact of globalization on the world, a fact that has been hammered home by the recent financial crisis," said Maddux. "Knowing that experiences abroad are critical for creative output makes study abroad programs and job assignments in other countries that much more important, especially for people and companies that put a premium on creativity and innovation to stay competitive."

Article: *"Cultural Borders and Mental Barriers: The Relationship Between Living Abroad and Creativity," William W. Maddux, PhD, INSEAD; Adam D. Galinsky, PhD, Kellogg School of Management at Northwestern University; Journal of Personality and Social Psychology, Vol. 96, No. 5.(Full text of the article is available from the APA Public Affairs Office and at http://www.apa.org/journals/releases/psp9651047.pdf)*

A Biological Basis for the 8-Hour Workday?

Penn researchers uncover 8- and 12-hour cycles of gene activity in mice

PHILADELPHIA - The circadian clock coordinates physiological and behavioral processes on a 24-hour rhythm, allowing animals to anticipate changes in their environment and prepare accordingly. Scientists already know that some genes are controlled by the clock and are turned on only one time during each 24-hour cycle. Now, researchers at the University of Pennsylvania School of Medicine and the Salk Institute for Biological Studies found that some genes are switched on once every 12 or 8 hours, indicating that shorter cycles of the circadian rhythm are also biologically encoded. Using a novel time-sampling approach in which the investigators looked at gene activity in the mouse liver every hour for 48 hours, they also found 10-fold more genes controlled by the 24-hour clock than previously reported.

This the first report where researchers have found other periodicities than the 24-hour cycle functioning in a live animal.

These findings, which appear in the April issue of PLoS Genetics, have implications for better understanding disruptions to normal circadian rhythms that contribute to a host of pathologies such as cardiovascular and metabolic disease, cancer, and aging-related disorders

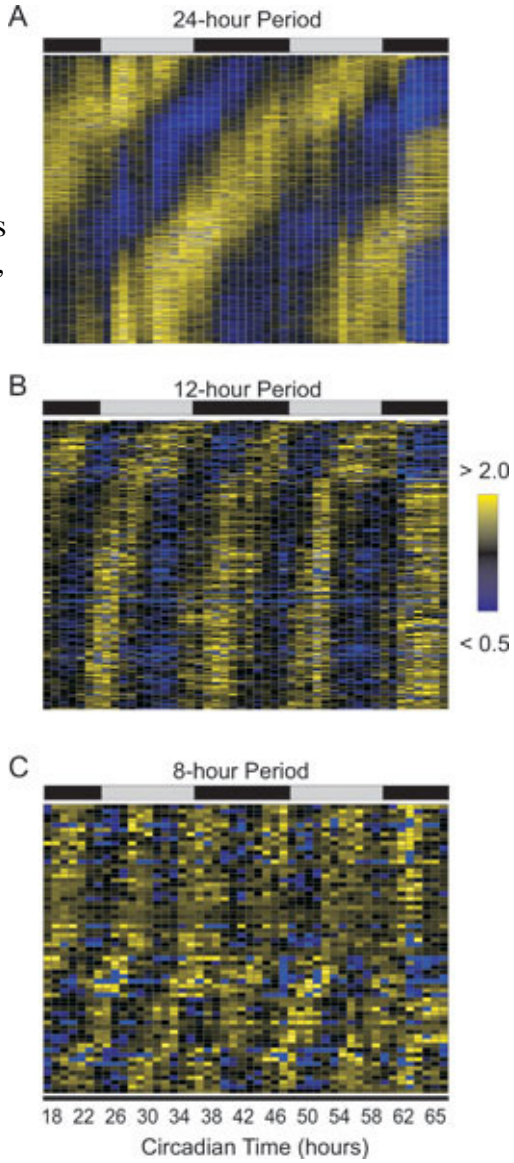
"The principal frequency, which is not a surprise, is the 24-hour cycle, and it is the most prevalent," says senior author John Hogenesch, PhD, Associate Professor of Pharmacology in the Institute for Translational Medicine and Therapeutics at Penn. "What was a surprise to us – although we set up the experiment to see exactly this – are the 12-hour and the 8-hour cycles.

To uncover these shorter oscillations, the Hogenesch and Salk team isolated RNA from the livers of mice every hour for 48 hours.

Microarray analysis showed that more than 3,000 genes were expressed on a circadian rhythm – which account for approximately 4% of all of the genes expressed in the liver. Additionally, 260 genes were expressed on a 12-hour cycle and 63 genes were expressed on an 8-hour cycle. The investigators saw similar 12-hour gene expression patterns in five other tissues.

"There is an obvious biological basis to a 12-hour rhythm, "Hogenesch says. "The 12-hour genes predicted dusk and dawn. These are two really, really stressful transitions that your body goes through and your mind goes through. Anybody who has young children realizes that they are more likely to cry around those times – and you're more likely to cry with them." The shift in gene expression controlled by these harmonics can help an animal prepare for the behavioral and physiological changes that accompany the shift from light to dark and back.

"We have less of a handle on the 8-hour rhythms," he says, "but the fact that we can see them reliably means to me there is the possibility that there could be a biological basis to an 8-hour cycle."



Time course of gene expression of 24-, 12-, and 8-hour periods. Bright yellow depicts gene expression twice that of the median level while bright blue depicts expression less than 50 percent of the median level. The time of peak expression of 24-hour cycling genes show a roughly equal distribution over the course of a day. In contrast, peak expression of both 12-hour peaks correlate with subjective dusk and dawn. **Michael Hughes, PhD, University of Pennsylvania School of Medicine**

Parallel experiments using RNA samples from synchronized tissue culture cells uncovered only genes that cycled on a 24-hour rhythm and showed no evidence of the shorter oscillations, suggesting that some of the timing cues are systemically controlled and some are controlled by the cell itself.

Feeding appears to control one of the 12-hour gene expression peaks. Mice consume about 20% of their daily calories right after they wake at dusk, which is near one gene expression peak. When the researchers restricted feeding to a different time of day one 12-hour peak disappeared and the other became more

pronounced. “We were left with the autonomously driven circadian protein transcription – the 24-hour component – which was unshifted by the feeding change,” Hogenesch says.

The high-density time sampling had an additional payoff: The team gained a sharper picture of the genes controlled by the 24-hour circadian clock. “We were able to more precisely measure the number of protein transcripts and the identity of the transcripts than we were able to with less frequent time sampling.

“The largest previously identified sets included 400 to 500 circadian-controlled genes and now we have 3,000 that are oscillating in the liver,” says Hogenesch. Using improved statistical methods also led to better accuracy. “We were able to more precisely say that, for example, the pituitary gland has 10-fold fewer oscillating protein transcripts than the liver, and cell-autonomous models have 10-fold less than that.”

Co-first authors on the paper are Michael E. Hughes of Penn and Luciano DiTacchio of the Salk Institute for Biological Sciences, La Jolla, CA. Other co-authors included Kevin R. Hayes and Julie E. Baggs of Penn, and Christopher Vollmers, S. Pulivarthy, the Salk researchers were led by Dr. Satchidananda Panda, Assistant Professor in the Regulatory Biology Laboratory and also corresponding author of the manuscript.

The study was funded by the Pennsylvania Commonwealth Health Research Formula Funds, the National Institute of Neurological Disease and Stroke, the National Institute of Mental Health, the Pew Scholars Program in Biomedical Science, and the Whitehall Foundation.

Even modest exercise can reduce negative effects of belly fat

URBANA – A new University of Illinois study suggests that moderate amounts of exercise alone can reduce the inflammation in visceral fat - belly fat, if you will - that has been linked with metabolic syndrome, a group of risk factors that predict heart disease and Type 2 diabetes.

"In the study, the benefits of exercise were apparent, even without a change in diet. We saw improvements in insulin sensitivity, less fat in the liver, and less inflammation in belly fat," said Jeffrey Woods, a U of I professor of kinesiology and community health and faculty member in the U of I Division of Nutritional Sciences and the Integrative Immunology and Behavior Program.

Belly fat is particularly dangerous because it produces inflammatory molecules that enter the bloodstream and increase the risk of heart disease and diabetes, he said.

"Scientists now know that obesity is associated with a low-grade systemic inflammation. Obese people have higher levels of circulating inflammatory markers, such as C-reactive protein (CRP), which are produced and secreted by fat tissue. This inflammation then triggers the systemic diseases linked with metabolic syndrome, such as Type 2 diabetes and heart disease," he said.

In the study, Woods and his colleagues examined the effects of diet and exercise on the inflammation of visceral fat tissue in mice. A high-fat diet was first used to induce obesity in the animals. After 6 weeks, mice were assigned to either a sedentary group, an exercise group, a low-fat diet group, or a group that combined a low-fat diet with exercise for 6 or 12 weeks so the scientists could compare the effects in both the short and long term.

"The surprise was that the combination of diet and exercise didn't yield dramatically different and better results than diet or exercise alone," said Vicki Vieira, the lead author of the study.

"Unexpectedly, the only significant increase from 6 to 12 weeks in belly fat—the type of fat that triggers these inflammatory diseases--was in the mice who were sedentary, which suggests that exercise is an effective behavioral approach to reduce the accumulation of visceral fat even when fat in the diet is high," she said.

Woods says that is a promising finding. "The benefits of exercise were apparent even if the animals were still eating a high-fat diet. That tells me that exercise could decrease or prevent these life-threatening diseases by reducing inflammation even when obesity is still present."

"The good news is that this was a very modest exercise program. The mice ran on a treadmill only about one-fourth of a mile five days a week. For humans, that would probably translate into walking 30 to 45 minutes a day five days a week," he noted.

"Even if you struggle with dieting, we believe you can still reduce the likelihood of developing obesity-related inflammatory diseases, such as Type 2 diabetes and heart disease, by adding a modest amount of exercise to your life," said Woods.

These results were reinforced by the scientists' study of sedentary older adults published in a recent issue of Brain, Behavior and Immunity (BBI). In that 10-month study, one group of sedentary older adults participated in three 45- to 60-minute cardiovascular exercise sessions per week, while another group focused on exercises to improve non-cardiovascular flexibility and balance for 75 minutes twice a week.

"At the end of the study, the 'cardio' group had lower levels of C-reactive protein (CRP), less belly fat, and improved general fitness than the 'flex' group," said Ph.D. candidate Vieira.

"The lower CRP levels were partially mediated by the reduction in trunk fat," she explained.

The mouse study was published in the American Journal of Physiology, Endocrinology and Metabolism. Co-authors are V.J. Vieira, R.J. Valentine, K. Wilund, N. Antao, T. Baynard, and J.A. Woods, all of the University of Illinois. The study was funded by the National Institutes of Health and the American College of Sports Medicine.
Co-authors of the BBI study are V.J. Vieira, L. Hu, R.J. Valentine, E. McAuley, E.M. Evans, T. Baynard, and J.A. Woods of the University of Illinois. Funding was provided by the National Institutes of Health.

Type of vitamin B1 could treat common cause of blindness

GALVESTON, Texas - University of Texas Medical Branch at Galveston researchers have discovered that a form of vitamin B1 could become a new and effective treatment for one of the world's leading causes of blindness.

Scientists believe that uveitis, an inflammation of the tissue located just below the outer surface of the eyeball, produces 10 to 15 percent of all cases of blindness in the United States, and causes even higher rates of blindness globally. The inflammation is normally treated with antibiotics or steroid eye drops.

In a paper appearing in the May issue of the journal Investigative Ophthalmology and Visual Science, however, the UTMB researchers describe striking results achieved with benfotiamene, a fat-soluble form of vitamin B1. In their experiments, they first injected laboratory rats with bacterial toxins that ordinarily produce a reaction mimicking uveitis. When those rats are fed benfotiamene, they fail to develop any signs of the inflammatory disorder.

"Benfotiamene strongly suppresses this eye-damaging condition and the biochemical markers we associate with it," said UTMB associate professor Kota V. Ramana, senior author of the study. "We're optimistic that this simple supplementation with vitamin B1 has great potential as a new therapy for this widespread eye disease."

The researchers' data shows benfotiamene works by suppressing the activation of a crucial signaling molecule called NF-kappa B, which is normally triggered by the stress caused by infection. Shutting down NF-kappa B, they said, prevents the runaway production of inflammatory proteins that generates uveitis.

Benfotiamene's low cost, rapid absorption by the body and lack of negative side effects make it an ideal candidate for uveitis prevention, according to Ramana.

"Already, clinical trials have shown that benfotiamene is absorbed better than thiamine [the most common form of vitamin B1] and significantly improved diabetic polyneuropathy in patients, and it's already taken as a supplement for diabetic complications," Ramana said.

Stem cell eye 'patch' to save sight gets cash boost

* 11:04 24 April 2009 **by Andy Coghlan**

A small patch of cells that protects the eye from age-related blindness could begin trials in patients within two years in the UK. The pioneering treatment could be one of the first successful applications originating from embryonic stem cells (ESC), the cells in embryos that can grow into all tissues of the body.

Because embryos are destroyed when ESCs are obtained, anti-abortion groups have opposed development of treatments based on them. More recently, they've claimed that ESC research is unnecessary because it's now possible to make ordinary tissue into embryonic-like cells called "induced pluripotent" stem cells (iPS). Success of the eye patch would demonstrate that ESCs can indeed lead to valuable treatments, in this case to prevent blindness.

In a major boost for the treatment today, the pharmaceutical company Pfizer announced that it would be funding clinical development of the treatment and helping to win permission from regulatory authorities to proceed with trials.

"This offers such an opportunity for patients, and it's time to start mapping that regulatory pathway towards trials," says Ruth McKernan, chief scientific officer of Pfizer Regenerative Medicine.

Vital for sight

Pfizer will be taking forward the work in collaboration with Pete Coffey, head of the team at University College London that has pioneered the work. He and his colleagues have found a way to change the ESCs into retinal pigment epithelium (RPE) cells, which are vital for sight but deteriorate with age, leading to blindness caused by a condition called age-related macular degeneration (AMD).

Coffey's team makes the cells into a single-layered RPE "carpet", which underlays and nourishes the photoreceptor cells that actually process light and generate images. The RPE also "vacuums up" debris produced by retinal cells.

Coffey says that the cells are only needed to protect a very small area of the eye called the macula, which is the point at which the eye focuses. "You end up with a carpet, or patch, that's just 3 millimetres by 6, a monolayer of 40,000 to 60,000 cells," says Coffey.

"It sounds like a lot, but it's actually a very small number in cellular terms," says Coffey. He says that a single flask of the RPE cells in a murky brown liquid contains enough cells to treat as many as 1000 patients.

Superior cells

Already, Coffey and his colleagues have demonstrated that they can use the patches to save the sight of rats.

More recently, they've demonstrated that the patches can be transplanted safely into pigs, which have eyes about the same size as ours. Until the patches are tried out in humans, however, researchers cannot claim that the technology will save sight.

Coffey says that given successful regulatory approval and successful scale-up of RPE patch production by Pfizer, trials could begin within about two years.

Coffey says that at present, the only treatment for AMD is regular injections of a drug called Lucentis, but it only works for a "wet" form of the disease, which affects 10 per cent of patients. The patch, by contrast, repairs "dry" AMD, which accounts for 90 per cent of AMD cases, but is untreatable.

He also said that his team attempted first to make the RPEs from adult stem cells, but found that RPEs from embryonic stem cells were far superior, both in consistency and function.

Novel cancer drug reduces neuroblastoma growth by 75 percent

M. D. Anderson-developed drug starves cancer cells of energy source in pre-clinical studies

SAN DIEGO - Researchers from the Children's Cancer Hospital at The University of Texas M. D. Anderson Cancer Center have found a new drug that restricts the growth of neuroblastoma, a childhood brain cancer. The pre-clinical study was presented today in the plenary session at the 22nd annual meeting of the American Society of Pediatric Hematology/Oncology.

Alejandro Levy, M.D., fellow at the Children's Cancer Hospital at M. D. Anderson, presented research showing for the first time that the M. D. Anderson-developed drug, 3-BrOP, reduces tumor growth by more than 75 percent as a single agent. The study, conducted with human neuroblastoma cells transplanted into mice, showed how 3-BrOP, a glycolysis inhibitor, starved the cancer cells to death by shutting down their main energy source, glucose.

"We found that neuroblastoma cells, unlike healthy cells, are highly dependent on glycolysis for energy instead of more efficient means of energy production," said Levy. "Glycolysis is a process that breaks down sugar for energy, so by blocking that process with 3-BrOP, we are able to keep the tumors from producing energy, and this disrupts their ability to grow."

According to the American Cancer Society, approximately 650 children, mainly under the age of five, are diagnosed with neuroblastoma in the United States each year. Close to two-thirds of these children are diagnosed after the cancer has metastasized to other parts of the body. For these patients with high-risk neuroblastoma, long-term survival is less than 40 percent because the tumors are often resistant to traditional chemotherapy.

Pre-clinically, 3-BrOP has already been proven effective against other cancers including glioblastoma, colon cancer, lymphoma and acute leukemia. A Phase I clinical trial is planned to open this year for adult patients.

"As we explore alternative options to standard chemotherapy agents, we are finding drugs, like 3-BrOP, that have the potential to destroy cancer cells while leaving healthy cells unharmed," said Patrick Zweidler-McKay, M.D., Ph.D., assistant professor at the Children's Cancer Hospital and senior investigator of the study. "These drugs can often enhance the efficacy of other treatments, potentially leading to more successful combinations and better outcomes for our young patients."

Other investigators on the study were Lauren Akers, D.O., Maurizio Ghisoli, M.D., Timothy Graham, Lizhi Zeng, M.D., Riitta Nolo, M.D., Peter Zage, M.D., Ph.D., Wendy Fang, M.D., Sankaranarayanan Kannan, Ph.D., Anna Franklin, M.D., Peng Huang, M.D., Ph.D., and Patrick Zweidler-McKay, M.D., Ph.D.

Innovation: Mind-reading headsets will change your brain

* 18:18 23 April 2009 **by Tom Simonite**

This week, engineer Adam Wilson made global headlines by updating Twitter using his brainwaves. "USING EEG TO SEND TWEET" he explained.

Wilson's achievement was actually pretty trivial. He used a system called BCI2000, found in hundreds of laboratories across the globe, that can do the job of a keyboard for any software program. But it was significant precisely because it was trivial: mind-reading tech is going to have a massive impact this year.

In the coming months, cheap headsets that let you control technology with the electrical signals generated by your firing neurons will go on sale to the general public. Our relationship with technology – and our brains – will never be the same again.

Escaping the lab

Researchers have developed systems that read brainwaves – in the form of electroencephalogram (EEG) signals – in order to help people suffering from disabilities or paralysis control wheelchairs, play games Movie

Camera, or type on a computer. Now, two companies are preparing to market similar devices to mainstream consumers.

Australian outfit Emotiv will release a headset whose 16 sensors make it possible to direct 12 different movements in a computer game. Emotiv says the helmet can also detect emotions.

Compatible with any PC running Windows, it will ship later this year for $299. They have shown off a game where the player moves stones to rebuild Stonehenge using mind power alone.

Californian company NeuroSky has also built a device that can detect emotions: the firm says it can tell whether you are focused, relaxed, afraid or anxious, for example.

Rather than selling it directly to the public, NeuroSky is licensing its set-up to other companies, including Mattel, Nokia and Sega. Mattel, for example, will soon sell a game which involves players levitating a ball using thought alone (*see video*).

The Emotiv headset picks up the electrical activity of neurons firing inside a person's brain and interprets your thoughts to control a computer game **(Image: Emotiv)**

Mind hacks

These devices are remarkably cheap, especially when compared to the price tags on research-grade EEGs, which can run to hundreds of thousands of dollars. Emotiv's headset will retail for $299, while Mattel's game will cost just $80. At such low prices, these dirt-cheap brain interfaces will likely be popular – and not just with people who want to play with them.

Consider what happened when the most revolutionary interface of recent years appeared – the wireless controller of Nintendo's Wii games console. Legions of hackers started experimenting; and millions of people have now seen how the interface can be repurposed to make an industrial robot play tennis, track a person's head movements and make a normal TV display 3D images.

You can expect some similarly mind-blowing hacks to result once Emotiv and NeuroSky release their devices. That'll certainly help make for some compelling viewing on YouTube and accelerate the development of brain controllers.

But the most interesting consequence of the coming flood of brainware isn't technological at all. Parents, and anyone else whose schooldays are fading into memory, will be acutely aware that today's youngsters have a facility with interactive technology that can be acutely disorienting.

There's already speculation about how the internet, gaming and other interactive technology is changing the brains of the next generation – albeit not necessarily well-founded. But for the generation after that, it will be normal to control machines using thought alone. Given the awesome adaptability and plasticity of the human brain, how will our biological hardware and software will adapt?

Can internal 'brain music' be used in therapy?

* 17:07 24 April 2009 **by Colin Barras**

Does the brain naturally compose melodies to rival those by Mozart or Chopin? Researchers at the US Department of Homeland Security (DHS) think so. What's more, they suggest that piano renditions of an individual's cerebral music can help in dealing with insomnia and fatigue in the aftermath of a stressful experience. Psychologists, however, are sceptical of their claims.

The DHS researchers on the TechSolutions programme and in the Human Factors/Behavior Science Division hope to record the brain's natural activity during periods of calm or alertness. Human Bionics – a company specialising in neurotraining in Purcellville, Virginia – will convert the signal into an audible polyphonic melody. Individuals will be asked to listen to the tracks at various times during the day to either soothe the nerves or improve concentration levels.

Such technology was requested by local firefighters, coast guards, bomb squads and others working within the DHS, says DHS science spokesman John Verrico.

Lawrence Parsons, a psychologist at the University of Sheffield, UK, thinks the proposed work taps into a number of well-established research areas. "But I don't think they have a clue about what they're trying to do," he adds.

A little mood music

Biofeedback involves taking signals from the body and playing them back to individuals to affect their performance. "It's been used on and off for 20 years," says Parsons. In 2004 Fumiko Hoeft and colleagues at Stanford University showed that recording brain activity using a functional magnetic resonance imaging (fMRI)

scanner and then playing it back to volunteers helped them control pain. There are even proposals to use the biofeedback effect in the next generation of computer games.

"But the idea of making music from the brain and playing it back to an individual to recreate the original mood is crazy," Parsons says.

Instead, he thinks it's likely that the proposed mood-altering powers of the music are due not because the melodies emerge from the individual's brain, but simply because they are melodies in the first place. "If you're looking at music modulating someone's emotions, then lots of studies show that," he says. There is ongoing research to test the claims of music therapists.

Listen to an alertness track, which DHS researchers suggest has a "Mozart sound", or try the "melodic, subdued Chopin sonata" relaxing track.

Verrico thinks that underestimates personal taste in music. "Some people can listen to first chords of Pachelbel's Canon and feel their eyelids getting heavy, but others can listen to the whole thing without an impact," he says. "This study is more personalised that traditional music therapy because it's designed to sync up to what activates the individual's brain."

Key signatures

But Ulman Lindenberger, a psychologist at the Max Planck Institute for Human Development in Berlin, Germany, thinks that the brain is unlikely to respond particularly to its own music. Part of the problem is that converting the brain waves to an audible melody would likely strip the signal of its signature, leaving the individual unaware that the music is their own. That music might impact mood, but it's "highly questionable whether the effects would be any different if it was [from] the same person's brain or some other brain," says Lindenberger.

Parsons says that unless volunteers in the experiments are not told the provenance of the music they are played, yet another well-known phenomenon could be at work. "It sounds like a big fat placebo effect," he says. The placebo effect can produce powerful outcomes in treatment, and DHS researchers must be careful to guard against it influencing their studies, says Parsons.

While the study has some degree of coherency, "the researchers are mixing [a number of theoretical ideas] into a brood that makes no sense," says Parsons. ***Read more about the DHS research here***

Two-Pronged Model Could Help Foil Tough Cystic Fibrosis Infections

Dartmouth Medical School researchers have devised a novel approach for thwarting the relentless bacterial infections that thrive in the lungs of people with cystic fibrosis (CF), unlocking new possibilities against a tenacious and toxic hallmark of the common genetic disease.

Combining a mainstay antibiotic with drugs to deprive the bacteria of iron, which facilitates their persistent growth, appears to boost infection killing, they found.

Their research, reported in the American Journal of Respiratory Cell and Molecular Biology online and scheduled for publication, builds on the collaborative expertise of DMS microbiology and lung physiology labs studying cystic fibrosis infections.

Cystic fibrosis patients are plagued by infections of the bacteria Pseudomonas aeruginosa. Their mucous-clogged lungs are fertile incubators for the bacteria to breed and cluster in slimy communities called biofilms that become increasingly drug resistant and damaging. Tobramycin, the antibiotic routinely used against the microbes, can control, but not efficiently eliminate Pseudomonas established on CF airway cells.

Last year, the DMS researchers reported that it took far more tobramycin to destroy biofilm pockets than can be delivered to the lungs. Using a surrogate tissue culture system they created to simulate human airways, they determined that up to 10 times the maximum tobramycin dosage was needed. They were also studying iron overload in CF lungs. Airway cells with the CF gene mutation release more iron, and the bacteria depend on that iron to form their resilient biofilms, the investigators discovered.

Now, applying their findings to the clinical front, the team demonstrated that two agents already approved by the Federal Drug Administration to treat acute iron poisoning or overload can enhance the ability of tobramycin against Pseudomonas infection.

"The beauty is that we are mixing FDA-approved drugs-- antibiotics and iron chelators-- to potentiate the effect of tobramycin on biofilm formation," said lead author Dr. Sophie Moreau-Marquis, a research associate. "It's an exciting translational framework that opens the door to potentially treating CF patients, taking the novel model we developed from the lab hopefully to the clinic."

Co-authors of the study are DMS professors Dr. Bruce Stanton of physiology, who heads the laboratory where Moreau-Marquis works, and Dr. George O'Toole of microbiology and immunology.

The research combines two results: "We were first to show iron is definitive for biofilms forming on live human airway cells. And the highest concentration of tobramycin that can reach CF lungs is below what we've shown to be barely enough to eradicate biofilms on airway cells," Moreau-Marquis said.

The team used two FDA-approved iron chelators, deferoxamine and deferasirox, that can remove excess iron from the system by binding to the metal in a process called chelation. To mimic the clinical environment, they stuck to the maximum possible tobramycin dose of 1,000 micrograms per milliliter, mixed with a chelator.

The combination had a dramatic effect: it disrupted the mass of established and highly resistant bacteria in human airway cells by 90 percent and it also prevented formation of damaging biofilms. In contrast, neither an iron chelator nor tobramycin alone had such success.

"We built on the idea that if more iron helps bacteria to grow, maybe taking iron away will help kill them," said O'Toole. "The concept is to reformulate one of these iron chelators to be inhaled with tobramycin, which is already inhalable, to treat the bacteria locally in the lungs."

Still, the team found evidence that a chelator can get into lungs from the bloodstream. Using a permeable support in the lab, they mimicked giving tobramycin to the lung side and a chelator to the blood side and showed that the iron chelator is able to work its way through to lungs.

The researchers are working with the CF clinic at Dartmouth-Hitchcock Medical Center to develop clinical trials. Their study is part of Dartmouth's interdisciplinary Lung Biology and Cystic Fibrosis Research Development programs, and is supported by the National Institutes of Health and the Cystic Fibrosis Foundation.

Increased mortality associated with nocturia

Patients, physicians should be vigilant about underlying causes of nighttime urination

LINTHICUM, MD, April 26, 2009–Patients suffering from nocturia, the need to urinate at least twice during the night, may have a significantly increased risk for mortality. Researchers presented a study at the 104th Annual Scientific Meeting of the American Urological Association (AUA) showing that there was a significantly increased mortality rate in elderly patients living in a Japanese assisted-living facility who suffered from nocturia relative to other residents.

Researchers conducted a comprehensive geriatric assessment of 788 residents 70 years old or older to determine incidence of nocturia. Using data from a national health insurance system, researchers assessed differences in survival stratified by presence or absence of nocturia over three years. Researchers adjusted the models to control for age, sex, BMI, diabetes, hypertension, history of coronary heart disease, nephropathy, alcohol consumption, and use of tranquilizers, hypnotics or diuretics.

"Nighttime urination is not necessarily just a matter of getting older. Patients should talk to their doctor about what may be causing this," said Anthony Y. Smith, MD, an AUA spokesman. "There may be a very serious yet treatable condition involved."

Nakagawa, H; Niu, K; Hozawa, A; Ikeda, Y; Kaiho, Y; Masuda-Ohmori, K; Nagatomi, R; Tsuji, I; Arai, Y. Association between nocturia and mortality in a community-dwelling elderly population aged 70 years and over: results of a 3-year prospective cohort study in Japan. J Urol, suppl. 2009: 181, 4, abstract 20.

Whiter laundry and a surprising new treatment for kids' eczema

Bleach baths clear the rash and banish flare-ups of miserable skin disease

CHICAGO--- It's best known for whitening a load of laundry. But now simple household bleach has a surprising new role: an effective treatment for kids' chronic eczema.

Chronic, severe eczema can mar a childhood. The skin disorder starts with red, itchy, inflamed skin that often becomes crusty and raw from scratching. The eczema disturbs kids' sleep, alters their appearance and affects their concentration in school. The itching is so bad kids may break the skin from scratching and get chronic skin infections that are difficult to treat, especially from methicillin-resistant Staphylococcus aureus (MRSA).

Researchers from the Northwestern University Feinberg School of Medicine have discovered powerful relief in the form of diluted beach baths. It's a cheap, simple and safe treatment that drastically improves the rash as well as reduces flare-ups of eczema, which affects 17 percent of school-age children.

The study found giving pediatric patients with moderate or severe eczema (atopic dermatitis) diluted bleach baths decreased signs of infection and improved the severity and extent of the eczema on their bodies. That translates into less scratching, fewer infections and a higher quality of life for these children.

The typical treatment of oral and topical antibiotics increases the risk of bacterial resistance, something doctors try to avoid, especially in children. Bleach kills the bacteria but doesn't have the same risk of creating bacterial resistance.

Patients on the bleach baths had a reduction in eczema severity that was five times greater than those treated with placebos over one to three months, said Amy S. Paller, M.D., the Walter J. Hamlin Professor and chair of

dermatology, and professor of pediatrics, at the Feinberg School. Paller also is an attending physician at Children's Memorial Hospital.

The study will be published in the journal Pediatrics April 27.

"We've long struggled with staphylococcal infections in patients with eczema," Paller said. She noted more than two-thirds of eczema patients have evidence of staphylococcus on their skin, the bacteria that most commonly causes infection and worsens the eczema. "This study shows that simple household bleach, which we think decreases the staphylococcus on the skin, can help these children."

In the study, Paller and researchers treated 31 pediatric patients (6 months to 17 years old) who had eczema and a bacterial staph infection for 14 days with oral antibiotics. Half of the patients received bleach in their bath water (half a cup per full standard tub), while the other half received a look-alike placebo. Patients were also instructed to put a topical antibiotic ointment or placebo control into their nose (where the staphylococcus can also grow) for five sequential days of each month. All were instructed to bathe in the bleach twice a week, and soak for five to 10 minutes for three months.

Paller said bathing in the diluted bleach bath water was surprisingly odor-free because of the small amount of bleach added. "In our clinics, no one had the just-out-of-the-swimming pool smell," she said.

The research team saw such rapid improvement in the kids taking the real bleach baths that they terminated the study early because they wanted the children getting the placebo to get the same relief.

"The eczema kept getting better and better with the bleach baths and these baths prevented it from flaring again, which is an ongoing problem for these kids," Paller said. "We presume the bleach has antibacterial properties and decreased the number of bacteria on the skin, which is one of the drivers of flares."

Northwestern researchers launched the study to confirm their hunch about the potential of bleach baths, "since bleach has been used by hospitals in the past few years as a disinfectant to decrease MRSA," Paller said.

One interesting finding in the study was the eczema on the body, arms and legs improved dramatically with the bleach baths, but the face, which was not submerged in the bath, did not improve, further evidence of the positive effect of the bath.

As a result of the study, Paller suggests that kids who have eczema on their face close their eyes and mouths and dunk under the water to help improve the lesions. In her practice, patients have found that even daily bleach baths are well tolerated. The bleach baths may also be useful for individuals with frequent staphylococcus infection, whether related to eczema or not, and in adults with eczema and recurrent infections.

To help treat a rising number of severe cases of eczema, Northwestern's Feinberg School has recently opened an Eczema Care & Education Center (www.eczemacarecenter.com).

The new center offers patients one-on-one instruction for treating eczema, while a support group helps patients and their families cope with the emotional aspects of the disease.

"This is a disorder that can drive people crazy," said Peter Lio, M.D., director of the Eczema Care & Education Center and an assistant professor of dermatology and of pediatrics at the Feinberg School. "Eczema beats people down."

Lio said he just worked with an 11-year-old girl who had missed a half-year of school because of her severe eczema. "As we were working with her and demonstrating how to treat her skin, she started weeping," he said. "Between the tears, she said 'I'm crying because I know I'm going to get better.' "

Scientists believe eczema may be triggered by urban pollutants and toxins and/or allergies, and certainly shows a genetic tendency. "We don't have all the answers and are still learning about this disease," Lio said.