

Diabetes drug kills cancer stem cells in combination treatment in mice

PHILADELPHIA - In a one-two punch, a familiar diabetes drug reduced tumors faster and prolonged remission in mice longer than chemotherapy alone by targeting cancer stem cells, Harvard Medical School researchers reported in the September 14 online first edition of *Cancer Research*, a journal of the American Association for Cancer Research.

"We have found a compound selective for cancer stem cells," said lead researcher Kevin Struhl, Ph.D., the David Wesley Gaiser professor of biological chemistry and molecular pharmacology at Harvard Medical School. "What's different is that ours is a first-line diabetes drug."

These findings add to a growing body of preliminary evidence in cells, mice and people that metformin may improve breast cancer outcomes in people. In this study, the diabetes drug seemed to work independently of its ability to improve insulin sensitivity and lower blood sugar and insulin levels, all of which are also associated with better breast cancer outcomes.

The results fit within the cancer stem cell hypothesis, an intensely studied idea that small subsets of cancer cells have a special power to initiate tumors, fuel tumor growth and promote recurrence of cancer. Cancer stem cells appear to resist conventional chemotherapies, which kill the bulk of the tumor.

"There is a big desire to find drugs specific to cancer stem cells," said Struhl. "The cancer stem cell hypothesis says you cannot cure cancer unless you also get rid of the cancer stem cells. From a purely practical point of view, this could be tested in humans. It's already [in use as] a first-line diabetes drug."

The possible usefulness of a diabetes drug against cancer lends credence to an emerging idea that, in the vast and complex alphabet soup of molecular interactions within cells, a relatively few biological pathways will turn out to be most important for many different diseases, Struhl suggested.

In experiments led by postdoctoral fellows Heather Hirsch, Ph.D., and Dimitrios Iliopoulos, Ph.D., the combination of metformin and the cancer drug doxorubicin killed human cancer stem cells and non-stem cancer cells in culture. The researchers used four genetically distinct breast cancer cell lines.

In mice, pretreatment with metformin prevented the otherwise dramatic ability of human breast cancer stem cells to form tumors. In other mice where tumors took hold for 10 days, the combination therapy also reduced tumor mass more quickly and prevented relapse for longer than doxorubicin alone. In the two months between the end of treatment and the end of the experiment, tumors regrew in the mice treated with chemotherapy alone, but not in those who received both drugs. Metformin was ineffective in treating tumors when used alone.

"This is an exciting study," said Jennifer Ligibel, M.D., a medical oncologist at the Dana-Farber Cancer Institute and a Harvard Medical School instructor in medicine. Ligibel and colleagues at the National Cancer Institute of Canada Clinical Trials Group are developing a large-scale phase II trial and will study its metformin's impact on recurrence in women treated for early stage breast cancer.

"There is a lot of interest in studying metformin in breast cancer, but so far we do not have direct evidence that metformin will improve outcomes in patients," said Ligibel, who was not involved in the current study "That's what this trial is for."

So far, observational studies have suggested a lower risk of cancers, including breast cancer, and better response to chemotherapy in patients with diabetes who are treated with metformin, she said. Results of basic science studies have also suggested plausible biological mechanisms. The study from the Struhl lab suggests a potential new pathway through which metformin could have an effect on breast cancer cells, according to Ligibel.

In their search for compounds that selectively destroy cancer stem cells, researchers hope to improve cancer outcomes. But the story is never as simple in human cancers, according to Kornelia Polyak, M.D., Ph.D., a breast cancer researcher at the Dana-Farber Cancer Institute and an associate professor of medicine at Harvard Medical School.

Cancer stem cells are a shifty target, said Polyak, who was not involved in the current study. For example, any cancer cell can acquire the properties of a cancer stem cell, and cancer stem cells can change into non-stem cancer cells, which can be just as deadly. Clinical trials in people are needed to test these ideas, according to Polyak.

The study by Struhl and colleagues is an offshoot of a larger project in his lab to systematically track how gene activity changes when cells transform into cancer. These changes were remarkably similar to gene dynamics in diabetes and other inflammatory conditions.

The researchers reasoned that if a common genetic pathway underlies different diseases, drugs that work against one disease might work against another. In a screen, the most effective drug inhibiting the transformation of cells into cancer was metformin, which led to the experiments in this study. They were further encouraged by the low dose of metformin needed for the effect in the laboratory, compared to the

amount needed for analogous molecular experiments in basic diabetes research. The relative dosage for treating or preventing cancer is unknown and untested in people.

Struhl and Harvard Medical School have applied for a patent for a combined therapy of metformin and a lower dose of chemotherapy, which is being tested in animals. The National Institutes of Health and the American Cancer Society funded this research.

Fake video dramatically alters eyewitness accounts

Researchers at the University of Warwick have found that fake video evidence can dramatically alter people's perceptions of events, even convincing them to testify as an eyewitness to an event that never happened.

Associate Professor Dr Kimberley Wade from the Department of Psychology led an experiment to see whether exposure to fabricated footage of an event could induce individuals to accuse another person of doing something they never did.

In the study, published in *Applied Cognitive Psychology*, Dr Wade found that almost 50% of people shown fake footage of an event they witnessed first hand were prepared to believe the video version rather than what they actually saw.

Dr Wade's research team filmed 60 subjects as they took part in a computerised gambling task. The subjects were unknowingly seated next to a member of the research team as they both separately answered a series of multiple-choice general knowledge questions.

All subjects were given a pile of fake money to gamble with and they shared a pile of money that represented the bank. Their task was to earn as much money as possible by typing in an amount of money to gamble on the chances of them answering each question correctly. They were told the person who made the highest profit would win a prize. When they answered each question, subjects saw either a green tick on their computer monitor to show their answer was correct, or a red cross to show it was incorrect. If the answer was wrong, they would be told to return the money to the bank.

After the session, the video footage was doctored to make it look as if the member of the research team sat next to the subject was cheating by not putting money back into the bank.

One third of the subjects were told that the person sat next to them was suspected of cheating. Another third were told the person had been caught on camera cheating, and the remaining group were actually shown the fake video footage. All subjects were then asked to sign a statement only if they had seen the cheating take place.

Nearly 40% of the participants who had seen the doctored video complied. Another 10% of the group signed when asked a second time by the researchers. Only 10% of those who were told the incident had been caught on film but were not shown the video agreed to sign, and about 5% of the control group who were just told about the cheating signed the statement.

Dr Wade said: "Over the previous decade we have seen rapid advances in digital-manipulation technology. As a result, almost anyone can create convincing, yet fake, images or video footage. Our research shows that if fake footage is extremely compelling, it can induce people to testify about something they never witnessed."

Communication problems in dementia care cause physical strain

Excessive physical strain in dementia care is not so much related to equipment or the resident's body weight as it is due to communication problems and misunderstandings. This is shown in a new study from the Sahlgrenska Academy. Dementia not only affects the memory and other cognitive functions, but also motor skills such as the ability to walk.

'The symptoms of dementia are very individual and can vary from one day to the next, and sometimes even from one moment to the next. This makes person transfers in dementia care very demanding for the personnel', says physiotherapist Cristina Wångblad, one of the researchers behind the study recently published in the scientific journal *Scandinavian Journal of Caring Sciences*.

The study investigates how nurses' aides at three dementia care facilities in western Sweden feel about person transfers in the workplace and what they do to reduce the physical strain. While the residents' body weight seems to be less relevant for how straining the personnel perceive their work to be, Wångblad found misunderstandings and communication problems to be much more important.

'A resident who is unable to read signals from the surroundings or who forgets what he or she is supposed to do reacts with anxiety, confusion and resistance. The personnel can avoid communication problems by explaining things with different words and by using body language, and thereby make person transfers much easier', says Synneve Dahlin Ivanoff, Professor of Occupational Therapy at the Sahlgrenska Academy.

Individual-specific knowledge about the residents also seems useful. For example, the personnel can make person transfers easier by giving appropriate instructions, using the right vocal pitch, assisting a resident in the way he or she prefers, and by knowing whether it is possible to ask a resident to move faster.

'The physiotherapists who train and educate dementia care personnel must be aware of the complexity of person transfers. The instructions on how residents should be moved ought to be tailored to each individual's needs and to each situation', says Wångblad.

Green tea component may help preserve stored platelets, tissues

Tampa, Fla. (September 14th, 2009) – In two separate studies, a major component in green tea, epigallocatechin-3-O-gallate (EGCG), has been found to help prolong the preservation of both stored blood platelets and cryopreserved skin tissues. Published in the current double issue of *Cell Transplantation* (18:5/6), now freely available on-line at <http://www.ingentaconnect.com/content/cog/ct>, devoted to organ preservation and transplantation studies from Japan, the two complimentary studies have shown that EGCG, known to have strong anti-oxidative activity, can prolong platelet cell "shelf life" via anti-apoptosis (programmed cell death) properties and preserve skin tissues by controlling cell division.

Dr. Suong-Hyn Hyon, lead author on both studies and associate professor in the Institute for Frontier Medical Sciences in Kyoto, Japan, says that EGCG, a green tea polyphenol, is a known anti-oxidation and anti-proliferation agent, yet the exact mechanism by which EGCG works is not yet known. However, some of the activity of EGCG is likely to be related to its surface binding ability.

Enhanced platelet preservation

Using standard blood banking procedures, the storage duration for platelet cells (PCs) is limited to five days internationally or three days in Japan. During storage, PCs undergo biochemical, structural and functional changes, and PCs may lose membrane integrity and haemostatic functions, such as aggregability and affinity for surface receptors. Thus, PC shortages often occur. When EGCG was added to blood platelet concentrates, aggregation and coagulation functions were better-maintained after six days, perhaps due to EGCG's anti-oxidative ability. Researchers suggested that EGCG inhibited the activation of platelet functions and protected the surface proteins and lipids from oxidation.

"Functions were restored by the maintained surface molecules with the detachment of ECGC by washing," noted Dr. Hyon. "EGCG may lead to an inhibition of platelet apoptosis and lower rates of cell death, offering a potentially novel and useful method to prolong platelet storage period."

EGCG enhances life of cryopreserved skin grafts

Another team of Japanese researchers studied the effects of using EGCG on frozen, stored skin tissues. As with platelet storage, the storage of skin tissue for grafting presents problems of availability and limitations on the duration of storage.

"To provide best outcomes, skin grafts must be processed and stored in a manner that maintains their viability and structural integrity until they are needed for transplantation," explained Dr. Hyon. "Transplant dysfunction often occurs as the result of oxidation. A better storage solution could prevent this."

It is known that polyphenols in green tea promote the preservation of tissues, such as blood vessels, cornea, islet cells, articular cartilage and myocardium at room temperature. Also, it is known that ECGC has stronger anti-oxidant activities than vitamin C because of its stereochemical structure and is reported to play an important role in preventing cancer and cardiovascular diseases.

This study examined how EGCG might help extend the preservation duration of frozen rat skin tissues and found that skin grafts could be protected from freeze-thaw injuries when EGCG was absorbed into various membrane lipids and proteins. Results of the study showed that EGCG enhanced the viability and stored duration of skin grafts up to seven weeks at 4 degrees C.

"The storage time of skin grafts was extended to 24 weeks by cryopreservation using EGCG and the survival rate was almost 100 percent," noted Dr. Hyon. "These studies highlight the benefits of using natural compounds such as ECGC to enhance the preservation of stored tissues, possibly due to their anti-oxidative properties" said Dr. Naoya Kobayashi, guest editor of this double issue of *Cell Transplantation*.

*Contact: Suong-Hyu Hyon, PhD, associate professor, Research Center for Nano Medical Engineering, Institute for Frontier Medical Sciences, Kyoto University, 53 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507 Japan.
Tel: +81 75 751 4125, Email: biogen@frontier.kyoto-u.ac.jp*

Popular stomach acid reducer triples risk of developing pneumonia

WINSTON-SALEM, N.C. – A popular stomach-acid reducer used to prevent stress ulcers in critically ill patients needing breathing machine support increases the risk of those patients contracting pneumonia threefold, according to researchers at Wake Forest University School of Medicine.

Hospital-acquired pneumonia is the leading cause of infection-related deaths in critically ill patients. It increases hospital stays by an average of seven to nine days, cost of care, and the risk of other complications.

"As best we can tell, patients who develop hospital-acquired pneumonia or ventilator-acquired pneumonia have about a 20 to 30 percent chance of dying from that pneumonia," said senior study author David L. Bowton,

M.D., professor and head of the Section on Critical Care in the Department of Anesthesiology. "It's a significant event."

The study, published in a recent issue of CHEST, compared treatment with two drugs that decrease stomach acid: ranitidine, marketed under the name Zantac™, and pantoprazole, marketed under the name Protonix™.

Both drugs decrease stomach acid, but the newer pantoprazole is considered more powerful and has become the drug of choice in many hospitals.

However, in the analysis of 834 patient charts, the researchers found that hospitalized cardiothoracic surgery patients treated with pantoprazole were three times more likely to develop pneumonia.

"We conducted this study, in part, because we thought we were seeing more pneumonias than we were used to having," said study co-author Marc G. Reichert, Pharm.D., pharmacy coordinator for surgery at Wake Forest University Baptist Medical Center.

Both acid-reducing drugs can make the stomach a more hospitable place for bacteria to colonize. Patients on breathing machines sometimes develop pneumonia when stomach secretions reflux into the lungs.

Current treatment guidelines to prevent pneumonia recommend raising the head of the bed for patients on breathing machines, which reduces the risk of stomach secretions getting into the lungs. But the study's findings suggest some other steps could keep critically ill patients from developing ventilator-associated pneumonia.

Doctors should consider whether an acid reducer is needed at all, Bowton said. The occurrence of stress ulcer bleeding has gone down in recent years, perhaps because patients with breathing tubes are fed earlier, and food in the stomach may neutralize or reduce the effects of stomach acid.

Bowton added that in cases where an acid reducer is needed, ranitidine is recommended, given the apparent decreased risk in developing pneumonia.

Doctors should stop using the drug as soon as the risk of bleeding passes – once the patient is off the breathing machine and eating, either on his/her own or through a feeding tube.

"Stopping the drugs earlier appears to be the best thing for patients," Reichert said.

Todd A. Miano, Pharm.D., formerly of Wake Forest University Baptist Medical Center and now with the Hospital of the University of Pennsylvania, is the study's lead author. Co-authors, all from Wake Forest University School of Medicine, are Timothy T. Houle, Ph.D., and Drew A. MacGregor, M.D., of the Department of Anesthesiology; and Edward H. Kincaid, M.D., of the Department of Cardiothoracic Surgery.

Pfizer to pay huge fine for improper drug promotion

BY ANY standard, the \$2.3 billion sum that pharmaceutical giant Pfizer will pay to settle charges of improper drug promotion is big. But will it change anything?

Doctors can prescribe medications in situations other than those approved by drug regulators, but drug firms in the US are not allowed to promote these "off-label" uses.

The payout settles claims by whistleblowers and the US government that Pfizer broke these rules for a range of drugs including the painkiller Bextra, pulled from the market in 2005 because of evidence suggesting it might increase the risk of heart attack and stroke.

The sum represents less than three weeks of sales for Pfizer, based on 2008 figures - a significant loss but by no means catastrophic. "It sends out a clear message," says Merrill Goozner, formerly of the Center for Science in the Public Interest in Washington DC. "Whether the message gets heard or not is a different question." Given the huge profits to be made from drug sales, he says, the incentives to bend the rules remain strong.

Jupiter had brief encounter with icy companion

* 13:37 14 September 2009 by MacGregor Campbell

The planet Jupiter seems to be as promiscuous as its Olympian namesake. New calculations reveal that in the middle of the last century it had a fling with a wayward comet, which for 12 years joined the gas giant's harem of moons. The finding helps to explain how comets move from the outer solar system into inner, sometimes Earth-threatening orbits.

Comet Kushida-Muramatsu is the fifth object known to have been captured by Jupiter as a temporary moon. The most famous of these brief companions, Shoemaker-Levy 9, crashed into the planet in 1994.

Astronomers Katsuhiko Ohtsuka of the Tokyo Meteor Network, Japan, and David Asher of Armagh Observatory in Northern Ireland used observations from the discovery of Kushida-Muramatsu in 1993 and its return in 2001 to calculate its orbit over the previous century.

Their model shows that the comet entered Jupiter's neighbourhood from the outer solar system in 1949 and dallied in a highly irregular orbit, coming perilously close to the planet's surface three times before being thrown into the inner solar system around 1962.

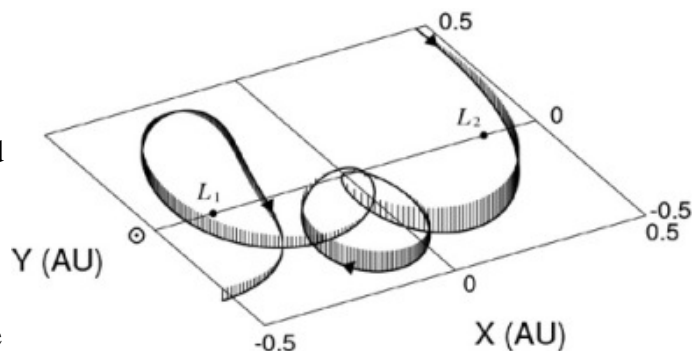
Uncertainty in the observations makes the comet's path impossible to determine exactly, so Ohtsuka and Asher ran over 200 scenarios for how events could have unfolded. "We backtracked everything possible that

could have happened in the past century that would be consistent with the observations," says Asher. Each scenario varied slightly in the timing and exact shape of orbit, but all of them showed that Kushida-Muramatsu orbited Jupiter for around 12 years.

Solar system sweeper

Brian Marsden of the Harvard-Smithsonian Center for Astrophysics in Cambridge, Massachusetts, says that predicting the orbit is more complicated than Ohtsuka and Asher's approach, which took account of gravity alone, because there could also be some small forces exerted on the comet by material evaporating from its surface.

"Probably it did happen," says Marsden of the comet's tryst with the gas giant, "but I don't think you can give the dates very precisely."



This illustration shows one possible path that the comet Kushida-Muramatsu took around Jupiter (located at centre of axes) (Illustration: Ohtsuka/Asher)

Jupiter made headlines earlier this summer when an amateur astronomer noticed the "bruise" left by an unknown object's impact. Along with the impact of Shoemaker-Levy 9, this illustrates Jupiter's capacity for sweeping up space debris, protecting Earth from the risk of bombardment.

But Kushida-Muramatsu's escape suggests that the giant planet can sometimes have a more delicate touch with its companions, helping them move into the inner solar system. Some of these comets will move into Earth-threatening orbits.

Kushida-Muramatsu's future is unclear, says Asher. It could stay in the inner solar system or it could end up orbiting Jupiter again some time in the next hundred years, perhaps to be thrown back among the outer planets. He presented the results (PDF) at the European Planetary Science Congress in Potsdam, Germany, on Monday.

Study Shows Common Pain Cream Could Protect Heart During Attack

Cincinnati - New research from the University of Cincinnati shows that a common, over-the-counter pain salve rubbed on the skin during a heart attack could serve as a cardiac-protectant, preventing or reducing damage to the heart while interventions are administered. These findings are published in the Sept. 14 edition of the journal *Circulation*.

Keith Jones, PhD, a researcher in the department of pharmacology and cell biophysics, and scientists in his lab have found that applying capsaicin to specific skin locations in mice caused sensory nerves in the skin to trigger signals in the nervous system. These signals activate cellular "pro-survival" pathways in the heart which protect the muscle. Capsaicin is the main component of chili peppers and produces a hot sensation. It is also the active ingredient in several topical medications used for temporary pain relief.

Capsaicin is approved for use by the U.S. Food and Drug Administration.

Jones is working with Neal Weintraub, MD, a UC Health cardiologist and director of UC's cardiovascular diseases division, and other clinicians to construct a translational plan to test capsaicin in a human population.

"Topical capsaicin has no known serious adverse effects and could be easily applied in an ambulance or emergency room setting well in advance of coronary tissue death," Jones says. "If proven effective in humans, this therapy has the potential to reduce injury and/or death in the event of a coronary blockage, thereby reducing the extent and consequences of heart attack."

Researchers observed an 85 percent reduction in cardiac cell death when capsaicin was used. They also found that a small incision made on the abdomen triggered an 81 percent reduction.

"Both this and the capsaicin effect are shown to work through similar neurological mechanisms. These are the most powerful cardioprotective effects recorded to date. "This is a form of remote cardioprotection, using a skin stimulus that activates cardioprotection long before the blocked coronary artery is opened, Jones says."

Weintraub adds that this finding offers an important distinction between existing therapies.

"All of the current interventions require the vessel to be opened before doctors can act, and since it takes time to elicit protection, tissue dies," he says. "This treatment will protect the heart before the vessel is opened while producing a strong protective effect that is already active when we open the vessel."

Jones and Weintraub think that skin - the main sensor and largest human body organ - has evolved to protect animals, including humans, in a variety of ways. "By activating these sensors in the nervous system, via skin, we think that a response to preserve and protect the heart is triggered," Weintraub says.

"We think that this technique is fooling the body into sending out protective signals," Jones adds. "This may be similar to the way certain acupuncture treatments work; there may be a neurological basis. In a broad sense, this work may provide a 'Rosetta stone' for translating alternative medicine techniques - like acupuncture - to

Western medicine. Perhaps we can understand the biological mechanisms of how alternative treatments may be successful for patients.”

Now, researchers will further explore this concept by investigating which sensors are associated with certain aspects of organ protection - and how much of specific stimuli are needed to produce the desired responses.

“This could help create favorable outcomes for those who are experiencing stroke, shock or are in need of an organ transplant, and the best part is that it is done non-invasively and is relatively inexpensive,” Jones says.

But he warns against rubbing capsaicin on your belly if you feel like you are having a heart attack.

“We don’t know if it will work for all indications, for all patients, and we don’t know if it will work over an extended amount of time,” he says. “A major goal is testing this therapy in clinical trials, but we still need to study more about dosage and application - where we put it on the body for the best results. However, this has tremendous clinical potential and could eventually save lives.”

This study was funded by the National Institutes of Health and by the University of Cincinnati. Jones and Weintraub have filed a patent for this funding but have received no honoraria from the makers of capsaicin.

Texas A&M researcher shows possible link between 1918 El Niño and flu pandemic

Research conducted at Texas A&M University casts doubts on the notion that El Niño has been getting stronger because of global warming and raises interesting questions about the relationship between El Niño and a severe flu pandemic 91 years ago. The findings are based on analysis of the 1918 El Niño, which the new research shows to be one of the strongest of the 20th century.

El Niño occurs when unusually warm surface waters form over vast stretches of the eastern Pacific Ocean and can affect weather systems worldwide. Using advanced computer models, Benjamin Giese, a professor of oceanography who specializes in ocean modeling, and his co-authors conducted a simulation of the global oceans for the first half of the 20th century and they find that, in contrast with prior descriptions, the 1918-19 El Niño was one of the strongest of the century. Giese's work will be published in the current "Bulletin of the American Meteorological Society," and the research project was funded by NOAA (National Oceanic and Atmospheric Administration) and the National Science Foundation.

Giese says there were few measurements of the tropical Pacific Ocean in 1918, the last year of World War I, and the few observations that are available from 1918 are mostly along the coast of South America. "But the model results show that the El Niño of 1918 was stronger in the central Pacific, with a weaker signature near the coast," Giese explains. "Thus the limited measurements likely missed detecting the 1918 El Niño."

Giese adds, "The most commonly used indicator of El Niño is the ocean temperature anomaly in the central Pacific Ocean. By that standard, the 1918-19 El Niño is as strong as the events in 1982-83 and 1997-98, considered to be two of the strongest events on record, causing some researchers to conclude that El Niño has been getting stronger because of global warming. Since the 1918-19 El Niño occurred before significant warming from greenhouse gasses, it makes it difficult to argue that El Niño s have been getting stronger."

The El Niño of 1918 coincided with one of the worst droughts in India, he adds. "It is well known that there is a connection between El Niño and the failure of the Indian monsoon, just as there is a well-established connection between El Niño and Atlantic hurricane intensity," Giese says. In addition to drought in India and Australia, 1918 was also a year in which there were few Atlantic hurricanes.

The research also raises questions about El Niño and mortality from the influenza pandemic of 1918. By mid-1918, a flu outbreak – which we now know was the H1N1 strain that is of great concern today – was sweeping the world, and the resulting fatalities were catastrophic: At least 25 million people died worldwide, with some estimates as high as 100 million deaths. India was particularly hard hit by the influenza.

"We know that there is a connection between El Niño and drought in India," Giese notes.

"It seems probable that mortality from influenza was high in India because of famine associated with drought, so it is likely that El Niño contributed to the high mortality from influenza in India."

The flu epidemic of 1918, commonly called the "Spanish Flu," is believed to be the greatest medical holocaust in history. It lasted from March of 1918 to June of 1920, and about 500 million people worldwide became infected, with the disease killing between 25 million to 100 million, most of them young adults. An estimated 17 million died in India, between 500,000 to 675,000 died in the U.S. and another 400,000 died in Japan. Could the events of 1918 be a harbinger of what might occur in 2009?

Giese says there are some interesting parallels. The winter and spring in 1918 were unusually cold throughout North America, just at the time influenza started to spread in the central U.S. That was followed by a strengthening El Niño and subsequent drought in India. As the El Niño matured in the fall of 1918, the influenza became a pandemic.

With a moderate to strong El Niño now forming in the Pacific and the H1N1 flu strain apparently making a vigorous comeback, the concerns today are obvious, Giese adds.

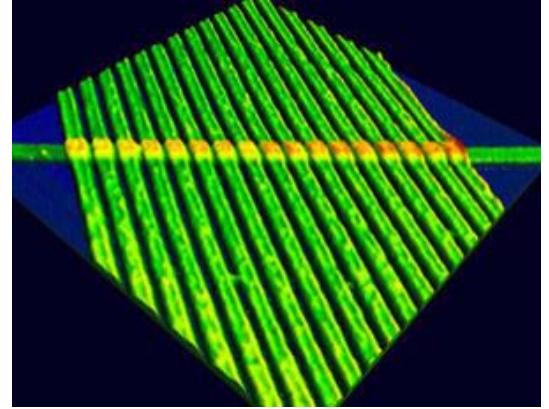
Electronics 'missing link' united with rest of the family

* 16:40 14 September 2009 by Colin Barras

In the 18 months since the "missing link of electronics" was discovered in Hewlett-Packard's laboratories in Silicon Valley, California, memristors have spawned a hot new area of physics and raised hope of electronics becoming more like brains.

Now the same team have upgraded a standard silicon chip with a layer of memristors to show that the novel component can play nicely with existing computing hardware.

That suggests it may not be long before they reach the market. And that in turn is good news for manufacturers, who need to find a new way to keep computer power growing: the methods that have shrunk computers in recent years look to have reached their limits.



Bridging the gap. Memristors can integrate with existing computing hardware. (Image: J. J. Yang, HP Labs)

Decreasing returns

Memristors behave a bit like resistors, which simply resist the flow of electric current. But rather than only respond to present conditions, a memristor can also "remember" the last current it experienced.

That's an ability that would usually require many different components. "Each memristor can take the place of 7 to 12 transistors," says Stan Williams, head of HP's memristor research. What's more, it can hold its memory without power.

By contrast, "transistors require power at all times and so there is a significant power loss through leakage currents", Williams explains.

A memristor's memory of its last current can be read by watching how it creates a new memory as it responds to a new current. They are made from a double layer of semiconducting titanium dioxide – the pigment in white paint.

Memristor array

Williams and his colleagues patterned 10,000 memristors on top of an ordinary CMOS chip.

"The biggest technical challenge for building the hybrid circuit was the fact that the CMOS circuit had a highly irregular surface," says Williams. Even bumps only one ten-thousandth of a millimetre high would be too large, so complex physical and chemical polishing was required.

The memristor array is made from a criss-crossing grid of 100-by-100 conducting wires. Each junction between two wires sandwiches titanium dioxide and acts as a memristor. A series of copper connections link the guts of the original chip with its new memristive top coat.

Flexible chip

That new memristor array can take over some tasks of the CMOS circuit beneath.

"The new hybrid system lifts the data-routing network and the switches out of the CMOS plane," says Williams.

"This will greatly free up the space on the CMOS layer for more devices, effectively increasing the density of circuits," he says, without the need to shrink the transistors any further.

Adding the memristors has given a fixed silicon chip similar properties to a field-programmable gate array, a kind of chip that can be physically reconfigured on the fly to prototype new circuit designs without building many fixed designs, says Williams.

It has also proved that memristors can integrate with standard silicon hardware.

Learning machines

The similarities between memristive circuits and the behaviour of some simple organisms suggests the hybrid devices could also open the way for "neuromorphic" computing, says Williams, in which computers learn for themselves, like animals.

Wei Lu, a memristor researcher at the University of Michigan in Ann Arbor, says the new device is a "significant step forward" in the development of nanoelectronic circuits.

Showing that nanoscale memristors can be made on top of existing chips "will certainly stimulate additional interest from the semiconductor industry and academia", he says.

The speed of such hybrid devices needs to improve, Lu adds. "However, continued development of the memristor devices may fundamentally change the way we design and fabricate integrated circuits in the future."

Journal reference: Nano Letters, DOI: 10.1021/nl901874j

Personal Health
Early Warning for a Deadly Kidney Disease

By JANE E. BRODY

Carol Johnson, an otherwise healthy woman in her 60s, was at her wits' end. Despite a good diet and regular exercise, she was gaining weight - 20-plus pounds. Her blood pressure was too high, even though she was taking three drugs for it. And she didn't feel well.

Since 2005, two doctors had told her she had a high blood level of creatinine, a product of muscle breakdown that can suggest abnormal kidney function. Yet neither doctor could figure out why. Even repeated kidney infections failed to alert her current doctor to the real problem.

Then, in March 2008, Mrs. Johnson, a retired special-education teacher living in Independence, Mo., noticed an advertisement for a free screening test offered by the National Kidney Foundation.

The test, part of a nationwide program called KEEP (for Kidney Early Evaluation Program), can serve as an early warning sign for a disease that often shows no symptoms until patients are on the verge of kidney failure. It uses a formula to convert the creatinine reading to a better measure of how well the kidneys are filtering wastes from the blood - the EGFR, or estimated glomerular filtration rate. (The precise rate, called the GFR, is measured by a much more involved test.)

Mrs. Johnson's EGFR was 49, well below the normal reading of 90 or above and a sign that she had chronic kidney disease. Suspecting that she was taking more medication than her kidneys could handle, her doctor stopped two of them.

And using information she found on the Web, Mrs. Johnson made some changes on her own. She cut out red meat, colas and sweets. She started eating still more vegetables and whole grains. And she kept to her daily exercise program, alternating among a gym workout, water aerobics and brisk walking.

Within six months Mrs. Johnson, now 67, had lost the extra weight, and her blood pressure and EGFR were normal. "If not for going to KEEP and finding out what was really wrong," she said in an interview, "I would have accepted the fact that nothing more could be done."

Multibillion-Dollar Problem

Like many other Americans with chronic kidney disease, Mrs. Johnson might have ended up with a heart attack or stroke, bone disease or kidney failure. Once kidneys fail, patients must undergo regular dialysis or have a kidney transplant, procedures that add billions of dollars to the nation's health care costs.

The kidney foundation undertook the KEEP program nine years ago because family doctors and internists often fail to order an EGFR when performing routine blood tests on patients at risk for kidney disease - even, as happened to Mrs. Johnson, when there are hints of kidney malfunction.

Fully half of the first 11,000 people whose blood and urine were tested in the KEEP program had evidence of kidney disease, but only 3 percent of them knew that before being screened.

Belgian nephrologists writing in *The Mayo Clinic Proceedings* in 2006 reported that physicians were often unaware of the severity of kidney malfunction because they relied solely on a creatinine measure. They noted that as many as four out of five patients with chronic kidney disease were referred to a specialist for treatment late in the disease, within six months of needing dialysis or a transplant.

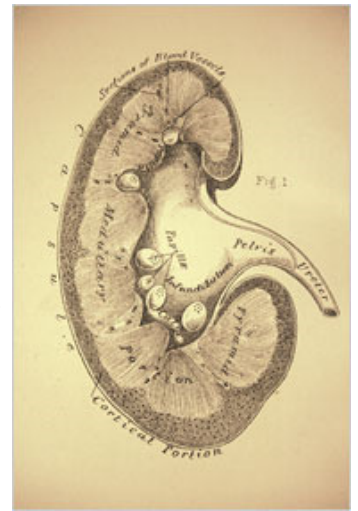
According to the latest national surveys, 26 million Americans have chronic kidney disease, and the numbers rise daily as more people become overweight and develop diabetes or high blood pressure, the two leading causes of kidney malfunction.

The KEEP program, which has so far examined more than 130,000 participants, screens adults with the most common risk factors for chronic kidney disease - diabetes, high blood pressure or a family history of kidney disease. To find nearby upcoming screenings, go to www.kidney.org and click on the "Get Tested" box, or call the foundation at (800) 622-9010.

Follow-up surveys of 72,000 people who have taken advantage of the free community-based screenings indicate that the test has prompted many to take action, like seeing a physician, adjusting their diets and doing more to control their blood pressure and diabetes.

Constellation of Risks

Chronic kidney disease is a life-threatening condition even for the young and middle-aged. Men under 55 and women under 65 identified through the KEEP program as having chronic kidney disease had twice the risk of heart attack or stroke, and four times the risk of dying, as those free of the disease, according to a study led by Dr. Peter A. McCullough of the William Beaumont Hospital in Royal Oak, Mich.



Dr. McCullough explained that kidney damage caused biological changes that accelerated injury to blood vessels throughout the body. He urged that all adults at risk for kidney disease, including smokers, be routinely checked for protein in their urine and reduced kidney function. Those found to have a kidney problem should also be tested for abnormalities that can result in bone disease or calcium deposits in blood vessels, he said.

Dr. Joseph A. Vassalotti, chief medical officer of the kidney foundation, said that in addition to the leading risk factors, many other conditions could increase the risk for chronic kidney disease. Among them are heart disease, lupus, amyloidosis (a buildup of amyloid proteins in the body), chronic kidney infection, polycystic kidney disease, hepatitis B or C, and multiple myeloma.

In addition, kidney damage can result from overuse of corticosteroids or of nonsteroidal anti-inflammatory drugs like ibuprofen and naproxen, from excessive cola consumption and from exposure to certain environmental toxins and radiological materials like barium.

The risk of developing kidney failure is also higher among Hispanics, African-Americans and American Indians than other ethnic groups, partly because of higher rates of high blood pressure and diabetes and poorer access to medical care.

As with Mrs. Johnson, if kidney problems are caught early and their underlying cause is corrected or properly treated, kidney damage and other complications can be slowed or halted, and sometimes even reversed.

As Sally Burrows-Hudson, a registered nurse in Sunnyvale, Calif., and a specialist in kidney disease, wrote in *The American Journal of Nursing*, "When patients at risk for chronic kidney disease are identified early and treated aggressively, the disease progression can be slowed or stopped, complications can be prevented or controlled, and clinical outcomes can be favorable."

Basics

An Organ of Many Talents, at the Root of Serious Ills

By NATALIE ANGIER

Should anybody in the reliably pestilent health care debate be casting about for a mascot organ to represent some of the biggest medical crises that we Americans face, allow me to nominate a nonobvious candidate: the pancreas.

It may lie in the hidden depths of the abdominal cavity, and its appearance, size and purpose may be obscure to the average person. Yet the pancreas turns out to be a linchpin in two epidemics that are all too familiar.

As the organ entrusted with the manufacture of insulin and other hormones that help control blood sugar, the pancreas gone awry is a source of diabetes, which afflicts more than 23 million people in this country, including the newest member of the Supreme Court.

And as the tireless brewer of digestive juices that help shear apart the amalgamated foodstuffs that we consume each day, the pancreas is at the frontlines of our expanding waistlines, the mass outbreak of fatness that has already claimed 60 percent of Americans and shows no sign of slackening.

Researchers are discovering that the pancreas helps mediate much of the appetite-related cross talk between the brain and the gastrointestinal tract, the streams of chemical signals that say, I'm starving down here, how about some dinner, or, enough already, step away from that dessert cart and no one will be hurt. By better understanding the precise role of the pancreas in conveying sensations of hunger or satiety, suggested Rodger A. Liddle of Duke University Medical School, we may find new ways to combat obesity.

Other researchers are intrigued by the pancreas's ability to shield itself from harm, to churn out huge quantities of enzymes that can rapidly reduce a cheeseburger and fries to so many particles of amino acids, carbohydrates and fats, without digesting its own tissue in the process. They suspect that the organ's set of self-protective mechanisms has a terrible downside, and helps explain why pancreatic cancer can be so difficult to treat - insights that are just beginning to offer hope in the fight against one of the most lethal of all malignancies.

If you've been remiss in appreciating your pancreas, don't feel bad: the ancients were, too. Early anatomists were certainly aware of the pancreas but mostly ignored it, and the organ's name reflects that ho-hum attitude. Pancreas is Greek for all-meat, a reference to its seeming homogeneity from one end to the other.

Much of the neglect may well have been practical. "The pancreas has always been difficult to study," Dr. Liddle said. For one thing, it's hidden. Measuring some six to eight inches in length, and slippery and lobular to the touch, the yellowish-brown pancreas is located deep in the abdomen, wedged between the stomach and the spinal cord and extending horizontally right above the waistline. Think of it as an oblong eel, the tail tucked into the stomach, the head butting up against the curve of the duodenum, of the small intestine.

Add to that inaccessibility a prima donna sensitivity. "If you do anything to the pancreas, you initiate an inflammatory response," Dr. Liddle said. "It tends to become inflamed more easily than other organs." In fact, inflammation of the pancreas, or pancreatitis, is a relatively common and often debilitating condition, brought on by excess alcohol, drug reactions, gallstones, genetic predisposition or other reasons. Unfortunately, said Dr.

Anthony Kalloo, a professor of medicine at the Johns Hopkins University School of Medicine, the symptoms of pancreatitis, like chronic abdominal pain radiating into the back, could be misdiagnosed or dismissed as a hypochondriac's lament. As a result, Dr. Kalloo said, patients do not always receive the right pain medications, the optimal diet, surgery when necessary.

For all the difficulty of studying the pancreas, researchers eventually came to appreciate the organ as a gland of many talents, serving both an exocrine role - secreting its products through ducts, as the breast secretes milk and the sweat glands perspiration - and an endocrine role, fabricating hormones and squirting them into the bloodstream, as the ovaries and testes dispense sex hormones and the thyroid thyroxine.

Roughly 90 percent of the pancreas is devoted to its exocrine role of generating digestive enzymes and funneling them into the small intestine, a burbling broth that flows forth from the pancreas at a rate of perhaps a quart a day.

The other 10 percent of pancreatic tissue consists of so-called islet cells, the endocrine players that synthesize insulin and glucagon to manipulate and titrate blood sugar, the body's energy currency, as needed. In people with Type 1, or juvenile-onset, diabetes - among them Justice Sonia Sotomayor of the Supreme Court - an autoimmune reaction ends up destroying many of these islet cells, resulting in the need for lifelong insulin injections. Among sufferers of Type 2, or adult-onset, diabetes, the reasons for insulin imbalance are more varied, and the condition can often be treated through diet and exercise alone.

Imagine the pancreas as a tree, Dr. Liddle suggested. The trunk and branches are the ducts that deliver digestive juices, the leaves the factories that make digestive enzymes, and the islet cells birds' nests scattered throughout - in the tree but not of it.

When cancer strikes, it generally arises in the ductal tissue of the pancreas, the woody parts of our metaphoric tree, and intriguingly, they feel the part. "These tumors are rock-hard masses," said Peter Olson, an oncology researcher at the University of California, San Francisco. "They're white on dissection, very tough and fibrous."

Pancreatic cancer is almost impossible to cure. About 34,000 Americans will be diagnosed with it this year, and nearly as many will die of it. As doctors have long known, some of that lethality is positional: there is no easy way to screen the deep-set pancreas for early signs of malignancy, and by the time symptoms arise, the cancer has already spread to other organs.

Another reason for the ferocity, however, might be the nature of the tumors themselves. Most cancers are thought to spur the growth of new blood vessels to supply them with the extra oxygen and nutrients necessary for frenzied cell division, but pancreatic tumors are markedly devascularized. "The number of blood vessels in a pancreatic tumor is 10 percent what it is in normal tissue, of the pancreas or anywhere else," said David A. Tuveson of the Cambridge Research Institute in England. The results are devastating. In the anoxic microenvironment beneath the fibrous, bloodless capsule, any malignant cells that survive become increasingly unstable and virulent, like superroaches proliferating in the wake of a pesticide bomb. Moreover, without blood vessels, nothing can get into the tumor to kill the renegade cells, so chemotherapy is almost useless.

Reporting recently in the journal *Science* on results with genetically engineered mice, Dr. Tuveson and his colleagues described a new approach to treating pancreatic cancer, in which the tumors were revascularized and thus made sensitive to cancer drugs. Clinical trials are now under way to test the basic strategy in people, and with all due caveats, Dr. Tuveson said, "I am cautiously optimistic."

Methane mining could trigger killer gas cloud

* 15 September 2009 **by Shanta Barley**

BENEATH the shimmering surface of Africa's Lake Kivu, a deadly time bomb awaits. A "gold rush" to extract valuable methane from the lake's depths might trigger an outburst of gas that could wash a deadly, suffocating blanket over the 2 million people who live around Kivu's shores.

The lake, which is almost half a kilometre deep in places, is on Rwanda's north-west border with the Democratic Republic of the Congo (see map) and contains a vast reservoir of dissolved methane. Many companies are extracting the gas to burn for electricity production, and the governments of both nations are aggressively courting further investment in extraction plants.

Now a group of biochemists warns that if unregulated extraction continues unabated, it could trigger a catastrophic outgassing of carbon dioxide - another dissolved gas abundant in the lake's depths. Such a disaster occurred at Lake Nyos in Cameroon in 1986, killing 1700 people. Kivu contains 300 times more CO₂ than Nyos did, warns Alfred Wüest, a bio-geochemist based at the Swiss Federal Institute of Aquatic Science and Technology (Eawag).

Like Nyos, Lake Kivu is permanently stratified: a deep layer of dense water laden with CO₂, methane, salt and nutrients is locked away beneath a surface layer of fresh water. Methane is generated by lake-bed bacteria that feed on a stream of dead algae sinking from the surface. The CO₂ enters through volcanic seeps.

So far, the Rwandan government has established one methane extraction plant on the lake, and two companies - Contour Global and Rwanda Investment Group - are running pilot projects. At least two more plants are in the pipeline, says Eva Paul of Rwanda's Ministry of Infrastructure. These will support the country's plan to expand electricity access from 6 per cent of the Rwandan population to 16 per cent by 2012.

According to a report by 15 researchers at Eawag and other institutes, certain current practices could trigger a catastrophic outgassing when methane extraction becomes widespread, as it will in the near future.

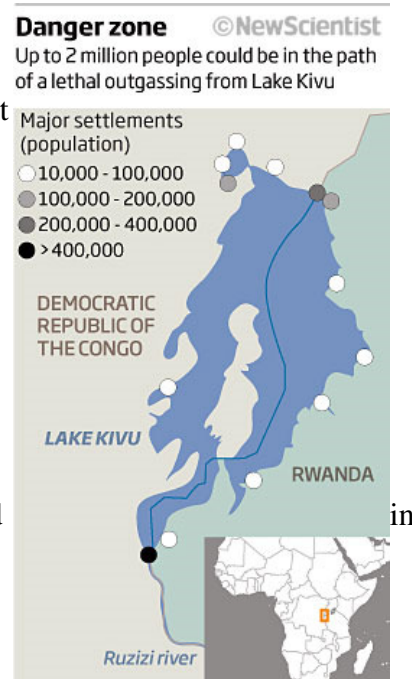
Perhaps the most dangerous practice is pumping waste water into the lake's shallows. "If degassed water is dumped at the surface, it sinks, mixing water and salts between the lake's layers," says George Kling, an expert on the Lake Nyos disaster at the University of Michigan, Ann Arbor, who was not involved in the report. Enough mixing would disrupt the density stratification of the lake, and could bring huge volumes of CO₂-rich water to the surface. The pressure reduction would cause the CO₂ to bubble out of solution. Instead, waste water must be re-injected where it came from, the report recommends, at a depth greater than 270 metres.

Unfortunately, there's an economic incentive for companies to pump waste water into the shallows, says Finn Hirslund of COWI, a Danish environmental and engineering consultancy. This nutrient-rich water triggers algal blooms that then die and sink, helping to form even more methane. "If companies mess around with the lake's density structures and accidentally trigger an entirely avoidable and deadly gas outburst, it will be a crime against humanity," he says. If companies trigger a deadly gas outburst, it will be a crime against humanity.

The Rwandan government, which commissioned the report, received it in June, but none of the recommendations has been applied or enforced so far, claims Kling. "There are no regulations in place as far as I know," he says. "Our hope is that we can get the governments to require and enforce regulations."

Hirslund believes that the Rwandan government has been too eager to win investment. "They have failed to put in place sufficient regulations to prevent malpractice," he says.

Rwandan officials insist that they are enforcing regulations. "All the recommendations within the report are sincerely followed," says Paul. But she admits that while all new facilities will be obliged to follow the rules, the government's own plant will not be bound.



Weeding out marijuana: Researchers close in on engineering recognizable, drug-free Cannabis plant

U of Minnesota researchers identify genes producing THC

In a first step toward engineering a drug-free Cannabis plant for hemp fiber and oil, University of Minnesota researchers have identified genes producing tetrahydrocannabinol (THC), the psychoactive substance in marijuana. Studying the genes could also lead to new and better drugs for pain, nausea and other conditions.

The finding is published in the September issue of the *Journal of Experimental Botany*. Lead author is David Marks, a professor of plant biology in the College of Biological Sciences.

The study revealed that the genes are active in tiny hairs covering the flowers of Cannabis plants. In marijuana, the hairs accumulate high amounts of THC, whereas in hemp the hairs have little. Hemp and marijuana are difficult to distinguish apart from differences in THC.

With the genes identified, finding a way to silence them - and thus produce a drug-free plant - comes a step closer to reality. Another desirable step is to make drug-free plants visually recognizable. Since the hairs can be seen with a magnifying glass, this could be accomplished by engineering a hairless Cannabis plant.

The researchers are currently using the methods of the latest study to identify genes that lead to hair growth in hopes of silencing them.

"We are beginning to understand which genes control hair growth in other plants, and the resources created in our study will allow us to look for similar genes in *Cannabis sativa*," said Marks.

"Cannabis genetics can contribute to better agriculture, medicine, and drug enforcement," said George Weiblen, an associate professor of plant biology and a co-author of the study.

As with Dobermans and Dachshunds, marijuana and hemp are different breeds of the same species (*Cannabis sativa*), but marijuana contains much more THC than hemp, which is a source of industrial fiber and nutritious oil. Hemp was raised for its fiber - which is similar to cotton but more durable - in the United States until legislation outlawed all *Cannabis* plants because they contain THC. Today, marijuana contains as much as 25 percent THC, whereas hemp plants contain less than 0.3 percent.

Hemp was once a popular crop in the upper Midwest because it tolerates a cool climate and marginal soils that won't support other crops but, after drug legislation, hemp fiber was replaced by plastic and other alternatives. Recent popular demand for hemp products has led some states to consider the economic and environmental benefits of hemp. North Dakota legislation aims to reintroduce it as a crop, and Minnesota is considering similar legislation. At the same time, California and other states permit the medicinal use of marijuana.

"I can't think of a plant so regarded as a menace by some and a miracle by others," says Weiblen, who is one of the few researchers in the United States permitted to study *Cannabis* genetics. In 2006, Weiblen and colleagues developed a DNA "fingerprinting" technique capable of distinguishing among *Cannabis* plants in criminal investigations.

Two treatment innovations improve heart function after heart attack

Study highlights:

- * Supersaturated oxygen given during treatment for a STEMI heart attack can reduce heart muscle damage.
 - * The larger the area of heart muscle threatened, the greater the reduction in damage.
- * Supersaturated oxygen doesn't increase a patient's risk of serious ill effects, such as death or stroke.
 - * Manually removing a blood clot during angioplasty provided greater recovery of heart function.

DALLAS, Sept. 15, 2009 - Supersaturated oxygen (SSO2) administered during catheter-based treatments for heart attack can significantly reduce heart muscle damage, according to a new study reported in *Circulation: Cardiovascular Interventions*, a journal of the American Heart Association.

In another study from the same issue, a different group of researchers found that manually removing a blood clot provided greater recovery of heart function after a heart attack.

"The greatest benefits were seen in the patients most at risk," said Gregg W. Stone, M.D., lead author of the SSO2 study, and professor of medicine at Columbia University Medical Center in New York, N.Y. "The larger the heart attack, the more heart muscle salvaged."

SSO2 - highly concentrated oxygen mixed in blood and delivered to the area of heart muscle dying after a heart attack - showed promise in animal studies and a previous human trial (AMIHOT-I). So Stone and his colleagues conducted AMIHOT-II with a similar protocol, focusing on patients with anterior ST-segment elevation myocardial infarctions (STEMIs) who were treated within six hours of heart attack symptoms.

"STEMIs are the large attacks," Stone said. "They have a really bad early prognosis because there is so much heart muscle lost." When a large area of the heart is damaged, heart failure is more likely.

Of the 733,000 Americans who suffer acute coronary syndromes (i.e. heart attack or chest pain) each year, 361,000 (almost half) have a STEMI. Catheter-based percutaneous coronary intervention (PCI) is a procedure that can effectively open blocked arteries in STEMI patients.

The AMIHOT-II researchers studied 301 STEMI patients who arrived within six hours after the onset of symptoms at 20 sites in four countries. The researchers randomized 222 to receive PCI plus SSO2 - infused for 90 minutes during treatment - and 79 to PCI only. Some of their analyses also included data pooled from 101 patients from the AMIHOT-I.

Major study findings included:

- * In AMIHOT-II patients, heart damage 14 days after treatment averaged 26.5 percent of the left ventricle for PCI-only patients and 20 percent for the PCI plus SSO2 group. Pooled data from both AMIHOT studies showed 25 percent damage in PCI-only patients and 18.5 percent in the SSO2 group.

- * Among 154 patients whose left ventricle ejected less than 40 percent of the blood with each contraction prior to treatment, the PCI-only group had 33.5 percent damage versus 23.5 percent in the SSO2 patients. "For patients with large heart attacks, this is the first therapy shown to be beneficial in an adequately powered, multicenter trial," Stone said.

- * In those with more than 40 percent blood ejection, muscle damage was 16.5 percent in PCI-only patients and 12.5 percent in the SSO2 group, which is a similar relative reduction in heart attack size as in patients with larger attacks, but a smaller absolute reduction.

- * Researchers found no significant differences between the two groups of AMIHOT-II patients in the levels of blood markers that indicate a heart attack, or in the percentage of heart muscle at risk of dying, which was measured three hours after treatment.

* At 30 days post-op, the pooled data showed the two groups had similar percentages of major adverse events - death, another heart attack, reopening the same heart artery and stroke: 4.7 percent for the SSO2 patients and 5.1 percent for PCI-only group.

"Some scientists have questioned the safety of SSO2 in heart patients, but only a few major and minor problems occurred in AMIHOT-II, and the study met all of its pre-defined safety endpoints," Stone said.

In the same issue of *Circulation: Cardiovascular Interventions*, Francesco Liistro, M.D., and colleagues at San Donato Hospital in Arezzo, Italy, reported that manually removing a blood clot during PCI provides STEMI patients greater heart muscle perfusion and recovery of left ventricle function.

In their single-center study, researchers randomized 55 patients to clot aspiration and 56 to standard PCI. In PCI, a physician typically inflates a balloon on a catheter tip to flatten a clot against the vessel wall, and then inserts a metal-mesh stent to prop the vessel open.

Instead of using a balloon, which leaves clot debris in the blood, the team pushed a special catheter into the blockage and sucked the clot into the tube to remove it from the body before stenting.

Major study findings included:

* The ST-segment of an electrocardiogram returned to normal in 39 (71 percent) of the clot-aspiration group versus 22 (39 percent) of those getting standard PCI.

* Ninety-six percent of aspiration patients reached TIMI grade 3, the desired blood flow through the opened artery, compared to 82 percent for the standard PCI group.

* Aspiration patients showed a higher rate of artery perfusion, as measured by ultrasound, than those getting standard PCI, 85 percent versus 64 percent.

Co-authors with Stone are: Jack L. Martin, M.D.; Menko-Jan de Boer, M.D.; Massimo Margheri, M.D.; Ezio Bramucci, M.D.; James C. Blankenship, M.D.; D. Christopher Metzger, M.D.; Raymond J. Gibbons, M.D.; Barbara S. Lindsay, R.N.; Bonnie H. Weiner, M.D.; Alexandra J. Lansky, M.D.; Mitchell W. Krucoff, M.D.; Martin Fahy, M.Sc.; and W. John Boscardin, Ph.D. TherOx, Inc. funded the AMIHOT-II study.

Co-authors with Liistro are: Simone Grotti, M.D.; Paolo Angioli, M.D.; Giovanni Falsini, M.D.; Kenneth Ducci, M.D.; Silvia Baldassarre, M.D.; Alessandra Sabini, M.D.; Rossella Brandini, M.D.; Eugenia Capati, M.D.; and Leonardo Bolognese, M.D. Author disclosures are on the manuscripts.

UT scientists discover link between protein and lung disease

HOUSTON - (Sept. 10, 2009) - In a development that could lead to a novel approach to the treatment of a devastating lung disease, biochemists at The University of Texas Health Science Center at Houston report they are the first to link the osteopontin (OPN) protein to chronic obstructive pulmonary disease (COPD). Findings appear online and will be in the January 2010 print issue of *The FASEB Journal*, the journal of The Federation of American Societies for Experimental Biology.

More than 12 million Americans are currently diagnosed with this incurable illness, which is the fourth leading cause of death, the National Heart Lung and Blood Institute reports. In the United States, the term COPD includes two main conditions - emphysema and chronic obstructive bronchitis.

The researchers were able to prevent COPD features in a mouse model by genetically removing osteopontin. To gauge the applicability of their findings to humans, the investigators analyzed the airways of people with COPD and found elevated levels of the protein.

"This is an important crossover study," said Michael Blackburn, Ph.D., the study's senior author and professor in the Department of Biochemistry and Molecular Biology at The University of Texas Medical School at Houston. "Because we can show osteopontin is elevated in people with COPD, this suggests that osteopontin could serve as both an indicator of disease progression and a therapeutic target."

In the study, researchers induced COPD features in mice and then compared symptoms experienced by mice with osteopontin and those without. The mice without the protein had less inflammation and lung disease. "The lack of osteopontin in the mice prevented the COPD features," said Daniel Schneider, the study's lead author and an M.D./Ph.D. candidate at the UT Health Science Center at Houston.

"This paper reveals exciting new information on the pathogenetic mechanisms involved in the development of chronic obstructive pulmonary disease and emphysema," said Richard J. Castriotta, M.D., professor and director of the Pulmonary, Critical Care and Sleep Medicine Division at the UT Medical School at Houston and medical director of the Sleep Disorder Center at Memorial Hermann - Texas Medical Center.

The study stems from research in Blackburn's laboratory involving a signaling molecule named adenosine, which can orchestrate the process of inflammation in wound healing. Adenosine can also activate a cell surface receptor associated with COPD named A2B and produce osteopontin. Blackburn's decade-long research has focused on blocking the A2B receptor. With the new study linking osteopontin to COPD, Blackburn believes his laboratory may have uncovered a protein that could lead to a more targeted approach to treating emphysema.

Schneider said; "As a physician scientist, one goal of drug development is to offer more specific drug targets to treat the disorder and osteopontin provides a specific target that may be associated with fewer side effects." "This paper adds a new element, osteopontin, to the mix by discovering its significant role in the development of COPD with emphysema ... It's still too early to be used clinically, but there may be a place for osteopontin in the future as an indicator of lung disease in progress that leads to COPD and emphysema," Castriotta said.

Blackburn is director of the Graduate Program in Biochemistry and Molecular Biology at the UT Medical School.

Schneider is a graduate research assistant at The University of Texas Graduate School of Biomedical Sciences at Houston and is a recipient of a T32 training grant by the Center for Clinical and Translational Sciences at the UT Health Science Center at Houston.

The study is titled "Adenosine and osteopontin contribute to the development of chronic obstructive pulmonary disease." Other contributors from the Department of Biochemistry and Molecular Biology were graduate students Janci C. Lindsay and Yang Zhou, as well as senior research assistant Jose G. Molina.

The study was funded by the National Institutes of Health and the National Center for Research Resources.

Scary Music Is Scarier with Your Eyes Shut

TAU brain scientist says findings could lead to new neurological treatments

The power of the imagination is well-known: it's no surprise that scary music is scarier with your eyes closed. But now neuroscientist and psychiatrist Prof. Talma Hendler of Tel Aviv University's Functional Brain Center says that this phenomenon may open the door to a new way of treating people with Alzheimer's, Parkinson's and other neurological diseases.

In her new study, Prof. Hendler found that the simple act of voluntarily closing one's eyes - instead of listening to music and sounds in the dark - can elicit more intense physical responses in the brain itself. This finding may have therapeutic value in treating people with brain disorders. Her research was just published in PLoS One and builds on her 2007 study published in Cerebral Cortex.

Prof. Hendler's research suggests that, when our eyes are closed, a region in our brain called the amygdala is fired up. The experience of scary music becomes more emotionally and physically intense. And the converse of the scary music effect may be true: happy music could produce a joyous effect when our eyes are shut as well.

Listening to sounds with our eyes closed seems to wire together a direct connection to the regions of our brains that process emotions, says Prof. Hendler. "Music is a relatively abstract emotional carrier," says Prof. Hendler. "It can easily take one's subjective personal experience and manipulate it. Our new findings, however, suggest that the effect is not only subjective. Using a functional MRI (fMRI), we can see that distinct changes in the brain are more pronounced when a person's eyes are not being used."

Alfred Hitchcock in the laboratory

Dr. Yulia Lerner, a post-doctoral fellow at Prof. Hendler's lab, had 15 healthy volunteers listen to spooky Hitchcock-style music, and then neutral sounds with no musical melody. They listened to these twice, once with their eyes open and a second time with their eyes shut, as she monitored their brain activity with an fMRI. While volunteers were listening to the scary music, Dr. Lerner found that brain activity peaked when the subjects' eyes were closed. This medical finding corresponded to volunteer feedback that the subjects felt more emotionally charged by the scary music.

The amygdala, the region of the brain in which emotions are located, was significantly more active when the subjects' eyes were closed. "It's possible that closing one's eyes during an emotional stimulation, like in our research, may help people through a variety of mental states. It synchs connectivity in the brain," Dr. Hendler says. "We don't know exactly how or why this happens - it's like a light switch gets turned off, allowing the brain to better integrate the highs and lows of the emotional experience when the eyes are shut."

Music brings balance to the brain and more readily integrates the affective and cognitive centers of our mind. Music may help us think better and even improve our learning abilities. But, she warns, more studies are needed before you let your teen crank up the hip-hop music as a study aid.

Applications for dementia and systemic brain disorders

"This study is the first time scientists have looked inside the brain non-invasively, to examine what happens to the brain under these conditions," says Prof. Hendler. Small physical behaviors can radically alter the balance and color of emotions. Not long ago in U.S. classrooms, teachers found that hyperactive students learned better while standing, rather than sitting at their desks. Now, Prof. Hendler's latest study with scary music is "just an example of how a small manipulation in one's physical state such as eyes open or shut can change our mental experience," she says.

The findings, researchers hope, can be applied to therapies that achieve more significant and longer-lasting effects without chemical intervention. While her study just touches on the connection of physical and emotional activity in the brain, Prof. Hendler doesn't rule out music therapy in alleviating symptoms in chronic mental disorders such as depression, Schizophrenia and Parkinson's, in the future.

First solid evidence for a rocky exoplanet

Mass and density of smallest exoplanet finally measured

The longest set of HARPS measurements ever made has firmly established the nature of the smallest and fastest-orbiting exoplanet known, CoRoT-7b, revealing its mass as five times that of Earth's. Combined with CoRoT-7b's known radius, which is less than twice that of our terrestrial home, this tells us that the exoplanet's density is quite similar to the Earth's, suggesting a solid, rocky world. The extensive dataset also reveals the presence of another so-called super-Earth in this alien solar system.

"This is science at its thrilling and amazing best," says Didier Queloz, leader of the team that made the observations. "We did everything we could to learn what the object discovered by the CoRoT satellite looks like and we found a unique system."

In February 2009, the discovery by the CoRoT satellite [1] of a small exoplanet around a rather unremarkable star named TYC 4799-1733-1 was announced one year after its detection and after several months of painstaking measurements with many telescopes on the ground, including several from ESO. The star, now known as CoRoT-7, is located towards the constellation of Monoceros (the Unicorn) at a distance of about 500 light-years. Slightly smaller and cooler than our Sun, CoRoT-7 is also thought to be younger, with an age of about 1.5 billion years.

Every 20.4 hours, the planet eclipses a small fraction of the light of the star for a little over one hour by one part in 3000 [2]. This planet, designated CoRoT-7b, is only 2.5 million kilometres away from its host star, or 23 times closer than Mercury is to the Sun. It has a radius that is about 80% greater than the Earth's.

The initial set of measurements, however, could not provide the mass of the exoplanet. Such a result requires extremely precise measurements of the velocity of the star, which is pulled a tiny amount by the gravitational tug of the orbiting exoplanet. The problem with CoRoT-7b is that these tiny signals are blurred by stellar activity in the form of "starspots" (just like sunspots on our Sun), which are cooler regions on the surface of the star. Therefore, the main signal is linked to the rotation of the star, which makes one complete revolution in about 23 days.

To get an answer, astronomers had to call upon the best exoplanet-hunting device in the world, the High Accuracy Radial velocity Planet Searcher (HARPS) spectrograph attached to the ESO 3.6-metre telescope at the La Silla Observatory in Chile. "Even though HARPS is certainly unbeaten when it comes to detecting small exoplanets, the measurements of CoRoT-7b proved to be so demanding that we had to gather 70 hours of observations on the star," says co-author François Bouchy.

HARPS delivered, allowing the astronomers to tease out the 20.4-hour signal in the data. This figure led them to infer that CoRoT-7b has a mass of about five Earth masses, placing it in rare company as one of the lightest exoplanets yet found.

"Since the planet's orbit is aligned so that we see it crossing the face of its parent star - it is said to be transiting - we can actually measure, and not simply infer, the mass of the exoplanet, which is the smallest that has been precisely measured for an exoplanet [3]," says team member Claire Moutou. "Moreover, as we have both the radius and the mass, we can determine the density and get a better idea of the internal structure of this planet."

With a mass much closer to that of Earth than, for example, ice giant Neptune's 17 Earth masses, CoRoT-7b belongs to the category of "super-Earth" exoplanets. About a dozen of these bodies have been detected, though in the case of CoRoT-7b, this is the first time that the density has been measured for such a small exoplanet. The calculated density is close to Earth's, suggesting that the planet's composition is similarly rocky.

"CoRoT-7b resulted in a 'tour de force' of astronomical measurements. The superb light curves of the space telescope CoRoT gave us the best radius measurement, and HARPS the best mass measurement for an exoplanet. Both were needed to discover a rocky planet with the same density as the Earth," says co-author Artie Hatzes.

CoRoT-7b earns another distinction as the closest known exoplanet to its host star, which also makes it the fastest - it orbits its star at a speed of more than 750 000 kilometres per hour, more than seven times faster than the Earth's motion around the Sun. "In fact, CoRoT-7b is so close that the place may well look like Dante's Inferno, with a probable temperature on its 'day-face' above 2000 degrees and minus 200 degrees on its night face. Theoretical models suggest that the planet may have lava or boiling oceans on its surface. With such extreme conditions this planet is definitively not a place for life to develop," says Queloz.

As a further testament to HARPS' sublime precision, the astronomers found from their dataset that CoRoT-7 hosts another exoplanet slightly further away than CoRoT-7b. Designated CoRoT-7c, it circles its host star in 3 days and 17 hours and has a mass about eight times that of Earth, so it too is classified as a super-Earth. Unlike CoRoT-7b, this sister world does not pass in front of its star as seen from Earth, so astronomers cannot measure its radius and thus its density.

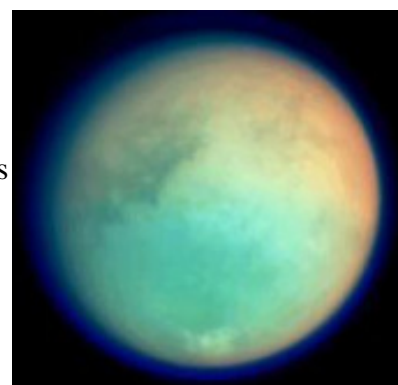
Given these findings, CoRoT-7 stands as the first star known to have a planetary system made of two short period super-Earths with one that transits its host.

Saturn's moon Titan has a foggy bottom

FOG has been spotted on Titan, the first evidence that the Earth isn't the only body in the solar system to have a hydrological cycle. Yet Titan's cycle is based on methane.

Saturn's moon Titan is known to have lakes, clouds and river beds, hinting that surface liquid evaporates and returns as rain. But proof is lacking: the lakes might not evaporate, the clouds might not rain, and the river beds might be relics from a wetter past.

Now Michael Brown of the California Institute of Technology in Pasadena and his team have used NASA's Cassini spacecraft to view methane fog at Titan's south pole. The only explanation is evaporated surface methane condensing into humid air, say the team (www.arxiv.org/abs/0908.4087).



Fog at Titan's south pole is evidence of the evaporation of liquid methane on the surface and its subsequent condensation into humid air (Image: NASA/JPL/Space Science Institute)

Durians and booze: worse than a stinking hangover

ACCORDING to Asian folklore, eating the famously pungent durian - known as the "king of fruits" - along with alcohol can kill you. Now intrepid researchers have confirmed there may be some truth in this supposition. It is the first time combining a fruit with booze has been scientifically linked to an adverse reaction.

John Maninang and Hiroshi Gemma from the University of Tsukuba, Japan, wondered if the reported side effects were due to durian's high sulphur content impairing alcohol breakdown. In test tubes they found that durian extract inhibited the activity of aldehyde dehydrogenase - an enzyme that clears toxic breakdown products - by up to 70 per cent (Food Chemistry, DOI: 10.1016/j.foodchem.2009.03.106).

Detractors complain about the rotting smell of durian, says Gemma. "Now we know that it may smell of danger too."

Cases of liver cancer reduced in a younger population vaccinated for HBV

A 20-year follow-up study revealed a dramatic drop in liver cancer cases among 6- to 19-year-olds who were vaccinated for the hepatitis B virus at birth, according to a study published online September 16 in the Journal of the National Cancer Institute.

In July 1984, a universal vaccination program was initiated among newborn children in Taiwan to prevent the hepatitis B virus infection, which can predispose to the development of hepatocellular carcinoma, a primary malignancy of the liver.

For this study, Mei-Hwei Chang, M.D., of the Department of Pediatrics, National Taiwan University Hospital in Taipei, and colleagues collected data from almost 2,000 patients with hepatocellular carcinoma who were aged 6-29 years at diagnosis in Taiwan between 1983 and 2004. Age- and sex-specific incidence were compared among vaccinated and unvaccinated birth cohorts with regression models.

Sixty-four cases of hepatocellular carcinoma were found among people vaccinated in almost 38 million person-years vs. 444 cancers among unvaccinated people in almost 80 million person-years.

A few individuals have developed liver cancer despite the program. Analysis of their records shows that most of these patients, however, were not given enough doses of the vaccine, or were insufficiently protected when they were born to hepatitis B-infected mothers, according to the study.

"These data suggest that the effectiveness of the universal HBV immunization program to prevent hepatocellular carcinoma has extended beyond childhood and into young adulthood over the past two decades," the authors write.

Scientists cure color blindness in monkeys

GAINESVILLE, Fla. - Researchers from the University of Washington and the University of Florida used gene therapy to cure two squirrel monkeys of color blindness - the most common genetic disorder in people.

Writing online Wednesday in the journal Nature, scientists cast a rosy light on the potential for gene therapy to treat adult vision disorders involving cone cells - the most important cells for vision in people.

"We've added red sensitivity to cone cells in animals that are born with a condition that is exactly like human color blindness," said William W. Hauswirth, Ph.D., a professor of ophthalmic molecular genetics at the UF College of Medicine and a member of the UF Genetics Institute and the Powell Gene Therapy Center.

"Although color blindness is only moderately life-altering, we've shown we can cure a cone disease in a primate, and that it can be done very safely. That's extremely encouraging for the development of therapies for human cone diseases that really are blinding."

The finding is also likely to intrigue millions of people around the world who are colorblind, including about 3.5 million people in the United States, more than 13 million in India and more than 16 million in China. The problem mostly affects men, leaving about 8 percent of Caucasian men in the United States incapable of discerning red and green hues that are important for everyday things like recognizing traffic lights.

"People who are colorblind feel that they are missing out," said Jay Neitz, Ph.D., a professor of ophthalmology at the University of Washington. "If we could find a way to do this with complete safety in human eyes, as we did with monkeys, I think there would be a lot of people who would want it. Beyond that, we hope this technology will be useful in correcting lots of different vision disorders."

The discovery comes about 10 years after Neitz and his wife Maureen Neitz, Ph.D., a professor of ophthalmology at the University of Washington and senior author of the study, began training two squirrel monkeys named Dalton and Sam.

In addition to teaching the animals, the Neitz research group worked with the makers of a standard vision-testing technique called the Cambridge Colour Test to perfect a way the monkeys could "tell" them which colors they were seeing.

The tests are similar to ones given to elementary children the world over, in which students are asked to identify a specific pattern of colored dots among a field of dots that vary in size, color and intensity. The researchers devised a computer touch screen the monkeys could use to trace the color patterns. When the animals chose correctly, they received a reward of grape juice.

Likewise, decades were spent by Hauswirth and colleagues at the University of Florida to develop the gene-transfer technique that uses a harmless adeno-associated virus to deliver corrective genes to produce a desired protein.

In this case, researchers wanted to produce a substance called long-wavelength opsin in the retinas of the monkeys. This particular form of opsin is a colorless protein that works in the retina to make pigments that are sensitive to red and green.

"We used human DNAs, so we won't have to switch to human genes as we move toward clinical treatments," said Hauswirth, who is also involved in a clinical trial with human patients to test gene therapy for the treatment of Leber congenital amaurosis, a form of blindness that strikes children.

About five weeks after the treatment, the monkeys began to acquire color vision, almost as if it occurred overnight.

"Nothing happened for the first 20 weeks," Neitz said. "But we knew right away when it began to work. It was if they woke up and saw these new colors. The treated animals unquestionably responded to colors that had been invisible to them."

It took more than a year and a half to test the monkeys' ability to discern 16 hues, with some of the hues varying as much as 11-fold in intensity.

Dalton is named for John Dalton, an English chemist who realized he was colorblind and published the first paper about the condition in 1798.

"We've had Dalton and Sam for 10 years. They are like our children," Neitz said. "This species are friendly, docile monkeys that we just love. We think it is useful to continue to follow them - it's been two years now that they've been seeing in color, and continuing to check their vision and allowing them to play with the computer is part of their enrichment."

With the discovery, the researchers are the first to address a vision disorder in primates in which all photoreceptors are intact and healthy, providing a hint of gene therapy's full potential to restore vision.

About 1 in 30,000 Americans have a hereditary form of blindness called achromatopsia, which causes nearly complete color blindness and extremely poor central vision. "Those patients would be targets for almost exactly the same treatment," Hauswirth said.

Even in common types of blindness such as age-related macular degeneration and diabetic retinopathy, vision could potentially be rescued by targeting cone cells, he said.

"The major thrust of the study is you can ameliorate if not cure color blindness with gene therapy," said Gerald H. Jacobs, Ph.D., a research professor of psychology at the University of California, Santa Barbara, who was not involved in the research. "There are still questions about safety, but in these monkeys at least, there were no untoward effects. Those who are motivated to ameliorate their color defect might take some hope from the findings.

"This is also another example of how utterly plastic the visual system is to change," Jacobs said. "The nervous system can extract information from alterations to photopigments and make use of it almost instantaneously."

GPs' gut feelings defined

'Gut feelings' experienced by GPs play a substantial role in their diagnostic reasoning process, but always in combination with analytical reasoning. Gut feelings can be separated into the sense of alarm and the sense of reassurance. Researchers writing in the open access journal BMC Family Practice worked with 27 medical opinion leaders to closely define the concepts, which will allow future research to evaluate the effectiveness of this 'gut-compass'.

Erik Stolper, from Maastricht University, The Netherlands, worked with a team of researchers to carry out the consensus procedure. He said, "Uncertainty and unpredictability are common phenomena in general practice. Although gut feelings play a role in dealing with this uncertainty, studies about their validity are lacking. In order to facilitate such research, we've created a well-supported definition of the two types of gut feeling, alarm and reassurance".

The researchers' panel eventually concluded that a sense of alarm means that a GP perceives an uneasy feeling, as they are concerned about a possible adverse outcome. They might not have found any specific indications yet; it is a sense of 'there's something wrong here'. Stolper said, "A 'sense of alarm' activates the diagnostic process by stimulating a GP to formulate and weigh up working hypotheses that might involve a serious outcome. If possible, the GP needs to initiate specific management to prevent serious health problems. The sense will decrease as the diagnosis and the right management become clearer".

The sense of reassurance means that a GP feels secure about the further management and course of a patient's problem, even though he/she may not be certain about the diagnosis: everything fits in. Speaking about the possible applications of these findings, Stolper said, "Our next step will be to construct and validate a questionnaire as a tool to evaluate gut feelings as well as the diagnostic work-up and the contribution of major potential determinants like experience and contextual knowledge. Actually, we aim to enhance the positive effects of gut feelings in the diagnostic process and to reduce their potential undesirable effects".

Notes to Editors 1. Consensus on gut feelings in general practice

Erik Stolper, Paul Van Royen, Margje Van de Wiel, Marloes Van Bokhoven, Paul Houben, Trudy Van der Weijden and Geert Jan Dinant BMC Family Practice (in press)

Pursuing a Battery So Electric Vehicles Can Go the Extra Miles

By JOHN MARKOFF

SAN JOSE, Calif. - A future generation lithium-air battery might be the much sought after power source for electric vehicles with ranges that match gasoline powered cars of today.

The interest in the as-yet-unproven technology was underscored this summer when I.B.M. said it had begun to pursue a tenfold improvement in battery storage, with hopes of reaching the goal before the end of the next decade.

I.B.M. executives said the company was unlikely to enter the battery business directly but was aiming toward a partnership that would marry its hardware and systems design expertise with ultralight battery technology.

Such a strategy would follow the lead of Tesla Motors, a new California company that produced a high-end electric roadster based on a computerized and sensor-based battery system. Tesla put 6,800 standard lithium-ion battery cells designed for consumer electronic products into a 992 pound package.

"I strongly believe that climbing this Mount Everest of 10 times better, given resources, time and patience, will happen," said Winfried Wilcke, a physicist and I.B.M.'s senior manager for nanoscale science and technology here at the Almaden Research Center. "This is simply so overwhelming in its simplicity and its clarity and the socioeconomic consequences it would have, that it deserves a Manhattan-like effort."

Battery experts met at the center for two days last month. The meeting highlighted both the promise of several types of new battery technology as well as the stumbling blocks.

Burton Richter, who won a Nobel Prize in Physics, expressed optimism about the progress in battery technology. "We have a wonderful confluence of people who are concerned about security, and people concerned about the environment, which makes batteries and electrical transportation a big deal," Dr. Richter said.

Lithium-ion batteries, the technology of choice for hybrid and electric car makers, have limited energy capacity. Researchers working on lithium-air and lithium-sulfur alternatives said at the I.B.M. conference that they would broaden the market for solar cars if safety issues could be overcome.

Lithium-ion batteries have the potential to deliver about 585 watt-hours of electricity per kilogram, while lithium-sulfur has a theoretical potential of about 2,600 watt-hours, and lithium-air batteries might reach targets well above 5,000 watt-hours.

If they can be perfected, lithium-air batteries would be ideal for transportation applications, given their potential for high energy capacity and low weight. And, unlike zinc-air batteries, it should be possible to make them rechargeable.

The difficulty of developing such batteries is great. Scientists at the I.B.M. conference spelled out a range of challenges, like safety concerns and lowering the cost of the batteries, which now add thousands of dollars to the price of electric vehicles.

Nadav Enbar, an energy analyst at IDC Corp., said that despite I.B.M.'s optimism, the advent of lithium-air batteries was unlikely in the near term. Mr. Enbar cited the long testing cycles that new battery technologies must go through as the most significant challenge the company would face.

Jeff Dahn, a materials scientist at Dalhousie University in Halifax, Nova Scotia, warned that several of the battery efforts were at risk of repeating the mistakes of the past. Dr. Dahn described a rigorous testing program at a Canadian startup for a new consumer battery technology created during the mid-1980s. Buyers of the batteries recharged them in ways that led to dangerous failures and their eventual recall.

But Dr. Wilcke, of I.B.M., said many of the problems cited by Dr. Dahn had been solved.

Lunar Craters May Be Chillest Spots in Solar System

By KENNETH CHANG

The shadowy craters near the south pole of the Moon may be the coldest places in the solar system, colder than even Pluto, NASA scientists reported Thursday as they unveiled some of the first findings from the Lunar Reconnaissance Orbiter spacecraft.

"We're looking at the Moon with new eyes," said Richard Vondrak, the mission's project scientist.

The orbiter, launched in June, officially began its one-year mission to map the Moon's surface this week. But during three months of turning on, testing and calibration of its seven instruments, it had already begun returning data. Notably, its camera captured pictures of the Apollo landing sites, including some of the tracks that the astronauts left on the surface.

In the newly released data, thermal measurements showed that daytime temperatures over much of the surface reached 220 degrees Fahrenheit - hotter than boiling water - before plummeting to frigidness at night.

But the bottoms of the craters, which lie in permanent darkness, never warm above minus 400. Those ultracold temperatures have trapped and held deposits of ice for several billion years. The ice could prove a valuable resource to future explorers, not only as drinking water but also, when the water molecules are broken apart, hydrogen and oxygen.

If it exists, the ice could also hold a detailed historical record of past comet impacts on the Moon, which would provide new hints of the early conditions in the solar system.

A second instrument detected slow-moving neutrons, which indicate the presence of hydrogen in the polar regions. The hydrogen is most likely in the form of water, and that data support the findings of the Lunar Prospector spacecraft a decade ago.

In a twist, the reconnaissance orbiter found hydrogen not only in some craters but also in some areas outside of the craters. Also, some of the craters did not appear to have hydrogen.

That means the water - or some other hydrogen-containing molecule like methane - lies beneath the surface. "It would be very durable there," Dr. Vondrak said. "What we don't know is the abundance and how deep it is buried."

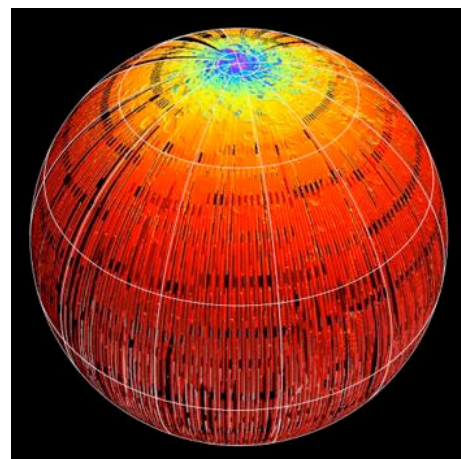
Getting to the material at the bottom of the craters could be difficult. An instrument that maps the topography by bouncing a laser beam off the surface has found the sides of the craters to be steep and rough terrain.

The primary mission of the Lunar Reconnaissance Orbiter, gathering data on the Moon from an altitude of 31 miles to prepare for the return on astronauts, will continue for a year. After that, it will continue to operate to gather information for scientists.

Tiny ancestor is T. rex blueprint

By Judith Burns Science reporter, BBC News

A 3m-long dinosaur fossil from China which predates T. rex by 60 million years is a blueprint for the mighty carnivore, say researchers. They tell Science magazine that the fossil displays the same features as T. rex but in miniature. The new species, *Raptorex kriegsteini*, would have weighed around 65kg; its descendants were 90 times as massive. Scientists believe it could be the "missing link" between earlier species of dinosaur and T. rex.



The 125-million-year-old specimen suggests that *T. rex*'s characteristic big head with enhanced jaw, relatively small forearms and huge back legs were inherited from this much smaller dinosaur, and that the body type changed little over millions of years except in size.

Long-armed relatives

In the past 10 years, fossils from earlier and more primitive species have been discovered in rocks between 100 and 176 million years old (Middle Jurassic to Early Cretaceous Periods) in Europe, North America and China.



*The skull of *R. kriegsteini* is dwarfed by the skull of a full-sized descendant*

These previous finds have confirmed that the Tyrannosaur family of dinosaurs is descended from small-bodied, long-armed predecessors. But there has been little evidence of a direct link between these relatively small dinosaurs and the massive fossils of *T. rex*.

The team believes that *Raptorex kriegsteini* is that link. It looks identical to a big *T. rex*, even down to the shape of the skull with its enlarged olfactory bulbs, which would have given it the same acute sense of smell as *T. rex*.

Lead researcher Dr Paul Sereno, from the University of Chicago, said: "It's as close to the proverbial missing link on a lineage as we might ever get for *T. rex*."

"From the teeth to the enlarged jaw muscles, the enlarged head, the small forelimbs, the lanky, running, long hind-limbs with the compressed foot for hunting prey: we see this all, to our great surprise, in an animal that is basically the body weight of a human or 1/90th the size that ultimately this lineage would reach in *T. rex* at the end of the Cretaceous."

Theory overturned

The team believes that the new fossil completely overturns accepted opinion on the evolution of tyrannosaurs.

Until now it had been thought that their strange body shape evolved as a consequence of their large size.

The fossil record bears out the previous theory that as tyrannosaurs developed truly giant size over time, they needed to modify their entire skeletons so they could continue to function as predators as they grew.

According to co-author Stephen Brusatte of the American Museum of Natural History in New York: "*Raptorex*, the new species, really throws a wrench into this observed pattern."

"Here we have an animal that's 1/90th or 1/100th of the size of *T. rex*, about my size, but with all the signature features - the big head, the strong muscles, the tiny little arms - that were thought to be necessary adaptations for a large body predator. "So really we can say that these features did not evolve as a consequence of large body size but rather that they evolved as an efficient set of predatory weapons in an animal that was just 1/100th of the size of *T. rex* and that lived 60 million years before *T. rex*."

The fossil record tells us that tyrannosaurs only grew to huge sizes during the final 20 million years of the Cretaceous.

Dr Brusatte said: "So that means that for most of their evolutionary history, about 80% of the time that they were on Earth, tyrannosaurs were small animals that lived in the shadow of other types of very large dinosaur predators. "In short, much of what we thought we know about tyrannosaur evolution turns out to be either simplistic or out-and-out wrong."

Fossil hunter

Dr Sereno estimates that this specimen of *Raptorex kriegsteini* was a young adult when it died.

The team made casts of the bones and reconstructed the animal as they believe it would have appeared. They think it would have been 1m high and that it would have had similar feathers to an ostrich.

It would have preyed on small birds and other smaller scampering animals that lived around the lake beds where it was discovered.

The researchers say that fragments of sand and sediment on the skeleton indicate that it came from an area of northeastern China rich in fossils. It was dug up illicitly and spirited out of the country and ultimately sold.

It is named after Henry Kriegstein, a private collector, who bought it from a dealer. He contacted Dr Sereno three years ago, asked him to analyse the specimen, and agreed to give it back to science and ultimately to China. It is now in a museum in Inner Mongolia. Mr Kriegstein is a co-author on the paper.

Dr Sereno said: "I hope this is a pathway that other important specimens will follow."

"This is more than just a Chinese specimen. It has given us some real insights into our own tyrannosaurs here in North America. So it really belongs to science. It belongs to the world."

Too much radiation for astronauts to make it to Mars

* 16 September 2009 by David Shiga

FORGET the risk of exploding rockets or getting sideswiped by a wayward bit of space junk. Radiation may be the biggest hurdle to human exploration beyond low-Earth orbit and could put a damper on a recently proposed mission to Mars orbit.

A panel tasked by the White House with reviewing NASA's human space flight activities (New Scientist, 22 August, p 8) suggests sending astronauts to one of Mars's moons, Phobos or Deimos, among other possibilities raised in its report released last week (<http://tinyurl.com/mbajav>).



A trip to Phobos comes with extras (Image: NASA/JPL)

From such a perch, astronauts could use remote-controlled robots to explore the Martian surface and retrieve samples - from the planet as well as the moon itself - for later close-up study on Earth. This would avoid the need to develop expensive hardware to land humans on a body with substantial gravity, like Mars.

"I, for one, would go to Phobos or Deimos in a heartbeat, even without any hope of landing on Mars," says planetary scientist Pascal Lee of the Mars Institute, a California-based research organisation.

But the insidious threat of space radiation in the form of galactic cosmic rays could keep astronauts confined much closer to home.

The rays are actually speeding protons and heavier atomic nuclei that rain onto our solar system from all directions. They can slice through DNA molecules when they pass through living cells and the resulting damage can lead to cancer.

People on the ground are protected by our planet's atmosphere and magnetic field, which also provide some protection to astronauts on the International Space Station. Lunar missions are short enough to keep radiation risks low, and the moon itself blocks half of the incoming particles. Crews on long journeys beyond low-Earth orbit would have no such protection.

Relatively lightweight aluminium or plastic shielding can block charged particles from the sun. But it would take impractically thick and heavy shields to stop the higher-energy galactic cosmic rays. "Shielding is not a solution to the risk problem," says Frank Cucinotta, chief scientist for radiation studies at NASA's Johnson Space Center in Houston, Texas. Alternative technologies - which would generate bubbles of plasma that could protect spacecraft without adding much weight - are still at an early stage of development.

So how dangerous would a trip to Mars orbit be? Estimates of how much a given dose of space radiation increases the risk of cancer are fraught with uncertainty. But calculations by Cucinotta and his colleagues suggest the trip would not meet NASA's existing rules, which aim to keep each astronaut's lifetime risk of fatal cancer from space radiation below 3 per cent.

For journeys outside Earth's magnetic field, astronauts could reach that limit in less than 200 days in a spacecraft with aluminium walls nearly 4 centimetres thick, according to worst-case scenario estimates (Radiation Measurements, DOI: 10.1016/j.radmeas.2006.03.011).

But the White House panel expects a round-trip mission to a Martian moon would take four times as long, lasting 750 days. Since such trips would expose astronauts to more radiation than is currently allowed, the panel asked NASA if it would consider simply accepting higher risks for the missions. Steven Lindsey, head of NASA's astronaut office, thinks most astronauts would probably be open to the idea. "It depends on the individual," he says. "I've got crew members that will fly on anything."

Guide on lung cancer in 'never-smokers': A different disease and different treatments **Sixth largest cancer killer**

A committee of scientists led by Johns Hopkins investigators has published a new guide to the biology, diagnosis and treatment of lung cancer in never-smokers, fortifying measures for what physicians have long known is a very different disease than in smokers.

"It is becoming increasingly clear that the genetic, cellular, and molecular nature of lung cancer in many never-smokers is different from that of smoking-related lung cancers, and there is good evidence now that the best treatment and prevention strategies for never-smokers may be different as well," says Charles M. Rudin, M.D., Ph.D., associate director for Clinical Research at the Johns Hopkins Kimmel Cancer Center. Lung cancer in never-smokers is the sixth leading cause of cancer-related deaths in the U.S.

Exposure to second-hand smoke and radon gas are thought to play important roles in causing the disease in never-smokers. Radon, which leaks into homes from naturally occurring uranium in soil, is known to be the leading cause of these cancers in U.S. populations, but about half of never-smokers with lung cancer cannot be

explained by known risk factors identified in the guide, which also include asbestos, indoor wood-burning stoves, and aerosolized oils caused by cooking.

The guide, published as three papers in the September 15 issue of *Clinical Cancer Research*, resulted from a two-day meeting of 13 lung cancer experts who convened at Johns Hopkins in 2007. The committee reviewed available evidence from several hundred studies published by experts in public health, epidemiology, molecular biology, pathology and oncology to identify distinctive characteristics of never-smokers with lung cancer.

Among the guide's recommendations is one calling on organizers of lung cancer clinical trials to classify subjects by their smoking status and evaluate outcomes accordingly. Committee members suggest that never-smokers should be consistently defined as people who have smoked less than 100 cigarettes in their lifetime.

"Patients who never smoked respond better to a certain class of drugs called EGFR inhibitors, because lung cancer in these patients more often contain mutations in the EGFR gene," says Rudin. EGFR normally promotes cell growth and development, and when mutated, allows the uncontrolled growth of cells that is the hallmark of cancer. "There are other examples of success in specifically targeting genetic changes in never-smokers with lung cancer, such as treatments of tumors with alterations in the EML4-ALK gene, and a genomewide association study exclusively on this population could tell us more."

Committee participant William Pao, M.D., associate professor at the Vanderbilt-Ingram Cancer Center in Nashville, TN, has established a repository of tissue specimen samples from non-smokers with lung cancer as a first step in such a study.

According to the experts, lung cancer in never-smokers usually presents at an advanced stage with non-specific symptoms like cough and chest pain. Rudin says it is often incorrectly treated as a respiratory illness with antibiotics and asthma medications. Doctors rarely suspect lung cancer since these patients have no smoking history, he adds.

"Besides second-hand smoke and radon exposure, we still have a gap of knowledge in explaining the causes of lung cancer in never-smokers," says Jonathan Samet, M.D., professor and Flora L. Thornton Chair of the Department of Preventive Medicine at the University of Southern California and formerly of the Johns Hopkins Bloomberg School of Public Health.

Lung cancer in non-smokers accounts for 10 to 15 percent of lung cancer cases in the U.S., according to the guide, which amounts to approximately 20,000 Americans annually. Survival rates are poor for most people with any kind of lung cancer.

Rudin says that lung cancer in never-smokers tends to occur more often in women and in certain populations in East Asia. This may be due to women's increased exposure to indoor pollutants caused by cooking oils and wood-burning stoves.

The experts also recommend a closer look at genetic trends in populations with early-age onset of the disease. *The two-day workshop and development of the guide were funded by the Flight Attendant Medical Research Institute (FAMRI). As part of a settlement with the American tobacco industry, flight attendants, who historically have been exposed to second-hand smoke in airplane cabins, won \$300 million to create FAMRI, which funds research on the early detection and treatment of diseases associated with tobacco-smoke exposure.*

In addition to Rudin, Samet and Pao, participants included Erika Avila-Tang and James G. Herman from Johns Hopkins; Curtis C. Harris and Susan Olivo-Marston from the National Cancer Institute; Fred R. Hirsch from the University of Colorado; Ann G. Schwartz from Wayne State University, Kirsi H. Vahakangas from the University of Kuopio; Paolo Boffetta from the International Agency for Research on Cancer; and Lindsay M. Hannan and Michael J. Thun from the American Cancer Society.

Barrow researcher finds natural hydrogel helps heal spinal cord

Research led by a scientist at the Barrow Neurological Institute at St. Joseph's Hospital and Medical Center has shown injecting biomaterial gel into a spinal cord injury site provides significantly improved healing. The project that also included researchers from Purdue University and Arizona State University indicates that a "practical path" to treatment may be found for spinal injury patients.

The research led by the Mark Preul, MD of Barrow and Alyssa Panitch, PhD of Purdue was published in the *Journal of Neurosurgery*. Their study found that injection of an engineered hydrogel made up mainly of hyaluronic acid (a naturally-occurring body substance) into the spinal cord injury site decreases scarring and promotes a realignment of the spinal cord fibers around the injury site.

The hyaluronic acid which forms a scaffold-like configuration may help to structurally stabilize the spinal cord injury site. Tracing of cells in the brain stem after injury showed much higher levels in the hydrogel treated animals compared to animals which did not receive the treatment, and approached nearly normal levels. Treated animals had higher functional scores than non-treated animals.

The work was presented at the Annual Meeting of the American Association of Neurological Surgeons in San Diego where it won the Synthes Prize for Spine Research.

"Spinal cord injury is devastating to civilian and military populations – especially to the young. There has been little progress toward paradigms of regeneration and few results that show real, sustained functional recovery," says Dr. Preul. "We've been so pre-occupied with regeneration, but that is a highly complicated and difficult to define goal. This project is a synergy of neurosurgeons and bioengineers that attempts repair of the SCI lesion cavity using a tissue-engineering biomaterials approach."

Dr. Preul says his team's goal is to find ways to structurally allow the body to better heal itself. "In this project we did not add anything to the hyaluronic acid. It may be that adding growth factors or cells into the gel matrix may allow even better results."

Although clinical trials are likely years off, Dr. Preul says these results show "we may be on a practical path that can give hope to the many people who suffer this sort of injury."

The current research was supported by a \$450,000 grant from the Arizona Biomedical Research Commission.

Introduced Japanese white-eyes pose major threat to Hawaii's native and endangered birds

In the late 1920s, people intentionally introduced birds known as Japanese white-eyes into Hawaiian agricultural lands and gardens for purposes of bug control. Now, that decision has come back to bite us.

A recent increase in the numbers of white-eyes that live in old-growth forests is leaving native bird species with too little to eat, according to a report published online on September 17th in *Current Biology*, a Cell Press publication. The findings show that introduced species can alter whole communities in significant ways and cause visible harm to the birds that manage to survive.

"Native Hawaiian songbirds cannot rear normal-size offspring in the presence of large numbers of introduced Japanese white-eyes," said Leonard Freed of the University of Hawaii at Manoa. "Their growth is stunted."

"Just as there are permanent effects of stunted growth in human children, there are permanent effects in adult birds," added Rebecca Cann, also of the University of Hawaii at Manoa. "Birds cannot use their shorter bills to feed efficiently for themselves or when feeding their young. Stunted birds have higher death rates than normal size birds. The Japanese white-eye is causing this problem for native Hawaiian birds by depleting the food available for growth, survival, and breeding."

Undernourished birds are left more susceptible to other threats, including infectious diseases. "Birds can only tolerate malaria if they have adequate nutrition to mount an immune response," Freed said. "They can only tolerate chewing lice if they have adequate nutrition to replace heat lost through plumage degraded by the lice."

The threat posed by the white-eyes came as a surprise to the researchers. That's because over more than a decade of study, it had seemed as though the white-eyes were living in peaceful coexistence with other birds, including the endangered Hawaii akepa.

But sometime after the year 2000, the researchers began to notice that young akepa were disappearing. The akepa fledglings that were seen were noticeably underweight. Other native birds had many broken wing and tail feathers - a sign of malnutrition - and suffered from a major increase in chewing lice. The researchers sounded an alarm, alerting the US Fish and Wildlife Service of the problem, but nothing was done, and two-thirds of the akepa in their long-term study site had disappeared by 2006.

Although Hawaiian birds face many threats, such as malaria, yellow-jacket wasps, and parasitoid wasps escaped from biological control of insects, the researchers were able to show that the white-eyes are most likely responsible for the decline of 7 of 8 native forest birds in a major portion of a national wildlife refuge. Young birds in a site with fewer white-eyes continued to grow normally, they found, despite potentially greater challenges from malaria and parasitoids. In other parts of Hawaii where white-eyes are flourishing, native species are suffering a similar fate.

The white-eyes are yet another example of the threats that introduced species can pose. When white-eyes were introduced, "no one at that time could have imagined that they would invade native forests," Cann said. "This is a problem with all introduced species. It is impossible to predict how they will respond to the new environment. The white-eye is a member of a bird family famous for expanding its range and consuming new types of prey, even to the point that individuals that colonize a new habitat may vary among themselves in the prey items they consume. But that was not known in 1929."

Even today, Freed said, foreign species continue to be put to work in risky ways. "Right now, realtors are using alien catfish to clean up the algae-ridden swimming pools of abandoned foreclosed houses in Florida. What if some escape during a flood into streams and lakes?"

The researchers include Leonard A. Freed, and Rebecca L. Cann, of the University of Hawaii at Manoa, Honolulu, HI.

Robots get smarter by asking for help

* 17 September 2009 by Jim Giles

ASKING someone for help is second nature for humans, and now it could help robots overcome one of the thorniest problems in artificial intelligence.

That's the thinking behind a project at Willow Garage, a robotics company in Palo Alto, California. Researchers there are training a robot to ask humans to identify objects it doesn't recognise. If successful, it could be an important step in developing machines capable of operating with consistent autonomy.

Object recognition has long troubled AI researchers. While computers can be taught to recognise simple objects, such as pens or mugs, they often make mistakes when the lighting conditions or viewing angle change. This makes it difficult to create robots that can navigate safely around buildings and interact with objects, a problem Willow Garage encountered when building its Personal Robot 2 (PR2).

Where AI struggles, humans excel, finding this sort of recognition task almost effortless. So Alex Sorokin, a computer scientist at the University of Illinois at Urbana-Champaign, who collaborates with Willow Garage, decided to take advantage of this by building a system that allows PR2 to ask humans for help.

The system uses Amazon's Mechanical Turk, an online marketplace which pairs up workers with employers that have simple tasks they need completing. The robot takes a photo of the object it doesn't recognise and sends it to Mechanical Turk. Workers can then use Sorokin's software to draw an outline around an object in the image and attach a name to it, getting paid between 3 and 15 cents for each image they process.

In initial tests, the robot moved through Willow Garage's offices, sending images to be processed every few seconds. Labelled images started coming back a few minutes later. The accuracy rate was only 80 per cent, but Sorokin says this can be improved by paying other workers to verify that the responses are valid.

Sorokin believes his system will help robots learn about new environments. A cleaning robot, for example, could spend its first week in a new building taking pictures and having people label them, helping it to build up a model of the space and the objects it contained. If it got stuck, it could always ask for help again.

"This is a fantastic idea," says John Leonard, a roboticist at the Massachusetts Institute of Technology. Potentially this could allow robots to operate for long periods without direct intervention from a human operator, he adds.

The next step for the programmers is to enable PR2 to make sense of the human responses and then act upon them, Sorokin says.

Negative public opinion an early warning signal for terrorism, Princeton professor says

An analysis of public opinion polls and terrorist activity in 143 pairs of countries has shown for the first time that when people in one country hold negative views toward the leadership and policies of another, terrorist acts are more likely to be carried out.

Princeton University economist Alan Krueger and co-author Jitka Malečková of Charles University in the Czech Republic have found that there is a strong relationship between attitudes expressed toward a foreign country -- indicated in surveys on foreign leaders' performance -- and the occurrence of terrorism against that country. The research is detailed in the Sept. 18 issue of the journal *Science*.

"Public opinion appears to be a useful predictor of terrorist activity," said Krueger, the Bendheim Professor in Economics and Public Policy. He has held a joint appointment since 1987 in Princeton's Department of Economics and the Woodrow Wilson School of Public and International Affairs. "This is the first study to relate public opinion across countries to concrete actions such as terrorism," he added.

Until now, the notion that public attitudes can contribute to terrorism has been inadequately explored, Krueger noted. The study's findings are significant, he said, because public opinion provides a valuable early warning signal of terrorism and helps researchers better understand the causes of terrorism.

The researchers carried out their study by mining public opinion polls of residents in 19 countries in the Middle East and northern Africa conducted by Gallup. Respondents were asked whether they approved of the job performance of the leaders of nine large countries. Those countries, selected because they are world powers in terms of size, population or military strength, are the United States, Canada, China, France, Germany, India, Japan, Russia and the United Kingdom. The opinions, both positive and negative, were then linked to the number of terrorist attacks conducted against the nine world powers by people from the 19 countries between 2004 and 2008. The terror attacks were compiled by the National Counterterrorism Center.

In findings that are consistent with his earlier work, Krueger said there is not a direct connection between poverty and terrorism, contrary to a popular view. Economic status has more to do with target countries than it does with the states where the attacks originate, according to Krueger. Countries with advanced economies as well as a high degree of civil liberties, he said, are most likely to be the targets of terrorism.

The study does not explain whether terrorists act in response to public opinion or whether they are simply reacting just like the larger public to external events, he noted. In either case, however, he noted that public opinion surveys can provide a powerful indication of the likelihood of terrorist activity.

Krueger hypothesized that greater disapproval of another country's leaders or policies may result in more terrorist acts because it increases the number of people who provide material support and encouragement for terrorism, and increases the number of people interested in joining cells and carrying out terrorist acts themselves.

Extending the analysis, the researchers proposed that new leadership and policies in a country - such as the election of President Barack Obama in the United States - might change opinions in other countries and alter terrorist activity.

Krueger has published many papers about the origins of terrorism, and he has urged terrorism experts to apply the rigorous techniques of social science to questions concerning terrorism and its effects.

Krueger is currently on leave from Princeton, working as the assistant secretary for economic policy and chief economist at the U.S. Department of Treasury. The research was conducted while Krueger was at Princeton and submitted before he assumed his position with the government. The contents of the paper do not necessarily reflect the views of the U.S. government. Work on the project was partly supported by a grant from the European Commission to the European Security Economics project.

Researchers make rare meteorite find using new camera network in Australian desert

Researchers have discovered an unusual kind of meteorite in the Western Australian desert and have uncovered where in the Solar System it came from, in a very rare finding published today in the journal *Science*.

Meteorites are the only surviving physical record of the formation of our Solar System and by analysing them researchers can glean valuable information about the conditions that existed when the early Solar System was being formed. However, information about where individual meteorites originated, and how they were moving around the Solar System prior to falling to Earth, is available for only a dozen of around 1100 documented meteorite falls over the past two hundred years.



This is Bunburra Rockhole, the meteorite, at the discovery site. Imperial College London

Dr Phil Bland, the lead author of today's study from the Department of Earth Science and Engineering at Imperial College London, said: "We are incredibly excited about our new finding. Meteorites are the most analysed rocks on Earth but it's really rare for us to be able to tell where they came from. Trying to interpret what happened in the early Solar System without knowing where meteorites are from is like trying to interpret the geology of Britain from random rocks dumped in your back yard."

The new meteorite, which is about the size of cricket ball, is the first to be retrieved since researchers from Imperial College London, Ondrejov Observatory in the Czech Republic, and the Western Australian Museum, set up a trial network of cameras in the Nullarbor Desert in Western Australia in 2006.

The researchers aim to use these cameras to find new meteorites, and work out where in the Solar System they came from, by tracking the fireballs that they form in the sky. The new meteorite was found on the first day of searching using the new network, by the first search expedition, within 100m of the predicted site of the fall. This is the first time a meteorite fall has been predicted using only the data from dedicated instruments.

The meteorite appears to have been following an unusual orbit, or path around the Sun, prior to falling to Earth in July 2007, according to the researchers' calculations. The team believes that it started out as part of an asteroid in the innermost main asteroid belt between Mars and Jupiter. It then gradually evolved into an orbit around the Sun that was very similar to Earth's. The other meteorites that researchers have data for follow orbits that take them back, deep into the main asteroid belt.

The new meteorite is also unusual because it is composed of a rare type of basaltic igneous rock. The researchers say that its composition, together with the data about where the meteorite comes from, fits with a recent theory about how the building blocks for the terrestrial planets were formed. This theory suggests that the igneous parent asteroids for meteorites like today's formed deep in the inner Solar System, before being scattered out into the main asteroid belt. Asteroids are widely believed to be the building blocks for planets like the Earth so today's finding provides another clue about the origins of the Solar System.

The researchers are hopeful that their new desert network could yield many more findings, following the success of their first meteorite search.

Dr Bland added: "We're not the first team to set up a network of cameras to track fireballs, but other teams have encountered problems because meteorites are small rocks and they're hard to find in vegetated areas. Our solution was quite simple - build a fireball network in a place where it's easy to find them. The Nullarbor Desert

is ideal because there's very little vegetation and dark rocks show up really easily on the light desert plain. "It was amazing to find a meteorite that we could track back to its origin in the asteroid belt on our first expedition using our small trial network. We're cautiously optimistic that this find could be the first of many and if that happens, each find may give us more clues about how the Solar System began," said Dr Bland.

The researchers' network of cameras takes a single time-lapse picture every night to record any fireballs in the sky. When a meteorite falls, researchers can then use complex calculations to uncover what orbit the meteorite was following and where the meteorite is likely to have landed, so that they can retrieve it.

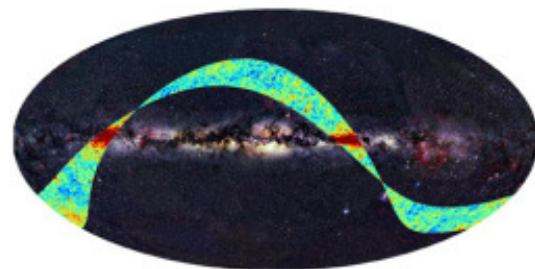
Probe gets clearest glimpse yet of cosmic dawn

* 21:40 17 September 2009 by **David Shiga**

The Planck spacecraft has obtained its first peek at the afterglow of the big bang, revealing it in unprecedented detail. Its first map of the entire sky is set to be complete in about six months.

The European Space Agency spacecraft was launched into space on 14 May. It is observing the glow of hot gas from just 380,000 years after the big bang – about 13.73 billion years ago – called the cosmic microwave background.

The detailed properties of this background may contain hints of hidden extra dimensions or multiple universes, as well as providing clues to what caused a brief, early period of incredibly rapid cosmic expansion.



The microwave strip observed by Planck (multi-coloured curve) is superimposed on a visible-light image of the sky, which is dominated by the disc of our Milky Way galaxy (Image: ESA/LFI/HFI Consortium/Axel Mellinger)

Planck began surveying the microwave background on 13 August, a few weeks after reaching its planned perch 1.5 million kilometres from Earth at a point called L2 and cooling its detectors to within 0.1 °C above absolute zero. Now, the Planck team has released the probe's first image, an observational strip covering about 5 per cent of the sky.

Best yet

Slight variations in temperature from place to place in the early universe give the image its mottled appearance. "With a few per cent of the data in, you can see it's working well and delivering good stuff," says team member George Efstathiou of the University of Cambridge.

Planck is expected to provide the most detailed all-sky map of the cosmic microwave background yet, improving on the best current map, obtained by NASA's Wilkinson Microwave Anisotropy Probe (WMAP), which launched in 2001. Planck's detectors have more than 10 times the sensitivity of WMAP's, and about 2.5 times the angular resolution. "Every strip that Planck scans, we're getting data that is many, many times more sensitive than WMAP," Efstathiou told New Scientist.

Although Planck was only designed to observe the sky for 15 months, the team believes it could last for more than 30 months, based on new estimates of how long its coolant will last. The extra time will allow Planck to measure the radiation with even greater precision, since it will scan the entire sky four times – two more than originally planned.

New vitamin K analysis supports the triage theory

Modest vitamin/mineral deficiencies increase age-related disease

September 16, 2009 - Oakland, CA – An important analysis conducted by Children's Hospital Oakland Research Institute scientists suggests the importance of ensuring optimal dietary intakes of vitamin K to prevent age-related conditions such as bone fragility, arterial and kidney calcification, cardiovascular disease, and possibly cancer (1). Vitamin K is concentrated in dark green plants such as spinach or Swiss chard, and is either not present or present in only small amounts in most multivitamin pills.

This finding comes from Associate Staff Scientist, Joyce McCann, PhD, and Senior Scientist, Bruce Ames, PhD, who analyzed data from hundreds of published articles dating back to the 1970's. Their review was designed to test Dr. Ames' "trriage" theory that provides a new basis for determining the optimum intake of individual vitamins and minerals (also called micronutrients), and has major implications for preventive medicine. The analysis, which strongly supports his theory, will be published in the October 2009 issue of the American Journal of Clinical Nutrition.

Dr. Ames proposed the triage theory in 2006 (2,3) to explain numerous observations from his own lab and the scientific literature. The theory explains why diseases associated with aging like cancer, heart disease, and dementia (and the pace of aging itself) may be unintended consequences of mechanisms developed during evolution to protect against episodic vitamin/mineral shortages. If correct, the triage theory has widespread implications for public health because modest vitamin/mineral deficiencies are quite common. The theory also

suggests a new scientifically based and consistent strategy for establishing optimal vitamin/mineral intake standards, and it provides a research strategy to uncover early biomarkers of chronic disease.

Vitamin K is known as the "Koagulation" vitamin because about half of the 16 known proteins that depend on vitK are necessary for blood coagulation. The other vitK-dependent proteins are involved in a variety of different functions involving the skeletal, arterial, and immune systems.

Average intakes of vitamin K in the United States and the United Kingdom are less even than currently recommended intakes, which are primarily based on levels to ensure adequate coagulation. McCann & Ames' analysis supports recommendations by some experts that non-clotting functions requiring vitamin K may need higher intakes than are currently recommended.

McCann says, "Encouraging support for the triage theory from our vitamin K analysis suggests that experts aiming to set micronutrient intake recommendations for optimal function and scientists seeking mechanistic triggers leading to diseases of aging may find it productive to focus on micronutrient-dependent functions that have escaped evolutionary protection from deficiency."

This vitamin K analysis is the first in a series of literature-based studies conducted by Drs. Joyce McCann and Ames to test the basic premises of the triage theory. As a reviewer of the manuscript notes, "...this review provides a unique perspective of consequences of vitamin K insufficiency and may serve as an important future reference, as new vitamin K dependent proteins are identified and new (non-clotting) functions of vitamin K are elucidated. More broadly, an assessment of micronutrient sufficiency from the perspective of triage theory may provide a valuable point of view, as current recommendations for nutrient intakes are reconsidered."

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Rare genetic disease successfully reversed using stem cell transplantation

Scripps Research scientists correct gene defect in mice that causes lethal symptoms in children

LA JOLLA, CA – A recent study by Scripps Research Institute scientists offers good news for families of children afflicted with the rare genetic disorder, cystinosis. In research that holds out hope for one day developing a potential therapy to treat the fatal disorder, the study shows that the genetic defect in mice can be corrected with stem cell transplantation.

"After meeting the children who suffer from this disease, like an 18-year-old who has already had three kidney transplants, and the families who are desperately searching for help, our team is committed to moving toward a cure for cystinosis, a lysosomal storage disorder," says principal investigator Stephanie Cherqui, assistant professor in the Department of Molecular and Experimental Medicine. "This study is an important step toward that goal."

In the study, which is published in the September 17, 2009 print edition of the journal *Blood*, the Scripps Research team used bone marrow stem cell transplantation to address symptoms of cystinosis in a mouse model. The procedure virtually halted the cystine accumulation responsible for the disease and the cascade of cell death that follows.

Cystine is a byproduct of the break down of cellular components the body no longer needs in the cell's "housekeeping" organelles, called lysosomes. Normally, cystine is shunted out of cells, but in cystinosis a gene defect of the lysosomal cystine transporter causes it to build up, forming crystals that are especially damaging to the kidneys and eyes.

A Rare But Devastating Disease

While cystinosis is rare - affecting an estimated 500 people in the United States and 2,000 worldwide - it is devastating. Three types of cystinosis have been described based on the age at diagnosis and the amount of cystine in cells: infantile onset, adolescent onset, and adult onset. Children as young as six months can begin to suffer renal dysfunction, which grows progressively worse with time. Other symptoms include diabetes, muscular disease, neurological dysfunction, and retinopathy. Infantile onset is the most common, as well as the most severe, form of the disease.

The only available drug to treat cystinosis, cysteamine, while slowing the progression of kidney degradation, does not prevent it, and end-stage kidney failure is inevitable.

"Cysteamine must be given every six hours, so children have to be woken up each night to take this drug, which has unpleasant side effects, and many others to treat various symptoms," Cherqui says. "So although there is treatment, it is difficult treatment that does not cure the disease."

"Surprised and Encouraged"

In the new study, the researchers found that transplanted bone marrow stem cells carrying the normal lysosomal cystine transporter gene abundantly engrafted into every tissue of the experimental mice. This led to an average drop in cystine levels of about 80 percent in every organ. In addition to preventing kidney dysfunction, there was less deposition of cystine crystals in the cornea, less bone demineralization, and an improvement in motor function.

"The results really surprised and encouraged us," says Cherqui, who as a doctoral student in France in 1998 helped discover the gene involved in cystinosis. "Because the defect is present in every cell of the body, we did not expect a bone marrow stem cell transplant to be so widespread and effective."

Cherqui, who generated the mouse model in 2000 that is currently used to study cystinosis, says that adult bone marrow stem cell therapy is particularly well suited as a potential treatment for cystinosis because these cells target all types of tissues. In addition, stem cells reside in the bone marrow for the duration of a patient's life, becoming active as needed, a particular benefit for a progressive disease like cystinosis.

The work of Cherqui and her colleagues may have wider applications for other genetic diseases, providing proof of principle that adult stem cell transplants may be successful in humans for genetic diseases with systemic defects, especially those of a progressive nature.

Cherqui expects to spend the next several years analyzing the safety of genetically modified autologous (obtained from the same individual) bone marrow transplants in the cystinosis mouse and other models before moving on to human clinical trials.

In addition to Cherqui, authors of the study "Successful treatment of the murine model of cystinosis using bone marrow cell transplantation" include first author Kimberly Syres of Scripps Research; Frank Harrison, Matthew Tadlock, and Daniel R. Salomon of Scripps Research; James V. Jester and Jennifer Simpson of the University of California, Irvine; and Subhojit Roy of the University of California, San Diego. This work was funded by the Cystinosis Research Foundation.

Researchers prolong the half-life of biopharmaceutical proteins Biotech innovation could extend dosing intervals, simplify production

Many biopharmaceuticals comprise small proteins that are quickly eliminated from the body. Scientists at the Technische Universitaet Muenchen (TUM) combine such small proteins with a kind of molecular balloon that swells and thus prolongs the half-life of the proteins in the body. The TUM spin-off XL-Protein GmbH has now started to further develop this new technology with blockbuster potential.

People who suffer from hepatitis B are often treated with the tissue hormone interferon. However, there is a problem: Interferon is a very small protein, which is filtered from the blood via the kidneys after only a short time. For the patient this means a high-dose injection every other day to keep the effect of the substance from wearing off prematurely.

However, interferon stays in the body much longer when chemically coupled with a synthetic PEG (polyethylene glycol) molecule. PEG is a random coil long-chain polymer string that swells by adsorbing water. That way the PEG molecule becomes large enough that it does not fit through the fine pores of the kidneys – the attached interferon remains in the circulatory system longer, and the patient will need an injection only every one to two weeks.

Using genetic engineering, TU Muenchen scientist Prof. Arne Skerra and his coworkers from the Chair of Biological Chemistry at the Center for Life and Food Sciences Weihenstephan have now developed an amino acid string that tangles up similarly to PEG and also swells in the presence of water. However, unlike many PEG compounds, there is no danger of this biological polymer accumulating in the body. In fact – over an extended period of time – it is discharged or biologically broken down. That happens because this amino acid string (polypeptide) consists of three of the 20 naturally occurring amino acids: proline, alanine and serine, or in short, PAS.

The protein substance interferon, which itself consists of amino acids, can thus be easily generated in "PASylated" form. In first trials with animals, TUM scientists established that PASylated interferon has a half-life in the blood that is prolonged by a factor of 60, which should allow a significant extension of dosing intervals during medicinal therapy.

A further advantage is the simplified biotechnological production: The DNA segments carrying the information for the PAS amino acid sequence and for the interferon can simply be attached to each other and then, for instance, used for transforming bacteria. The bacteria then produce the PASylated interferon in one

piece, thus making much fewer production steps necessary in comparison with the chemical coupling of PEG. According to Skerra, "this will lead to a significant drop in production cost."

In principle all small proteins currently used as medication or in development in pharmaceutical companies – for example, growth factors or functional antibody fragments – can be PASylated. Thus there could be a huge market for the new technology. Consequently, Prof. Skerra and his team initiated the founding of a new biotech company, XL-Protein GmbH (<http://www.xl-protein.com>), which started its operations last spring. "Our technology has the potential to give birth to a whole new generation of blockbuster medications," the TUM biochemist is convinced. Several of the new drugs are already at an advanced stage of preclinical development.

Cheap, Quick Bedside "Eye Movement" Exam Outperforms Mri For Diagnosing Stroke In Patients With Dizziness

Small study demonstrates possibilities of reducing unnecessary MRI tests and improving safety

September 18, 2009-In a small "proof of principle" study, stroke researchers at Johns Hopkins and the University of Illinois have found that a simple, one-minute eye movement exam performed at the bedside worked better than an MRI to distinguish new strokes from other less serious disorders in patients complaining of dizziness, nausea and spinning sensations.

Results of the study of 101 patients, who were already at higher than normal risk of stroke because of factors including high blood pressure or high cholesterol, were published online ahead of print on Sept. 17 in *Stroke*. The patients were all seen at OSF St. Francis Medical Center in Peoria, Ill.

The project, spearheaded by a Johns Hopkins neurologist in collaboration with colleagues at the University of Illinois in Peoria, found that the quick, extremely low-cost exam caught more strokes than the current gold standard of MRI, suggesting that if further research on broader populations confirms these results, physicians may have a way to improve care and avoid the high costs of MRI in some cases.

"The idea that a bedside exam could outperform a modern neuroimaging test such as MRI is something that most people had given up for dead, but we've shown it's possible," says David E. Newman-Toker, M.D., Ph.D., assistant professor of neurology at the Johns Hopkins University School of Medicine.

Dizziness is a common medical problem, Newman-Toker says, responsible for 2.6 million emergency room visits annually in the United States. While the vast majority of dizziness complaints are caused by benign inner-ear balance problems, about 4 percent are signals of stroke or transient ischemic attack (TIA, a condition that often warns of impending stroke in the coming days or weeks). Because more than half of patients with dizziness who are experiencing strokes show none of the classic stroke symptoms - one-sided weakness, numbness, or speech problems - emergency room physicians are estimated to misdiagnose at least a third of them, losing the chance for quick and effective treatment.

"We know that time is brain, so when patients having a stroke are sent home erroneously, the consequences can be really serious, including death or permanent disability," says Jorge C. Kattah, M.D., chairman of neurology at OSF St. Francis Medical Center, who co-led the study.

The study of eye movement tests was suggested by previous research showing that people experiencing a stroke have eye-movement alterations that correlate with stroke-damage to various brain areas and that these are distinct from eye-movement alterations seen with benign ear diseases. Some patients, for example, can't immediately adjust their eye position if their heads are quickly turned to the side, or they experience jerky eye movements as they try to focus on a doctor's finger when looking to either side.

Newman-Toker and his colleagues at the University of Illinois College of Medicine in Peoria wondered whether testing eye movements in dizzy patients might help them sort out which ones were having a stroke from those with other problems.

All of the patients in the current study were seen after complaining of severe dizziness that had lasted for several hours continuously, and all had at least one risk factor for stroke. The researchers selected them to increase the chance that they would find strokes in this population. None of the patients had a history of previous dizzy spells and more than half sought care at the Peoria medical center's ER, though some were inpatients at the hospital or were transferred from other area hospitals.

The researchers gave each patient an exam comprised of three eye-movement tests: looking for inability to keep the eyes stable as patients heads were rotated rapidly to either side, looking for jerkiness as patients tracked a doctor's finger to look right and left, and checking eye position to see if one eye was higher than the other. Each patient then received an early MRI, the highest-quality neuroimaging test available to confirm stroke in dizzy patients. Patients with eye tests suggesting stroke but without stroke on the first MRI scan underwent a repeat scan.

In the end, 69 patients were diagnosed with stroke and 25 with inner-ear conditions. The remainder had other neurological problems. Using only the three eye-movement tests, the researchers had correctly diagnosed all of

the strokes and 24 of 25 with inner-ear conditions. By contrast, initial MRI scans were falsely negative in eight of the 69 stroke patients, who were later correctly diagnosed with follow-up MRIs.

Though the researchers emphasize the need to verify their results in a larger and more general population of patients with dizziness, Newman-Toker says the initial findings are “incredibly promising.” If they hold true, he adds, testing eye movements could have several advantages over MRI beyond reliable diagnostics. For example, while the wait time for an MRI can be several hours or more, physicians can perform all three eye-movement tests in a minute or less. Also, the eye-movement tests are “basically free,” compared to \$1000 or more for an MRI, Newman-Toker says.

“In an era where cost containment is butting up against issues of quality in health care delivery, there’s tremendous potential for bedside approaches like ours that could reduce costs while improving quality at the same time,” says Newman-Toker.

For more information, go to: http://www.hopkinsmedicine.org/neurology_neurosurgery/experts/team_member_profile/516F40C024FCA3D4B4B633D0E080FE1B/David_Newman-Toker

Medications Effective in Reducing Risks for Breast Cancer Can Also Cause Serious Side Effects

Although tamoxifen, raloxifen and tibolone dramatically reduce the risk of invasive breast cancer, some patients experience adverse effects

PORTLAND, Ore. - Three drugs that reduce a woman's chance of getting breast cancer also have been shown to cause adverse effects, according to a new report from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health & Human Services.

The report is based on a study led by Heidi D. Nelson, M.D., M.P.H., research professor in the Oregon Evidence-Based Practice Center at Oregon Health & Science University and medical director of the Women and Children's Program and Research Center at Providence Health & Services. It is published online in the Sept. 15 issue of the *Annals of Internal Medicine*.

The study is the first to make a direct, comprehensive comparison of drugs that reduce the risk of breast cancer so that women and their health care providers can assess their potential effectiveness and adverse effects. It compares the use of tamoxifen, raloxifene and tibolone to reduce the risks of getting breast cancer in women without pre-existing cancer.

Tamoxifen, raloxifene and tibolone can be prescribed to women with a family history of breast cancer or other risk factors, but prescribing practices vary widely. According to the study, all three drugs significantly reduce invasive breast cancer in midlife and older women, but benefits and adverse effects can vary depending on the drug and the patient.

Breast cancer is the second most commonly diagnosed cancer among women (after skin cancer), with more than 190,000 new cases diagnosed each year in the United States. It is estimated to cause more than 40,000 deaths per year. The National Cancer Institute estimates that nearly 15 percent of women born today will develop breast cancer in their lifetimes. Most cases of breast cancer occur in women with no specific risk factors other than age and gender, although family history of breast and ovarian cancer is associated with higher risk.

Tamoxifen, a selective estrogen receptor modulator (SERM), was approved by the Food and Drug Administration in 1998 to reduce risk for breast cancer in women at high risk of developing the disease. Its use to reduce the risk of breast cancer is accepted clinical practice, although it is primarily used for treatment rather than risk reduction.

The study compared tamoxifen with another SERM, raloxifene, which is primarily used to prevent and treat osteoporosis and was approved by the FDA for breast cancer risk reduction in 2007. A third drug, tibolone, which has not been approved by the FDA for use in the United States but is commonly used in other countries to treat menopausal symptoms and osteoporosis, also was included in the study.

The study found that all three drugs reduce the occurrence of breast cancer but have various side effects. The most common side effects for tamoxifen are flushing and other vasomotor symptoms (e.g., night sweats, hot flashes), vaginal discharge and other vaginal symptoms such as itching or dryness; for raloxifene, side effects include vasomotor symptoms and leg cramps; and for tibolone, side effects include vaginal bleeding.

The study also found that each drug carried risks of adverse effects. Tamoxifen increases risks of endometrial cancer, hysterectomies and cataracts compared with the other drugs. Tamoxifen and raloxifene increase risk of blood clots, although tamoxifen's risk is greater. Tibolone carries an increased risk of stroke, according to the study.

The study also examined the drugs' effectiveness and harms based on age, menopausal status, estrogen use and family history of breast cancer, and sought to identify the kinds of women who might be good candidates

for therapy, although the evidence is limited in this area. The investigators called for more research to more clearly identify characteristics of patients who would benefit from these drugs while suffering the least harm.

"Before applying the findings of the report to practice, clinicians must ensure that women understand their individual risks for breast cancer and can favorably balance these with the unwanted effects of risk-reducing medications," explained Nelson.

The report, Comparative Effectiveness of Medications to Reduce Risk of Primary Breast Cancer in Women, is the latest analysis from the Agency's Effective Health Care Program. That program, authorized by the Medicare Prescription Drug Improvement, and Modernization Act of 2003, represents an important federal effort to compare alternative treatments for health conditions and make the findings public. The program is intended to help patients, doctors, nurses, and others choose the most effective treatments. Information, including the new report, can be found at www.effectivehealthcare.ahrq.gov.

Nevada professor discovers new way to calculate body's 'Maximum Weight Limit'

For immediate release: Sept. 18, 2009 Nevada professor discovers new way to calculate body's "Maximum Weight Limit" RENO, Nev. - Most of us are familiar with the term, Body Mass Index, or BMI, as an index to determine healthy body weight. But, calculating BMI involves a complex formula: weight in pounds is multiplied by 703, and then divided by height in inches squared. Charts or online calculators are then used to show a "healthy weight range" given an individual's height that corresponds to the "healthy range BMI." For example, a BMI chart indicates that a healthy range BMI of 19 to 24 translates to a "healthy weight range" of 120 to 150 pounds for a 5-foot, 6-inch individual.

If this sounds way too complicated to you, you're not alone. George Fernandez, a professor of applied statistics and director of the Center for Research Design and Analysis at the University of Nevada, Reno, set out to give people a simpler way of calculating their healthy weight, and one that wouldn't require charts or online calculators. In addition, he doesn't think the "range" approach sticks in individuals' minds. "We need a "Maximum Weight Limit, or MWL," he said, "one number that we know we can't go over, just like a speed limit."

So, using SAS software and statistical procedures, he discovered a much simpler way of calculating a Maximum Weight Limit, which closely corresponds to weight recommendations listed on BMI charts. But, you don't need to calculate or know your BMI, nor do you need a chart or online calculator to figure out your Maximum Weight Limit. Fernandez will present his Maximum Weight Limit calculation at the Nevada Public Health Association Conference, 1:30 p.m., Sept. 22 at the University of Nevada, Reno's Joe Crowley Student Union, Room 423.

"It's a very simple calculation that most of us can do in our heads," he explained. For men and women, there is a baseline height and weight. For men, the baseline is 5-feet, 9-inches tall and a Maximum Weight Limit of 175 pounds, meaning that a 5-foot, 9-inch tall man should weigh no more than 175 pounds. For women, the baseline is 5-feet tall and a Maximum Weight Limit of 125 pounds. "These are nice round numbers that people can easily remember: 5-feet, 9-inches tall, 175 pounds for man; and 5-feet tall, 125 pounds for a woman," explained Fernandez.

From that starting point, you simply calculate how much taller or shorter you are, in inches. Then, if you are man, you add or subtract 5 pounds for every inch you are taller or shorter than 5 feet, 9 inches. So, if you are 5-feet, 11-inches tall, you are 2 inches taller than the baseline of 5 feet, 9 inches. You add 5 pounds for each of those 2 inches, 10 pounds, to the baseline Maximum Weight Limit of 175. So, your Maximum Weight Limit is 185 (175 pounds plus 10 pounds). Women add or subtract 4.5 pounds for each inch they differ from the baseline height of 5-feet tall.

These Maximum Weight Limits correspond very closely to BMIs of 25.5 for men and 24.5 for women. A BMI of 18.5 to 25 BMI is diagnosed as the "healthy range." Fernandez used a slightly lower BMI base for women and a slightly higher one for men because, on average, women have less muscle mass than men. Although some have debated using BMI as a means for calculating healthy weight because it does not take into account factors such as muscle mass, for example, it has been shown to work as a basis for calculating a healthy weight for more than 90 percent of the population and is the most universally used index in weight management programs.

"Now people can calculate their own Maximum Weight Limit, based on the BMI index, but without any calculators or charts," Fernandez said. "And, all they have to remember is that one number, 185 pounds for example, which is easier for most people than retaining a weight range, such as 155 to 185 pounds."

Fernandez also noted that this simple formula could be very useful in medically underserved areas of the world, and for individuals without access to technology and charts.

"Anyone, anywhere can calculate their Maximum Weight Limit if they know their height and this simple formula," he said. "People can calculate this in their heads and remember this."

New rabies vaccine may require only a single shot... not 6

The current standard post-exposure regimen is not feasible in the developing world, where rabies is endemic

Philadelphia - A person, usually a child, dies of rabies every 20 minutes. However, only one inoculation may be all it takes for rabies vaccination, according to new research published in the Journal of Infectious Diseases by researchers at the Jefferson Vaccine Center. A replication-deficient rabies virus vaccine that lacks a key gene called the matrix (M) gene induced a rapid and efficient anti-rabies immune response in mice and non-human primates, according to James McGettigan, Ph.D., assistant professor of Microbiology and Immunology at Jefferson Medical College of Thomas Jefferson University.

"The M gene is one of the central genes of the rabies virus, and its absence inhibits the virus from completing its life cycle," Dr. McGettigan said. "The virus in the vaccine infects cells and induces an immune response, but the virus is deficient in spreading." The immune response induced with this process is so substantial that only one inoculation may be sufficient enough, according to Dr. McGettigan. In addition, the vaccine appears to be efficient in both pre-exposure and post-exposure settings.

Currently, the World Health Organization standard for rabies infection is post-exposure prophylaxis. The complex regimen in the United States requires six different shots over 28 days: five of the rabies vaccine and one of rabies immunoglobulin. The current standard vaccine is made from inactivated rabies virus, whereas the experimental vaccine is made from a live rabies virus. The virus is modified by removing the M gene, thus inhibiting its spread within the vaccine recipient.

Worldwide, the annual number of rabies-related deaths is estimated to be 40,000 to 70,000. The disease is endemic in developing areas, where the six-shot post-exposure regimen is not feasible for many people due to cost and availability. According to the World Health Organization, approximately 10 million people worldwide receive the post-exposure regimen, which presents a financial burden to both industrialized and developing countries.

"Developing countries do not have the resources to vaccinate people six times after exposure, so many of these 10 million do not receive the full regimen," Dr. McGettigan said. "Therefore, simpler and less expensive vaccine regimens are needed. The alternative may also be to treat people pre-exposure, as they are with many of the current vaccines used. Although our vaccine was tested primarily to be a post-exposure vaccine, the data we collected show it would be effective as a pre-exposure vaccine as well."

Dr. McGettigan recently was awarded a four-year \$1.5 million R01 grant from the National Institutes of Health to continue his research on novel rabies vaccine approaches.

Well

With Soap and Water or Sanitizer, a Cleaning That Can Stave Off the Flu

By TARA PARKER-POPE

It sounds so simple as to be innocuous, a throwaway line in public-health warnings about swine flu. But one of the most powerful weapons against the new H1N1 virus is summed up in a three-word phrase you first heard from your mother: wash your hands.

A host of recent studies have highlighted the importance and the scientific underpinning of this most basic hygiene measure. One of the most graphic was done at the University of California, Berkeley, where researchers focused video cameras on 10 college students as they read and typed on their laptops.

The scientists counted the times the students touched their faces, documenting every lip scratch, eye rub and nose pick. On average, the students touched their eyes, noses and lips 47 times during a three-hour period, once every four minutes. Hand-to-face contact has a surprising impact on health. Germs can enter the body through breaks in the skin or through the membranes of the eyes, mouth and nose.

The eyes appear to be a particularly vulnerable port of entry for viral infections, said Mark Nicas, a professor of environmental health sciences at Berkeley. Using mathematical models, Dr. Nicas and colleagues estimated that in homes, schools and dorms, hand-to-face contact appears to account for about one-third of the risk of flu infection, according to a report this month in the journal Risk Analysis.

In one study of four residence halls at the University of Colorado, two of the dorms had hand sanitizer dispensers installed in every dorm room, bathroom and dining area, and students were given educational materials about the importance of hand hygiene. The remaining two dorms were used as controls, and researchers simply monitored illness rates.

During the eight-week study period, students in the dorms with ready access to hand sanitizers had a third fewer complaints of coughs, chest congestion and fever. Over all, the risk of getting sick was 20 percent lower in the dorms where hand hygiene was emphasized, and those students missed 43 percent fewer days of school.

Young children benefit, too. In a study of 6,000 elementary school students in California, Delaware, Ohio and Tennessee, students in classrooms with hand sanitizers had 20 percent fewer absences due to illness. Teacher absenteeism in those schools dropped 10 percent.

Better hand hygiene also appears to make a difference in the home, lowering the risk to other family members when one child is sick. Harvard researchers studied nearly 300 families who had children 5 or younger in day care. Half the families were given a supply of hand sanitizer and educational materials; the other half were left to practice their normal hand washing habits.

In homes with hand sanitizers, the risk of catching a gastrointestinal illness from a sick child dropped 60 percent compared with the control families. The two groups did not differ in rates of respiratory illness rates, but families with the highest rates of sanitizer use had a 20 percent lower risk of catching such an illness from a sick child.

Regular soap and water and alcohol-based hand sanitizers are both effective in eliminating the H1N1 virus from the hands. In February, researchers in Australia coated the hands of 20 volunteers with copious amounts of a seasonal H1N1 flu virus. The concentration of virus was equivalent to the amount that would occur when an infected person used a hand to wipe a runny nose.

When the subjects did not wash their hands, large amounts of live virus remained even after an hour, said the lead author, Dr. M. Lindsay Grayson, a professor of medicine at the University of Melbourne. But using soap and water or a sanitizer virtually eliminated the presence of the virus.

Frequent hand washing will not eliminate risk. When an infected person coughs or sneezes, a bystander might be splattered by large droplets or may inhale airborne particles. In a recent Harvard study of hand sanitizer use in schools, hand hygiene practices lowered risk for gastrointestinal illness but not upper respiratory infections.

Still, it is a good idea to wash your hands regularly even if you're not in contact people who are obviously ill. In a troubling finding, a recent study of 404 British commuters found that 28 percent had fecal bacteria on their hands. In one city, 57 percent of the men sampled had contaminated hands, according to the study, which was published this month in the journal *Epidemiology and Infection*.

"We were surprised by the high level of contamination," said Gaby Judah, a researcher at the London School of Hygiene and Tropical Medicine. Ms. Judah added that many of the contaminated commuters reported that they had washed their hands that morning. They may have been embarrassed to admit they hadn't washed, or they may have picked up the bacteria on their hands during their commute.

For all those reasons, the Centers for Disease Control and Prevention, with other health organizations around the world, urge frequent hand washing with soap and water or alcohol-based hand sanitizers. (They also repeat some advice you may not have heard from your mother: cough or sneeze into the crook of your elbow, not your bare hands.) And as hospitals put stricter hand hygiene programs in place, absentee rates during cold and flu season also drop.

"Statistically, you can't determine a causal relationship, but it's very suggestive," said Dr. Neil O. Fishman, infectious disease specialist at the University of Pennsylvania. "Our vaccination rates remained relatively stable, so what else changed? The only thing different was that hand hygiene rates increased."

Belatedly, Egypt Spots Flaws in Wiping Out Pigs

By Michael Slackman

CAIRO - It is unlikely anyone has ever come to this city and commented on how clean the streets are. But this litter-strewn metropolis is now wrestling with a garbage problem so severe it has managed to incite its weary residents and command the attention of the president. "The problem is clear in the streets," said Haitham Kamal, a spokesman for the Ministry of State for Environmental Affairs. "There is a strict and intensive effort now from the state to address this issue." But the crisis should not have come as a surprise.

When the government killed all the pigs in Egypt this spring - in what public health experts said was a misguided attempt to combat swine flu - it was warned the city would be overwhelmed with trash.

The pigs used to eat tons of organic waste. Now the pigs are gone and the rotting food piles up on the streets of middle-class neighborhoods like Heliopolis and in the poor streets of communities like Imbaba.

Ramadan Hediya, 35, who makes deliveries for a supermarket, lives in Madinat el Salam, a low-income community on the outskirts of Cairo. "The whole area is trash," Mr. Hediya said. "All the pathways are full of trash. When you open up your window to breathe, you find garbage heaps on the ground."

What started out as an impulsive response to the swine flu threat has turned into a social, environmental and political problem for the Arab world's most populous nation.

It has exposed the failings of a government where the power is concentrated at the top, where decisions are often carried out with little consideration for their consequences and where follow-up is often nonexistent, according to social commentators and government officials.

“The main problem in Egypt is follow-up,” said Sabir Abdel Aziz Galal, chief of the infectious disease department at the Ministry of Agriculture. “A decision is taken, there is follow-up for a period of time, but after that, they get busy with something else and forget about it. This is the case with everything.” Speaking broadly, there are two systems for receiving services in Egypt: The government system and the do-it-yourself system. Instead of following the channels of bureaucracy, most people rely on an informal system of personal contacts and bribes to get a building permit, pass an inspection, get a driver’s license - or make a living.

“The straight and narrow path is just too bureaucratic and burdensome for the rich person, and for the poor, the formal system does not provide him with survival, it does not give him safety, security or meet his needs,” said Laila Iskandar Kamel, chairwoman of a community development organization in Cairo.

Cairo’s garbage collection belonged to the informal sector. The government hired multinational companies to collect the trash, and the companies decided to place bins around the city.

But they failed to understand the ethos of the community. People do not take their garbage out. They are accustomed to seeing someone collecting it from the door.

For more than half a century, those collectors were the zabaleen, a community of Egyptian Christians who live on the cliffs on the eastern edge of the city. They collected the trash, sold the recyclables and fed the organic waste to their pigs - which they then slaughtered and ate.

Killing all the pigs, all at once, “was the stupidest thing they ever did,” Ms. Kamel said, adding, “This is just one more example of poorly informed decision makers.”

When the swine flu fear first emerged, long before even one case was reported in Egypt, President Hosni Mubarak ordered that all the pigs be killed in order to prevent the spread of the disease.

When health officials worldwide said that the virus was not being passed by pigs, the Egyptian government said that the cull was no longer about the flu, but was about cleaning up the zabaleen’s crowded, filthy, neighborhood. That was in May.

Today the streets of the zabaleen community are as packed with stinking trash and as clouded with flies as ever before. But the zabaleen have done exactly what they said they would do: they stopped taking care of most of the organic waste. Instead they dump it wherever they can or, at best, pile it beside trash bins scattered around the city by the international companies that have struggled in vain to keep up with the trash.

“They killed the pigs, let them clean the city,” said Moussa Rateb, a former garbage collector and pig owner who lives in the community of the zabaleen. “Everything used to go to the pigs, now there are no pigs, so it goes to the administration.”

The recent trash problem was compounded when employees of one of the multinational companies - men and women in green uniforms with crude brooms dispatched around the city - stopped working in a dispute with the city. The government says that the dispute has been resolved, but nothing has been done to repair the damage to the informal system that once had the zabaleen take Cairo’s trash home.

The garbage is only the latest example of the state’s struggling to meet the needs of its citizens, needs as basic as providing water, housing, health care and education.

The government announced last week that schools would not be opened until the first week of October to give the government time to prepare for a potential swine flu outbreak, a decision that could have been made anytime over the past three months, while schools were closed for summer break, critics said.

Officials in the Ministry of Health and other government ministries said they had not made this decision - and that they had counseled against pre-emptive school closings.

It appears to have been ordered by the presidency and carried out by the governors, who also ordered that all private schools, already in class, be shut down as well.

“We did not propose or call for postponing schools, so the reason is not with us,” said an official in the Ministry of Health who spoke on the condition of anonymity because the person was not authorized to speak to the news media.

The heads of three large governorates, or states, in Egypt announced Wednesday that their strategy for keeping schoolchildren safe was to take classes, which on average are crowded with more than 60 students, and split them in half and have children attend school only three days a week, another decision that was criticized. There have been more than 800 confirmed cases of H1N1 in Egypt, and two flu-related deaths.

“The state is troubled; as a result the system of decision making is disintegrating,” said Galal Amin, an economist, writer and social critic. “They are ill-considered decisions taken in a bit of a hurry, either because you’re trying to please the president or because you are a weak government that is anxious to please somebody.” Cairo’s streets have always been busy with children and littered with trash.

Now, with the pigs gone, and the schools closed, they are even more so.

“The Egyptians are really in a mess,” Mr. Amin said. *Mona el-Naggar contributed reporting.*

F.D.A. to Require Strict Warning on Anti-Nausea Drug

By Gardiner Harris

In a clear break with the Bush administration, the Food and Drug Administration has decided to require makers of an intravenous anti-nausea drug that had been the subject of a Supreme Court case to put a strict warning on its label. The drug, Phenergan, which is also known as promethazine, can cause gangrene and serious tissue damage when unintentionally injected into an artery.

In 2000, Diana Levine, a Vermont musician, had her hand and forearm amputated after such a mistaken injection. She sued Wyeth, the drug's maker, claiming the company should have put a more forceful warning on the drug's label. She won a \$6.8 million judgment.

Wyeth appealed to the Supreme Court, arguing that the F.D.A. had decided a less severe warning was adequate. Conservative legal scholars hoped the case would lead the Supreme Court to throw out thousands of similar lawsuits filed against drug makers claiming inadequate warnings.

While the case was pending, Bush administration appointees at the F.D.A. said that lawsuits often undermined their efforts to give consumers a balanced view of the risks and benefits of drugs since the threat of litigation sometimes led companies to warn about too many potential risks. Officials wrote rules that had the effect of strengthening Wyeth's claims.

The fundamental issue was whether Wyeth or the F.D.A. was most responsible for warning consumers about the potential risks of Wyeth's drugs. The Bush administration argued that the F.D.A. was the only agency with enough expertise to regulate drug makers and that its decisions should not be second-guessed by courts.

Had the administration strengthened the warning on Phenergan while Ms. Levine's case was being considered, the action might have undermined Wyeth's case by confirming Ms. Levine's argument that the previous warning was inadequate.

The F.D.A.'s new ruling, made Wednesday, resulted from a review of reports of "severe tissue injury, including gangrene, requiring amputation."

The change suggests that the Obama administration may view lawsuits as helpful to its work, a position that had been the policy of the drug agency before the Bush administration.