EKG can show false positive readings for diagnosing heart condition

The electrical measurements on the electrocardiogram can often mislead physicians in diagnosing the heart condition left ventricular hypertrophy, causing other screening tests to be ordered before a definitive conclusion can be made, according to a Henry Ford Hospital study.

The study of 500 patients found a false positive reading between 77 and 82 percent in patients screened by electrocardiogram, and a false negative reading between 6 percent to 7 percent in the same patient population.

The electrocardiogram also showed a high negative predictive reading, which reflects the absence of left ventricular hypertrophy. Physicians rely on several electrocardiogram measurements for diagnosing the heart condition.

Researchers evaluated the electrocardiogram data against coronary CT scans taken of patients. CT scans are considered highly accurate for diagnosing left ventricular hypertrophy, or LVH.

An electrocardiogram, or EKG, measures electrical activity of a heartbeat; a CT scan uses X-rays to take clear, detailed images of the heart. The study is being presented at the American Heart Association's annual scientific conference Nov. 14-18 in Orlando.

"The EKG criteria for diagnosing left ventricular hypertrophy have a very poor sensitivity," says Mohamad Sinno, M.D., cardiology fellow at Henry Ford Hospital and lead author of the study. "So when the EKG shows left ventricular hypertrophy, it doesn't allow the physician to make an accurate assessment, and further screening tools such as cardiac CT, MRI scan, or an echocardiogram are warranted."

LVH, a condition in which the lower-left chamber of the heart grows abnormally thick, affects more than 16 percent of the adult population in the United States. It is caused by an underlying medical condition, most commonly high blood pressure, but often does not show symptoms until later in the disease process.

If left untreated, LVH has been shown to be an independent predictor for future adverse cardiovascular disease such as heart attacks, strokes, heart failure, arrythmias and death.

The study was funded by Henry Ford Hospital, 09-SS-A-18116-AHA.

Migraine raises risk of most common form of stroke

Women more at risk than men; risk particularly high in those with visual symptoms

Pooling results from 21 studies, involving 622,381 men and women, researchers at Johns Hopkins have affirmed that migraine headaches are associated with more than twofold higher chances of the most common kind of stroke: those occurring when blood supply to the brain is suddenly cut off by the buildup of plaque or a blood clot.

The risk for those with migraines is 2.3 times those without, according to calculations from the Johns Hopkins team, to be presented Nov. 16 at the American Heart Association's (AHA) annual Scientific Sessions in Orlando. For those who experience aura, the sighting of flashing lights, zigzag lines and blurred side vision along with migraines, the risk of so-called ischemic stroke is 2.5 times higher, and in women, 2.9 times as high.

Study participants, mostly in North America and Europe, were between the ages 18 and 70, and none had suffered a stroke prior to enrollment.

Senior study investigator and cardiologist Saman Nazarian, M.D., says the team's latest analysis, believed to be the largest study of its kind on the topic, reinforces the relationship between migraine and stroke while correcting some discrepancies in previous analyses. For examples, a smaller combination study in 2005 by researchers in Montreal showed a bare doubling of risk, yet mixed together different mathematical measures of risk, while the Hopkins study kept them separate, pooling together only like measures. As well, another half dozen recent and smaller studies from Harvard University yielded mixed results, some showing a link between migraines and ischemic stroke, while one did not show a tie-in.

Nazarian says that while nearly 1,800 articles have been written about the relationship between migraine and ischemic stroke, the Hopkins review was more selective, combining only studies with similar designs and similar groups of people, and more comprehensive, including analysis of unpublished data.

"Identifying people at highest risk is crucial to preventing disabling strokes," says Nazarian, an assistant professor at the Johns Hopkins University School of Medicine and its Heart and Vascular Institute. "Based on this data, physicians should consider addressing stroke risk factors in patients with a history or signs of light flashes and blurry vision associated with severe headaches."

Prevention and treatment options for migraine, he says, range from smoking cessation and taking anti-blood pressure or blood-thinning medications, such as aspirin. In women with migraines, stopping use of oral contraceptives or hormone replacement therapy may be recommended.

Such widespread use of hormone-controlling drugs is what Nazarian says may explain why women with migraines have such high risk of ischemic stroke. Contraceptives and other estrogen therapies are both known

to contribute to long-term risk factors for cardiovascular diseases and stroke, such as high blood pressure and increased reactivity by clot-forming blood platelets.

Nazarian says the researchers' next steps are to evaluate if preventive therapies, especially aspirin, offset the risk of ischemic stroke in people with migraines.

Funding support for the study, performed entirely at Hopkins, was provided by the National Institutes of Health Clinical Research Scholars Program.

Other researchers involved in this study were Susan Kahn, M.D., M.Sc.; Miranda Jones, M.P.H.; Monisha Jayakumar, M.P.H.; and Deepan Dalal, M.P.H. The lead study investigator was June Spector, M.D., M.P.H., a former postdoctoral research fellow at Hopkins, now in Seattle.

(Presentation title: Migraine headache and the risk of ischemic stroke, a systemic review and meta-analysis of observational studies.) For additional information, go to:
http://www.hopkinsmedicine.org/heart_vascular_institute/experts/physician_profile.html?profile=BA950FA2FC9595743865305E3B2DDE57&directory=1B2D0F30B59D39A341B0C23CB2B204D9

Marker of oxidative stress predicts heart disease outcomes

Judging from the number of juices and teas advertised as containing antioxidants, consumers are aware of the dangers of oxidative stress. But what is the best way to measure it – and fight it?

Doctors at Emory University School of Medicine have identified a substance in the blood that may be useful in predicting an individual's risk for heart disease. The substance is cystine, an oxidized form of the amino acid cysteine and an indirect measure of oxidative stress.

In a study of more than 1,200 people undergoing cardiac imaging at Emory because of suspected heart disease, people with high levels of cystine in the blood were twice as likely to have a heart attack or die over the next few years.

Riyaz Patel, MD, a postdoctoral researcher at Emory's Cardiovascular Research Group, is presenting the results Monday at the American Heart Association Scientific Sessions meeting in Orlando. Patel was part of a team led by Arshed Quyyumi, MD, professor of medicine (cardiology) at Emory University School of Medicine.

When considered independently of variables such as the presence of diabetes, high levels of cystine still predicted future trouble, Patel says. In the current research, high levels means the quarter of the group of patients with the highest levels.

"Cystine could be a valuable marker of cardiovascular risk, but it also has a direct harmful effect on cells, so reducing it may be a valuable treatment strategy," he says. "What's exciting is there are already known ways to intervene and drive down cystine levels in patients."

For example, a previous study has shown that supplementing the diet with zinc can lower cystine levels, he says.

Several studies have shown that levels of oxidized cysteine in the blood tend to rise as people age. Smoking and alcohol consumption are also linked with higher levels of oxidized cysteine.

Cysteine is itself a short-lived precursor to glutathione, one of the main antioxidants found inside cells, says Dean P. Jones, PhD, professor of medicine and director of the Clinical Biomarkers Laboratory at Emory University School of Medicine. "We need to have a continuous supply of cysteine, but it is too reactive for us to have very much at any one time," he says. "We are not sure why the oxidized form of cysteine accumulates with aging and disease. But our studies show that when it accumulates, it activates inflammation in cells."

Jones and his colleagues have shown that when white blood cells are exposed to high levels of cystine, they display signs of inflammation and become stickier. That makes them more likely to adhere to blood vessels in the heart, an event that contributes to the development of heart disease.

The team has found that levels of cystine do not correlate with C-reactive protein, a blood marker of inflammation other scientists have studied for a possible relationship with heart disease. The team's future plans include comparing cystine to other markers of inflammation and understanding the relationships between them.

Reference: *Effects of long-term zinc supplementation on plasma thiol metabolites and redox status in patients with age-related macular degeneration. SE Moriarty-Craige, KN Ha, P. Sternberg, M. Lynn, S. Bressler, G. Gensler, D.P. Jones. Am J Ophthalmol. 143(2):206-211 (2007)*

UCI researchers create compound that boosts anti-inflammatory fat levels

Discovery could lead to new immune-response drugs for allergies, illnesses and injuries

Irvine, Calif. – UC Irvine pharmacology researchers have discovered a way to boost levels of a natural body fat that helps decrease inflammation, pointing to possible new treatments for allergies, illnesses and injuries related to the immune system.

For decades, it has been known that this fat, called palmitoylethanolamide (PEA), is a potent anti-inflammatory substance that reduces both allergic symptoms and occurrences of rheumatic fever, but researchers understood little about how PEA works. In a study appearing online in the Proceedings of the National Academy of Sciences, Daniele Piomelli, the Louise Turner Arnold Chair in Neurosciences at UCI, and colleagues found that

levels of PEA are tightly regulated by immune system cells. In turn, PEA helps control the activity of these cells, which are called into action to fight infection, disease and injury in the body.

In addition, they found that PEA – also present in foods like eggs and peanuts – is deactivated by a protein called N-acylethanolamine-hydrolyzing acid amidase, which is an enzyme that breaks down molecules controlling cell inflammation.

Using a combination of molecular modeling and chemical library screening, the researchers created a novel compound that blocks the action of this protein. When given to rodents, the compound increased the levels of PEA in their immune cells and reduced the amount of inflammation elicited by an inflammatory substance. Furthermore, when administered to the spinal cords of mice after spinal cord injury, the compound decreased inflammation associated with the trauma and improved the recovery of motor function.

"These findings are very exciting for the field of medicine because most drugs for inflammatory conditions are effective in only a portion of the population and have serious side effects," Piomelli says. "This compound shows wide-scale promise."

He adds that the PEA-boosting compound is a prime candidate for development into a range of immune-response drugs. This possibility will be explored through a research collaboration between UCI and the Italian Institute of Technology in Genoa.

List makers take note: 10 technologies that made news in 2009 and warrant watching in 2010

WASHINGTON — A first-of-its kind inhalable measles vaccine for developing countries, where the disease remains a scourge. A "nanogenerator" that could recharge iPods and other electronic devices with a shake. And for Fido and Fluffy, a long-awaited once-a-month pill for both ticks and fleas.

It's list season, the time to prepare inventories of what stood out in 2009 and holds promise for the year ahead. Those three advances are among more than 250 research advances publicized in 2009 by the American Chemical Society (ACS) Office of Public Affairs. With 154,000 members, ACS is the world's largest scientific society. The advances were selected from among 34,000 scientific reports published during 2009 in ACS's 34 peer-reviewed journals, and 18,000 technical papers presented at ACS's two National Meetings. For a look at more than 250 other advances, publicized in the ACS News Service Weekly PressPac or National Meeting press releases, click here. If you use any of these discoveries in articles, please credit the journal or the American Chemical Society. Here is a sampler:

1. **Needle-free, inhalant powder measles vaccine could save thousands of lives** Scientists are reporting development of the first dry powder inhalable vaccine for measles. The vaccine is moving toward clinical trials next year in India, where the disease still sickens millions of infants and children and kills almost 200,000 annually, according to a report presented at the 238th ACS National Meeting. Robert Sievers, Ph.D., who leads the team that developed the dry-powder vaccine, said it's a perfect fit for use in back-roads areas of developing countries. Those areas often lack the electricity for refrigeration, clean water and sterile needles needed to administer traditional liquid vaccines.

2. **Toward home-brewed electricity with "personalized solar energy"** New scientific discoveries are moving society toward the era of "personalized solar energy," in which the focus of electricity production shifts from huge central generating stations to individuals in their own homes and communities. That's the topic of a report by an international expert on solar energy published in ACS' *Inorganic Chemistry*, a bi-weekly journal. It describes a long-awaited, inexpensive method for solar energy storage that could help power homes and plug-in cars in the future while helping keep the environment clean.

3. **"Frozen smoke:" The ultimate sponge for cleaning up oil spills** Scientists in Arizona and New Jersey are reporting that aerogels, a super-lightweight solid sometimes called "frozen smoke," may serve as the ultimate sponge for capturing oil from wastewater and effectively soaking up environmental oil spills. The scientists, lead by Robert Pfeffer, packed a batch of tiny aerogel beads into a vertical column and exposed them to flowing water containing soybean oil to simulate the filtration process at a wastewater treatment plant. They showed that the aerogel beads absorbed up to seven times their weight and removed oil from the wastewater at high efficiency, better than many conventional sorbent materials. Their study appeared in ACS' *Industrial & Engineering Chemistry Research*, a bi-weekly journal.

4. **New nanogenerator may charge iPods and cell phones with a wave of the hand** Imagine if all you had to do to charge your iPod or your BlackBerry was to wave your hand, or stretch your arm, or take a walk? You could say goodbye to batteries and never have to plug those devices into a power source again. In research presented at the ACS's 237th National Meeting, scientists from Georgia described technology that converts mechanical energy from body movements or even the flow of blood in the body into electric energy that can be used to power a broad range of electronic devices without using batteries.

5. **First broad spectrum anti-microbial paint to kill "superbugs"** Scientists in South Dakota are reporting development of the first broad-spectrum antimicrobial paint, a material that can simultaneously kill not just disease-causing bacteria but mold, fungi, and viruses. Designed to both decorate and disinfect homes, businesses, and health-care settings, the paint is the most powerful to date, according to the new study. It appeared in the monthly ACS' *Applied Materials & Interfaces*. The paint shows special promise for fighting so-called "superbugs," antibiotic-resistant microbes that infect hospital surfaces and cause an estimated 88,000 deaths annually in the United States, the researchers say.

6. **Tobacco plants yield the first vaccine for the dreaded "cruise ship virus"** Taking that "cruise of a lifetime" could soon be friendlier to your health. Scientists have used a new vaccine production technology to develop a vaccine for norovirus, a dreaded cause of diarrhea and vomiting that may be the second most common viral infection in the United States after the flu. Sometimes called the "cruise ship virus," this microbe can spread like wildfire through passenger liners, schools, offices and military bases. The new vaccine is unique in its origin - it was "manufactured" in a tobacco plant using an engineered plant virus. The research was presented at the 238th ACS National Meeting.

7. **Once-a-month pill for both fleas and ticks in Fido and Fluffy** Scientists in New Jersey are describing discovery and successful tests of the first once-a-month pill for controlling both fleas and ticks in domestic dogs and cats. Their study appears in the ACS' *Journal of the Medicinal Chemistry*, a bi-weekly publication. Peter Meinke and colleagues at Merck Research Laboratories note the need for better ways of controlling fleas and ticks, driven in part by increases in pet ownership. In tests on fleas and ticks in dogs and cats, a single dose of the new pill was 100 percent effective in protecting against both fleas and ticks for a month. There were no signs of toxic effects on the animals.

8. **Toward the design of greener, more eco-friendly consumer products** So you're a manufacturer about to introduce a new consumer product to the marketplace. Will that product or the manufacture of the product contribute to global warming through the greenhouse effect? Until now, there was no clear way to answer that question. Scientists are reporting development of a new method for screening molecules and predicting how certain materials, ranging from chemicals used in carpeting to electronics, will contribute to global warming. Their study was published in the ACS' *Journal of Physical Chemistry A*, a weekly publication.

9. **A "shrimp cocktail" to fuel cars and trucks** Call it a "shrimp cocktail" for your fuel tank. Scientists in China are reporting development of a catalyst made from shrimp shells that could transform production of biodiesel fuel into a faster, less expensive, and more environmentally friendly process. Their study appeared in ACS' *Energy & Fuels*, a bi-monthly journal. In laboratory tests, the shrimp shell catalysts converted canola oil to biodiesel (89 percent conversion in three hours) faster and more efficiently than some conventional catalysts.

10. **Toward an "electronic nose" to sniff out kidney disease in exhaled breath** Scientists in Israel have identified the key substances in exhaled breath associated with healthy and diseased kidneys — raising expectations, they say, for development of long-sought diagnostic and screening tests that literally sniff out chronic renal failure (CRF) in its earliest and most treatable stages. Their report appeared in *ACS Nano*, a monthly journal. The scientists describe tests of an experimental "electronic nose" on exhaled breath of laboratory rats with no kidney function and normal kidney function. The device identified 27 so-called volatile organic compounds that appear only in the breath of rats with CRF.

Accidental discovery produces durable new blue pigment

CORVALLIS, Ore. – An accidental discovery in a laboratory at Oregon State University has apparently solved a quest that over thousands of years has absorbed the energies of ancient Egyptians, the Han dynasty in China, Mayan cultures and more – the creation of a near-perfect blue pigment.

Through much of recorded human history, people around the world have sought inorganic compounds that could be used to paint things blue, often with limited success. Most had environmental or durability issues. Cobalt blue, developed in France in the early 1800s, can be carcinogenic. Prussian blue can release cyanide. Other blue pigments are not stable when exposed to heat or acidic conditions.

But chemists at OSU have discovered new compounds based on manganese that should address all of those concerns. They are safer to produce, much more durable, and should lead to more environmentally benign blue pigments than any being used now or in the past. They can survive at extraordinarily high temperatures and don't fade after a week in an acid bath. The findings were just published in the Journal of the American Chemical Society, and a patent has been applied for on the composition of the compound and the process used to create it. The research was funded by the National Science Foundation.

"Basically, this was an accidental discovery," said Mas Subramanian, the Milton Harris Professor of Materials Science in the OSU Department of Chemistry. "We were exploring manganese oxides for some

interesting electronic properties they have, something that can be both ferroelectric and ferromagnetic at the same time. Our work had nothing to do with looking for a pigment.

"Then one day a graduate student who is working in the project was taking samples out of a very hot furnace while I was walking by, and it was blue, a very beautiful blue," he said. "I realized immediately that something amazing had happened."

What had happened, the researchers said, was that at about 1,200 degrees centigrade – almost 2,000 degrees Fahrenheit – this otherwise innocuous manganese oxide turned into a vivid blue compound that could be used to make a pigment able to resist heat and acid, be environmentally benign and cheap to produce from a readily available mineral.

The newest – and possibly the best – blue pigment in world history was born, due to manganese ions being structured in an unusual "trigonal bipyramidal coordination" in the presence of extreme heat.

"Ever since the early Egyptians developed some of the first blue pigments, the pigment industry has been struggling to address problems with safety, toxicity and durability," Subramanian said.

The pigment may eventually find uses in everything from inkjet printers to automobiles, fine art or house paint, researchers say. The scientists said in their journal article that the new compound yields "a surprisingly intense and bright blue color," and they have outlined its structure and characteristics in detail. Collaborating on the work were researchers in the Materials Department at the University of California/Santa Barbara.

"A lot of the most interesting discoveries are not really planned, we've seen that throughout history," Subramanian said. "There is luck involved, but I also teach my students that you have to stay alert to recognize something when it happens, even if it isn't what you were looking for. Luck favors the alert mind."

Researchers discover heart disease in 3,500-year-old mummies

Abstract 537/Poster 1037

Study highlights:

* CT scans of mummies revealed calcium deposits in their artery walls.
* These deposits are an indication of clogged or hardened arteries, a sign of heart disease.
* Heart disease was not unusual in humans living 3,000 years ago, researchers said.

ORLANDO, FLA. - Hardening of the arteries has been detected in 3,500-year-old mummies, so we may have to look beyond modern risk factors to fully understand heart disease, according to research presented American Heart Association's Scientific Sessions 2009.

Although atherosclerotic cardiovascular disease is commonly ascribed to modern risk factors, this study found evidence of the disease which causes heart attacks and strokes in ancient Egyptian mummies.

The study, presented by Randall C. Thompson, M.D., professor of medicine at the Mid America Heart Institute in Kansas City, was conducted by a unique collaboration of imaging experts, Egyptologists and preservationists who sought the most direct evidence possible. Using six-slice computed X-ray tomography (CT) scans, they systematically examined 20 mummies housed in the Museum of Antiquities in Cairo, Egypt to see if heart and blood vessel tissue was present and to learn its condition.

The mummies dated from 1981 B.C. to 364 A.D. Social status could be determined for most of them - all were of high social status. The researchers found evidence of blood vessels or heart tissue in 13 of the mummies, and in four they could see an intact heart. Definite atherosclerosis, in other words a build-up of fat, cholesterol, calcium and other substances in the inner walls of blood vessels, was present in three and probable atherosclerosis in an additional three. Calcification was significantly more common in the mummies estimated to be 45 years or older at the time of death. Researchers found no difference in calcification between men and women. The most ancient mummy with findings diagnostic of atherosclerosis died approximately 1530 to 1570 B.C

The investigators concluded that atherosclerosis is not only a disease of modern man, but was present and not unusual in humans living 3000 years ago.

Co-authors are L. Samuel Wann, M.D.; Adel H. Allam, M.D.; Michael I. Miyamoto, M.D.; Hany A. Amar, Pharm.D.; Ibrahem Badr, Ph.D.; Abdelhalium Nureldin, Ph.D.; Jennifer J. Thomas, Ph.D.; and Gregory S. Thomas, M.D., M.P.H. Author disclosures are on the abstract. The study was funded by Siemens, National Bank of Egypt and Mid-America Heart Institute.

Toddlers insensitive to fear go on to commit crimes

* 11:20 17 November 2009 **by Ewen Callaway**

Even at the tender age of 3, children who will go on to be convicted of a crime are less likely to learn to link fear with a certain noise than those who don't. This may mean that an insensitivity to fear could be a driving force behind criminal behaviour.

Adult criminals tend to be fearless, but whether this characteristic emerges before or after they commit a crime wasn't clear, says Adrian Raine, a psychologist at the University of Pennsylvania in Philadelphia.

To find out, Raine and colleague Yu Gao turned to data from a 1970s study, collected as part of a decades-long project to understand the biological and environmental factors underlying mental illness.

Back then, researchers led by Raine's former research supervisor had measured the sweat response of about 1800 3-year-olds in Mauritius when they were exposed to two different sounds. One sound was always followed by a noisy blare, the other by nothing. The children learned to anticipate which sound preceded the blare, and sweated in response to it – an indicator of fear.

Decades later, Raine's own team looked to see if any of the subjects had criminal records and found 137 that did. The team discovered that, as toddlers, these people had sweated significantly less in anticipation of the blare compared with subjects of similar race, gender and background for whom no criminal record was found.

Reducing crime

"I think it's a very interesting, potentially important finding," says Joseph Newman, a psychologist at the University of Wisconsin-Madison. However, he cautions that the existence of early predictors of criminal behaviour does not mean that some children are born criminals. "There are many causes of crime, and there are many things that underlie fear conditioning," he says.

The differences in fear sensitivity are likely to be innate, at least in part: dysfunction in the amygdala, a brain area important for processing fear, has previously been linked to psychopathic behaviour, and genetic factors must underlie some of these differences.

However, numerous children who showed muted responses to fearful cues never fell foul of the law, Raine says. "Is this a throw-away-the-key approach to criminals? Absolutely not," he says.

Raine emphasises that environment can make someone less likely to commit a crime. He points to other studies from his team, also based on data from Mauritius, which indicate that manipulating a child's surroundings with improved nutrition, more exercise and cognitive stimulation, can reduce the chance they will commit a crime later on in life.

Journal reference: American Journal of Psychiatry, DOI: 10.1176/app1.ajp.2009.09040499

Really?

The Claim: A Person Can Contract Two Colds at One Time

By ANAHAD O'CONNOR

THE FACTS The rhinovirus that causes most cases of the common cold comes in many strains — at least 99, to be exact.

As a result, it has long been theorized that a person could be sickened with more than one cold strain at the same time. But recent studies of the common cold and its behavior in the human body have revealed some surprises.

In a study published in the journal Science this year, a team of researchers showed that when two strains of the virus infected a person, they could link up and swap genetic material in a process called recombination, which was once thought to be impossible in the rhinovirus. The study demonstrated that in a typical cold season, when many strains are circulating, recombination could cause new strains to emerge rapidly.

But it is not clear how often this happens. In another study published this year in PLoS One, an online open-access journal, scientists in China followed 64 children with colds and found evidence of recombination events and what they called "triple infections": children carrying both a cold strain and other respiratory viruses, like influenza or adenovirus. But ultimately only a small fraction carried multiple strains of rhinovirus.

On a practical level, there is no evidence that carrying two cold strains necessarily results in longer or more severe symptoms. And in fact, studies show that in up to a quarter of cases in adults, a cold infection may result in no symptoms at all.

THE BOTTOM LINE A single person can carry multiple cold strains at one time.

How fish is cooked affects heart-health benefits of omega-3 fatty acids

Abstract 1404/Poster 2071

Study highlights:

* Baked or boiled fish is associated with more benefit from heart-healthy omega-3 fatty acids than fried, salted or dried fish.

* Caucasian, Japanese-American and Latino men may be more likely to get the health benefits of fish than African-American or Hawaiian men, perhaps because of how their fish is prepared or genetic predisposition.

* Omega-3s from plant sources such as soy may do more to improve women's heart health than fish sources.

ORLANDO, FLA - If you eat fish to gain the heart-health benefits of its omega-3 fatty acids, baked or boiled fish is better than fried, salted or dried, according to research presented at the American Heart Association's Scientific Sessions 2009.

And, researchers said, adding low-sodium soy sauce or tofu will enhance the benefits.

"It appears that boiling or baking fish with low-sodium soy sauce (shoyu) and tofu is beneficial, while eating fried, salted or dried fish is not," said Lixin Meng, M.S., lead researcher of the study and Ph.D. candidate at the University of Hawaii at Manoa. "In fact, these methods of preparation may contribute to your risk. We did not directly compare boiled or baked fish vs. fried fish, but one can tell from the (risk) ratios, boiled or baked fish is in the protective direction but not fried fish."

The findings also suggest that the cardioprotective benefits vary by gender and ethnicity — perhaps because of the preparation methods, genetic susceptibility or hormonal factors.

Many studies have suggested that eating omega-3 fatty acids reduces the risk of heart disease; however, little is known about which source is most beneficial.

In this study, researchers examined the source, type, amount and frequency of dietary omega-3 ingestion among gender and ethnic groups. Participants were part of the Multiethnic Cohort living in Hawaii and Los Angeles County when they were recruited between 1993 and 1996. The group consisted of 82,243 men and 103,884 women of African-American, Caucasian, Japanese, Native Hawaiian and Latino descent ages 45 to 75 years old with no history of heart disease.

Researchers divided their intake of canned tuna, other canned fish, fish excluding shell fish, or soy products that contain plant omega-3s (soy, tofu and shoyu) into quintiles, quartiles, or tertiles when applicable. They also surveyed the preparation methods: raw, baked, boiled; fried; salted or dried. The initial study did not consider grilled fish.

Those in the highest quintile consumed a median 3.3 grams of omega-3 fatty acids a day. The lowest quintile consumed a median of 0.8 grams a day.

Omega-3 intake was inversely associated with overall risk of death due to heart disease in men - a trend mainly observed in Caucasians, Japanese Americans and Latinos. However, there weren't many blacks or Hawaiians in the study, so the results should be interpreted cautiously, Meng said.

Overall, men who ate about 3.3 grams per day of omega-3 fatty acids had a 23 percent lower risk of cardiac death compared to those who ate 0.8 grams daily.

"Clearly, we are seeing that the higher the dietary omega-3 intake, the lower the risk of dying from heart disease among men," Meng said.

Japanese and Hawaiians eat fish more often compared to whites, blacks and Latinos, and they prepare fish in a variety of methods, Meng noted.

For women, the omega-3 effect was cardioprotective at each level of consumption but not consistently significant, Meng said. Salted and dried fish was a risk factor in women.

In contrast, adding less than 1.1 gram/day shoyu and teriyaki sauce at the dinner table was protective for men but not for greater than 1.1 gram/day. For women, shoyu use showed a clear inverse relationship to death from heart disease. She noted that shoyu that is high in sodium can raise blood pressure, so she stressed low-sodium products. Eating tofu also had a cardioprotective effect in all ethnic groups.

"My guess is that, for women, eating omega-3s from shoyu and tofu that contain other active ingredients such as phytoestrogens, might have a stronger cardioprotective effect than eating just omega-3s," said Meng, noting that further studies are needed to confirm the hypothesis.

During the average 11.9 years of follow-up, 4,516 heart-related deaths occurred in the group, according to state and national death records, which were cross-referenced through the end of 2005.

The study didn't consider possible dietary changes over time; subjects who were diagnosed with heart disease after their baseline food intake surveys might have modified their eating habits. Further, the study didn't account for the possible effects of fish-oil supplementation.

In light of these limitations, the researchers plan to include subjects' dietary patterns over time and a cross-validation of their omega-3 levels through blood analysis.

"Our findings can help educate people on how much fish to eat and how to cook it to prevent heart disease," Meng said. "Alternately, if it is verified that the interactions between fish consumption, risk factors and ethnicity are due to genetic susceptibility, the heart-disease prevention message can be personalized to ethnic groups, and future study could identify susceptibility at the genetic level."

Co-authors are Lynne Wilkens, Dr.P.H., and Laurence Kolonel, M.D., Ph.D.

Author disclosures are on the abstract. An American Heart Association Pacific Mountain Pre-doctoral Fellowship grant funded the study. The data for this research is based on Multiethnic Cohort Study of Diet and Cancer under the NIH grant R37 CA054281.

***Editor's note:** The American Heart Association recommends eating fish (particularly fatty fish) at least two times a week and eating tofu and other forms of soybeans, canola, walnut and flaxseed, and their oils. Learn specific information on the recommendations.*

Treatment with folic acid, vitamin B12 associated with increased risk of cancer, death

Patients with heart disease in Norway, a country with no fortification of foods with folic acid, had an associated increased risk of cancer and death from any cause if they had received treatment with folic acid and vitamin B12, according to a study in the November 18 issue of JAMA.

Most epidemiological studies have found inverse associations between folate (a B vitamin) intake and risk of colorectal cancer, although such associations have been inconsistent or absent for other cancers, according to background information in the article. "Experimental evidence suggests that folate deficiency may promote initial stages of carcinogenesis, whereas high doses of folic acid may enhance growth of cancer cells. Since 1998, many countries, including the United States, have implemented mandatory folic acid fortification of flour and grain products to reduce the risk of neural-tube birth defects," the authors write. "Recently, concerns have emerged about the safety of folic acid, in particular with respect to cancer risk."

Marta Ebbing, M.D., of Haukeland University Hospital, Bergen, Norway, and colleagues analyzed the results of two Norwegian homocysteine-lowering trials among patients with ischemic heart disease, where there was a statistically nonsignificant increase in cancer incidence in the groups assigned to folic acid treatment. The researchers examined whether folic acid treatment was associated with cancer outcomes and all-cause mortality after extended follow-up. "Because there is no folic acid fortification of foods in Norway, this study population was well suited for such an investigation," they write.

The two randomized, placebo-controlled clinical trials included 6,837 patients with ischemic heart disease who were treated with B vitamins or placebo between 1998 and 2005, and were followed up through December 31, 2007. Patients were randomized to receive oral treatment with folic acid (0.8 mg/d), plus vitamin B12 (0.4 mg/d), plus vitamin B6 (40 mg/d) (n = 1,708); folic acid (0.8 mg/d) plus vitamin B12 (0.4 mg/d) (n = 1,703); vitamin B6 alone (40 mg/d) (n = 1,705); or placebo (n = 1,721). During study treatment, median (midpoint) serum folate concentration increased more than 6-fold among participants given folic acid.

The researchers found that after a median 39 months of treatment and an additional 38 months of post-trial observational follow-up, 288 participants (8.4 percent) who did not receive folic acid plus vitamin B12 vs. 341 participants (10.0 percent) who received such treatment were diagnosed with cancer, a 21 percent increased risk. A total of 100 patients (2.9 percent) who did not receive folic acid plus vitamin B12 vs. 136 (4.0 percent) who received such treatment died from cancer, a 38 percent increased risk. A total of 16.1 percent of patients who received folic acid plus vitamin B12 vs. 13.8 percent who did not receive such treatment died from any cause.

"Results were mainly driven by increased lung cancer incidence in participants who received folic acid plus vitamin B12. Vitamin B6 treatment was not associated with any significant effects," the authors write.

"Our results need confirmation in other populations and underline the call for safety monitoring following the widespread consumption of folic acid from dietary supplements and fortified foods."

(JAMA. 2009;302[19]:2119-2126. Available pre-embargo to the media at www.jamamedia.org)

Editor's Note: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Editorial: *Assessing Cancer Prevention Studies - A Matter of Time*

Bettina F. Drake, Ph.D., M.P.H., and Graham A. Colditz, M.D., Dr.P.H., of the Alvin J. Siteman Cancer Center and Washington University in St. Louis School of Medicine, write in an accompanying editorial that longer-term studies are needed.

"Preventive interventions require long-term evaluation. While the report by Ebbing et al provides important short-term data, the findings do not nullify the potential long-term benefits that folic acid fortification may have on population health. The time frame for benefit for some preventive interventions may span decades, although smoking cessation may be unique among lifestyle changes that produce a rapid reduction in cancer risk."

(JAMA. 2009;302[19]:2152-2153. Available pre-embargo to the media at www.jamamedia.org)

Personal Health

A Dental Shift: Implants Instead of Bridges

By JANE E. BRODY

If I have one serious regret about my age, it is that my permanent teeth developed before New York, my hometown, got fluoridated water. I first lost a permanent molar to decay in my early 20s, and the resulting bridge has had to be replaced several times in subsequent decades, ultimately as a four-part apparatus.

Now that has to go as well. Because I could not floss and clean properly under the bridge and between the supporting crowns, I developed a severe periodontal infection.

Dr. Michael Zidile, the young periodontist I consulted, took one look at my mouth and said: “This is not how we do restorations nowadays. A bridge is not a permanent solution and makes it too hard for most people to keep their gums and underlying bone healthy. Now we do implants and individual crowns where needed.”

More out of curiosity than distrust - and before I invested thousands of dollars and countless hours on new teeth - I did my own homework and got a second opinion. Dr. Zidile, I learned, is correct. In an overwhelming majority of cases, implants to replace lost teeth are by far the best long-term solution for maintaining a healthy mouth. Also, because they rarely need to be replaced, in the long run they are more economical than bridges.

A Growing Option

Implants for replacing lost teeth have come a long way in the 25 years since I last wrote about them in this column. Better materials, procedures and professional experience result in far fewer problems than occurred in the early years of implants.

Critical to their success, however, is proper selection of both patients and practitioners - and, after the implant, a commitment to good oral hygiene. Dental implants must be treated like natural teeth: kept clean and free of plaque through proper brushing, flossing and periodic professional cleanings.

"Bridges are not the standard of care anymore," Dr. Lawrence J. Kessler, a periodontist and associate professor of surgery at the University of Miami School of Medicine, told me in an interview. "For most people who lose teeth, implants are the treatment of choice."

Implants do not decay, and adjacent healthy teeth do not require crowns to support them. And because it is easy to clean and floss between implants, the gum tissue and underlying bone are more likely to remain healthy.

With a bridge, if one of the supporting crowned teeth breaks or develops decay or nerve damage, the bridge and its three or more crowns must be removed and replaced.

Implants can replace individual lost teeth or many teeth in a row. For those who have lost most of their teeth, implants can be used to anchor a full or partial denture. About half a million implants are placed each year in this country. On average, the total cost of an implant to replace a single tooth is $3,500 to $4,000 (more if other procedures are required), or about one-third more than the cost of a bridge. But while bridges have an average life span of 10 years, an implant can last a lifetime.

Many insurance companies now cover implants, but most people do not have dental insurance and must pay out of pocket. If cost is an issue, consider treatment at a dental college, where implants may be available at reduced rates as part of the teaching process.

Not a Quick Procedure

The basic technique involves surgically inserting a titanium screw - the implant - into the supporting bone, which can be done under local anesthesia in less than an hour, and attaching a small fake tooth called an abutment, followed by a crown. The resulting tooth looks and feels like a natural one.

The procedure is a lengthy one. Unlike a bridge, which can be completed in two weeks, implants usually take about eight weeks for the screw to become firmly attached to bone before the final crown can be placed. "A patient's health, not age, determines suitability for an implant," Dr. Kessler said. "I just did implants for a 93-year-old who needed them to fit a partial denture. I put two implants in a man when he was 85 and five more when he was 88, with no problems either time. "If cases are chosen well, implants are very successful - 96 to 97 percent successful. And they rarely fail down the road."

A most important element is having enough bone in the jaw to support the implant, although in some cases bone cells removed during drilling for the implant or taken from elsewhere in the mouth can be used to fill in gaps. "If someone has diabetes or is a smoker," Dr. Kessler said, "the chances of success are reduced because a poorer blood supply diminishes the fusion of bone cells to the implant."

Also important is healthy gum tissue, free of periodontal disease. Before I could undergo an implant procedure, I had to have periodontal treatment to get rid of the plaque, tartar and infection on the tooth roots and gum tissue around my bridge and supporting crowns.

In some cases when a tooth must be pulled, an implant can be placed right after the extraction, with the advantage of limiting bone loss in the area. When bone is not being stimulated, it tends to break down. I consider myself lucky that although I've had this troublesome bridge for many decades, my underlying bone has remained healthy enough to support an implant.

Choosing a Doctor

Just as any physician can legally perform surgery, any dentist can legally do implants. Be sure to choose someone thoroughly trained in the technique. Taking a weekend course in implantology is rarely adequate. There are risks involved in placing implants, including damage to a nerve or sinus cavity, which are magnified when the practitioner lacks adequate training.

Implants were once done mainly by oral and maxillofacial surgeons, most of whom operated independently of dentists. Now at least as many implants are placed by periodontists who are schooled in the technique and who coordinate their work closely with the patient's dentist. Ideally, the periodontist should be board-certified.

Just as you might ask for referrals for a prospective nanny or house cleaner, consider asking to speak with other patients of the practitioner before deciding to proceed with an implant. Though every case is different, at the least you can determine how well you are likely to be cared for.

Immediate, aggressive spending on HIV/AIDS could end epidemic

Money available to treat HIV/AIDS is sufficient to end the epidemic globally, but only if we act immediately to control the spread of the disease. That was the conclusion of a study just published in the open-access journal, BMC Public Health. This approach defies conventional thinking, which recommends gradual spending over 15-20 years. Canadian Researchers found that an aggressive program over five years is the only way to end the epidemic given our current resources. The study, part of a supplement on "The OptAIDS project: towards global halting of HIV/AIDS," was based on a leading-edge mathematical model developed by mathematicians and biologists, who recently earned acclaim for a study on how best to handle a planetary invasion by zombies.

Professor Robert J. Smith? and his team from the University of Ottawa, as well as researchers from York University and the University of Manitoba, developed the mathematical model to examine how best to eliminate HIV/AIDS worldwide, given the large amounts of money that have been committed to fighting the disease. They found that the $60 billion currently committed to fighting HIV/AIDS might suffice to end the epidemic globally. However, spending this money over the proposed 15-20 years will almost certainly fail, given the ability of HIV/AIDS to spread through travel and migration.

Recent scientific advances combined with education campaigns and condoms have been very effective in reducing the incidence of the disease in many countries and regions. However, the incidence of infection is still on the rise in many countries too. Over an extended timeframe of 15-20 years, travel and immigration will make it impossible to contain the disease to these regions. As a result, they predict that the spread of the disease will continue to outpace treatment.

This breakthrough finding was the culmination of numerous international studies looking at how epidemics spread globally, the infrastructure required to contain epidemics, how different countries are managing the disease, and the resources required to manage the HIV/AIDS epidemic, under the OptAIDS project umbrella.

"The OptAIDS project grew out of a frustration with existing attempts to tackle the disease," says Professor Smith? "HIV/AIDS is mostly addressed at a community or national level, when it needs to be tackled globally."

The team is now working to develop a model for how best to spend existing resources in the developing world to contain the disease before it spreads beyond our reach.

Notes to Editors:

1. The question mark after the author's name is part of his surname and not a typographical mistake

2. The OptAIDS project: towards global halting of HIV/AIDS

Research and reviews Supplement editor: Robert Smith? BMC Public Health (in press)

After the embargo, published articles available at the journal website: http://www.biomedcentral.com/bmcpublichealth/

Common herbal medicine may prevent acetaminophen-related liver damage, says Stanford researcher

STANFORD, Calif. - A well-known Eastern medicine supplement may help avoid the most common cause of liver transplantation, according to a study by researchers at the Stanford University School of Medicine. The finding came as a surprise to the scientists, who used a number of advanced genetic and genomic techniques in mice to identify a molecular pathway that counters acetaminophen toxicity, which leads to liver failure.

"I didn't know anything about the substance that was necessary for the pathway's function, so I had to look it up," said Gary Peltz, MD, PhD, professor of anesthesiology. "My postdoctoral fellow, whose parents and other family members in Asia were taking this compound in their supplements, started laughing. He recognized it immediately."

The molecule was S-methylmethionine, which had been marketed as an herbal medicine known as Vitamin U for treatment of the digestive system. It is highly abundant in many plants, including cabbage and wheat, and is routinely ingested by people. Coincidentally, Garnett Cheney, MD, at Stanford University performed a series of studies in the 1950s in which he used the compound to treat peptic ulcers.

Peltz is the senior author of the research, which will be published online Nov. 18 in Genome Research. The experiments were conducted in Peltz's laboratory at Roche Palo Alto in Palo Alto, Calif., where Peltz worked before coming to Stanford in July 2008. He is continuing the research at Stanford. The first author of the paper, Hong-Hsing Liu, MD, PhD, is now a postdoctoral scholar in Peltz's Stanford lab.

Acetaminophen is a pain reliever present in many over-the-counter cold and flu medicines. It is broken down, or metabolized, in the body into byproducts - one of which can be very toxic to the liver. At normal, therapeutic levels, this byproduct is easily deactivated when it binds to a naturally occurring, protective molecule called

glutathione. But the body's glutathione stores are finite, and are quickly depleted when the recommended doses of acetaminophen are exceeded.

Unfortunately, the prevalence of acetaminophen makes it easy to accidentally exceed the recommended levels, which can occur by dosing more frequently than indicated or by combining two or more acetaminophen-containing products. However, severe liver damage can occur at even two to three times the recommended dose (the maximum adult dose is 4 grams per day; toxic daily levels range from 7 to 10 grams).

"It's a huge public health problem," said Peltz. "It's particularly difficult for parents, who may not realize that acetaminophen is in so many pediatric medicines." Acetaminophen overdose is the most common cause of liver transplantation in this country. The only effective antidote is an unpalatable compound called NAC that can induce nausea and vomiting, and must be administered as soon as possible after the overdose.

Peltz and his colleagues used 16 inbred strains of laboratory mice for their investigations. Most strains are susceptible to acetaminophen toxicity, but one is resistant. They compared how the drug is metabolized by the different strains and looked for variations in gene expression and changes in endogenous metabolites in response to acetaminophen administration. They identified 224 candidate genes that might explain the resistant strain's ability to ward off liver damage, and then plumbed computer databases to identify those involved in metabolizing acetaminophen's dangerous byproducts.

One, an enzyme called Bhmt2, fit the bill: It helped generate more glutathione, and its sequence varied between the resistant and non-resistant strains of mice. Bhmt2 works by converting the diet-derived molecule S-methylmethionine, or SMM, into methionine, which is subsequently converted in a series of steps into glutathione. The researchers confirmed the importance of the pathway by showing that SMM conferred protection against acetaminophen-induced liver toxicity only in strains of mice in which the Bhmt2 pathway was functional.

"By administering SMM, which is found in every flowering plant and vegetable, we were able to prevent a lot of the drug's toxic effect," said Peltz. He and his colleagues are now working to set up clinical trials at Stanford to see whether it will have a similar effect in humans. In the meantime, though, he cautions against assuming that dosing oneself with SMM will protect against acetaminophen overdose.

"There are many pathways involved in the metabolism of this drug, and individuals' genetic backgrounds are tremendously variable. This is just one piece of the puzzle; we don't have the full answer," he said. However, if subsequent studies are promising, Peltz envisions possibly a co-formulated drug containing both acetaminophen and SMM or using SMM as a routine dietary supplement.

The research was partially funded by the Institute of General Medical Sciences and the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health and by Roche. Peltz and Liu are the co-inventors on a patent filed on the use of SMM to prevent acetaminophen toxicity in humans. SandHill Bio, a drug discovery startup co-founded by Peltz, is further investigating the potential therapeutic applications of the finding.

Bigger not necessarily better, when it comes to brains

Professor Lars Chittka

Tiny insects could be as intelligent as much bigger animals, despite only having a brain the size of a pinhead, say scientists at Queen Mary, University of London.

"Animals with bigger brains are not necessarily more intelligent," according to Lars Chittka, Professor of Sensory and Behavioural Ecology at Queen Mary's Research Centre for Psychology and University of Cambridge colleague, Jeremy Niven. This begs the important question: what are they for?

Research repeatedly shows how insects are capable of some intelligent behaviours scientists previously thought was unique to larger animals. Honeybees, for example, can count, categorise similar objects like dogs or human faces, understand 'same' and 'different', and differentiate between shapes that are symmetrical and asymmetrical.

"We know that body size is the single best way to predict an animal's brain size," explains Chittka, writing in the journal Current Biology, today. "However, contrary to popular belief, we can't say that brain size predicts their capacity for intelligent behaviour."

Differences in brain size between animals is extreme: a whale’s brain can weigh up to 9 kg (with over 200 billion nerve cells), and human brains vary between 1.25 kg and 1.45 kg (with an estimated 85 billion nerve cells). A honeybee’s brain weighs only 1 milligram and contains fewer than a million nerve cells.

While some increases in brain size do affect an animal's capability for intelligent behaviour, many size differences only exist in a specific brain region. This is often seen in animals with highly developed senses (like

sight or hearing) or an ability to make very precise movements. The size increase allows the brain to function in greater detail, finer resolution, higher sensitivity or greater precision: in other words, more of the same.

Research suggests that bigger animals may need bigger brains simply because there is more to control - for example they need to move bigger muscles and therefore need more and bigger nerves to move them.

Chittka says: "In bigger brains we often don't find more complexity, just an endless repetition of the same neural circuits over and over. This might add detail to remembered images or sounds, but not add any degree of complexity. To use a computer analogy, bigger brains might in many cases be bigger hard drives, not necessarily better processors."

This must mean that much 'advanced' thinking can actually be done with very limited neuron numbers. Computer modelling shows that even consciousness can be generated with very small neural circuits, which could in theory easily fit into an insect brain.

In fact, the models suggest that counting could be achieved with only a few hundred nerve cells and only a few thousand could be enough to generate consciousness. Engineers hope that this kind of research will lead to smarter computing with the ability to recognise human facial expressions and emotions.

Need for emergency airway surgery for hard-to-intubate patients reduced

Johns Hopkins program offers model as more patients appear with hard to navigate airways

Be prepared, that old Boy Scout motto, is being applied with great success to operating room patients whose anatomy may make it difficult for physicians to help them breathe during surgery, Johns Hopkins researchers report in a new study.

When patients undergo general anesthesia, they stop breathing on their own and anesthesiologists must quickly insert a tube into the airway as a first step in machine-assisted breathing. The researchers showed that a comprehensive program designed to help physicians quickly identify and treat anesthetized patients in which placement of this tube is difficult has dramatically reduced the need for high-risk emergency surgical procedures to open obstructed airways.

At the heart of the program is a rolling cart armed with most any supply a physician would need to navigate a difficult airway and restart breathing, from flexible scopes and long catheters to medications and a surgical airway kit, just in case. While it may sound simple, the standardized cart cuts out the need for operating room staff to race here and there during a crisis to track down the gear needed to get oxygen flowing again, says Lauren C. Berkow, M.D., one of the study's leaders.

"It seems an obvious solution, but it's not what people are used to doing," says Berkow, an assistant professor of anesthesiology and critical care medicine at the Johns Hopkins University School of Medicine. "People had to run to five different places to get the right equipment.

"The stakes are pretty high. Oxygen is vital. Time is of the essence. You want to make sure you have everything you need and know how to use it when that patient with an emergency rolls through the door."

During the four years before Johns Hopkins put its difficult airway program into place, an average of 6.5 patients a year needed to have their airways opened surgically. Over the 11 years that followed — ending in December 2006 - an average of just 2.2 patients a year needed the emergency procedure. In the past year, Berkow says, no patients at Johns Hopkins have needed unplanned emergency airway surgery.

The findings are published online and will be in the December issue of the journal Anesthesia & Analgesia.

The cart is but one part of Hopkins' difficult airway program. Doctors have been educated how to spot someone with a potentially life-threatening obstruction and how to use the items on the cart to properly deal with it. When it is difficult to put a breathing tube in place for a particular patient, that information goes into the patient's electronic health record so future providers will be aware of and prepared to deal with potential problems.

The decrease in the number of surgical airway procedures at Hopkins occurred despite an increase in patients reported to have a "difficult airway" as well as an overall increase in the number of patients receiving anesthesia per year, Berkow says. Airway-related deaths also declined after the initiation of the program, but the difference was not statistically significant because of the small numbers.

More patients are appearing with difficult airways, she says, as the population gets older, sicker and larger - all signals that inserting a breathing tube could be tricky. Presently, only one to 10 percent of patients have difficult airways, Berkow says. A miniscule number of those will require surgical intervention - an incision just below the Adam's apple or into the trachea — to ensure air is getting into the lungs.

"We took disorganization and created an organized, standardized system, which we've continued to adapt and update as new technology comes out. We keep all of our staff updated on the system," Berkow says, "and we found it improves outcomes."

The research was supported by funding from the Medic Alert Foundation and a grant from MCIC Vermont, Inc.

Other Johns Hopkins researchers on the paper include Robert S. Greenberg, M.D.; Kristin H. Kan; Elizabeth Colantuoni, Ph. D.; Lynette J. Mark, M.D.; Paul W. Flint, M.D.; Nasir Bhatti, M.D.; and Eugenie S. Heitmiller, M.D.
For more information: http://www.hopkinsmedicine.org/anesthesiology/Team/summaries/Berkow_Lauren.html
http://www.anesthesia-analgesia.org/cgi/rapidpdf/ane.0b013e3181b2531av1.pdf

When East meets West: Why consumers turn to alternative medicine

Alternative health remedies are increasingly important in the health care marketplace. A new study in the Journal of Consumer Research explores how consumers choose among the many available remedies.

"Examples of the wide array of health remedy options available to consumers include drugs, supplements, acupuncture, massage therapy, Ayurveda, and Traditional Chinese Medicine (to name a few). Such medical pluralism is common in both developed and developing countries and raises the questions: How do consumers choose among health remedies, and what are the consequences for a healthy lifestyle?" write authors Wenbo Wang (New York University), Hean Tat Keh (Beijing University), and Lisa E. Bolton (Pennsylvania State University).

The authors use "lay theories of medicine" to explain how consumers choose between Western medicine and its Eastern counterparts, Traditional Chinese Medicine (TCM) and Ayurvedic medicine.

"Western Medicine is primarily concerned with the material aspect of the body and views all medical phenomena as cause-effect sequences, relying on rigorous scientific studies and research that seeks empirical proof to all phenomena," write the authors. "On the other hand, TCM and Ayurvedic Medicine favor a holistic approach, view the mind and body as a whole system, and rely upon inductive tools and methods for treatment."

Based on a series of experiments and surveys in the United States, China, and India, the authors found that consumers prefer TCM (over Western medicine) when uncertain about the cause of an illness (i.e., diagnosis uncertainty)—because a holistic medicine tolerates uncertainty better than Western Medicine. Similarly, consumers prefer TCM (over Western medicine) because of lay beliefs that TCM offers an underlying cure (versus symptom alleviation by Western Medicine).

"These findings add to the growing debate over the regulation of health marketing and the delivery of health care, the role of direct-to-consumer advertising, and marketing efforts to promote a healthy lifestyle," the authors conclude.

Wenbo Wang, Hean Tat Keh, and Lisa E. Bolton. "Lay Theories of Medicine and a Healthy Lifestyle." Journal of Consumer Research: June 2010. A preprint of this article (to be officially published online soon) can be found at http://journals.uchicago.edu/jcr).

Common pain relief medication may encourage cancer growth

Although morphine has been the gold-standard treatment for postoperative and chronic cancer pain for two centuries, a growing body of evidence is showing that opiate-based painkillers can stimulate the growth and spread of cancer cells. Two new studies advance that argument and demonstrate how shielding lung cancer cells from opiates reduces cell proliferation, invasion and migration in both cell-culture and mouse models.

The reports--to be presented November 18, 2009, at "Molecular Targets and Cancer Therapeutics," a joint meeting in Boston of the American Association for Cancer Research, the National Cancer Institute, and the European Organization for Research and Treatment of Cancer--highlight the mu opiate receptor, where morphine works, as a potential therapeutic target.

"If confirmed clinically, this could change how we do surgical anesthesia for our cancer patients," said Patrick A. Singleton, PhD, assistant professor of medicine at the University of Chicago Medical Center and principal author of both studies. "It also suggests potential new applications for this novel class of drugs which should be explored."

The proposition that opiates influence cancer recurrence, prompted by several unrelated clinical and laboratory studies, has gradually gained support. It started with a 2002 palliative-care trial in which patients who received spinal rather than systemic pain relief survived longer. Soon after that, Singleton's colleague, anesthesiologist Jonathan Moss, noticed that several cancer patients receiving a selective opiate blocker in a compassionate-use protocol lived longer than expected. Two recent retrospective studies found that breast and prostate cancer patients who received regional rather than general anesthesia had fewer recurrences. In February, 2009, the Anesthesia Patient Safety Foundation highlighted the issue.

Moss's palliative-care patients were taking methylnaltrexone (MNTX), developed in the 1980s for opiate-induced constipation by the late University of Chicago pharmacologist Leon Goldberg. Goldberg modified an established drug that blocks morphine so that it could no longer cross the protective barrier that surrounds the

brain. So MNTX blocks morphine's peripheral side effects but does not interfere with its effect on pain, which is centered in the brain. It won FDA approval in 2008.

"These were patients with advanced cancer and a life expectancy of one to two months," Moss recalled, "yet several lived for another five or six. It made us wonder whether this was just a consequence of better GI function or could there possibly be an effect on the tumors."

So Singleton, Moss and colleagues, including Joe G.N. Garcia, MD, professor of medicine at the University of Chicago, began a series of studies looking at the many peripheral effects of opiates and the potential benefits of blocking those effects.

In laboratory studies, morphine can directly boost tumor-cell proliferation and inhibit the immune response. The researchers found that opiates also promote angiogenesis, the growth of new blood vessels, and decrease barrier function--effects that may exacerbate diseases involving vascular leakiness including acute lung injury in experimental models. In a surgical setting, decreased barrier function may make it easier for tumors to invade tissue and spread to distant sites. Increased angiogenesis helps cancers thrive in a new site.

In the studies to be presented Nov. 18, Singleton and colleagues focus on the mu opiate receptor as a regulator of tumor growth and metastasis and examine the ability of methylnaltrexone to attenuate these effects.

Using two different models of non-small cell lung cancer, the research teams showed that MNTX inhibited the tumor-promoting effects of opiates. In one study, using bronchioloalveolar carcinoma cells, MNTX blocked oncogenic signaling and prevented tumor-cell proliferation and migration.

In the other study, using Lewis lung carcinoma cells, mice without the mu opiate receptor did not develop the tumors that normal mice did when injected with cancer cells. The researchers further showed that MNTX reduced proliferation of cancer cells by 90 percent in normal mice. It also prevented invasion in cell culture and tumor growth and metastasis in mice.

The opioid receptor promotes Lewis lung cancer tumor growth, angiogenesis and metastasis, the authors conclude in a summary of the second study. "Methylnaltrexone attenuates these oncogenic effects."

"In conjunction with previous studies on opiate-induced angiogenesis by our laboratory and others, these experimental data suggest a plausible explanation for the epidemiologic observations," notes Moss, professor of anesthesiology and critical care at the University of Chicago. "If these laboratory studies are confirmed clinically, the selection of anesthetic technique used during the operative procedure and the possible use of opiate antagonists in the perioperative period may be important."

Additional contributors to the project include Frances Lennon, PhD, Biji Mathew, PhD, and Ravi Salgia, MD, all of the University of Chicago.

Immune system activated in schizophrenia

Researchers at the Swedish medical university Karolinska Institutet have discovered that patients with recent-onset schizophrenia have higher levels of inflammatory substances in their brains. Their findings offer hope of being able to treat schizophrenia with drugs that affect the immune system.

The causes of schizophrenia are largely unknown, and this hinders the development of effective treatments. One theory is that infections caught early on in life might increase the risk of developing schizophrenia, but to date any direct evidence of this has not been forthcoming.

Scientists at Karolinska Institutet have now been able to analyse inflammatory substances in the spinal fluid of patients with schizophrenia, instead of, as in previous studies, in the blood. The results show that patients with recent-onset schizophrenia have raised levels of a signal substance called interleukin-1beta, which can be released in the presence of inflammation. In the healthy control patients, this substance was barely measurable.

"This suggests that the brain's immune defence system is activated in schizophrenia," says Professor Göran Engberg, who led the study. "It now remains to be seen whether there is an underlying infection or whether the immune system is triggered by some other means."

According to the dominant hypothesis, schizophrenia is related to an overactive dopamine system. Previous studies have shown that interleukin-1beta can upset the dopamine system in rats in a similar way to schizophrenia in humans.

"We would have made terrific progress if we were one day able to treat schizophrenia patients with immunotherapy, as it might then be possible to interrupt the course of the disease at an early stage of its development," says Professor Engberg.

The group is now studying if the inflammatory process is only activated in connection with the development of schizophrenia, or whether chronic patients exhibit the same phenomenon.

Publication *J Söderlund, J Schröder, C Nordin, M Samuelsson, L Walther-Jallow, H Karlsson, S Erhardt, G Engberg*
Activation of brain interleukin-1² in schizophrenia *Molecular Psychiatry, vol.14; no. 12; November 2009*

Cancers' Sweet Tooth May Be Weakness

The pedal-to-the-metal signals driving the growth of several types of cancer cells lead to a common switch governing the use of glucose, researchers at Winship Cancer Institute of Emory University have discovered.

Scientists who study cancer have known for decades that cancer cells tend to consume more glucose, or blood sugar, than healthy cells. This tendency is known as the "Warburg effect," honoring discoverer Otto Warburg, a German biochemist who won the 1931 Nobel Prize in Medicine. Now a Winship-led team has identified a way to possibly exploit cancer cells' taste for glucose.

The results were published this week in the journal Science Signaling.

Normally cells have two modes of burning glucose, comparable to sprinting and long-distance running: glycolysis, which doesn't require oxygen and doesn't consume all of the glucose molecule, and oxidative phosphorylation, which requires oxygen and is more thorough.

Cancer cells often outgrow their blood supply, leading to a lack of oxygen in a tumor, says Jing Chen, PhD, assistant professor of hematology and medical oncology at Emory University School of Medicine and Winship Cancer Institute. They also benefit from glycolysis because leftovers from the inefficient consumption of glucose can be used as building blocks for growing cells. "Even if they have oxygen, cancer cells still prefer glycolysis," Chen says. "They depend on it to grow quickly."

Working with Chen, postdoctoral researcher Taro Hitosugi focused on the enzyme PKM2 (pyruvate kinase M2), which governs the use of glucose and controls whether cells make the switch between glycolysis and oxidative phosphorylation. PKM2 is found predominantly in fetal cells and in tumor cells.

In many types of cancer, mutations lead to over-activation of proteins called tyrosine kinases. Chen's team showed that tyrosine kinases turn off PKM2 in lung, breast, prostate and blood cancers. Introducing a form of PKM2 that is not sensitive to tyrosine kinases into cancer cells forces them to grow slower and be more dependent on oxygen, they found.

Because the active form of PKM2 consists of four protein molecules stuck together, having a tyrosine kinase flip the "off" switch on one molecule can dampen the activity for the others.

"People knew that tyrosine kinases might modify PKM2 for decades but they didn't think it mattered," Chen says. "We showed that such a modification is important and you even don't need that much modification of PKM2 to make a difference in the cells' metabolism."

PKM2 could be a good drug target, because both inhibiting it or activating it can slow down cancer cell growth. Biotechnology companies are already searching for ways to do so, Chen says.

Scientists from Dana Farber Cancer Institute, Yale University, Cell Signaling Technology Inc. and Novartis contributed to the paper. The research was supported by the National Institutes of Health, the American Cancer Society and the Multiple Myeloma Research Foundation. 1. Vincent Dollard: 404-778-4580

Reference: *T. Hitosugi et al. Tyrosine phosphorylation inhibits PKM2 to promote the Warburg effect and tumor growth. Sci. Signal. 2, ra73 (2009).*

Toward explaining why hepatitis B hits men harder than women

Scientists in China are reporting discovery of unusual liver proteins, found only in males, that may help explain the long-standing mystery of why the hepatitis B virus (HBV) sexually discriminates -- hitting men harder than women. Their study has been published online in ACS' Journal of Proteome Research, a monthly publication.

Shuhan Sun, Fang Wang and colleagues note that chronic hepatitis B seems to progress and cause liver damage faster in men, with men the main victims of the virus's most serious complications -- cirrhosis and liver cancer. Men infected with HBV also are 6 times more likely than women to develop a chronic form of the disease. About 400 million people worldwide have chronic hepatitis B, including a form that is highly infectious and can be transmitted through blood, saliva, and sexual contact.

In experiments with laboratory mice, the scientists found abnormal forms of apolipoprotein A-I (Apo A-I), a protein involved in fighting inflammation, in the livers of infected male mice but not infected females. They then identified abnormal forms of these Apo A-I proteins in blood of men infected with HBV, but not in women. In addition to explaining the gender differences, the proteins may provide important markers for tracking the progression of hepatitis B, the scientists suggest.

DOWNLOAD FULL TEXT ARTICLE: *"An altered pattern of liver apolipoprotein A-I is implicated in male chronic hepatitis B progression" http://pubs.acs.org/stoken/presspac/presspac/full/10.1021/pr900593r*

Scientists find molecular trigger that helps prevent aging and disease

Researchers at Mount Sinai School of Medicine set out to address a question that has been challenging scientists for years: How do dietary restriction - and the reverse, overconsumption - produce protective effects against aging and disease?

An answer lies in a two-part study led by Charles Mobbs, PhD, Professor of Neuroscience and of Geriatrics and Palliative Medicine at Mount Sinai School of Medicine, published in the November 17 edition of the journal Public Library of Science Biology. The study, titled "Role of CBP and SATB-1 in Aging, Dietary Restriction, and Insulin-Like Signaling," examines how dietary restriction and a high-caloric diet influence biochemical responses.

Dr. Mobbs and his colleagues unraveled a molecular puzzle to determine that within certain parameters, a lower-calorie diet slows the development of some age-related conditions such as Alzheimer's disease, as well as the aging process. How the diet is restricted—whether fats, proteins or carbohydrates are cut—does not appear to matter. "It may not be about counting calories or cutting out specific nutrients," said Dr. Mobbs, "but how a reduction in dietary intake impacts the glucose metabolism, which contributes to oxidative stress." Meanwhile, a high calorie diet may accelerate age-related disease by promoting oxidative stress.

Dietary restriction induces a transcription factor called CREB-binding protein (CBP), which controls the activity of genes that regulate cellular function. By developing drugs that mimic the protective effects of CBP – those usually caused by dietary restriction – scientists may be able to extend lifespan and reduce vulnerability to age-related illnesses.

"We discovered that CBP predicts lifespan and accounts for 80 percent of lifespan variation in mammals," said Dr. Mobbs. "Finding the right balance is key; only a 10 percent restriction will produce a small increase in lifespan, whereas an 80 percent restriction will lead to a shorter life due to starvation."

The team found an optimal dietary restriction, estimated to be equivalent to a 30 percent caloric reduction in mammals, increased lifespan over 50 percent while slowing the development of an age-related pathology similar to Alzheimer's disease.

The first part of the study looked at C. elegans, a species of roundworm, that were genetically altered to develop Alzheimer's disease-like symptoms. Dr. Mobbs and his team reduced the roundworms' dietary intake by diluting the bacteria the worms consume. In these types of roundworms, human beta amyloid peptide, which contributes to plaque buildup in Alzheimer's disease, is expressed in muscle, which becomes paralyzed as age progresses. This model allowed researchers to readily measure how lifespan and disease burden were simultaneously improved through dietary restriction.

The researchers found that when dietary restriction was maintained throughout the worms' adulthood, lifespan increased by 65 percent and the Alzheimer's disease-related paralysis decreased by about 50 percent. "We showed that dietary restriction activates CBP in a roundworm model, and when we blocked this activation, we blocked all the protective effects of dietary restriction," said Dr. Mobbs. "It was the result of blocking CBP activation, which inhibited all the protective effects of dietary restriction, that confirmed to us that CBP plays a key role in mediating the protective effects of dietary restriction on lifespan and age-related disease. "

In the second part of study, Dr. Mobbs and his team looked at the other end of this process: What happens to CBP in a high-calorie diet that has led to diabetes, a disease in which glucose metabolism is impaired? Researchers examined mice and found that diabetes reduces activation of CBP, leading Dr. Mobbs to conclude that a high-calorie diet that leads to diabetes would have the opposite effect of dietary restriction and would accelerate aging.

Dr. Mobbs hypothesizes that dietary restriction induces CBP by blocking glucose metabolism, which produces oxidative stress, a cellular process that leads to tissue damage and also promotes cancer cell growth. Interestingly, dietary restriction triggers CBP for as long as the restriction is maintained, suggesting that the protective effects may wear off if higher dietary intake resumes. CBP responds to changes in glucose within hours, indicating genetic communications respond quickly to fluctuations in dietary intake.

"Our next step is to understand the exact interactions of CBP with other transcription factors that mediate its protective effects with age," said Dr. Mobbs. "If we can map out these interactions, we could then begin to produce more targeted drugs that mimic the protective effects of CBP."

Full recovery now possible for an 'untreatable' mental illness

Innovative therapy that offers new hope

Patients coping with the chaos and misery of Borderline Personality Disorder now have reason for strong confidence in making major life changes through a new treatment, Schema Therapy. For the first time, three major outcome studies have shown that many patients with Borderline Personality Disorder can achieve full recovery across the complete range of symptoms. In one study Schema Therapy was shown to be more than twice as effective in bringing about full recovery as a widely-practiced traditional treatment (Transference Focused Psychotherapy). Schema Therapy was also found to be more cost-effective and to have a much lower dropout rate. In a second study group schema therapy led to even stronger outcomes than those in the previous investigation over a briefer period with a 0% drop out rate and a recovery rate of 94% over an 8 month period.

A third study, now in press, shows that individual Schema Therapy can be successfully implemented in regular mental health care settings with no loss of effectiveness.

While other specialized treatments for BPD have demonstrated empirical support, all but Schema Therapy have serious limitations in their impact on patients' functioning and quality of life and only Schema Therapy has demonstrated cost effectiveness. Schema Therapy is also associated with higher levels of patient and therapist satisfaction with the treatment.

The first of these large scale studies was reported in the Archives of General Psychiatry, published by the American Medical Association, the second published in the Journal of Behavioral Therapy and Experimental Psychiatry and the third will soon be appearing in Behavior Research and Therapy. Schema Therapy is an integrative approach that expands on the principles of cognitive-behavioral therapy.

According to the National Institute of Mental Health, Borderline Personality Disorder is found in about 1 to 2.5 percent of the general population although a recent large-scale epidemiological study reported a much higher estimate of 5.9%. This latter study indicates that BPD is potentially five to six times as prevalent as either schizophrenia or bipolar disorder.

Patients with the disorder live life on the edge: they're typically impulsive, unstable, exquisitely sensitive to rejection, have regular outbursts of anger, and live daily with extreme emotional pain. They often self-mutilate and make repeated suicide attempts. Identity problems, low stress tolerance, and fears of abandonment also make the disorder difficult for patients and for those who live with them. Many with BPD either cannot work or do not function at levels that could be expected in light of their intellectual capacities. As a result, the disorder carries high medical and societal costs, accounting for more than one in every five inpatient psychiatric admissions.

Until recently, psychotherapy offered help for only some of the symptoms of BPD. The best available alternatives, such as Dialectical Behavioral Therapy, relieve many of the self-destructive behavioral symptoms of the disorder, but have not been able to reduce many of the other core symptoms, especially those related to deeper personality change. New York-based psychologist Jeffrey Young, Ph.D. (on the faculty in the Dept. of Psychiatry at Columbia University) began to develop Schema Focused Therapy in the mid-1980s. Encouraged by its success, he established the first Schema Therapy Institute in the mid-1990s in Manhattan. Adopted by many clinicians in the United States, Europe, and Asia, the therapy came to the attention of researchers in the Netherlands who were developing a large-scale study of treatments for Borderline Personality Disorder. The clearly articulated approach of Schema Therapy lent itself well to a controlled outcome study.

In the first study, Dutch investigators, including Dr. Josephine Giesen-Bloo and Dr. Arnoud Arntz (the project leader), compared Schema Therapy (also known as Schema Focused Therapy or SFT) with Transference Focused Psychotherapy (TFP) in the treatment of Borderline Personality Disorder. 86 patients were recruited from 4 mental health institutes in the Netherlands. Patients in the study received two sessions per week of SFT or TFP for 3 years. After three years, full recovery was achieved in 45% of the patients in the SFT condition, and in 24% of those receiving TFP. One year later, the percentage fully recovered increased to 52% in the SFT condition and 29% in the TFP condition, with 70% of the patients in the SFT group achieving "clinically significant and relevant improvement". Moreover, the dropout rate was only 27% for SFT, compared with 50% for TFP, indicating that Schema Therapy instilled a greater sense of allegiance among patients.

Patients began to feel and function significantly better after the first year, with improvement occurring more rapidly in the SFT group. There was continuing improvement in subsequent years. Thus investigators concluded that both treatments had positive effects, with Schema Therapy clearly more successful. In the third study mentioned above, Dutch investigators including Dr. Marjon Nadort and Dr. Arnoud Arntz assessed the effectiveness of schema therapy in the treatment of BPD when utilized in regular mental health care settings. A total of 62 patients were treated in 8 mental health centers located in the Netherlands. The treatment was less intensive along a number of dimensions including a shift from twice weekly to once weekly sessions during the second year. Despite this, there was no lessening of effectiveness with recovery rates that were at least as high and similarly low drop out rates.

In the second study mentioned above investigators DR. Joan Farrell, Ida Shaw and Dr. Michael Webber at the Indiana University School of Medicine Center for BPD Treatment & Research tested the effectiveness of adding an eight-month, thirty-session schema therapy group to treatment-as-usual (TAU) for BPD with 32 patients. The drop out rate was 0% for those patients who received group schema therapy in addition to TAU and 25% for those who received TAU alone. At the end of treatment, 94% of the patients who received group schema therapy in addition to TAU compared to 16% of the patients receiving TAU alone no longer met BPD diagnostic criteria. The schema therapy group treatment led to significant reductions in symptoms and global improvement in functioning. The large positive treatment effects found in the group schema therapy study

suggest that the group modality may augment or catalyze the active ingredients of the treatment for BPD patients. A collaborative randomized controlled trial with 14 sites in six countries is in development to further explore this productive interaction between groups and schema therapy.

Schema Therapy is an integrative approach, founded on the principles of cognitive-behavioral therapy, then expanded to include techniques and concepts from other psychotherapies. Schema therapists help patients to change their entrenched, self-defeating life patterns – or schemas -- using cognitive, behavioral, and emotion-focused techniques. The treatment focuses on the relationship with the therapist, daily life outside of therapy, and the traumatic childhood experiences that are common in this disorder. Dr. Young believes that Schema Therapy's greater effectiveness arises in part from its use of "limited reparenting," which is not part of other approaches to BPD.

Both Schema Therapy and Transference Focused Psychotherapy focus on deeper personality change, in comparison to other recent treatments that have been limited to the reduction of specific behavioral symptoms of the disorder, such as self-mutilation. According to Dr. Young: "Other treatments for BPD, such as Dialectical Behavior Therapy, have also led to more effective coping skills and a significant reduction in self-harm. With Schema Therapy patients are, in addition, breaking free of lives of pain, self-hatred, and emptiness, making deeper personality changes, and significantly improving the quality of their lives."

Even the most intensive version of Schema Therapy mentioned in the first study was found to be cost effective. An economic analysis conducted by the authors of the study indicated that, for each year Schema Therapy patients were in the study, Dutch society benefited from a net gain of 4,500 Euros per patient (the equivalent of about 5,700 US dollars), despite the cost-intensive treatment. The savings over the course of several years after the completion of treatment could actually prove to be higher. The newest innovation, group schema therapy, is likely to be even more cost effective.

Schema therapists and researchers are hoping that these repeated validations of the effectiveness of Schema Therapy for patients with Borderline Personality Disorder -- that for so many years has been considered intractable—will lead to more research studies and will encourage more clinicians to learn Schema Therapy. They also hope that this study will convince healthcare insurers to reimburse the costs of effective longer-term psychotherapy for this painful and costly illness.

More information can be found at www.schematherapy.com and www.isst-online.com www.BPD-home-BASE.org or by contacting the Cognitive Therapy Center of New York in Manhattan, or the Schema Therapy Institute Midwest in Kalamazoo, Michigan.

Articles: *Farrell, J.; Shaw, I.; and Webber, M. A schema-focused approach to group psychotherapy for outpatients with borderline personality disorder: A randomized controlled trial. Journal of Behavior Therapy and Experimental Psychiatry Volume 40, Issue 2, June 2009, Pages 317-328*

Josephine Giesen-Bloo, MSc; Richard van Dyck, MD, PhD; Philip Spinhoven PhD; Willem van Tilburg MD, PhD; Carmen Dirksen, PhD; Thea van Asselt, Msc; Ismay Kremers, PhD; Marjon Nadort, MSc; and Arnoud Arntz, PhD. Outpatient Psychotherapy for Borderline Personality Disorder: a randomized trial of Schema focused therapy versus Transference focused therapy. Archives of General Psychiatry, 2006 , Vol. 63, No. 6, pp. 649-658.

Nadort, M.; Arntz, A.; Smit, J.; Giesen-Bloo, J.; Eikelenbooma, M.; Spinhoven,P.; vanAsselt, T.; Wensing, M.; vanDyck, R.; Implementation of out patient schema therapy for borderline personality Disorder with versus without crisis support by the therapist outside office hours: A randomized trial Behaviour Research and Therapy xxx (2009)1-13

Gene change in cannibals reveals evolution in action

* 14:27 19 November 2009 **by Andy Coghlan**

It's a snapshot of human evolution in progress. A genetic mutation protecting against kuru – a brain disease passed on by eating human brains – only emerged and spread in the last 200 years.

When members of the Fore people in Papua New Guinea died, others would eat the dead person's brain during funeral rituals as a mark of respect. Kuru passed on in this way killed at least 2500 Fore in the 20th century until the cause was identified in the late 1950s and the practice halted.

Identification of kuru and how it was spread helped researchers identify how BSE – mad cow disease – spread through the feeding of infected cattle brains to other animals, and how this eventually led to variant Creutzfeldt-Jakob disease (vCJD), which has killed 166 people so far in the UK.

Fore tribe women in 1957 suffering from kuru. The women are showing upper limb postures adopted to prevent postural tremors. From Philosophical Transactions of the Royal Society B **(Image: 2008 The Royal Society)**

Simon Mead of the British prion research centre at University College London says the discovery of an "anti-kuru" gene is the most clear-cut evidence yet of human evolution in action. "I hope it will become a textbook example of how evolution happens," he says. "It's a striking and timely example, given the 150th anniversary of the publication of Darwin's Origin of Species," he says.

Good mutations

Mead and his colleagues discovered the mutation after comparing stored DNA from 152 dead Fore victims of the disease with DNA from more than 3000 living Fore, including almost 560 who participated in the ritual eating of brains before it was banned.

In 51 survivors and their descendants, they discovered a hitherto-unknown variant of PRNP, the gene which makes prions, the proteins that spread the disease. These prions become malformed and in turn make all healthy prions they encounter malformed as well, in a chain reaction that ultimately destroys brains by turning them into a spongy mush.

The change in the gene comes at a position called codon 127. Throughout the animal kingdom, the codon contains the same amino acid, called glycine or "G", from each parent, giving the form G127G. To their astonishment, Mead and his colleagues found a variant of the codon never seen in nature before, in which one of the glycines has been swapped for a valine amino acid, giving the new variant the name G127V.

Initially, Mead and his colleagues thought that because the variant had never been seen before, it must have damaging rather than beneficial effects. "We thought we'd found the trigger for how kuru happens, that someone ate the brain of someone with the mutation and that's how the disease started spreading through the cannibalistic funeral feasts," he said.

"Instead, we found the complete opposite, which is that it was protective."

Inherited health

The mutation first arose about 200 years ago by accident in a single individual, who then passed it down to his or her descendants. "When the kuru epidemic peaked about 100 years back, there were maybe a couple of families who found that they and their children survived while all their neighbours were dying, and so on to today's generation, who still carry the gene," says Mead. "So it was a very sudden genetic change under intense selection pressure from the disease," he says.

None of the 152 victims of kuru had the protective gene, suggesting that it provides almost complete resistance to the disease. But it's not yet known whether the variant protects against other prion diseases. Mead said that experiments are already under way in mice deliberately given the new mutation, to see if they are protected against both kuru and vCJD.

Mead says that the team has evidence that the prion protein made by the new variant might prevent the abnormal version of the prion from multiplying, giving clues to how to treat or prevent vCJD with drugs.

In 2003, Mead and his colleagues discovered a much more common variant of the prion gene that provides protection against prion diseases. The variant's position in the gene, at codon 129, is just two units away from the new one.

The protective variant at codon 129 is called "MV", standing for the amino acids methionine and valine. All deaths except one from vCJD have so far been in people with the "MM" variant, suggesting that they are specially at risk.

Jose Ordovas, who studies genetics and nutrition at Tufts University, Boston, said the finding "really supports the concept of very rapid adaptation of humans to the environment".

Journal reference: New England Journal of Medicine, vol 361, p 2056

Reflux esophagitis due to immune reaction, not acute acid burn, UT Southwestern researchers report

DALLAS - Contrary to current thinking, a condition called gastroesophageal reflux disease (GERD) might not develop as a direct result of acidic digestive juices burning the esophagus, UT Southwestern Medical Center researchers have found in an animal study.

Rather, gastroesophageal reflux spurs the esophageal cells to release chemicals called cytokines, which attract inflammatory cells to the esophagus. It is those inflammatory cells, drawn to the esophagus by cytokines, that cause the esophageal damage that is characteristic of GERD. The condition is manifested by symptoms such as heartburn and chest pain.

“Currently, we treat GERD by giving medications to prevent the stomach from making acid,” said Dr. Rhonda Souza, associate professor of internal medicine at UT Southwestern and lead author of the study appearing the November issue of Gastroenterology. “But if GERD is really an immune-mediated injury, maybe we should create medications that would prevent these cytokines from attracting inflammatory cells to the esophagus and starting the injury in the first place.”

In the study, researchers created GERD in rats by connecting the duodenum to the esophagus. This operation allows stomach acid and bile to enter the esophagus. Researchers were surprised to learn that esophagitis didn't develop for a number of weeks after the operation.

"That doesn't make sense if GERD is really the result of an acid burn, as we all were taught in medical school," said Dr. Stuart Spechler, professor of internal medicine at UT Southwestern and senior author of the study. "Chemical injuries develop immediately. If you spill battery acid on your hand, you don't have to wait a month to see the damage."

About 40 percent of Americans suffer symptoms of GERD at some point, and 20 percent on a weekly basis, Dr. Souza said. Over the long term, GERD could eventually lead to esophageal cancer.

Previous studies had shown that if an animal esophagus is perfused with highly concentrated acid, esophageal damage develops quickly. In humans, however, the large majority of reflux episodes do not contain such highly concentrated acid, Dr. Souza said.

"In animal models of reflux esophagitis designed to mimic the human disease, researchers hadn't looked at the early events in the development of esophageal injury," Dr. Souza noted. "Most of those investigators have been interested in the long-term consequences of GERD, and we found virtually no published data about what happens later that induces gastroesophageal reflux."

Dr. Souza, who is also a staff physician at the Dallas Veterans Affairs Medical Center and part of the Harold C. Simmons Comprehensive Cancer Center at UT Southwestern, and Dr. Spechler, chief of gastroenterology at the Dallas VA, said the method they used to produce GERD in rats is a reasonable representation of how GERD develops in humans – acidic digestive juices from the stomach surge into the esophagus.

Soon after the operation, they expected to see the death of surface cells of the esophagus, and they expected to see the injury progress later to the deeper layers. Instead, they found the opposite. Three days after the surgery, there was no damage to surface cells, but the researchers did find inflammatory cells in the deeper layers of the esophagus. Those inflammatory cells didn't rise to the surface layer until three weeks after the initial acid exposure.

The next step for researchers is to conduct additional studies in humans.

Other UT Southwestern researchers involved in the study included Dr. Xiaofang Huo, postdoctoral researcher in internal medicine; Dr. Vivek Mittal, postgraduate trainee in internal medicine; Dr. Susanne Carmack, postgraduate trainee in pathology: Dr. Huiying Zhang, instructor of internal medicine; Dr. Robert Genta, clinical professor of pathology and internal medicine; Dr. Kathy Hormi-Carver, assistant professor of internal medicine; and Dr. Xi Zhang and Dr. Chunhua Yu, both research associates in internal medicine.

The study was supported by the Dallas VA Medical Center and the National Institutes of Health.

Water found in lunar impact probably came from comets

* 23:41 19 November 2009 **by Dana Mackenzie**, Houston

The mystery of where the moon's water came from may soon be solved. Evidence from NASA's LCROSS mission suggests much of it was delivered by comets rather than forming on the surface through an interaction with the solar wind.

In October, the mission crashed two impactors – a spent rocket stage and a few minutes later, the LCROSS spacecraft itself – into a crater near the moon's south pole. The spacecraft snapped images and took spectra of lunar debris kicked up by the rocket's impact and found that it contained the unmistakable signs of water.

Volatiles, including hydrocarbons known to be present in comets, have been detected in lunar material kicked up by NASA's LCROSS mission **(Image: T.A.Rector/I.P.Dell'Antonio/NOAO/AURA/NSF)**

Previous missions have also found hints of lunar water but its source has not been clear. One idea is that it forms when hydrogen atoms from the solar wind latch onto oxygen atoms in the lunar soil, creating hydroxyl and water.

But now, the evidence is mounting in favour of an alternative explanation – comet impacts. The data was discussed this week at the Lunar Exploration Analysis Group meeting, a gathering of 160 lunar scientists in Houston, Texas.

'Dirty iceballs'

The first line of evidence comes from compounds that vaporise readily, called volatiles. LCROSS found spectral signs of volatiles containing carbon and hydrogen – likely methane and ethanol – as well as others such as ammonia and carbon dioxide. "It appears that we impacted into a very volatile-rich area," LCROSS principal scientist Tony Colaprete told the conference.

These compounds should have been mostly lost to space billions of years ago, when the moon coalesced from the debris of an impact between the Earth and a Mars-sized object. Water formed through an interaction with the solar wind would therefore be relatively pure – and free of volatiles.

But comets, which are thought to have been responsible for many of the moon's impact scars, are "dirty iceballs" known to contain volatiles such as methane. "If you can nail down the source of the water [on the moon], that could tell us a lot about the cometary history of the moon for the last couple of billion years," says Larry Taylor of the University of Tennessee.

High concentrations

The second line of evidence pointing to comets comes from the amount of water detected. The solar wind is expected to form water in minute amounts, amounting to concentrations of no more than 1 per cent in the lunar soil.

LCROSS team members are still analysing the data, but calculations suggest the concentration of water is higher than that. "The data are consistent with a total hydrogen content in the range of several per cent," says Colaprete.

Beyond their link to comets, volatiles generated excitement at the meeting because of their value as a resource for human spaceflight. While water is important for survival on the moon, it is the water's hydrogen that can be used as rocket propellant.

The possibility of finding compounds like ethanol and methane, which can be used as fuel directly, makes the economic case for returning astronauts to the moon even sweeter. "LCROSS has given us our ticket back to the moon," says Noah Petro of NASA's Goddard Space Flight Center in Greenbelt, Maryland.

Let them eat snail

Nutritional giant snails could address malnutrition

A nutritionist in Nigeria says that malnutrition and iron deficiency in schoolchildren could be reduced in her country by baking up snail pie. In a research paper to be published in the International Journal of Food Safety, Nutrition and Public Health, she explains snail is not only cheaper and more readily available than beef but contains more protein.

Ukpong Udofia of the Department of Home Economics, at the University of Uyo, has looked at the moisture levels, protein content, and iron composition of the flesh of the giant West African land snail and compared it to beef steak. Snail pie is much more nutritious than a beef pie, she says.

Udofia and her research team baked pies of both varieties and asked young mothers and their children to try the tasty meal. Most of them preferred the taste and texture of the pies baked with the snail Archachatina marginata to those made with beef. The kids and their mothers judged the snail pies to have a better appearance, texture, and flavor. "Snail pie is recommended as a cheap source of protein and iron for school-age children and young mothers and could contribute in the fight against iron deficiency anemia," Udofia says.

"The land snail is a readily available and affordable source of animal protein, inhabits a lot of the green forest and swamps of most developing countries including Nigeria," Udofia adds, "It is also increasingly cultivated, although in the West it is more familiar as an unusual pet than a pie.

Iron deficiency and a lack of protein in the diet affect young mothers and their children in many developing countries including Nigeria, according to the World Health Organization leading to serious health problems. There is no quick fix for the problem of malnutrition in such countries, but alternative to high-cost meat products could help.

Snail meat contains protein, fat (mainly polyunsaturated fatty acid), iron, calcium, magnesium, phosphorus, copper, zinc, vitamins A, B6, B12, K and folate. It also contains the amino acids arginine and lysine at higher levels than in whole egg. It also contains healthy essential fatty acids such as linoleic and linolenic acids. The high-protein, low-fat content of snail meat makes it a healthy alternative food.

"Snail (Archachatina marginata) pie: a nutrient rich snack for school-age children and young mothers" in Int. J. Food Safety, Nutrition and Public Health, 2009, Vol. 2, 125-130

Finding More in "Most"

TAU shakes the world of linguistics with a scientific study of an everyday word

William Shakespeare, who knew a thing or two about words, advised that "An honest tale speeds best, being plainly told." But the exact meaning of plain language isn't always easy to find. Even simple words like "most" and "least" can vary greatly in definition and interpretation, and are difficult to put into precise numbers.

Until now. In a groundbreaking new linguistic study, Prof. Mira Ariel of Tel Aviv University's Department of Linguistics has quantified the meaning of the common word "most." To be published by the renowned

Cambridge University Press this year in Defining Pragmatics, this research "is quite shocking for the linguistics world," she says.

"I'm looking at the nature of language and communication and the boundaries that exist in our conventional linguistic codes," says Prof. Ariel. "If I say to someone, 'I've told you 100 times not to do that,' what does '100 times' really mean? I intend to convey 'a lot,' not literally '100 times.' Such interpretations are contextually determined and can change over time."

Exploring the simple word "most," Prof. Ariel was able to use science to solve a central conundrum in the linguistics field.

What do we mean by "most"?

Academic linguists have traditionally agreed that when we use the word "most" in English, we usually mean anything from 51 to 99 percent of given group of people or collection of objects. "Some linguists have argued that the word 'most' includes the 100% value as well, and that the meaning of 'most' is identical to that of 'more than half.' My study has proved them wrong," says Prof. Ariel.

Working with 60 volunteers from English-speaking countries including Australia, Britain and America, Prof. Ariel and her research team presented each candidate with a dialogue which included a reference to "most," then asked them to choose an appropriate response (one out of two provided for them). "We didn't directly ask them about how they interpreted the word 'most,' but based on the preferred responses, we were able to draw conclusions regarding the classical theory in the field."

When people use the word "most," the study found, they don't usually mean the whole range of 51-99%. The common interpretation is much narrower, understood as a measurement of 80 to 95% of a sample - whether that sample is of people in a room, cookies in a jar, or witnesses to an accident.

Prof. Ariel cautions that 80-95% is valid today but could shift over the next 100 years, for example.

A "most" interesting product of democracy

"That's the nature of language and communication. It changes in the span of a few centuries," Prof. Ariel says, as words evolve over time. "'Most' as a word came to mean "majority" only recently. Before democracy, we had feudal lords, kings and tribes, and the notion of "most" referred to who had the lion's share of a given resource - 40%, 30% or even 20%," she explains.

"Today, 'most' clearly has come to signify a majority - any number over 50 out of a hundred. But it wasn't always that way. A two-party democracy could have introduced the new idea that 'most' is something more than 50%."

In law, the precise interpretation of individual words is critical - it can win or lose a criminal or civil suit. In a recent court case, Prof. Ariel recalled, a couple ordered a red car, only to be delivered a burgundy car by the dealer. The dealer refused to take it back, arguing that burgundy is a shade of red. The court ruled against the couple because burgundy is indeed "red" in literal terms. But in this specific case, Prof. Ariel reasons, the court wasn't fair. It ruled against the couple's, and most people's, expectations of the color of a red car.

Whether one car is redder than another is clearly a matter of debate. But Dr. Ariel's study proves that when we use linguistic abstractions, we may be more precise than we think - that is, most (80-95%) of the time.

Shifting blame is socially contagious

New study from University of Southern California and Stanford University finds blame spreads rapidly

Merely observing someone publicly blame an individual in an organization for a problem – even when the target is innocent – greatly increases the odds that the practice of blaming others will spread with the tenacity of the H1N1 flu, according to new research from the USC Marshall School of Business and Stanford University.

Nathanael J. Fast, an assistant professor of management and organization at the USC Marshall School of Business and Larissa Tiedens, a professor of organizational behavior at Stanford, conducted four different experiments and found that publicly blaming others dramatically increases the likelihood that the practice will become viral. The reason: blame spreads quickly because it triggers the perception that one's self-image is under assault and must be protected.

The study called "Blame Contagion: The Automatic Transmission of Self-Serving Attributions" is believed to be the first to examine whether shifting blame to others is socially contagious. The results will be published in the November issue of Journal of Experimental Social Psychology.

"When we see others protecting their egos, we become defensive too," says Fast, the study's lead author. "We then try to protect our own self-image by blaming others for our mistakes, which may feel good in the moment." He adds that in the long run, such behavior could hurt one's reputation and be destructive to an organization and further to our society as a whole.

Tiedens said the study didn't specifically look at the impact of hard economic times, but it undoubtedly makes the problem worse. "Blaming becomes common when people are worried about their safety in an organization," she said. "There is likely to be more blaming going on when people feel their jobs are threatened."

Fast says that when public blaming becomes common practice – especially by leaders -- its effects on an organization can be insidious and withering: Individuals who are fearful of being blamed for something become less willing to take risks, are less innovative or creative, and are less likely to learn from their mistakes.

"Blame creates a culture of fear," Fast said, "and this leads to a host of negative consequences for individuals and for groups."

A manager can keep a lid on the behavior by rewarding employees who learn from their mistakes and by making a point to acknowledge publicly his or her own mistakes, Fast says. Managers may also want to assign blame, when necessary, in private and offer praise in public to create a positive attitude in the workplace.

Or, managers could follow the lead of companies such as Intuit, which implemented a "When Learning Hurts" session where they celebrated and learned from mistakes, rather than pointing fingers and assigning blame. The blame contagion research provides empirical evidence that such a practice can avoid negative effects in the culture of the organization.

Anyone can become a blamer, Fast says, but there are some common traits. Typically, they are more ego defensive, have a higher likelihood of being narcissistic, and tend to feel chronically insecure.

President Richard Nixon is one example the authors point to in the study. Nixon harbored an intense need to enhance and protect his self-image and, as a result, made a practice of blaming others for his shortcomings. His former aides reported that that this ego-defensiveness pervaded his administration. It was the culture of fear and blame that ultimately led to Nixon's political downfall.

The experiments showed that individuals who watched someone blame another for mistakes went on to do the same with others. In one experiment, half of the participants were asked to read a newspaper article about a failure by Governor Schwarzenegger who blamed special interest groups for the controversial special election that failed in 2005, costing the state $250 million. A second group read an article in which the governor took full responsibility for the failure.

Those who read about the governor blaming special interest groups were more likely to blame others for their own, unrelated shortcomings, compared with those who read about Schwarzenegger shouldering the responsibility.

Another experiment found that self-affirmation inoculated participants from blame. The tendency for blame to spread was completely eliminated in a group of participants who had the opportunity to affirm their self-worth.

"By giving participants the chance to bolster their self-worth we removed their need to self protect though subsequent blaming," says Fast.

The results have particularly important implications for CEOs. Executives and leaders would be wise to learn from such examples, Fast suggests, and instead display behaviors that help to foster a culture of psychological safety, learning, and innovation.

Tiny fungi replay the fall of the giant beasts

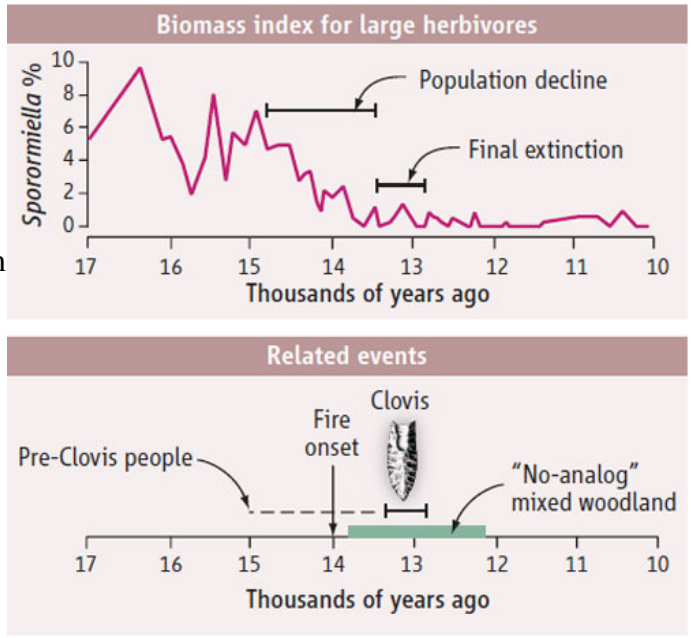
Around 15,000 years ago, North American was home to a wide menagerie of giant mammals - mammoths and mastodons, giant ground sloths, camels, short-faced bears, American lions, dire wolves, and more. But by 10,000 years ago, these "megafauna" had been wiped out. Thirty-four entire genera went extinct including every species that weighed over a tonne, leaving the bison as the continent's largest animal.

In trying to explain these extinctions, the scientific prosecution has examined suspects including early human hunters, climate change and even a meteor strike. But cracking the case has proved difficult, because most of these events happened at roughly the same time. To sort out this muddled chronology, Jacquelyn Gill has approached the problem from a fresh angle. Her team have tried to understand the final days of these giant beasts by studying a tiny organism, small enough to be dwarfed by their dung - a fungus called Sporormiella.

Sporormiella grows in the droppings of large plant-eating mammals and birds, and it leaves tell-tale spores in its wake. More spores mean more dung, so Sporormiella acts as a rough indicator of the number of herbivores in a given area. The fall of these beasts is reflected in falling numbers of spores.

Gill counted these spores in the sediment of Indiana's Appleman Lake, and compared them to counts of fossilised pollen and charcoal from the same soil. That allowed her to match the numbers of plant-eaters at any given time with the local plant species and the frequency of forest fires.

Using this fungal index, Gill has produced a detailed timeline of the changes in the Pleistocene. Her revised history argues against a role of climate change or alien rocks, but fails to clear early humans of the blame. More importantly, it suggests that many events that happened around the same time, such as an upheaval in the local plant communities and a rise in large infernos, were the result of the beasts' decline, rather than the cause of them



The spores revealed that the fall of the megafauna began in earnest around 14,800 years ago. By the 13,700 year mark, their numbers had fallen to less than 2% of their former glory. They never recovered, but it clearly took a few more millennia for the stragglers to succumb - the last bones of the great beasts date to around 11,500 years ago.

Changes in the local vegetation happened after the beasts started disappearing, around 13,700 years ago. Before this point, the environment was open grassland with the odd tree. Fires were a rarity. But without the suppressive mouths of the big plant-eaters, trees grew unchecked, producing a combo of vegetation you just don't see today. Large numbers of temperate deciduous trees like elm and ash happily coexisted with cold-loving conifers like larch and spruce.

And with them came fires, large infernos that broke out around 14,000 years ago and returned every century or so for the next few millennia. The pollen and charcoal of Appleman Lake tell the story of these changes, and also show that they came after the beasts' disappearance.

Right away, this timeline rules out the possibility that a collision with a large space object killed the megafauna. The proponents of that theory place the collision at around 13,000 years ago, after the giants had started to decline. And it's clear that extinctions were long, drawn-out affairs, rather than the relatively rapid annihilations you'd expect from an extraterrestrial impact.

Likewise, changing climate becomes an unlikelier suspect. The megafaunal extinction predated a rapid, millennium-long chill called the Younger Dryas that took place around 11,500 and 12,800 years ago. When the megafauna started dying, the Earth was going through a warming phase. That might well have affected them, but it didn't do so through the most obvious method - changing the plants they ate. After all, Gill's work tells us that the beasts' disappearance changed the plants, not the other way round.

What about humans, those pesky slayers of animals? Some scientists believed that North America's Clovis people specialised in hunting big mammals, causing a "blitzkrieg" of spear-throwing that drove many species to extinction. But these hunters only arrive in North America between 13,300 and 12,900 years ago, around a thousand years after the population crashes had begun.

If people were responsible, they must have been pre-Clovis settlers. There's growing evidence that such humans were around, but they weren't common or specialised. They may have contributed to the beasts' downfall, while Clovis hunting technology delivered a coup de grace to already faltering populati0ons.

By analysing the sediment at Appleman lake - spores, pollen, charcoal and all - Gill has replayed the history of the site, spanning the last 17,000 years. Her data rule out a few theories, but as she says, they "[do] not conclusively resolve the debate" about climate causes versus human ones. It's possible that similar studies at different sites and other continents will help to provide more clues.

Meanwhile, her study certainly tells us more about what happened in Earth's recent history, when a large swathe of hefty plant-eaters died off - a change from savannah to woodland, and more fires. This isn't just a matter of historical interest. The same events might be playing out today, as the largest modern land mammals suppress fires by eating flammable plants, and are facing a very real threat of extinction. History could well repeat itself. *Reference: Science 10.1126/science.1179504*

Dispensing prescription drugs in 3-month supplies reduces drug costs by a third

First study to quantify savings

Purchasing prescription drugs in a three-month supply rather than a one-month supply has long been regarded as a way to reduce the cost of drugs for patients and third-party payers. New research from the University of Chicago quantifies the savings for the first time.

An analysis of 26,852 prescriptions filled for 395 different drugs from 2000-2005 showed that patients who purchased their drugs in three-month supplies rather than with one-month supplies saved on average 29% in out-of-pocket costs. After factoring in third-party payers, including Medicare, Medicaid and insurance companies, total savings averaged 18%.

"These savings may not seem large to some, but they could help trim the cost of health care, which is especially important given the nationwide debate about how to finance health care reform," said G. Caleb Alexander, MD, MS, Assistant Professor of Medicine at the University of Chicago Medical Center and senior author of the study, which will be published in print November 20, 2009, in Applied Health Economics & Health Policy.

Although prescription drug costs represent only about 10% of the nation's total health care bill, they are one of the fastest growing sectors and affect a large proportion of patients.

"No matter what any health care reform package looks like, millions of Americans are burdened by prescription drugs costs, and this is one important way to help relieve that burden," Alexander said. "Other methods to lower prescription drug costs include substituting generic drugs for brand-name drugs and discontinuing non-essential medicines."

The drugs in this study were limited to those that were prescribed for common chronic conditions, including high cholesterol, hypertension, hypothyroidism and depression. Only patients who received both a one-month supply and a three-month supply during the same year in the same dose and quantity were included in the main analyses.

Forty-four percent of the prescriptions examined were dispensed in three-month supplies; the remainder were dispensed in one-month supplies. "This indicates that there is a significant amount of cost savings yet to be realized by converting from one-month supplies to three-month supplies," Alexander said.

The average monthly out-of-pocket cost for a one-month supply was $20.44 compared with $15.10 for a three-month supply yielding a 29% savings after adjustment for potential confounders. The corresponding numbers for the average monthly total costs were $42.72 and $37.95, respectively, yielding an 18% savings after adjustment for potential confounders.

If all the drugs in the study had been provided as three-month supplies, the out-of-pocket savings would have amounted to an estimated $148.6 million. Total savings would have amounted to $245.1 million. All figures are in 2005 dollars.

Patients' sex, race, level of education and number of chronic conditions did not seem to predict who was most likely to fill a 3-month supply, Alexander said. "We were surprised to find that there were no substantial systematic differences in the characteristics of individuals filling one-month and three-month supplies."

"Patients who are paying a lot each month for medicines - specially to treat chronic conditions—should investigate whether they can save money by using a three-month supply," he said. "Physicians need to keep this in mind as a potent way to help patients afford their medications."

'Frankenstein' fix lets asteroid mission cheat death

* 18:37 20 November 2009 **by David Shiga**

The beleaguered Hayabusa asteroid probe is back on track to return to Earth after a clever workaround coaxed one of its ion engines back to life.

The recovery is yet another reversal of fortune for the Japanese spacecraft, which has been plagued with problems since its visit to asteroid Itokawa in 2005.

It landed on the asteroid twice in November of that year, but its pellet gun – designed to dislodge material for collection – failed to fire. After an episode where it spun out of control and temporarily lost contact with Earth, engineers regained control and set it on a course back home.

The Hayabusa spacecraft is struggling to get back to Earth with possible samples of an asteroid **(Illustration: JAXA)**

Scientists are still eager to see the spacecraft return to Earth in case some loose asteroid bits accidentally made their way into the collection chamber during the landings.

But Hayabusa has been hobbling home without the full use of its four ion engines, which ionise xenon gas and then use electric fields to accelerate the ions, providing a steady – though weak – thrust.

One engine broke down shortly after launch and a second quit in 2007. When a third gave up the ghost on 4 November, it looked like Hayabusa would have too little power to ever get home.

Charge buildup

But the mission team has now cobbled together another working engine using parts from two sick ones, the Japan Aerospace Exploration Agency (JAXA) announced on Thursday.

One engine is still able to spit out positive ions for thrust, but can no longer squirt out negatively charged electrons, a step needed to prevent electric charge buildup on the spacecraft. The team got around this by spewing the required electrons from a second sick engine that retains this ability.

Now that Hayabusa in effect has two working ion engines again, it is back on track to return to Earth in June 2010, as had been planned before the 4 November glitch, JAXA says. If all goes well, it will drop its sample capsule in the Australian outback.

But Hayabusa project manager Jun'ichiro Kawaguchi of JAXA cautions that no one knows how long the cobbled-together engine will last. "This new configuration is very new to us and we are not sure ... how much we can count on [it]," he told New Scientist.

US could ban caffeine-alcohol drinks within months

THE US Food and Drug Administration is unimpressed by the fad for drinks that contain a double hit - alcohol and caffeine. Unless makers supply the FDA with scientific evidence that the drinks are safe they could be banned within months.

The agency is worried that consuming the drinks - which can mask the effect of alcohol - leads to rash behaviour, car crashes, violence and assaults. The FDA issued the ultimatum last week in response to a request made by the National Association of Attorneys General. "Caffeine added to alcohol poses a significant public health threat," said a task force headed by the attorney-generals of Utah, Guam and Connecticut.

The FDA allows caffeine concentrations of up to 200 parts per million in soft drinks, but adding caffeine to alcohol is unregulated. At least two of the 27 companies contacted have already withdrawn their drinks.

In 2006, Cecile Marczinski and Mark Fillmore of the University of Kentucky found that consumers of the drinks felt they were less inebriated than when imbibing alcohol alone, even though they made just as many errors in standard tests of alertness and reaction time.

Giraffes use 'supercharged' heart

By Jody Bourton Earth News reporter

For children and scientists alike the extraordinary shape of the giraffe has posed many questions. Why they have such long necks has so far been partly answered.

However, exactly how they maintain this neck, and get blood to a head that is two metres from their heart, has remained unknown. Now research reveals that giraffes have a small, powerful, supercharged heart that is different to that possessed by other similar mammals. Scientists have published the discovery in the journal Comparative Biochemistry and Physiology, Part A.

A long neck requires a special heart

Funny long neck

"There are not many animals that have evolved to have a very long neck," says giraffe expert Professor Graham Mitchell from the Centre of Wildlife Studies in Onderstepoort, South Africa. Prof Mitchell undertook the study along with Prof John Skinner from the Centre for Veterinary Wildlife Studies at the University of Pretoria South Africa.

"Giraffes have this very funny long neck, and two questions immediately arise, one is why and the other is how," he says.

The answer to the first question, says Prof Mitchell, is that a long neck probably confers a range of advantages, helping the animal feed on different browse, thermoregulate its body and be more vigilant.

But he wanted to find out more about how the giraffe (Giraffa camelopardalis) maintains such a long neck and is able to overcome its physiological constraints.

"Giraffes have this huge problem of having a head that is 2m away from the heart," Prof Mitchell says.

"So in a really big animal, how does it get blood up there?"

Under pressure

Most mammals have a relatively low blood pressure because their blood needs only move a short distance between head and heart. For the giraffe the distance is significant.

That creates two problems: a giraffe's heart must cope with the hydrostatic pressure exerted on it by the sheer amount of blood in the neck.

For blood to reach the head, the heart must then beat strongly enough to overcome this significant downward pressure caused by gravity.

Previous studies have found the giraffe has an extremely high blood pressure that is twice that found in other animals. But this study is the first to unravel the true nature of the giraffe heart and cardiovascular system. "For a long time it was thought that the origin of the high blood pressure was a really big heart and that was based on a single measurement based in the 1950s," says Prof Mitchell.

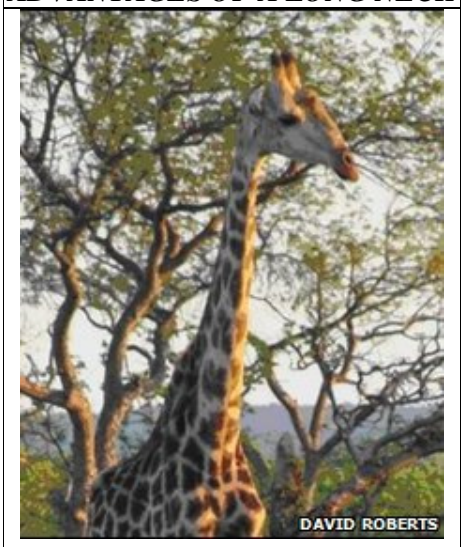
The researchers based their results on a range of measurements taken from giraffes culled in south eastern Zimbabwe between 2006 and 2009.

"Our concern was partly to explain the origin of high blood pressure and what physiological mechanisms operate to push the blood pressure to the level in the giraffe," he says. "We established that the heart is actually quite small. It's smaller than you'd expect in similar-sized animals, but the walls are incredibly thick," Prof Mitchell says. "You have a small but a very powerful heart delivering the blood pressure."

The researchers say giraffes are adapted to the high blood pressure and do not suffer as a consequence.

A giraffe's heart has evolved to have thick muscle walls and a small radius, giving it great power. The walls of the blood vessels also thicken with age as the giraffe's neck grows longer, to avoid rupturing under increasing pressure.

ADVANTAGES OF A LONG NECK



***Feeding**: enables giraffes to eat food that other animals cannot reach*
***Vigilance**: communication with other giraffes by sight and seeing predators from a distance*
***Thermoregulation**: provides a large surface area to lose heat in the hot sun*

Expanding vessels

The giraffe also has other specialist mechanisms to help deal with the high blood pressure, Prof Mitchell says.

"Blood pressure depends on the capacity of the cardiovascular system as well as the efficiency of the pump."

"Giraffes have got a way of adjusting the capacity of the cardiovascular system and are able to shrink and expand their blood vessels to change the volume of the cardiovascular system very efficiently."

From the data collected on the body dimensions of the dead giraffes, the researchers hope to reveal more about its extraordinary body, including insights into its range of vision and breathing.

Prof Mitchell says it will also be exciting to study the physiology of living giraffes using remote devices to collect data. "To measure blood pressure in a free living giraffe doing its thing, that would be really interesting," he says. "For people who study high blood pressure in humans, or people just like me who wonder how giraffes get it right."

Signs Swine Flu Wave May Have Peaked in U.S.

By DONALD G. McNEIL Jr.

Although federal health officials decline to use the word “peaked,” the current wave of swine flu appears to have done so in the United States.

Flu activity is coming down in all regions of the country, the Centers for Disease Control and Prevention said Friday, though it is still rising in Hawaii, Maine and some isolated areas.

The World Health Organization said Friday that there were “early signs of a peak” in much of the United States.

On Wednesday, the American College Health Association, which surveys over 250 colleges with more than three million students, said new cases of flu had dropped in the week ending Nov. 13. It was the first drop since school resumed in the fall, and it was significant - new cases were down 27 percent from the week before.

And on Friday, Quest Diagnostics, the country’s largest laboratory, said its tests of 142,000 suspected flu specimens since May showed that the flu peaked in late October.

Nonetheless, Dr. Anne Schuchat, the director of immunization and respiratory diseases at the C.D.C., chose her words carefully, saying: “I wish I knew if we had hit the peak. Even if a peak has occurred, half the people who are going to get sick haven’t gotten sick yet.”

Dr. Schuchat also noted that even when new infections topped out, hospitalizations and deaths were still on the way up, because most took place days or weeks later.

Privately, federal health officials say they fear that if they concede the flu has peaked, Americans will become complacent and lose interest in being vaccinated, increasing the chances of another wave. In New York, where cases peaked last May, vaccine clinics have gone begging for takers as long lines form in the rest of the country.

Epidemiologists expected a peak about now, because flu waves typically last six to eight weeks.

The current fall wave of new infections began in late August in the Southeast, where schools start earlier than on the East or West Coasts; it took several weeks to spread across the country and began falling in the Southeast two weeks ago. The drop was clearly not caused by the swine flu vaccine drive, which has not gone as fast as the authorities had hoped because the vaccine seed strain grew so slowly.

Only about 54 million doses are available now, and Dr. Schuchat said she wanted to “apologize for the frustration the public has been experiencing.”

Lone Simonsen, an epidemiologist at George Washington University, said she expected a third wave in December or January, possibly beginning in the South again.

“If people think it’s going away, they can think again,” Dr. Simonsen said.

Based on death rates in New York City and in Scandinavia, she has argued that both 1918 and 1957 had mild summer waves followed by two stronger waves, one in fall and one in midwinter.

Only 43 states are now reporting “widespread” flu activity, down from 48 two weeks ago.

As Dr. Schuchat noted, that is still above peak activity in a typical flu season.

The winter flu season usually starts in December; it is expected to return this year.

Since last week, 21 children and teenagers died of confirmed or suspected cases of the flu, Dr. Schuchat said. Based on her agency’s belief that three pediatric deaths take place for each confirmed one, about 600 children and teenagers have died since this epidemic began.

The World Health Organization said the flu appeared to be peaking in the United States and some Western European countries, like Belgium, Britain and Ireland. But it was moving rapidly east and north.

Canada’s outbreak is still intensifying, as is the one in Norway, and Eastern Europe and Central Asia, including Afghanistan, are seeing a surge in cases.

Norway reported finding a mutated virus in three people who died or were severely ill. The mutation, known as D222G on the receptor binding domain, allow the virus to grow deeper in the lungs.

The mutation does not appear to be circulating and may have spontaneously arisen in the three patients, said Geir Stene-Larsen, director of the Norwegian Institute of Public Health. Only 3 of Norway’s 70 tested samples had it.

Asked about that, Dr. Schuchat said the same mutation had also been found in mild cases in several countries and it did not make the virus resistant to vaccine or to treatment with drugs like Tamiflu. She said that she did not want to “underplay” it, but that “it’s too soon to say what this will mean long term.”

The D222G mutation allows the virus to bind to receptors on cells lining the lungs, which are slightly different from those in the nose and throat.

Henry L. Niman, a flu tracker in Pittsburgh, has been warning for a week that the same mutation has repeatedly been found in Ukraine, which is in the grips of a severe outbreak and where surprising numbers of people have died with lung hemorrhages.

Separate reports of Tamiflu-resistant virus also surfaced Friday. Duke University Medical Center said it had found four cases among its patients in six weeks, and British health authorities reported five in one Welsh hospital. Although Tamiflu resistance would be a serious worry for health officials, it was not clear that the strains were circulating outside the hospitals. Many isolated cases of resistant virus have been found.

Surface bacteria maintain skin's healthy balance

On the skin's surface, bacteria are abundant, diverse and constant, but inflammation is undesirable. Research at the University of California, San Diego School of Medicine now shows that the normal bacteria living on the skin surface trigger a pathway that prevents excessive inflammation after injury.

"These germs are actually good for us," said Richard L. Gallo, MD, PhD, professor of medicine and pediatrics, chief of UCSD's Division of Dermatology and the Dermatology section of the Veterans Affairs San Diego Healthcare System.

The study, to be published in the advance on-line edition of Nature Medicine on November 22, was done in mice and in human cell cultures, primarily performed by post-doctoral fellow Yu Ping Lai .

"The exciting implications of Dr. Lai's work is that it provides a molecular basis to understand the 'hygiene hypothesis' and has uncovered elements of the wound repair response that were previously unknown. This may help us devise new therapeutic approaches for inflammatory skin diseases," said Gallo.

The so-called "hygiene hypothesis," first introduced in the late 1980s, suggests that a lack of early childhood exposure to infectious agents and microorganisms increases an individuals susceptibility to disease by changing

how the immune system reacts to such "bacterial invaders." The hypothesis was first developed to explain why allergies like hay fever and eczema were less common in children from large families, who were presumably exposed to more infectious agents than others. It is also used to explain the higher incidence of allergic diseases in industrialized countries.

The skin's normal microflora – the microscopic and usually harmless bacteria that live on the skin – includes certain staphylococcal bacterial species that will induce an inflammatory response when they are introduced below the skin's surface, but do not initiate inflammation when present on the epidermis, or outer layer of skin.

In this study, Lai, Gallo and colleagues reveal a previously unknown mechanism by which a product of staphylococci inhibits skin inflammation. Such inhibition is mediated by a molecule called staphylococcal lipoteichoic acid (LTA) which acts on keratinocytes – the primary cell types found on the epidermis.

The researchers also found that Toll-like receptor 3 (TLR3) activation is required for normal inflammation after skin injury.

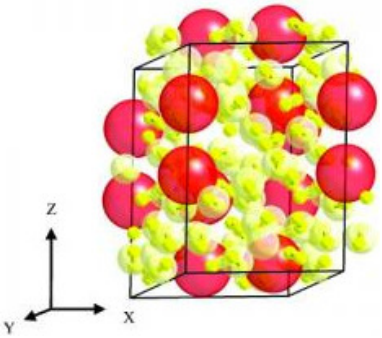
"Keratinocytes require TLR3 to mount a normal inflammatory response to injury, and this response is kept from becoming too aggressive by staphylococcal LTA," said Gallo. "To our knowledge, these findings show for the first time that the skin epithelium requires TLR3 for normal inflammation after wounding and that the microflora helps to modulate this response."

Additional contributors to the paper include Yuping Lai, Anna Di Nardo, Teruaki Nakatsuji, Anna L Cogen, Chun-Ming Huang and Katherine A. Radek, UCSD Division of Dermatology and the VA San Diego Healthcare System; Anke Leichtle and Allen F. Ryan, UCSD Department of Surgery/Otolaryngology and the VA San Diego Healthcare System; Yan Yang and Zi-Rong Wu, School of Life Science, East China Normal University, Shanghai; Lora V Hooper, Howard Hughes Medical Institute and University of Texas Southwestern Medical Center, Dallas; and Richard R Schmidt and Sonja von Aulock, University of Konstanz, Germany.

The study was funded by grants from the National Institutes of Health, and a US Veterans Administration Merit Award.

New hydrogen-storage method discovered

Washington, D.C.- Scientists at the Carnegie Institution have found for the first time that high pressure can be used to make a unique hydrogen-storage material. The discovery paves the way for an entirely new way to approach the hydrogen-storage problem. The researchers found that the normally unreactive, noble gas xenon combines with molecular hydrogen (H2) under pressure to form a previously unknown solid with unusual bonding chemistry. The experiments are the first time these elements have been combined to form a stable compound. The discovery debuts a new family of materials, which could boost new hydrogen technologies. The paper is published in the November 22, 2009, advanced online publication of Nature Chemistry.



This schematic shows the structure of the new material, Xe(H2)7. Freely rotating hydrogen molecules (red dumbbells) surround xenon atoms (yellow). Nature Chemistry

Xenon has some intriguing properties, including its use as an anesthesia, its ability to preserve biological tissues, and its employment in lighting. Xenon is a noble gas, which means that it does not typically react with other elements.

As lead author Maddury Somayazulu, research scientist at Carnegie's Geophysical Laboratory, explained: "Elements change their configuration when placed under pressure, sort of like passengers readjusting themselves as the elevator becomes full. We subjected a series of gas mixtures of xenon in combination with hydrogen to high pressures in a diamond anvil cell. At about 41,000 times the pressure at sea level (1 atmosphere), the atoms became arranged in a lattice structure dominated by hydrogen, but interspersed with layers of loosely bonded xenon pairs. When we increased pressure, like tuning a radio, the distances between the xenon pairs changed–the distances contracted to those observed in dense metallic xenon."

The researchers imaged the compound at varying pressures using X-ray diffraction, infrared and Raman spectroscopy. When they looked at the xenon part of the structure, they realized that the interaction of xenon with the surrounding hydrogen was responsible for the unusual stability and the continuous change in xenon-xenon distances as pressure was adjusted from 41,000 to 255,000 atmospheres.

Why was the compound so stable? "We were taken off guard by both the structure and stability of this material," said Przemek Dera, the lead crystallographer who looked at the changes in electron density at different pressures using single-crystal diffraction. As electron density from the xenon atoms spreads towards the surrounding hydrogen molecules, it seems to stabilize the compound and the xenon pairs.

"Xenon is too heavy and expensive to be practical for use in hydrogen-storage applications," remarked Somayazulu. "But by understanding how it works in this situation, researchers can come up with lighter substitutes."

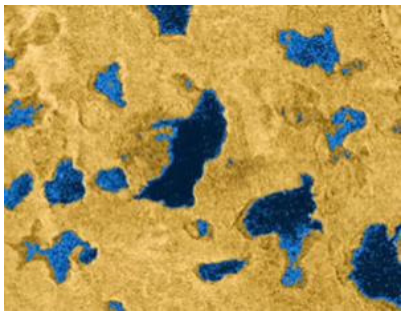
"It's very exciting to come up with new hydrogen-rich compounds, not just for our interest in simple molecular systems, but because such discoveries can be the foundation for important new technologies," commented Russell Hemley, director of the Geophysical Laboratory and a co-author. "This hydrogen-rich solid represents a new pathway to forming novel hydrogen storage compounds and the new pressure-induced chemistry opens the possibility of synthesizing new energetic materials."

This research was funded by the Department of Energy, Basic Energy Sciences hydrogen storage, and the National Science Foundation, Division of Materials Research.

Icy moon's lakes brim with hearty soup for life

* 00:24 23 November 2009 **by David Shiga**

Saturn's frigid moon Titan may be friendlier to life than previously thought. New calculations suggest Titan's hydrocarbon lakes are loaded with acetylene, a chemical some scientists say could serve as food for cold-resistant organisms.



Titan's hydrocarbon lakes, seen here in radar images, boast life-friendly chemistry **(Image: NASA/JPL)**

At about -180 °Celsius, Titan's surface is far too cold for liquid water. But two pairs of scientists proposed in 2005 that alien organisms might live instead in bodies of liquid hydrocarbons on the frigid moon. They suggested such organisms could eat acetylene that falls to the surface after forming in the atmosphere, combining it with hydrogen to gain energy. Since then, Titan has spotted dozens of lakes on Titan's surface, thought to be made of a mixture of liquid ethane and methane. But since no probe has directly sampled them, no one knows how much acetylene they might contain.

An estimate made in 1989 suggested bodies of liquid hydrocarbons on Titan would contain a few parts in 10,000 of acetylene.

But an updated estimate based on data from the Cassini-Huygens mission to Saturn now suggests the lakes contain much more food for any hungry alien life-forms that might be present. The new calculations were made by a team of scientists led by Daniel Cordier of the Ecole Nationale Supérieure de Chimie de Renne, France.

Right temperature

Data from the Cassini spacecraft and the Huygens probe, which parachuted to Titan's surface in 2005, helped Cordier's team re-calculate the lakes' likely composition. This depends on factors like a lake's temperature, which affects how easily chemicals will dissolve in it, and the rate various chemicals are produced in the atmosphere and rain onto the surface.

The team found that acetylene would be hundreds of times as abundant as the previous estimate, making up one part in 100 of the lake's content. "Having about a per cent of acetylene is potentially interesting from the life point of view," says team member Jonathan Lunine of the University of Arizona in Tucson. The idea of acetylene-eating organisms on Titan is "highly speculative" but intriguing, he says.

Separate layers

"I think the results are very exciting and further support the possibility for life on Titan," says Dirk Schulze-Makuch of Washington State University in Pullman, one of the scientists who proposed the possibility of acetylene-eating life in 2005. "Titan should be one of the two top targets for future astrobiology missions, the other being Mars."

But Tetsuya Tokano, a Titan researcher at the University of Cologne in Germany, says the exact amount of acetylene may be less important than other properties of the lakes that remain unknown, such as the existence of currents to keep them well-mixed. Tokano pointed out in a recent study that without mixing, hydrogen and acetylene would stay in separate layers of the lakes, limiting reactions between them that might otherwise power exotic organisms. *Journal reference: Astrophysical Journal Letters (in press)*

Grandmother monkeys care for baby

By Matt Walker Editor, Earth News

Two grandmother monkeys have been seen intervening to raise their own grandchildren, providing essential care including suckling the young. The scientists who witnessed the behaviour say it is the first unambiguous example of such behaviour shown by a non-human primate.

The observations were made in a free-ranging group of Japanese macaques living in Katsuyama, Japan.

Details of the grandmothers' actions are published in the journal Primates.

The same group of wild, free-ranging Japanese macaques (Macaca fuscata) have been studied since 1958, so scientists have kept a record of the birth date and blood relationships of each individual.

One scientist, Dr Masayuki Nakamichi at Osaka University in Japan, has been studying the animals' social interactions for 30 years. However, the behaviour of two macaque grandmothers surprised even him.

"We know that some monkeys... sometimes adopt infants. In most cases, it is females who have lost their own infants," Dr Nakamichi says. “However, in the present cases, the old, probably post-reproductive mothers started to take care of their young granddaughters. It is very unusual for females who have not had their own young offspring for years to start to take care of other infants."

Dr Nakamichi and colleagues at Osaka University first observed a monkey known to them as GM1, a 24-year-old female macaque, looking after her granddaughter GD1. The infant GD1 was the offspring of GM1's own daughter, known as M1. GM1 started looking after GD1 just 20 days after her birth.

And she intervened even more when the infant's mother M1 unexpectedly went missing from the troop. Then the grandmother held, groomed, carried and retrieved the abandoned and now two-month-old infant, even placing her nipples in the infant's mouth.

The grandmother looked after her granddaughter in this way for at least six days, before the mother returned and gradually resumed her role.

a+b) Grandmother GM1 retrieves her granddaughter GD1 then lets her suckle:
c) GMI then grooms her returning daughter who reunites with her own infant

Essential care

The second case involved a 23-year-old monkey dubbed GM2, who looked after her 14-month old granddaughter, GD2. In this case, the mother, M2, was busy nursing a second, younger infant.

So the grandmother stepped in, allowing her granddaughter to take her nipple on numerous occasions.

She was observed still looking after her granddaughter in this way 5 months later.

In both examples, the researchers believe the grandmothers were providing essential care.

Without the intervention of GM1, the scientists say her granddaughter would have died within two weeks.

Because GM1 had not had offspring for six years, she would not have been able to provide milk for the infant, but her actions would have protected her and kept her warm.

The second grandmother, GM2, did likely provide her granddaughter with nutritious milk, as the infant was seen actively suckling. It is likely that the repeated suckling by the granddaughter over a few weeks induced her to begin producing milk again.

Close relationships

The behaviour of the two elder monkeys offers support to an idea called the 'grandmother hypothesis'.

"It is an idea that post-reproductive grandmothers can play an important role in the survival of their grandchildren, although they cannot produce their own offspring," explains Dr Nakamichi. By doing so, he says, females can improve the chances that their own genes will be passed on down the generations.

The idea helps explain why mammals such as monkeys can live well beyond reproductive age, as by doing so, they can continue to promote the survival of their relations.

However, definitive evidence for the hypothesis has been difficult to obtain.

Numerous studies have shown that monkeys such as vervets, Japanese macaques and langurs will form close relationships with their grandchildren, investing time in them and occasionally helping to protect them.

Yet other studies on Japanese macaques, baboons and titi monkeys, for example, do not show that the presence of grandparents improves an infant's survival.

In other social mammals such as elephants, grandmothers may also occasionally help out with grandchildren.

But usually the grandmother has more offspring of her own, and does not provide essential, life-saving care.

"To our knowledge, there have been no reported cases in which, instead of a mother, a grandmother without dependant offspring has continuously provided essential care for the survival of her dependant grandchild, which is in accordance with the grandmother hypothesis," Dr Nakamichi and colleagues write in the journal Primates.

Dirt 'can be good for children'

Children should be allowed to get dirty, according to scientists who have found being too clean can impair the skin's ability to heal. Normal bacteria living on the skin trigger a pathway that helps prevent inflammation when we get hurt, the US team discovered. The bugs dampen down overactive immune responses that can cause cuts and grazes to swell, they say. Their work is published in the online edition of Nature Medicine.

Experts said the findings provided an explanation for the "hygiene hypothesis", which holds that exposure to germs during early childhood primes the body against allergies.

Many believe our obsession with cleanliness is to blame for the recent boom in allergies in developed countries.

'Good' bacteria

Researchers from the School of Medicine at University of California, San Diego, found a common bacterial species, known as Staphylococci , blocked a vital step in a cascade of events that led to inflammation.

By studying mice and human cells, they found the harmless bacteria did this by making a molecule called lipoteichoic acid or LTA, which acted on keratinocytes - the main cell types found in the outer layer of the skin. The LTA keeps the keratinocytes in check, stopping them from mounting an aggressive inflammatory response.

Head of the research Professor Richard Gallo said: "The exciting implication of the work is that it provides a molecular basis to understand the hygiene hypothesis and has uncovered elements of the wound repair response that were previously unknown. "This may help us devise new therapeutic approaches for inflammatory skin diseases."

The lobby group Parents Outloud said the work offered scientific support for its campaign to stop children being mollycoddled and over-sanitised. A spokeswoman for Allergy UK said there was a growing body of evidence that exposure to germs was a good thing. But she said more research was needed.

"Rates of allergy have tripled in the UK in the last decade. One in three people now has some kind of allergy.

"Some of this might be that people are better informed. But a lot of it is genetic as well as down to our environment," she said.

New research shows versatility of amniotic fluid stem cells

WINSTON-SALEM, N.C. – For the first time, scientists have demonstrated that stem cells found in amniotic fluid meet an important test of potential to become specialized cell types, which suggests they may be useful for treating a wider array of diseases and conditions than scientists originally thought.

Reporting in Oncogene, a publication of Nature Publishing Group, the research teams of Anthony Atala, M.D., director of the Wake Forest Institute for Regenerative Medicine, and Markus Hengstchläger, Ph.D., from the Medical University of Vienna, have shown that these amnion stem cells can form three-dimensional aggregates of cells known as embryoid bodies (EBs). It is believed that cells at this stage of development can be directed to become virtually any cell in the human body.

"This finding suggests that the amnion cells have greater potential than we originally thought and may be able to form many cell types," said Atala. "This could expand the number for diseases and conditions that they may be helpful for."

Atala's team is currently evaluating the cells for their potential to treat diabetes and kidney disease. They were the first to report success (Nature Biotechnology, Jan. 2007) in isolating stem cells from placenta and amniotic fluid, which surrounds the developing fetus. The current research is one of several projects designed to determine the potential of this new type of stem cell.

For the study, scientists generated two additional lines of stem cells from amniotic fluid using the same protocol developed by Atala's lab. They then investigated the incidence of EB formation in all three lines.

"Performing many independent experiments using different approaches, we demonstrate in the report that human amnion stem cells … can indeed form embryoid bodies," write the researchers in Oncogene. "Amnion cells are on the way to become an important source for both basic science and regenerative medicine."

In addition to the finding about EBs, the scientists identified a protein found inside cells (mTOR) as the regulator of EB formation. Hengstshläger, whose team was the first to provide evidence for the existence of stem cells in amniotic fluid, said that this finding may allow for new insights into the molecular mechanism of EB formation.

He said the cells may be a useful source for generating disease-specific stem cell lines for studying the differentiation process to determine what goes wrong in genetic diseases.

"These stem cells allow for studying the effects of mutations causing human genetic diseases on specific cell differentiation processes," he said.

Other potential advantages of the cells are that they can be grown in large quantities and are readily available during gestation and at the time of birth. "Whether these cells are as versatile as embryonic stem cells remains to be determined," said Atala, "but the current finding is certainly encouraging."

Atala stopped short of calling the cells pluripotent, which means the ability to form many cell types. He said while the cells meet some of the characteristics of pluripotency, such as versatility, they do not form tumors when implanted in animals, which is also considered a characteristic. The fact that the amnion cells are less likely to form tumors may be one advantage that they have over embryonic stem cells in their potential for clinical use.

Co-researchers were Alessandro Valli, Ph.D., Margit Rosner, student, Christiane Fuchs, MSc., Nicol Siegel, MSc., and Helmut Dolznig, Ph.D., from the Medical University of Vienna, Colin E. Bishop, Ph.D., from Wake Forest, and Ulrike Mädel, student, and Wilfried Feichtinger, M.D., from Wunschbaby Zentrum, in Vienna, Austria.