## More kidney stone disease projected due to global warming, researchers predict

DALLAS — July 14, 2008 — Global warming is likely to increase the proportion of the population affected by kidney stones by expanding the higher-risk region known as the "kidney-stone belt" into neighboring states, researchers at UT Southwestern Medical Center and UT Dallas have found.

Dehydration is one of the risk factors linked to kidney-stone disease, and the paper suggests global warming will exacerbate this effect. The researchers predict that by 2050, higher temperatures will cause an additional 1.6 million to 2.2 million kidney-stone cases, representing up to a 30 percent growth in some areas.

"This study is one of the first examples of global warming causing a direct medical consequence for humans," said Dr. Margaret Pearle, professor of urology at UT Southwestern and senior author of the paper, which appears in today's issue of Proceedings of the National Academy of Sciences.

"There is a known geographic variation in stone disease that has been attributed to regional differences in temperature," said Dr. Pearle. "When people relocate from areas of moderate temperature to areas with warmer climates, a rapid increase in stone risk has been observed. This has been shown in military deployments to the Middle East for instance."

Kidney-stone disease, or nephrolithiasis, is a common ailment. Kidney stones, which are solid crystals that form from dissolved minerals in urine, can be caused by both environmental and metabolic problems. Low volume of urine directly increases stone risk by increasing the concentration of stone-forming salts. They can arise from either taking in too little fluid or losing too much through dehydration.

Kidney-stones are more common in the warmer parts of the U.S. The Southeast is known as the "kidney-stone belt" because of the high incidence of kidney stones in the population living in Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, North Carolina, South Carolina and Tennessee.

To forecast climate change, Dr. Tom Brikowski, lead author of the study and associate professor of geosciences at UT Dallas, used models of global warming obtained from the Intergovernmental Panel on Climate Change's 2007 Fourth Assessment Report, in which predicted temperature increases are based on expectations of future greenhouse gases.

Using two studies that reported kidney-stone rates in various geographic regions and correlating regional stone rates with local mean annual temperatures, the investigators were able to derive two mathematical models relating temperature to kidney-stone risk. Both models of kidney-stone risk predicted that the current kidney-stone belt will expand with global warming, although the exact extent and location of the change was different. One model predicted that the increase will be concentrated in the southern half of the country, while the other model pointed to an increase in the upper Midwest. Taking into account the estimated future populations in those areas, increased temperatures are predicted to cause 1 million to 2 million more cases of kidney-stone disease.

"Obviously, this escalation is a problem when considering the costs associated with treating kidney-stone disease," said co-author Dr. Yair Lotan, assistant professor of urology at UT Southwestern. "Nationwide, the cost of treating these new kidney-stone cases could rise as high as $1 billion."

Similar climate-related changes in the prevalence of kidney-stone disease can be expected in other stone belts worldwide. Dr. Pearle and her colleagues plan to conduct future studies to understand the exact correlation of urine volume with environmental temperature.

*Visit http://www.utsouthwestern.org/urology for additional information about UT Southwestern's clinical services in urology.*

## 'Snapshots' of eyes could serve as early warning of diabetes

### *FA imaging, invented at U-M, measures metabolic stress in retina*

ANN ARBOR, Mich. — A new vision screening device, already shown to give an early warning of eye disease, could give doctors and patients a head start on treating diabetes and its vision complications, a new study shows.

The instrument, invented by two scientists at the University of Michigan Kellogg Eye Center, captures images of the eye to detect metabolic stress and tissue damage that occur before the first symptoms of disease are evident.

For people with diabetes — diagnosed or not — the new device could offer potentially significant advantages over blood glucose testing, the "gold standard" for diabetes detection.

The device takes a specialized photograph of the eye and is non-invasive, taking about five minutes to test both eyes.

In the July issue of Archives of Ophthalmology, Victor M. Elner, M.D., Ph.D., and Howard R. Petty, Ph.D., report on the potential of the new instrument to screen for diabetes and determine its severity. If further testing confirms the results to date, the new instrument may be useful for screening people who are at risk of diabetes but haven't been diagnosed.

"Our objective in performing this study was to determine whether we could detect abnormal metabolism in the retina of patients who might otherwise remain undiagnosed based on clinical examination alone," says Elner, professor, Department of Ophthalmology and Visual Sciences at U-M Medical School.

Metabolic stress, and therefore disease, can be detected by measuring the intensity of cellular fluorescence in retinal tissue. In a previous study, Petty and Elner reported that high levels of flavoprotein autofluorescence (FA) act as a reliable indicator of eye disease.

In their new study, Elner and Petty measured the FA levels of 21 individuals who had diabetes and compared the results to age-matched healthy controls. The Kellogg scientists found that FA activity was significantly higher for those with diabetes, regardless of severity, compared to those who did not have the disease. The results were not affected by disease severity or duration and were elevated for diabetics in each age group: 30 to 39 years, 40 to 49 years, and 50 to 59 years.

Given the increasing prevalence of diabetes, the FA device holds the potential to help address a leading and growing public health concern.

Some 24 million Americans have diabetes and an additional 57 million individuals have abnormal blood sugar levels that qualify as pre-diabetes, according to the latest report from the Centers for Disease Control and Prevention. In addition, 4.1 million people over the age of 40 suffer from diabetic retinopathy, an eye-related complication of diabetes that is the leading cause of blindness among working-age adults.

Twelve individuals in the study were known to have diabetic retinopathy, a disease in which blood vessels in the eye are damaged. The individuals with diabetic retinopathy in at least one eye had significantly greater FA activity than people with diabetes who do not have any visible eye disease.

"The abnormal readings indicated that it may be possible to use this method to monitor the severity of the disease," says Elner.

Petty, a biophysicist and imaging expert, explains that hyperglycemia — or high blood sugar — is known to induce cell death in diabetic tissue soon after the onset of disease but before symptoms can be detected clinically.

"Increased FA activity is the earliest indicator that cell death has occurred and tissue is beginning to break down," says Petty, professor of Ophthalmology and Visual Sciences, and professor of Microbiology and Immunology at the U-M Medical School. "FA serves as a 'spectral-biomarker' for metabolism gone awry, and we can use the results to detect and monitor disease."

Petty also observes that unlike glucose monitoring, elevation of FA levels reflects ongoing tissue damage. That knowledge, he says, could motivate patients to intensify their efforts to manage the disease.

The Michigan researchers also note that elevated FA does not always mean that an individual has diabetes. "Because of the prevalence of diabetes in our population, individuals with abnormally high FA would be prompted to undergo glucose tolerance testing," says Elner. "If the findings were negative for diabetes, we would look for other causes of ocular tissue dysfunction."

Both Elner and Petty agree that the device has great potential as a tool for diabetes screening and management. "So much damage occurs before the disease can be detected by a doctor," says Elner. "Early diagnosis will allow us to reduce organ damage and prevent many complications that accompany this disease."

*Elner and Petty have filed for patents and have formed a company, OcuSciences, Inc., to commercialize the metabolic imaging instrument.*

*Reference: "Rapid, Non-invasive Detection of Diabetes-induced Retinal Metabolic Stress," Archives of Ophthalmology, July 2008, Vol. 126, No. 7, pp. 934-938.*

## The 700-year-old Mexican mummy with a tummy ache

Remnants of the bacterium that causes stomach ulcers, Helicobacter pylori, (H. pylori) have been discovered in gastric tissue from North American mummies. A study of human remains believed to predate Columbus' discovery of the New World has shown for the first time that H. pylori infection occurred in native populations, according to research published in BioMed Central's open access journal, BMC Microbiology.

Yolanda Lòpez-Vidal and colleagues from the National Autonomous University of Mexico studied the stomach, tongue-soft palate and brains of two naturally mummified corpses - one young boy and one adult male. The researchers looked for the presence of telltale fragments of H. pylori DNA in the remains after amplification by polymerase chain reaction (PCR). According to Lòpez-Vidal, "Our results show that H. pylori infections occurred around 1350AD in the area we now know as Mexico".

Although previous research has suggested that H. pylori was present in these communities, this is the first evidence that it caused gastric infections. Lòpez-Vidal explains, "It is only through the use of the stomach tissue of these incredible mummies that we were able to make this discovery. Infection is established when the micro-

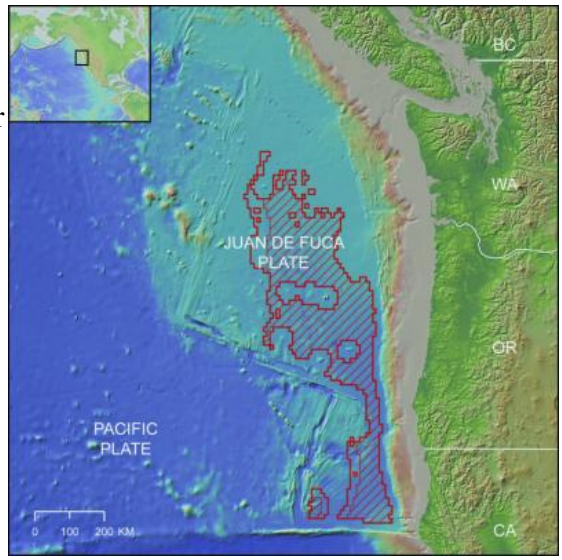
organism infiltrates the stomach lining and induces a local inflammatory response. This is unlike colonisation, which does not cause such a response and does not occur in the stomach".

As well as stomach ulcers, H. pylori causes gastritis, duodenitis, and cancer. It is a helix-shaped bacteria that is believed to be transmitted by the ingestion of food or water contaminated with faecal matter.

## Undersea volcanic rocks offer vast repository for greenhouse gas, says study

### *Drilling, experiments, target huge formations off West Coast*

Palisades, N.Y., July 14, 2008—A group of scientists has used deep ocean-floor drilling and experiments to show that volcanic rocks off the West Coast and elsewhere might be used to securely imprison huge amounts of globe-warming carbon dioxide captured from power plants or other sources. In particular, they say that natural chemical reactions under 78,000 square kilometers (30,000 square miles) of ocean floor off California, Oregon, Washington and British Columbia could lock in as much as 150 years of U.S. CO2 production. The findings are published today in the Proceedings of the National Academy of Sciences.




***Deep-sea basalt region for CO2 burial. Red outline shows where water depth exceeds 2,700 meters and sediment thickness exceeds 200 meters; hatched areas show where sediment thickness exceeds 300 meters. Seamounts and areas near plate boundaries or continental shelf are excluded.***

Interest in so-called carbon sequestration is growing worldwide. However, no large-scale projects are yet off the ground, and other geological settings could be problematic. For instance, the petroleum industry has been pumping CO2 into voids left by old oil wells on a small scale, but some fear that these might eventually leak, putting gas back into the air and possibly endangering people nearby.

Lead author David Goldberg, a geophysicist at Columbia University's Lamont-Doherty Earth Observatory, called the study "the first good evidence that this kind of carbon burial is feasible."

"We are convinced that the sub-ocean floor is a significant part of the solution to the global climate problem," said Goldberg. "Basalt reservoirs are understudied. They are immense, accessible and well sealed--a huge prize in the search for viable options." One of the main advantages, he said, is a chemical process between basalt and pumped-in CO2 that would convert the carbon into a solid mineral.

In their paper, Goldberg and his colleagues Taro Takahashi and Angela Slagle used previous deep-ocean drilling studies of the Juan de Fuca plate, some 100 miles off the Pacific coast, to chart a vast basalt formation that they say could be suitable for such pumping. Basalt, the basic stuff of the ocean floors, is hardened lava erupted from undersea fissures and volcanoes. In this region, much of it lies under some 2,700 meters (8,850 feet) of water, and 200 meters (650 feet) or more of overlying fine-grained sediment. Drilling by the Integrated Ocean Drilling Program has shown the rock is honeycombed with watery channels and pores that would provide room for pressurized CO2. The scientists have mapped out specific areas that they say are isolated from earthquakes, hydrothermal vents or other factors that might upset the system.

Ongoing experiments by Lamont scientists on land have shown that when CO2 is combined with basalt, the gas and components of the rock naturally react to create a solid carbonate—basically, chalk. Later this year, a separate team headed by Lamont geochemist Juerg Matter will begin pumping CO2 into a landbound basalt formation at a power plant near Reykjavik, Iceland—the first such large-scale demonstration. Basalts lie at or near the surfaces of other land areas including the northeast United States; the Caribbean; north and south Africa; and southeast Asia.

Goldberg says that undersea basalts, which are widespread, may be bigger, and better, than ones on land. At the depths studied, any CO2 that does not react with the rock will be heavier than seawater, and thus unable to rise. And in places like the Juan de Fuca, even if some did escape the rock, it would hit the overlying impermeable cap of clayey sediment.

Skeptics point out that getting the CO2 to such sites could be expensive and tricky. But Goldberg says the West Coast formations should be close enough to the land for delivery by pipelines or tankers. He called on government to study the details of how the idea might work, and whether it would be economically feasible. The United States currently spends about $40 million a year studying carbon sequestration, but nearly all of that goes to land-based research. "Forty million is about the opening-day box office for Finding Nemo," said Goldberg. We need policy change now, to energize research beyond our coastlines."

*Art or advance copies of the paper, "Carbon dioxide sequestration in deep-sea basalt," are available from the authors, PNAS, or The Earth Institute. Public release is EMBARGOED until 5pm EST, MONDAY, JULY 14, 2008*
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## Weeding out the highs of medical marijuana

Research exploring new ways of exploiting the full medicinal uses of cannabis while avoiding unwanted side-effects will be presented to pharmacologists today (Tuesday, 15 July) by leading scientists attending the Federation of European Pharmacological Societies Congress, EPHAR 2008.

Cannabis is a source of compounds known as cannabinoids, one of which, THC – the main chemical responsible for the 'high' – has long been licensed as a medicine for suppressing nausea produced by chemotherapy and for stimulating appetite, for instance, in AIDS patients.

More recently, the cannabis-based medicine Sativex was licensed both for the symptomatic relief of neuropathic pain in adults with multiple sclerosis and as an adjunctive analgesic treatment for adult patients with advanced cancer. Sativex contains approximately equal amounts of THC and the non-psychoactive plant cannabinoid, cannabidiol.

"THC works by targeting molecules in our bodies called cannabinoid receptors" said Roger Pertwee, Professor of Neuropharmacology at the University of Aberdeen, who is co-chairing the cannabis symposium.

"So some current research is focused on designing drugs that only target cannabinoid receptors in the part of the body relevant to the disease in question and not the receptors in the central nervous system involved in the unwanted effects of cannabis."

A further approach to avoiding the psychoactivity caused by THC involves harnessing the body's own cannabis, called 'endocannabinoids'.

"We don't have cannabinoid receptors just in case we come into contact with plant-derived chemicals that activate them but rather because we have our own molecules that do this," said Christopher Fowler, Professor of Pharmacology at Umea University, in Sweden, and co-chair of the meeting.

"The neat thing about endocannabinoids is that they are often produced only when we need them, such as when our bodies are damaged in some way; pain, for example, leads to a release of endocannabinoids in a region of the brain that is involved with pain control.

"The problem with this natural protective 'endocannabinoid system' is that it is too short-lived to be of great benefit – enzymes in our bodies quickly breakdown or metabolise the endocannabinoids negating their effect. It's a bit like a bathtub without a plug – the water is turned on but rapidly disappears down the plughole. This suggests an immediate target: block the plughole and the water will stay longer.

"Since the release of endocannabinoids is local, levels in other parts of the brain, stay low. This approach is under intense investigation and programmes for the development of new drugs targeting pain and possibly other disorders such as anxiety and depression are currently underway."

Speakers will report on promising studies that show improved strategies for targeting the endocannabinoid system, not only for pain relief, but also for treating other conditions, including stroke, liver diseases and, ironically, nicotine addiction and obesity.

Thus, as the conference will hear, there are some disorders in which endocannabinoid release appears to be detrimental to our health, one example being obesity, which can be treated with Acomplia*, a licensed synthetic medicine that acts by blocking cannabinoid receptors.

Professor Pertwee added: "THC in cannabis is of course well known for its ability to induce 'the munchies' and, as mentioned, is used in clinics to boost appetite. But my research group has discovered that another constituent of cannabis, THCV, acts in a similar way to Acomplia, blocking one of the cannabinoid receptors, so providing an alternative – and potentially better – treatment route in the fight against obesity.

"The conference will hear about some of the possible advantages THVC has over current obesity treatments, as well as data on the potential of cannabinoids to treat other conditions, including neurodegenerative disorders like Alzheimer's, Parkinson's and Huntington's disease."

***Notes for editors**:*
**Acomplia has been a licensed medicine for obesity in the UK and Europe for about two years and was accepted by the National Institute for Clinical Excellence (NICE) on June 28, 2008.*
*The 5th Congress of the Federation of European Pharmacological Societies, EPHAR 2008, is being held in Manchester, England, from Monday, 14 July, to Thursday, 17 July, inclusive.*
*For further information about EPHAR visit: http://www.ephar.org/index_fr.htm*
*For further information about the EPHAR 2008 Congress visit: http://www.ephar2008.org/*

## Was it a bird or was it a plane?

### *A new study of extinct flying reptiles*

Archaeopteryx is famous as the world's oldest bird, but reptiles were flying about some 50 million years earlier than that (225 million years ago), even before large dinosaurs roamed the Earth.

A new study of extinct reptiles called kuehneosaurs, by scientists from the University of Bristol, England, shows that these early flyers used extraordinary extensions of their ribs to form large gliding surfaces on the side of the body. The results are published today (15 July) in Palaeontology.

Kuehneosaurs, up to 70 centimetres (two feet) long, were first found in the 1950s in an ancient cave system near Bristol. Their lateral 'wings' were always assumed to be some form of flying adaptation, but their aerodynamic capability had never been studied before.

***Kuehneosauridae in the flesh: What Kuehneosaurus might have looked like, flying over a Triassic landscape*. Credit Simon Powell, University of Bristol**

Koen Stein, who did the work while a student studying for an MSc in palaeobiology at Bristol University, has shown that of the of the two genera found in Britain, Kuehneosuchus was a glider (it has elongate 'wings'), while Kuehneosaurus, with much shorter 'wings', was a parachutist. As the two forms are so alike in other respects, it is possible that they are males and females of the same animal.

Stein said: "We didn't think kuehneosaurs would have been very efficient in the air, but all the work up to now had been speculation, so we decided to build models and test them in the wind tunnel in the Department of Aerospace Engineering at Bristol.

"Surprisingly, we found that Kuehneosuchus was aerodynamically very stable. Jumping from a five-metre tree, it could easily have crossed nine metres distance before landing on the ground. The other form, Kuehneosaurus, was more of a parachutist than a glider."

So that Stein and his colleagues could work out how these creatures controlled their flight they had to model different skin flaps over the wing area." We also built webbed hands and feet and had an extra skin membrane between the legs on the models, but these made the flight of the animals unstable, suggesting that they probably did not have such features."

"This is a fantastic example of interdisciplinary research," said Professor Michael Benton, a member of the research team and Head of Department in Bristol. "Palaeontologists are keen to understand how all the amazing animals of the past operated and by collaborating with aerospace engineers we can be sure that model-making and calculations are more realistic."

*The paper: "The aerodynamics of the British Late Triassic Kuehneosauridae" by Koen Stein, Colin Palmer, Pamela G. Gill and Michael J. Benton is published in the July 15th issue of Palaeontology. Copies of the paper can be downloaded from here: https://www.bris.ac.uk/fluff/u/inclel/3MYOx9iGCQEJU_sYCOvaiwwy/*

*Koen Stein is now at the Institut für Paläontologie, Bonn, Germany. Colin Palmer, Pamela Gill and Michael Benton are based in Department of Earth Sciences, University of Bristol.*

## Positive thinking is prescription for the heart

Optimism is good for heart health, at least among men, a new study shows.

University of Rochester Medical Center researcher Robert Gramling, M.D., D.Sc., found that men who believed they were at lower-than-average risk for cardiovascular disease actually experienced a three times lower incidence of death from heart attacks and strokes.

The data did not support the same conclusion among women. One possible explanation for the gender difference, researchers said, is that the study began in 1990, a time when heart disease was believed to be primarily a threat to men. Therefore, women's judgments about how often heart attacks occur among average women might have been disproportionately low.

The study is published in the July-August issue of Annals of Family Medicine.

The 15-year surveillance study involved 2,816 adults in New England between the ages of 35 and 75 who had no history of heart disease. Researchers collected baseline data from 1990-1992; outcomes were obtained from the National Death Index records through December 2005.

Researchers were interested in measuring whether optimistic perceptions of risk might protect people from the fear-related coping behaviors (overeating comfort foods, too much alcohol, or avoiding the doctor) or the stress that can be associated with heart disease.

They asked people at the outset, "Compared with persons of your own age and sex, how would you rate your risk of having a heart attack or stroke in the next 5 years?"

Men's views were more discordant. Almost half of the men who self-rated their risk to be "low" would have been classified by objective medical tests as having "high" or "very high" risk. Most women who rated their risk to be "low" were far more accurate than the men.

"Clearly, holding optimistic perceptions of risk has its advantages for men," said Gramling, an assistant professor of Family Medicine and Community and Preventive Medicine.

If doctors are to accurately explain risks to patients, it's important for them to first understand how people perceive health risks. The study also pointed out that as genetic testing and advanced imaging continues to offer individuals more information about their future health, good communication is essential.

"It is not clear whether we should seek to disabuse people of optimistic 'misperceptions' in pursuit of changing behavior." Gramling said. "Perhaps we should work on changing behaviors by instilling more confidence in the capacity to prevent having a heart attack, rather than raising fears about having one."

*The National Human Genome Research Institute (ELSI branch) of the National Institutes of Health funded the study, which was conducted when Gramling was a faculty member at Brown University's Center for Primary Care and Prevention, Memorial Hospital in Rhode Island. He recently joined the Rochester Center to Improve Communication in Health Care, at the University of Rochester Medical Center. He is working on similar research funded by the National Institute of Nursing Research of the NIH.*

## Rx for time-crunched physicians

### *Communication skills increase efficiency of office visits without sacrificing patient satisfaction*

With their waiting rooms crowded and exam rooms full, many physicians say they are too busy to be good communicators. Those who study physician time-management think otherwise. Certain communication skills can foster efficiency and effectiveness during an office visit without sacrificing rapport with patients, according to researchers at the University of Washington (UW) and the University of Rochester.

Their guide to a smoother flow of communication between doctors and patients appears in the July 14 issue of the Archives of Internal Medicine. Their model is based on the authors' observation: "Effective communication in primary care must include skills that enhance the quality of care while helping patients and physicians use time wisely… Making the best use of available time is important for visits of any duration."

The researchers are Larry Mauksch, a UW behavioral scientist in family medicine who studies and teaches doctor/patient communications; David C. Dugdale, an internal medicine physician and director of the UW Hall Health Primary Care Center; Sherry Dodson, UW clinical medical librarian; and Ronald Epstein, professor of family medicine, psychiatry, and oncology at the University of Rochester School of Medicine and Dentistry and its Center to Improve Communication and Health Care.

A few of the lessons the researchers presented in the resulting article, "Relationship, Communication, and Efficiency in the Medical Encounter: Creating a Clinical Model from a Literature Review" are:

First, focus the purpose of the visit with the patient: Instead of addressing each issue as it surfaces, creating a list at the start enables the doctor to confirm which problem is most medically urgent or most important to the patient. This approach also reduces the "Oh, by the way" issues brought up at the end of the visit.

Then, understand the patient's perspective: Exploring the patient's viewpoint is useful for promoting self-management, suggesting healthy changes, assessing motivation, learning the patient's family and cultural beliefs, understanding the social and psychological problems that are diminishing the patient's ability to function, or getting to the root of medically unexplained symptoms.

Near the end, reach a mutual agreement on a plan: The physician and patient decide on approaches the patient is willing to follow to manage or prevent the health concerns explored during the visit.

**Throughout the office visit, it's helpful for physicians to:**

* Establish rapport and maintain the relationship: Some ways doctors do this are by eye contact, recognizing others in the room, or a brief warm greeting, such as, "Nice to see you." On the other hand, too much small talk steals away time from considering the patient's problems.

* Practice mindfully: This occurs when physicians pay close attention to their own beliefs and reduce distractions in order to observe their patients' response to what is being said and done, and adjust accordingly. For example, a doctor lecturing on excess weight might notice the patient withdrawing. The doctor stops and asks about the patient's views. A physician who doesn't continuously monitor the interaction or doesn't check in with the patient may cover areas of little interest to the patient, and miss significant issues.

* Track topics: Sometimes an interview veers off course, particularly when there are multiple topics and no clear agenda. Unless the conversation is redirected, it's likely that no clear decisions will be made on some problems before the end of the visit. Sharing an impression of what has and hasn't been covered and realigning by agreeing on what to talk about next can keep the discussion organized.

* Acknowledge cues: When a physician responds with empathy to a patient's cues, a patient may reveal beliefs and preferences that can shape a successful treatment plan. Also, once their concerns are taken into account, most patients don't keep restating them. This saves time.

"Visits with the doctor that contain these fundamental elements," Mauksch said, "lead to greater patient satisfaction, better adherence to medical regimes, increased self-management, better health outcomes, lower costs, and fewer malpractice claims. These skills enable physicians to do it right the first time, so they don't have to do it over."

"We've tried to propose a model of doctor/patient communications," Dugdale added, "that is at the intersection between what patients need and the reality of a doctor's world. These are skills that make a difference and that doctors can use throughout their entire careers."

**Some Facts on Doctors' Office Visits**

* During their careers, physicians conduct upwards of 100,000 patient interviews, making it the most common "medical procedure" in an office setting.
* The mean length of time spent with a doctor during an office visit: 18 minutes.
* Primary-care patients bring up 3 to 6 concerns per visit.
* A physician's communication style tends to remain the same regardless of the length of the visit.

**Teaching Doctors-in-Training How to Do Office Interviews**

Patient communications are addressed in medical schools and residency training programs, but after starting practice, many new doctors abandon what they learned.

Larry Mauksch, who is on the faculty of the UW Department of Family Medicine, said it's difficult for medical students to learn doctor/patient communications only through classroom lectures or reading. Medical student training at the University of Washington (UW) includes observations of actual, enacted and Web-taped doctor visits.

Trainees use checklists to monitor specific parts of a medical encounter and they learn to put a name to specific skills. Students rate video demonstrations that are missing core communication elements and identify strategies for improvement. They also observe one another to help each other learn. Communication skill building is a key component of the UW medical school's introduction to clinical medicine course for second-year medical students and the family medicine clerkship for third-year medical students.

Some senior medical students take a clinical clerkship that concentrates on patient-centered communication. Mauksch likens the method he uses to the training of an athlete or a musician, where students have many opportunities to try out their skills, get comments, and try again, with refinements.

"Students experience for themselves how specific communications skills help them avoid pitfalls in patient interactions and make better use of time," Mauksch said. "They see themselves becoming more effective and enjoy their work more."

## Ebola-like virus returns to Europe after 40 years

* 21:10 14 July 2008
* NewScientist.com news service
*** Ewen Callaway**

Marburg, a deadly haemorrhagic fever closely related to Ebola, is back in Europe, after a four-decade absence.

On Friday, 11 July, a 40-year old Dutch woman died in a quarantined ward of a hospital in Leiden, the Netherlands, less than two weeks after she returned from Uganda.

She had visited caves where she may have contracted the virus on 16 and 19 June, but she developed a fever and chills – early symptoms of Marburg – only after her return, on 2 July. More severe symptoms – such as liver failure and bleeding from multiple sites – struck two days after she was admitted to the hospital on 5 July.

***New Scientist takes a closer look at this mysterious and deadly virus.***

**Where does Marburg come from?**

The first reported cases occurred in the German city of Marburg in 1967 and originated in living monkeys at a monkey research facility. In total, 31 people in Marburg and Frankfurt in Germany and in Belgrade, now the capital of Serbia, contracted the disease and seven died.

After that, Marburg disappeared from Europe but has since flared up in South Africa, the Democratic Republic of Congo and Angola, where a 2004-2005 outbreak killed 355 of 399 people who contracted Marburg.

The virus's reservoir remained a mystery for a long time, but new research has pointed the finger squarely on cave-dwelling fruit bats. In 2007, a team of virus hunters found fragments of the virus's genome in a species called Rousettus aegyptiacus. The species also showed signs of an immune response against Marburg, which is unlikely to cause symptoms in the bats.

But the virus may be spread via other bats that don't stick to caves, according to Peter Walsh of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. Genetic sequences show similarities between viruses from Gabon and Angola, suggesting that some cave-to-cave transmissions occur.

**How deadly is the virus?**

That depends, according to the World Health Organization (WHO), which tracks outbreaks of the virus. The first human cases in Germany felled just a quarter of those infected, while more recent outbreaks in the Democratic Republic of Congo and Angola have killed 80 to 90% of those infected. There is no cure, and patients often die of haemorrhaging and massive organ failure.

**Is there a vaccine for Marburg?**

Not yet, but several research teams have made significant progress. In 2005, a team at Canada's National Microbiology Laboratory in Winnipeg genetically engineered an unrelated virus to produce a key Marburg protein. Macaques that received a single shot of this virus were immune to Marburg virus administered a month later.

US researchers at the National Institute of Health and in the Army took a similar approach against Ebola, stitching one of its proteins into a weakened cold virus. They say the same could be done with Marburg. Alternatively, a virus-free vaccine – made up of the proteins that coat Marburg's shell – might work, and one such vaccine has protected guinea pigs from Marburg infection.

So far, however, no vaccines against Marburg virus have been proven effective in humans.

**What should people do to protect against Marburg?**

Stay out of bat caves in countries known to have Marburg, such as Uganda, says the WHO and the Dutch government.

Human-to-human spread requires close contact with an infected person while they are showing symptoms. Because the most recent victim didn't show any symptoms while in Africa or on her flight home, only the people she came into contact with after 2 July are at risk. No one else has yet come down with Marburg.

## Devils get pregnant early to avoid cancer

* 22:00 14 July 2008
* NewScientist.com news service
*** Rachel Nowak**

In what seems like a desperate bid to survive, Tasmanian devils are showing precocious sexual behaviour in populations that have been ravaged by a fatal devil facial tumour disease.

A team led by ecologist Menna Jones of the University of Tasmania in Hobart, monitored the age at which females produced their first litter in five populations of Tasmanian devils (Sarcophilus harrisii), before and after the disease had become established.

Female Tasmanian devils – the largest of the carnivorous marsupials – usually breed at two, three and four years old, with up to four pups per litter, and then die at five or six years old.

The Jones team found that in populations where the infectious face cancer is established, life-expectancy falls to two to three years. In four out of five of those populations, between 13 and 80% of females bred at one year old – compared to less than 10% before the populations were affected.

"We found a 16-fold increase in precocious breeding. They are fitting in an extra litter when they are teenagers," says Jones.

The immediate trigger for early breeding is not known, but it could be because more food is available, with fewer animals competing for it, says Jones.

Several factors suggest that Tasmanian devils could rapidly evolve so that early breeding becomes an inherited trait, rather than one dictated by environment.

Tasmanian devils are dasyurid mammals, a family that is famous for its live-fast-and-die-young breeding strategy, in which animals invest in intense early reproduction at the expense of longevity. One of the best known examples is a tiny shrew-like marsupial called an antechinus - the males grow for 10 months, and then have sex for one month, forgoing food, and starving to death. By the time the females give birth there are no males left.

Devils share some of those traits – they are short-lived, and the males lose a quarter of their body weight during the breeding season.

"Rapid evolution tends to occur when you have high mortality. These animals are already predisposed to breeding early, and the disease is taking out all the individuals over one year in some areas – it's a very strong selective pressure," says Mathew Crowther, a wildlife biologist at the University of Sydney.

Devil facial tumour disease was first reported in 1996. By last year it had spread to more than half the animal's range in Tasmania, leading some experts to predict that the disease could make the animal extinct in the wild within 25 years.

"There's a little bit of hope that precocious breeding can keep the devil population ticking over. But with such heavy mortality, and all reproduction [now] having to occur in one season, they are very vulnerable," says Crowther.

The devil facial tumour disease is believed to be only the second known example of a disease that is spread by the transfer of cancerous cells from one animal to another, in this case when the animals bite.

*Journal reference: Proceedings of the National Academy of Sciences (DOI: 10.1073/pnas.0711236105)*

## Breast self-exams do not appear to reduce breast cancer deaths

It is a staple of women's health advice and visits to the OB/GYN: the monthly breast self-exam to check for lumps or other changes that might signal breast cancer. However, a review of recent studies says there is no evidence that self-exams actually reduce breast cancer deaths.

Instead, the practice may be doing more harm than good, since it led to almost twice as many biopsies that turned up no cancer in women who performed the self-exams, compared to women who did not do the exams.

"At present, screening by breast self-examination or physical examination [by a trained health worker] cannot be recommended," Jan Peter Kosters, Ph.D., and Peter Gotzsche, Ph.D., of the Nordic Cochrane Centre, conclude in the review.

However, the authors recognize that some women will want to continue with breast self-exams and women should always "seek medical advice if they detect any change in their breasts that might be breast cancer," Kosters said.

"We suggest that the lack of supporting evidence…should be discussed with these women to enable them to make an informed decision," he said.

Carolyn Runowicz, director of The Carole and Ray Neag Comprehensive Cancer Center at the University of Connecticut Health Center, encourages women to do the self-exams if they are comfortable with them, noting that 50 percent to 60 percent of women detect their own breast masses.

"I think what we are seeing is that women are familiar with their breast through breast self-exam and when there is a lump, they notice the difference," she said.

The new review appears in the latest issue of The Cochrane Library, a publication of The Cochrane Collaboration, an international organization that evaluates medical research. Systematic reviews like this one draw evidence-based conclusions about medical practice after considering both the content and quality of existing medical trials on a topic.

In the two large studies of 388,535 women in Russia and China included in the review, women who used self-breast exams had 3,406 biopsies, compared with 1,856 biopsies in the group that did not do the exams. At the same time, there was no significant difference in breast cancer deaths between the two groups.

The China study published data on how breast cancers detected in the women were treated. Rates of both mastectomy and breast-conserving surgery such as lumpectomy were very similar between the exam and no-exam groups.

***FOR MORE INFORMATION*** *Health Behavior News Service: (202) 387-2829 or www.hbns.org.*

*Kosters JP, Gotzsche PC. Regular self-examination or clinical examination for early detection of breast cancer. The Cochrane Database of Systematic Reviews 2008, Issue 3.*

## Stomach bug appears to protect kids from asthma, says NYU study

### *H. pylori may strengthen the immune system*

NEW YORK, July 15, 2008 – A long-time microbial inhabitant of the human stomach may protect children from developing asthma, according to a new study among more than 7,000 subjects led by NYU Langone Medical Center researchers. Helicobacter pylori, a bacterium that has co-existed with humans for at least 50,000 years, may lead to peptic ulcers and stomach cancer. Yet, kids between the ages of 3 and 13 are nearly 59 percent less likely to have asthma if they carry the bug, the researchers report. The study appears in the July 15, 2008, online issue of The Journal of Infectious Diseases.

"Our findings suggest that absence of H. pylori may be one explanation for the increased risk of childhood asthma," says Yu Chen, Ph.D., assistant professor of epidemiology at New York University School of Medicine and a co-author of the study. "Among teens and children ages 3 to 19 years, carriers of H. pylori were 25 percent less likely to have asthma."

The impact was even more potent among children ages 3 to 13: they were 59 percent less likely to have asthma if they carried the bacterium, the researchers report. H. pylori carriers in teens and children were also 40 percent less likely to have hay fever and associated allergies such as eczema or rash.

These results, which follow on from similar findings in adults published by the same authors last year, are based on an analysis of data gathered from 7,412 participants in the fourth National Health and Nutrition Survey (NHANES IV) conducted from 1999 to 2000 by the National Center for Health Statistics.

Dr. Chen collaborated on the survey with Martin J. Blaser, M.D., the Frederick H. King Professor of Internal Medicine, chair of the department of medicine, and professor of microbiology at NYU Langone Medical Center. Dr. Blaser has studied H. pylori for more than two decades.

Asthma has been rising steadily for the past half-century. Meanwhile H. pylori, once nearly universal in humans, has been slowly disappearing from developed countries over the past century due to increased antibiotic use, which kills off the bacteria, and cleaner water and homes, explains Dr. Blaser. Data from NHANES IV showed that only 5.4 percent of children born in the 1990s were positive for H. pylori, and that 11.3 percent of the participants under 10 had received an antibiotic in the month prior to the survey.

The rise in asthma over the past decades, Dr. Blaser says, could stem from the fact that a stomach harboring H. pylori has a different immunological status from one lacking the bug. When H. pylori is present, the stomach is lined with immune cells called regulatory T cells that control the body's response to invaders. Without these cells, a child can be more sensitive to allergens.

"Our hypothesis is that if you have Helicobacter you have a greater population of regulatory T-cells that are setting a higher threshold for sensitization," Dr. Blaser explains. "For example, if a child doesn't have Helicobacter and has contact with two or three cockroaches, he may get sensitized to them. But if Helicobacter is directing the immune response, then even if a child comes into contact with many cockroaches he may not get sensitized because his immune system is more tolerant."

In other words, the presence of the bacteria in the stomach may influence how a child's immune system develops: if a child does not encounter Helicobacter early on, the immune system may not learn how to regulate a response to allergens. Therefore, the child may be more likely to mount the kinds of inflammatory responses that trigger asthma.

"There's a growing body of data that says that early life use of antibiotics increases risk of asthma, and parents and doctors are using antibiotics like water," Dr. Blaser says. "The reality is that Helicobacter is disappearing extremely rapidly. In the NHANES IV study, less than six percent of U.S. children had Helicobacter, and probably two generations ago it was 70 percent. So, this is a huge change in human micro-ecology. The disappearance of an organism that's been in the stomach forever and is dominant is likely to have consequences. The consequences may be both good—less likelihood of gastric cancer and ulcers later in life—and bad: more asthma early in life."

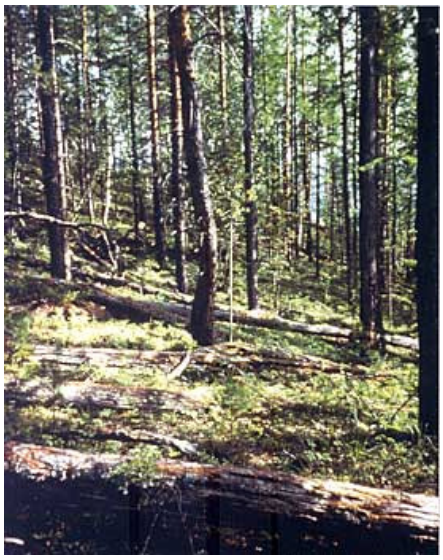
## Tunguska catastrophe: Evidence of acid rain supports meteorite theory

Moscow/Bologna/Halle. The Tunguska catastrophe in 1908 evidently led to high levels of acid rain. This is the conclusion reached by Russian, Italian and German researchers based on the results of analyses of peat profiles taken from the disaster region. In peat samples corresponded to 1908 permafrost boundary they found significantly higher levels of the heavy nitrogen and carbon isotopes 15N and 13C. The highest accumulation levels were measured in the areas at the epicentre of the explosion and along the trajectory of the cosmic body. Increased concentrations of iridium and nitrogen in the relevant peat layers support the theory that the isotope effects discovered are a consequence of the Tunguska catastrophe and are partly of cosmic origin. It is estimated that around 200,000 tons of nitrogen rained down on the Tunguska region in Siberia at that time. "Extremely high temperatures occurred as the meteorite entered the atmosphere, during which the oxygen in the atmosphere reacted with nitrogen causing a build up of nitrogen oxides," Natalia Kolesnikova told the Russian news agency RIA Novosti on last Monday. Mrs. Kolesnolova is one of the authors of a study by Lomonosov Moscow State University, the University of Bologna and the Helmholtz Centre for Environmental Research (UFZ), which was published in the journal Icarus in 2003.

***In 1927 Professor Leonid Kulik took the first photographs of the massive destruction of the taiga forest after the Tunguska catastrophe.*** **Photo: Professor Leonid Kulik**

The Tunguska event is regarded as one of the biggest natural disasters of modern times. On 30 June 1908 one or more explosions took place in the area close to the Tunguska River north of Lake Baikal. The explosion(s) flattened around 80 million trees over an area of more than 2000 square kilometres. The strength of the explosion is estimated to have been equivalent to between five and 30 megatons of TNT. That is more than a thousand times as powerful as the Hiroshima bomb. This almost unpopulated region of Siberia was first studied in 1927 by Professor Leonid A. Kulik. There are a number of different theories about what caused the catastrophe. However, the majority of scientists assume that it was caused by a cosmic event, such as the impact of a meteorite, asteroid or comet. If it had exploded in the atmosphere just under five hours later, St. Petersburg, which was the capital of Russia at that time, would have been completely destroyed because of the Earth's rotation.

***Evgeniy Kolesnikov photographed the same place 60 years later. The fallen trunks are still there, with the taiga growing in between them.*** **Photo: Evgeniy M. Kolesnikov/ Lomonosov-Universität Moskau**



In two expeditions in 1998 and 1999, Russian and Italian researchers took peat profiles from various locations within the Siberian disaster area. The type of moss studied, Sphagnum fuscum, is very common in the peat material and obtains its mineral nutrients exclusively from atmospheric aerosols, which means that it can store terrestrial and extraterrestrial dust. Afterwards, the samples were analysed in laboratories at the University of Bologna and the Helmholtz Centre for Environmental Research (UFZ) in Halle/Saale. Among other things, the UFZ specialises in isotope analyses of sediments, plants, soil and water and it was asked to help by the team of Moscow researchers led by Dr Evgeniy M. Kolesnikov. Kolesnikov, who has been investigating the Tunguska event for 20 years, has been to Leipzig University and UFZ twice as a guest researcher with the help of the German Research Foundation (DFG) to consult with the isotope experts. "The levels of accumulation of the heavy carbon isotope 13C measured right on the 1908 permafrost boundary in several peat profiles from the disaster area cannot be explained by any terrestrial process. This suggests that the Tunguska catastrophe had a cosmic explanation and that we have found evidence of this material," explains Dr Tatjana Böttger of the UFZ. Possible causes would be a C-type asteroid like 253 Mathilde, or a comet like Borelly. **Tilo Arnhold**

## Turning on hormone tap could aid osteoporosis fight

A potential new drug that 'opens the taps' for the release of useful hormones could stimulate new bone growth – and may eventually bring relief to osteoporosis sufferers.

The exciting potential of so-called negative allosteric modulators will be put under the microscope at a special symposium at The Federation of European Pharmacological Societies (EPHAR) 2008 Congress at The University of Manchester, UK, today (Wednesday, July 16).

European pharmacologists meeting in Manchester will present work that focuses on the stimulation of parathyroids – tiny glands located above the thyroids that control the release of the parathyroid (PTH) hormone into the bloodstream.

When the concentration of calcium is too low in the blood's plasma, PTH is released and acts on various tissues to increase the level of calcium in the blood. This calcium then activates the calcium sensing receptor on the parathyroid cell, which then reduces PTH release.

The first POSITIVE allosteric modulator was recently introduced into clinical practice for treating patients displaying high levels of PTH in the plasma – such as those with chronic kidney disease on dialysis and those displaying hypercalcaemia with parathyroid cancer. It mimics the effect of calcium on the receptor and so reduces PTH release.

But now attention is switching to NEGATIVE allosteric modulators, which have been shown in pre-clinical trials to block the effect of calcium on the parathyroid cell and thus increase the release of PTH in the serum.

"Daily administration of a negative allosteric modulator of the calcium sensing receptor should promote a sustained increase of PTH in such a way that it will stimulate new bone formation," said symposium organiser Martial Ruat, a neuropharmacologist at the government funded Centre National de la Recherche Scientifique in France.

"Now clinical trials will have to demonstrate the effectiveness and suitability of negative allosteric modulators for treating osteoporosis in humans."

While pharmacologists are excited and encouraged by results so far, Dr Ruat says it will be at least another eight to 10 years before negative allosteric modulators are passed for use in patients "Osteoporosis is a complex

disease and the timescale might be rather long," says Dr Ruat, who is himself carrying out research to learn more about the potential benefits of both negative and positive allosteric modulators.

He added: "The calcium sensing receptor is also found in the kidney, the intestine, in some vascular and bone cells and also in the brain. We still need to identify the roles of this receptor in these tissues before being able to specify novel applications of these drugs."

Negative and positive allosteric modulators are also being studied by European pharmacologists with a view to identifying the functions of calcium sensing receptors in the control of blood pressure.

## LSUHSC study finds high-dose HBO2 therapy extends survival window after cardiopulmonary arrest

New Orleans, LA – A ground-breaking study by researchers at the School of Medicine at LSU Health Sciences Center New Orleans published in the August 2008 issue of Resuscitation has major implications for the #1 cause of death of Americans -- sudden cardiac arrest. The researchers stopped the heart of laboratory swine kept at room temperature, declared them dead from cardiac arrest, waited 25 minutes, and then resuscitated them with high doses of oxygen using hyperbaric oxygen therapy. The American Heart Association statistics on sudden death have shown that if a patient's heart is not restarted within 16 minutes with CPR, medications, and electric shocks, 100% of patients die.

"To resuscitate any living organism after 25 minutes of heart stoppage at room temperature has never been reported and suggests that the time to successful resuscitation in humans may be extended beyond the stubborn figure of 16 minutes that has stood for 50 years," notes Dr. Keith Van Meter, Clinical Professor of Medicine and Chief of the Section of Emergency Medicine at LSU Health Sciences Center New Orleans, who led the study.

The study involved the use of three groups of laboratory swine. All swine underwent cardiac arrest for 25 minutes during which time they received no artificial breathing, CPR, medications, or electric shocks. After 25 minutes the swine were randomly divided into 3 groups. The first group remained at normal pressure. The second group was given standard-dose hyperbaric oxygen, and the third group was given high-dose hyperbaric oxygen, a dose that is nearly 1/3 more than the highest dose currently given to humans. Advanced cardiac life support (ACLS) was started on animals in all groups for a two-hour resuscitation period. After the two-hour resuscitation period, four of the six animals in the high-dose hyperbaric oxygen group could be resuscitated. None of the subjects in the other groups were able to be resuscitated.

"The present study shows that short-term high-dose hyperbaric oxygen is an effective resuscitation tool and is safe in a small multiplace hyperbaric chamber," concludes Dr. Van Meter. "A rehearsed team can easily load a patient in cardiopulmonary arrest into a small multiplace chamber in the pre-hospital or hospital setting without interrupting CPR or advanced cardiac life support. Successful resuscitation at 25 minutes suggests that if high dose hyperbaric oxygen is used at the current ACLS limit of 16 minutes, a greater survival may be achieved in humans and allow application of more definitive treatment such as clot dissolving drugs."

*The research team also included LSU Health Sciences Center New Orleans faculty Diana Barratt, MD, MPH, Heather Murphy-Lavoie, MD, Paul G. Harch, MD, James Moises, MD, and Nicolas Bazan, MD, PhD. and*

*Future studies are planned to further refine knowledge about this important addition to resuscitation and survival procedures.*

## Scientists demonstrate means of reducing Alzheimer's-like plaques in fly brain

### *But overexpression of Neprilysin causes other serious pathologies*

Neuroscientists at Cold Spring Harbor Laboratory (CSHL) are part of a collaboration that has succeeded in demonstrating that overexpression of an enzyme in the brain can reduce telltale deposits causally linked with Alzheimer's disease.

CSHL Professor Yi Zhong, Ph.D., whose lab studies genetic mechanisms involved in neurodegenerative illnesses, helped develop a line of transgenic fruit flies that was central in the experiments. Transgenic organisms express genes that occur naturally in other species. In this instance, the fruit flies were engineered to express a human gene that codes for the production of an enzyme called neprilysin, or NEP.

**Beta amyloid and the pathology of Alzheimer's**

NEP enzymes are known from prior experiments to degrade protein deposits in the brain that are characteristic of Alzheimer's . The protein clumps -- sheet-like plaques between brain cells called beta amyloid deposits -- have been found in the autopsied brains of human Alzheimer's patients.

Two types of beta amyloid sheets are associated with Alzheimer's plaques. Scientists have suspected that so-called Aβ42 plaques -- those structurally composed of 42-amino acid beta amyloid peptides -- are involved in the genesis of the illness. "But the mechanism by which Aβ42 reaches pathological levels in the brains of late-onset patients is not well understood," Dr. Zhong explained.

Past experiments in transgenic mice expressing human beta amyloid had shown that a deficiency of NEP caused a series of serious problems. The deficiency accelerated the formation of amyloid plaques, caused dysfunction in the synapses, or gaps, across which nerve cells in the brain communicate, and caused memory defects.

**Reversing the process: mixed results**

In new experiments, Dr. Zhong and other team members, who include Kanae Iijima-Ando, Ph.D., of the Farber Institute for Neurosciences and neuroscientists from Thomas Jefferson University in Philadelphia, sought to turn the tables. If NEP deficiency caused pathology, what would happen if NEP enzymes were expressed in above-normal amounts in brain cells affected by beta amyloid plaques?

Using transgenic fruit flies, the team found that by overexpressing human NEP in fly neurons, accumulation of Aβ42 inside the neurons was reduced. The scientists also observed that outright death of neurons due to Aβ42 plaques was suppressed.

At the same time, the experiment produced results that were not at all encouraging. Although NEP overexpression fought off plaques, chronic overexpression in the fly brain caused age-related degeneration of the axons that connect nerve cells, and also shortened the lifespan of the flies. The team believes that this effect was caused by the unintended impact of chronic NEP activity upon a critical gene-regulating protein, a transcription factor called CREB.

The team wants to test whether the life-shortening impact of NEP overexpression upon CREB occurs in transgenic mammals -- for instance, in mice, which are genetically closer to humans than flies.

"We have succeeded in demonstrating both protective and detrimental aspects of high NEP activity in the fly brain," Dr. Zhong said. "We also noted a reduction of NEP activity in fly brains that correlates with age. These are intriguing clues about mechanisms that contribute to the causation of Alzheimer's.

"We must now seek additional knowledge about the physiological mechanisms that underlie age-dependent downregulation of NEP in flies. This is a powerful genetic model system that we hope will lead us to discover novel therapeutics to combat Alzheimer's, a disease that devastates so many people every year."

*"Overexpression of Neprilysin Reduces Alzheimer Amyloid-β42 (Aβ42)-induced Neuron Loss and Intraneuronal Aβ42 Deposits but Causes a Reduction in cAMP-responsive Element-binding Protein-mediated Transcription, Age-dependent Axon Pathology, and Premature Death in Drosophila" appears in the Journal of Biological Chemistry, and can be viewed online at: doi:10.1074/jbc.M710509200. The compete citation is: Kanae Iijima-Ando, Stephen A. Hearn, Linda Granger, Christopher Shenton, Anthony Gatt, Hsueh-Cheng Chiang, Inessa Hakker, Yi Zhong, and Koichi Iijima.*

## Scientists close in on source of X-rays in lightning

GAINESVILLE, Fla. — University of Florida and Florida Institute of Technology engineering researchers have narrowed the search for the source of X-rays emitted by lightning, a feat that could one day help predict where lightning will strike.

“From a practical point of view, if we are going to ever be able to predict when and where lightning will strike, we need to first understand how lightning moves from one place to the other,” said Joseph Dwyer, a professor in the department of physics and space sciences at FIT. “At present, we do not have a good handle on this. X-rays are giving us a close-up view of what is happening inside the lightning as it moves.”

An article detailing the UF and FIT team’s findings appears this week in the online edition of Geophysical Research Letters, published by the American Geophysical Union.

The researchers used an array of electric field and X-ray detectors at a UF/FIT-operated lightning research facility in North Florida to hunt the source of X-rays emitted by lightning strokes. Their main conclusion: As the lightning comes down from the cloud toward the ground in 30- to 160-foot stages known as “steps” in a “step leader” process, the X-rays shoot out just below each step, mere millionths of a second after the step completes.

“Nobody understands how lightning makes X-rays,” said Martin Uman, a professor of electrical and computer engineering. “Despite reaching temperatures five times hotter than the surface of the sun, the temperature of lightning is still thousands of times too cold to account for the X-rays observed.”

That said, Uman added, “It’s obviously happening. And we have put limits on how it’s happening and where it’s happening.”

As far back as 1925, theorists predicted that thunderstorms and lightning might make X-rays. However, scientists spent decades seeking evidence, with little success. Then in 2001 and 2002, researchers at New Mexico Institute of Mining and Technology, the University of Florida and Florida Tech reported solid confirmation that lightning does indeed produce large quantities of X-rays. Scientists worldwide have been seeking to understand and explain the phenomenon since then, Uman said.

The New Mexico Tech researchers detected high-energy radiation from natural lightning. The UF/FIT's International Center for Lightning Research Laboratory, located on a military base in Clay County, triggers lightning using wire-trailing rockets fired into passing storm clouds. In 2002, Uman's team showed "triggered lightning" produces X-rays.

In the latest research, electrical engineering doctoral student Joey Howard, the paper's lead author, and other UF/FIT researchers used a series of electric field detectors and sodium iodide X-ray detectors to try to probe X-rays more closely.

In the 2002 paper, the UF/FIT researchers confirmed that X-rays are produced by the stepped leader in natural lightning. In the latest paper, they narrowed the production of X-rays to the beginning of each step of the step leader, based on data gathered from one natural lightning strike and one triggered strike, Uman said.

"We could see when the electric field arrived at the sequence of stations, and it was the same with the X-rays," Uman said. "We then went back and calculated what the source location was for the field and the X-ray."

Dwyer said the research is one more step toward using X-rays to understand how lightning travels.

"A spark that begins inside a thunderstorm somehow manages to travel many miles to the ground, where it can hurt people and damage property," he said. "Now, for the first time, we can actually detect lightning moving toward the ground using X-rays. So just as medical X-rays provide doctors with a clearer view inside patients, X-rays allow us to probe parts of the lightning that are otherwise very difficult to measure."

Uman said the research will continue with more expensive, faster and more sensitive X-ray detectors. One area of future interest, he said, is whether lightning strikes to airplanes could produce X-rays harmful to passengers.

## Who's the brightest star of all?

* 22:13 15 July 2008
* NewScientist.com news service
*** Ker Than**

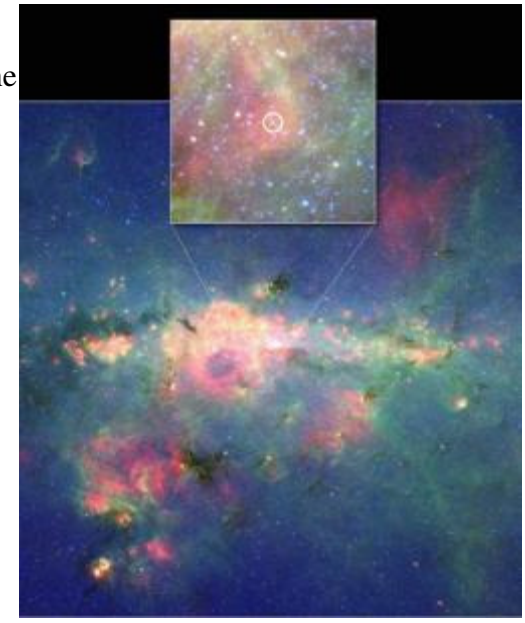
There's a new contender for the title of the Milky Way's brightest star.

The star had been discovered previously in the Peony nebula near the galaxy's dusty centre. But infrared observations taken from the ground and with NASA's Spitzer Space Telescope have pierced the dust to reveal just how bright the star is.

It boasts a wattage of about 3.2 million Suns. That is close to the output of Eta Carinae, the current record holder, which shines with the light of about 4.7 million Suns. However, measuring stellar brightness is not an exact science, and the stars may actually radiate similar amounts of light.

"As we get better measurements, these things change around a bit," says Michelle Thaller at NASA's Jet Propulsion Laboratory in California, who was not involved in the study.

It's possible that the galaxy's brightest star has not even been discovered yet. "There are probably other stars just as bright if not brighter in our galaxy that remain hidden from view," says team leader Lidia Oskinova of Potsdam University in Germany.



***The Peony nebula (reddish cloud around white circle) near the galactic centre is home to a star that rivals the stellar powerhouse Eta Carinae in brightness*** **(Image: NASA/JPL-Caltech/Potsdam Univ)**

**New stars**

Both Eta Carinae and the Peony nebula star are evolved blue giants known as "Wolf-Rayet" stars, which have masses of 100 to 200 Suns. Either could self-destruct as a supernova at any moment.

The Peony nebula star lies about 26,000 light years away and Eta Carinae about 7500 light years away. "For all we know, they may have already blown themselves up and we're just waiting for the light to get to us to tell us that," Thaller told New Scientist.

For Thaller and other astronomers, knowing which blue giant is the brightest is less important than understanding what role the massive stars play in galactic evolution.

"These are real drivers of a galaxy's life cycle," Thaller says. "When these things go off, they will probably kick off a new generation of stars." *Journal reference: Astronomy & Astrophysics (forthcoming)*

## UT Pathologists Believe They Have Pinpointed Achilles Heel of HIV

HOUSTON—(July 3, 2008)—Human Immunodeficiency Virus (HIV) researchers at The University of Texas Medical School at Houston believe they have uncovered the Achilles heel in the armor of the virus that continues to kill millions.

Scientists in UT Houston laboratory of Sudhir Paul, Ph.D., may have uncovered a chink the armor of the deadly HIV virus. Pictured from left to right are: Paul, Yasuhiro Nishiyama, Ph.D., and Stephanie Planque.

Scientists in UT Houston laboratory of Sudhir Paul, Ph.D., may have uncovered a chink the armor of the deadly HIV virus. Pictured from left to right are: Paul, Yasuhiro Nishiyama, Ph.D., and Stephanie Planque.

The weak spot is hidden in the HIV envelope protein gp120. This protein is essential for HIV attachment to host cells, which initiate infection and eventually lead to Acquired Immunodeficiency Syndrome or AIDS. Normally the body's immune defenses can ward off viruses by making proteins called antibodies that bind the virus. However, HIV is a constantly changing and mutating virus, and the antibodies produced after infection do not control disease progression to AIDS. For the same reason, no HIV preventative vaccine that stimulates production of protective antibodies is available.

The Achilles heel, a tiny stretch of amino acids numbered 421-433 on gp120, is now under study as a target for therapeutic intervention. Sudhir Paul, Ph.D., pathology professor in the UT Medical School, said, "Unlike the changeable regions of its envelope, HIV needs at least one region that must remain constant to attach to cells. If this region changes, HIV cannot infect cells. Equally important, HIV does not want this constant region to provoke the body's defense system. So, HIV uses the same constant cellular attachment site to silence B lymphocytes - the antibody producing cells. The result is that the body is fooled into making abundant antibodies to the changeable regions of HIV but not to its cellular attachment site. Immunologists call such regions superantigens. HIV's cleverness is unmatched. No other virus uses this trick to evade the body's defenses."

Paul is the senior author on a paper about this theory in a June issue of the journal Autoimmunity Reviews. Additional data supporting the theory are to be presented at the XVII International AIDS Conference Aug. 3-8 in Mexico City in two studies titled "Survivors of HIV infection produce potent, broadly neutralizing IgAs directed to the superantigenic region of the gp120 CD4 binding site" and "Prospective clinical utility and evolutionary implication of broadly neutralizing antibody fragments to HIV gp120 superantigenic epitope."

First reported in the early 1980s, HIV has spread across the world, particularly in developing countries. In 2007, 33 million people were living with AIDS, according to a report by the World Health Organization and the United Nations.

Paul's group has engineered antibodies with enzymatic activity, also known as abzymes, which can attack the Achilles heel of the virus in a precise way. "The abzymes recognize essentially all of the diverse HIV forms found across the world. This solves the problem of HIV changeability. The next step is to confirm our theory in human clinical trials," Paul said.

Unlike regular antibodies, abzymes degrade the virus permanently. A single abzyme molecule inactivates thousands of virus particles. Regular antibodies inactivate only one virus particle, and their anti-viral HIV effect is weaker.

"The work of Dr. Paul's group is highly innovative. They have identified antibodies that, instead of passively binding to the target molecule, are able to fragment it and destroy its function. Their recent work indicates that naturally occurring catalytic antibodies, particularly those of the IgA subtype, may be useful in the treatment and prevention of HIV infection," said Steven J. Norris, Ph.D., holder of the Robert Greer Professorship in the Biomedical Sciences and vice chair for research in the Department of Pathology and Laboratory Medicine at the UT Medical School at Houston.

The abzymes are derived from HIV negative people with the autoimmune disease lupus and a small number of HIV positive people who do not require treatment and do not get AIDS. Stephanie Planque, lead author and UT Medical School at Houston graduate student, said, "We discovered that disturbed immunological events in lupus patients can generate abzymes to the Achilles heel of HIV. The human genome has accumulated over millions of years of evolution a lot of viral fragments called endogenous retroviral sequences. These endogenous retroviral sequences are overproduced in people with lupus, and an immune response to such a sequence that resembles the Achilles heel can explain the production of abzymes in lupus. A small minority of HIV positive people also start producing the abzymes after decades of the infection. The immune system in some people can cope with HIV after all."

Carl Hanson, Ph.D., who heads the Retrovirus Diagnostic Section of the Viral and Rickettsial Disease Laboratory of the California Department of Public Health, has shown that the abzymes neutralize infection of

human blood cells by diverse strains of HIV from various parts of the world. Human blood cells are the only cells that HIV infects.

"This is an entirely new finding. It is a novel antibody that appears to be very effective in killing the HIV virus. The main question now is if this can be applied to developing vaccine and possibly used as a microbicide to prevent sexual transmission," said David C. Montefiori, Ph.D., director of the Laboratory for AIDS Vaccine Research & Development at Duke University Medical Center. The abzymes are now under development for HIV immunotherapy by infusion into blood. They could also be used to guard against sexual HIV transmission as topical vaginal or rectal formulations.

"HIV is an international priority because we have no defense against it," Paul said. "Left unchecked, it will likely evolve into even more virulent forms. We have learned a lot from this research about how to induce the production of the protective abzymes on demand. This is the Holy Grail of HIV research -- development of a preventative HIV vaccine."

Major contributors to the research from the UT Medical School include Yasuhiro Nishiyama, Ph.D., and Hiroaki Taguchi, Ph.D., both with the Department of Pathology and Laboratory Medicine, and Miguel Escobar, M.D., of the Department of Pediatrics. Maria Salas and Hanson, both with the Viral and Rickettsial Disease Laboratory, contributed.

The journal article is titled "Catalytic antibodies to HIV: Physiological role and potential clinical utility". The research was funded by the National Institutes of Health and the Texas Higher Education Coordinating Board.

## Vitamin A pushes breast cancer to form blood vessel cells

Washington, DC – Researchers at Georgetown University Medical Center have discovered that vitamin A, when applied to breast cancer cells, turns on genes that can push stem cells embedded in a tumor to morph into endothelial cells. These cells can then build blood vessels to link up to the body's blood supply, promoting further tumor growth.

They say their findings, published in the July 16 online issue of PLoS ONE, is a proof of principle of the new – and controversial – "vasculogenic mimicry" theory, proposing that, as needed, tumors build their own blood pipelines. This is very different from the well-accepted role of tumor angiogenesis, when tumors send signals to blood vessels to grow toward the cancer.

The study's senior author, Stephen W. Byers, Ph.D., a professor of oncology and cell biology at Georgetown's Lombardi Comprehensive Cancer Center, also says that this study helps explain why retinoids--natural or synthetic vitamin A agents--have had mixed results in treating cancer. "Finding that vitamin A may cause some breast cancer cells to form blood vessels brings up the rather disturbing notion that treatment with these drugs may actually stimulate tumor growth," says Byers.

For example, use of beta-carotene, the most important dietary precursor of vitamin A and the chemical that makes carrots orange, has been found to increase lung cancer progression in a large clinical trial. Additionally, fenretinide, a synthetic retinoid, appears to reduce the risk of second breast cancers in premenopausal women, but increase the risk in postmenopausal women, Byers says.

"None of this means that people should avoid foods rich in vitamin A, or should refuse to take their vitamins," he says. "What led us to this study is that previous research on retinoids implied that they may be effective in a preventative setting, but may actually have a negative effect after tumor initiation and during progression."

The researchers demonstrated that treating the cells with RA turns on 81 genes that are associated with endothelial cells, such as vascular endothelial (VE) cadherin, which plays a role in binding endothelial cells together into a structure. When they then mixed the treated cancer cells with endothelial cells taken from human umbilical cord blood, structures similar to blood vessels developed within the tumor masses grown in culture.

This makes sense, says Byers, because vitamin A is known to be necessary for embryonic development precisely because it helps to "differentiate" stem cells, pushing them to become required tissue. In the same way, taking too much vitamin A can result in birth defects.

So, in cancer cells, vitamin A seems to be turning on cancer stem cells, allowing them to form the blood vessel tissue -- needed most as tumors develop. Independent formation of these vessels is what has been proposed in the vasculogenic mimicry theory, developed by Mary Hendrix, , Ph.D., of Northwestern University, Byers says.

"Like many scientists, I was not an advocate of this notion because it seemed too far fetched, but now, based on these findings and my years of working on retinoids and breast cancer, I am a believer," he says. "And what this study tells us is that treating stem cells that have retained the ability to become cell types other than breast with differentiating agents such as vitamin A may cause an inappropriate cell to develop - in this case potentially promoting tumor vasculogenesis and growth, which is not a desired effect."

While there is much work yet to do to further define the molecular mechanisms by which endothelial cells form within tumors and assemble themselves into blood vessels, Byers says that these findings open a new door to drug development. "Cancer drugs based on stopping host-derived angiogenesis have met with mixed success, and we think there could be new ways to target and halt the ability of tumor cells themselves to contribute to their own blood supply," he says.

*The study was funded by grants from the National Institutes of Health and the Department of Defense. Co-authors include Georgetown University Medical Center researchers Yoshimi Endo, M.D., Ph.D., Kamla Deonauth, Ph.D., and Priya Prahalad BS, (co-first authors of the study) and Yuelin Zhu Ph.D.*

## Tongue Orchids' Sexual Guile: Utterly Convincing

**By CAROL KAESUK YOON**

**TRICKY** ***Tongue orchids of Australia, excellent mimics of female wasps.***

Orchids, gorgeous and elegant, are also some of the most deceitful flowers, having evolved sometimes elaborate ruses to lure pollinators.

In a new study of the most brazen of these botanical cheats, the species that entice pollinators with false promises of sex, scientists have discovered that one group of orchids has taken the art of manipulation to shameless heights.

Sexually deceptive orchids, as biologists have long known, look and can even smell so much like a female insect that males will try to mate with the flower in a sometimes vigorous process that can result in pollination. But scientists now report that the tongue orchids of Australia are such thoroughly convincing mimics of female wasps that males not only try to mate with them, but they actually do mate with them — to the point of ejaculation.

"It's always been described as pseudocopulation," said Anne Gaskett, a graduate student at Macquarie University in Australia and the lead author of the study. "But it looked like true copulation to me."

The discovery that orchids can induce such an extreme response is more than just bizarre natural history, because biologists have always assumed that the sexual misrepresentations of orchids were harmless to the duped males, no more than a comical exercise in frustration.

Yet the study, published last month in The American Naturalist, suggests a potentially huge cost to the wasps.

"If males waste all their sperm on orchids," Ms. Gaskett asked, "what have they got to offer a real female?"

Beyond that, why, scientists asked, would orchids do such an evolutionarily foolish thing? Why would a flower evolve to compromise the ability of its pollinator to reproduce?

So many orchids treat their pollinators so nastily, with false promises of food and sex or the occasional dunking of insect visitors into bucket-shaped petals full of liquid, that naturalists have puzzled over the relationship for more than a century.

Darwin was so consumed by the odd interactions that after "The Origin of Species," his next book was an entire volume on the subject, "The Various Contrivances by Which Orchids Are Fertilized by Insects."

In the case of the tongue orchids and their dupe wasps, at least, scientists say they may have deciphered why these flowers abuse their visitors: the treatment of the wasps may, in fact, be very much to the orchids' advantage.

In wasps, the sex of an individual, male or female, is determined by a peculiar genetic system known as haplodiploidy. In this system, females are produced by an egg from their mother and a sperm from their father. But males have just half of the genetic complement and are produced by females from just an egg, without the aid of a male or a single drop of sperm.

For an orchid that is pollinated just by males, depleting sperm that would be used just to produce females might not be a drawback at all. It could even be a plus, because some female wasps without sufficient sperm tend to produce more sons — or, from the orchid's perspective, more pollinators.

Increasing the numbers of males, scientists say, could even make males a bit more desperate and less discriminating — another potential advantage for an orchid trying to fool a male into giving the not-quite-right-looking fake female sitting immobile inside its petals a try.

# Gene Variation May Raise Risk of H.I.V., Study Finds

**By NICHOLAS WADE**

A genetic variation that once protected people in sub-Saharan Africa from a now extinct form of malaria may have left them somewhat more vulnerable to infection by H.I.V., the virus that causes AIDS. The gene could account for 11 percent of the H.I.V. infections in Africa, explaining why the disease is more common there than expected, researchers based in Texas and London say. The researchers said their finding had no immediate public health consequences. But if confirmed, it would offer an important insight into the biology of the virus.

The genetic variation has been studied in United States Air Force personnel, whose H.I.V. infections have been followed for 25 years. African-Americans who carried the variation were 50 percent more likely to acquire H.I.V. than African-Americans who did not, although their disease progressed more slowly, say researchers led by Sunil K. Ahuja, director of the Veterans Administration H.I.V./AIDS Center, San Antonio, and Matthew J. Dolan of the Uniformed Services University in Bethesda, Md. Their results were reported Wednesday in the journal Cell Host & Microbe.

David B. Goldstein, geneticist who studies H.I.V. at Duke University, said that the new result "would be pretty exciting if it holds up" and that many other researchers would now test it. "If the results are confirmed, it would mean that selection for resistance to malaria has created a vulnerability to infection with HIV-1," he said, referring to the principal form of the virus.

The genetic variation, called a SNP, or snip, involves a change in one unit of DNA. This particular snip has a far-reaching consequence. It prevents red blood cells from inserting a certain protein on their surface. The protein is called a receptor because it receives signals from a hormone known as CCL5, which is part of the immune system's regulatory system.

The receptor is also used by a malarial parasite called Plasmodium vivax to gain entry to the red blood cells it feeds on. About 10,000 years ago, people in Africa who possessed the SNP variation gained a powerful survival advantage from not being vulnerable to the ancestor of Plasmodium vivax. The SNP eventually swept through the population and the vivax parasite died out in Africa, to be replaced by its current successor, Plasmodium falciparum. More than 90 percent of people in Africa now lack the receptor on their red blood cells, as do about 60 percent of African-Americans.

The possibility that the receptor has a bearing on H.I.V. infection first occurred to Robin Weiss, a biologist at University College, London, after he noticed that the virus seemed to be hitchhiking on red blood cells. Dr. Weiss, who wrote the new report with Dr. Ahuja and Dr. Dolan, showed in laboratory tests that H.I.V. latches onto the receptor in place of its intended guest, the CCL5 hormone.

The Texas-London research team is not certain how lack of the receptor promotes H.I.V. infection, but Dr. Ahuja said the red blood cells acted like a sponge for CCL5. Because CCL5 is known to obstruct multiplication of the virus, having lots of the hormone in the bloodstream may prevent infection. Conversely, people whose blood cannot soak up the hormone could be more vulnerable.

Dr. Weiss said the red blood cell receptor was similar to another receptor, CCR5, which occurs on the surface of the white blood cells that are H.I.V.'s major target. A small percentage of Europeans have a mutation that prevents the CCR5 receptor from being displayed on the surface of white blood cells, and they are protected against H.I.V.

It is somewhat puzzling that the absence of the two receptors has the opposite effect — vulnerability to H.I.V. when the red cell receptor is missing, protection from it when the white cell receptor is withdrawn. The researchers offer an explanation that they concede is far from straightforward.

"If you found the paper plain sailing, most of my students didn't," Dr. Weiss said. As is often the case with provocative new findings, the researchers may have some way to go before convincing others that their observation is correct. Dr. Goldstein said that in parts of the United States, African-Americans have a higher infection rate than European-Americans, and that patients with a higher proportion of African genes may be more vulnerable to H.I.V. for reasons unconnected to the SNP. Nonetheless, the SNP would show up in a greater proportion of infected people simply because of their African heritage. If so, the gene's apparent association with H.I.V. infection could be just coincidental, not causal. The researchers took steps to rule out this possibility, but Dr. Goldstein said those steps might not have been adequate.

Dr. Carl Dieffenbach, director of the AIDS division of the National Institute of Allergy and Infectious Diseases, said the new finding, if confirmed, would be intriguing because it pointed to the many ways in which pathogens have shaped the body's receptors. Although H.I.V. is too recent an infection to have left an evolutionary mark on the genome, human ancestors would have been exposed to malarial parasites and to S.I.V., which infects monkeys, and the genome still bears the marks of these challenges to survival. Better knowledge of these adaptations will help understand the biology of H.I.V. infection, he said.

# Trial for Vaccine Against H.I.V. Is Canceled

**By LAWRENCE K. ALTMAN**

Plans for a large human trial of a promising government-developed H.I.V. vaccine in the United States were canceled Thursday because a top federal official said scientists realized that they did not know enough about how H.I.V. vaccines and the immune system interact.

The decision is a major setback in an effort to develop an H.I.V. vaccine that began 24 years ago when government health officials promised a marketed vaccine by 1987. Health officials have long contended that such a vaccine would be their best weapon to control the AIDS pandemic.

A number of other H.I.V. vaccines are in various stages of testing around the world. But there had been high hopes for the government's trial because the potential vaccine was among a new class that sought to stimulate the immune system in a different way.

The official who canceled the government trial, Dr. Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases, said it was becoming clearer that more fundamental research and animal testing would be needed before an H.I.V. vaccine was ever marketed.

Scientists say that developing a vaccine against H.I.V. is one of the most difficult scientific endeavors in history because of the uncanny nature of the virus.

The government vaccine — known as PAVE, for Partnership for AIDS Vaccine Evaluation — was similar to a much-heralded vaccine that failed last year. That vaccine was developed by Merck, and Dr. Fauci's agency helped pay for the Merck trials.

Dr. Fauci said he reached his decision to cancel the coming trial after meeting with scientists to try to understand why the Merck vaccine had failed. He said he had concluded that scientists must go a step at a time because they did not yet know fundamental facts like which immune reactions are the most important in preventing the infection.

Dr. Fauci said the new trial was intended to determine whether the vaccine could significantly lower the amount of H.I.V. in the blood of those who become infected. He said a smaller trial was needed to figure out whether the vaccine could do that before large trials were conducted.

"Show me that the vaccine works by lowering the amount of H.I.V. in the blood," Dr. Fauci said. "Then we will move to a larger trial that will document the link with a particular immune response." He added that until then, "doing a large trial is not justified."

Dr. Alan Bernstein, executive director of the Global HIV Vaccine Enterprise, said that his organization supported Dr. Fauci's decision and that there was an "urgent need for a diversity of new approaches to H.I.V. vaccine design."

For instance, Dr. Bernstein said, recent laboratory advances, which allow scientists to look at hundreds of genes simultaneously, "offer immense promise in helping us understand how to design new H.I.V. vaccine candidates that can achieve long-lasting immune protection."

The trial canceled Thursday was supposed to have started enrolling 8,500 volunteers last October to receive the PAVE vaccine, developed by the infectious diseases agency. PAVE is a consortium of federal agencies and key federally financed organizations involved in developing and evaluating experimental H.I.V. vaccines. It seeks to create an effective H.I.V. vaccine that no pharmaceutical company or institution is likely to accomplish on its own.

The PAVE trial had been postponed after a test of the Merck vaccine failed in its two main objectives: to prevent infection and to lower the amount of H.I.V. in the blood among those who became infected. Also, the findings among the 3,000 participants in nine countries in which the Merck vaccine was tested suggested it might have increased the risk of becoming infected.

After a safety monitoring committee detected the problems with the Merck vaccine in September, the company quickly halted its study.

Scientists have found no obvious explanation for the failure of the Merck vaccine, which had been considered the most promising candidate.

The Merck vaccine was the first of a new class of H.I.V. vaccines to get to an advanced stage in human testing. The vaccine was made from a weakened version of a common cold virus, adenovirus type 5, which served as a way to deliver three synthetically produced genes — gag, pol and nef — from the AIDS virus. Three doses of the vaccine were injected over six months.

Scientific analyses found that the highest risk of H.I.V. infection among recipients of the Merck vaccine was in males who both were uncircumcised and had pre-existing antibodies to adenovirus type 5.

After the failure of Merck trial, the government reduced the number of potential volunteers to 2,400; they would have included circumcised gay men who had no pre-existing antibodies to adenovirus type 5. The scaled-back study would have cost about $63 million, compared with $140 million for the initial design.

At a news conference in 1984, top federal officials said they were optimistic that a marketable H.I.V. vaccine would be available in three years. Since then, AIDS researchers have been divided about how fast to test experimental vaccines.

Many urge caution out of fear that failures could destroy confidence among uninfected people most at risk who would be needed as volunteers in future trials.

But equally vocal groups call for testing everything as soon as the research shows promise because of the urgent need for a vaccine.

In an unrelated development, researchers at Duke University reported new findings Thursday showing that H.I.V. stuns the immune system earlier than scientists previously understood.

The window of opportunity in stopping H.I.V. may be a matter concerning the first few days, not weeks, after the virus enters the body, a team headed by Dr. Barton Haynes reported in The Journal of Virology.

The findings were based on a study of 30 individuals newly infected with H.I.V., and the National Institutes of Health paid for the study.

## Men and women may need different diets: research

Diet can strongly influence how long you live and your reproductive success, but now scientists have discovered that what works for males can be very different for females.

In the first study of its kind, the researchers have shown that gender plays a major role in determining which diet is better suited to promoting longer life or better reproductive success.

In the evolutionary "battle of the sexes", traits that benefit males are costly when expressed in females and vice versa. This conflict may have implications for human diet, aging and reproduction, says a team of scientists from UNSW, the University of Sydney and Massey University.

"When it comes to choosing the right diet, we need to look more closely to the individual, their sex and their reproductive stage in life," says Associate Professor Rob Brooks, Director of the Evolution and Ecology Research Centre at the University of New South Wales. "It may be, for example, that women in their child-bearing years need a different diet to those who are post-menopausal.

"It also underlines the important lesson that what we want to eat or, if you like, what we're programmed to eat, is not necessarily best for us." The researchers are conducting long-term studies on Australian black field crickets and have discovered that the lifespan of both males and females is maximised on high-carbohydrate, low-protein diets, they say in the latest issue of Current Biology.

But reproductive success differs dramatically between the sexes when the carbohydrate-protein balance is changed: males live longest and have the greatest reproductive success with a diet that favours carbohydrates to protein by eight-to-one, whereas females have greatest success when the ratio is just one-to-one. Given a choice, however, females eat only a small amount more protein than males. The shared ability to sense and choose food dooms both males and females to eat a diet that is a compromise between what is best for each sex.

"Male and female crickets maximise their fitness on different diets," says UNSW's Dr Alexei Maklakov, the study's lead author. "Despite that, the dietary preferences of the sexes are very similar. Instead of selecting foods in a sex-specific manner, males and females select 'intermediate' diets that are less than optimal for both sexes.

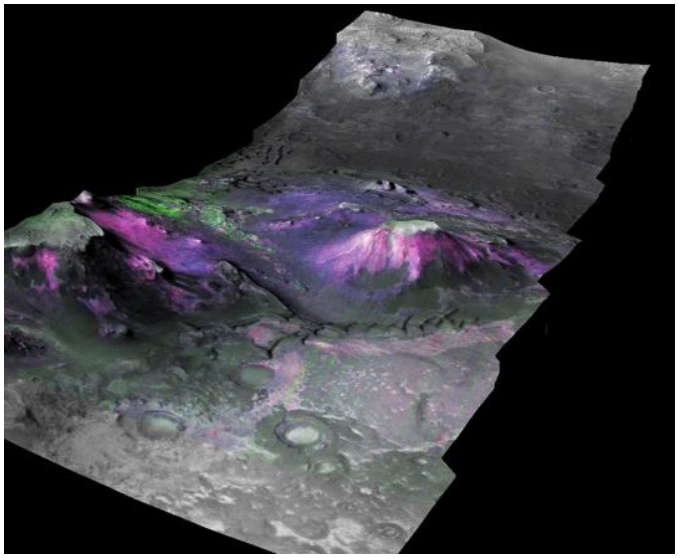
The researchers believe the sexes share most of their genes and this fact can constrain the evolution of sex differences in traits such as diet choice, because many of the same genes are likely to be responsible for trait expression in both sexes.

Significance for humans – "Men and women invest differently in reproduction, a difference that is even more marked than that between male and female crickets," says Rob Brooks. "Think of the tremendous amounts of energy and protein required of a mother in carrying a baby to term and breastfeeding. We also know that men and women need to eat different diets - think of the careful attention we pay to what expectant mothers eat.

"What men and women need to eat might be more dramatically different than we had realised. However, men and women eat very similar diets and our results suggest that our tastes and food preferences could be a shared compromise, as they are in crickets."

## New Findings Show Diverse, Wet Environments on Ancient Mars

Mars once hosted vast lakes, flowing rivers and a variety of other wet environments that had the potential to support life, according to two new studies based on data from the Compact Reconnaissance Imaging Spectrometer for Mars (CRISM) and other instruments on board NASA's Mars Reconnaissance Orbiter (MRO).



"The big surprise from these new results is how pervasive and long-lasting Mars' water was, and how diverse the wet environments were," says Scott Murchie, CRISM's principal investigator at the Johns Hopkins University Applied Physics Laboratory (APL), in Laurel, Md.

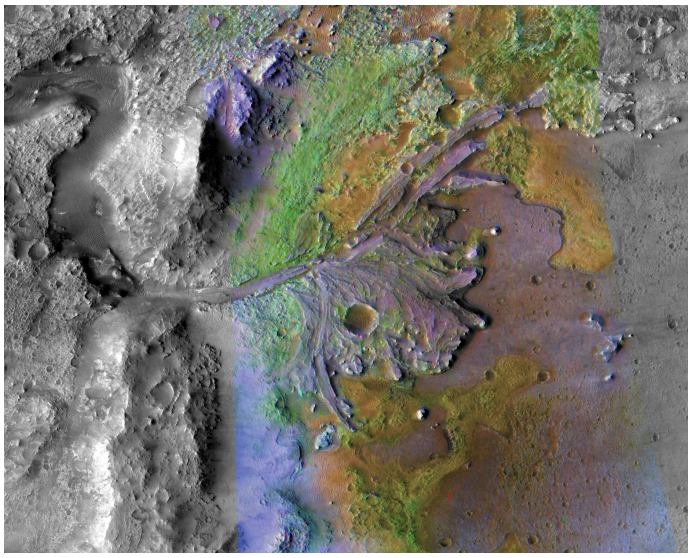
One study, published in the July 17 issue of Nature, shows that vast regions of the ancient highlands of Mars—which cover about half the planet—contain clay minerals, which can form only in the presence of water. Volcanic lavas buried the clay-rich regions during subsequent, drier periods of the planet's history, but impact craters later exposed them at thousands of locations across the planet.

**Water-Rich Terrain** ***This three-dimensional image of a trough in the Nili Fossae region of Mars shows a type of minerals called phyllosilicates (in magenta and blue hues) concentrated on the slopes of mesas and along canyon walls. The abundance of phyllosilicates shows that water played a sizable role in changing the minerals of a variety of terrains in the planet's early history.*** **NASA/JPL/JHUAPL/University of Arizona/Brown University.**

The clay-like minerals, called phyllosilicates, preserve a record of the interaction of water with rocks dating back to what is called the Noachian period of Mars' history, about 4.6 to 3.8 billion years ago. This period corresponds to the earliest years of the solar system, when Earth, the moon and Mars sustained a cosmic bombardment by comets and asteroids. Rocks of this age have largely been destroyed on Earth by plate tectonics; they are preserved on the moon, but were never exposed to liquid water. The phyllosilicate-containing rocks on Mars therefore preserve a unique record of liquid water environments—possibly suitable for life—in the early solar system.

"The minerals present in Mars' ancient crust show a variety of wet environments," says John Mustard, a member of the CRISM team from Brown University in Providence, R.I., and lead author of the Nature study. "In most locations the rocks are lightly altered by liquid water, but in a few locations they have been so altered that a great deal of water must have flushed though the rocks and soil. This is really exciting because we're finding dozens of sites where future missions can land to understand if Mars was ever habitable and if so, to look for signs of past life."

A companion study, published in the June 2 issue of Nature Geosciences, finds that the wet conditions persisted for a long time. Thousands to millions of years after the clays were formed, a system of river channels eroded them out of the highlands and concentrated them in a delta where the river emptied into a crater lake slightly larger than California's Lake Tahoe, about 25 miles (40 kilometers) in diameter. "The distribution of clays inside the ancient lakebed shows that standing water must have persisted for thousands of years," says Bethany Ehlmann, another member of the CRISM team from Brown and lead author of the study of the ancient lake within Jezero Crater. "Clays are wonderful at trapping and preserving organic matter, so if life ever existed in this region, there's a chance of its chemistry being preserved in the delta."



**Organic Cemetery?** ***A color-enhanced image of the delta in Jezero Crater, which once held a lake. Researchers led by CRISM team member and Brown graduate student Bethany Ehlmann report that ancient rivers ferried clay-like minerals (shown in green) into the lake, forming the delta. Clays tend to trap and preserve organic matter, making the delta a good place to look for signs of ancient life.*** **NASA/JPL/JHUAPL/MSSS/Brown University.**

CRISM's combination of high spatial and spectral resolutions—better than any previous imaging spectrometer sent to Mars—reveals variations in the types and composition of the phyllosilicate minerals. By combining data from CRISM and MRO's Context Imager (CTX) and High Resolution Imaging Science Experiment (HiRISE), the team has identified three principal classes of water-related minerals dating to the early Noachian period: aluminum-phyllosilicates, hydrated silica or opal, and the more common and widespread iron/magnesium-phyllosilicates. The variations in the minerals suggest that different processes, or different types of watery environments, created them.

"Our whole team is turning our findings into a list of sites where future missions could land to look for organic chemistry and perhaps determine whether life ever existed on Mars," says APL's Murchie.

APL, which has built more than 150 spacecraft instruments over the past four decades, led the effort to build CRISM, and operates the instrument in coordination with an international team of researchers from universities, government and the private sector. The Jet Propulsion Laboratory of the California Institute of Technology, Pasadena, manages the Mars Reconnaissance Orbiter mission for NASA's Science Mission Directorate. Lockheed Martin Space Systems, Denver, is the prime contractor for the project and built the spacecraft.

## Eruptions wiped out ocean life 94 million years ago

University of Alberta scientists contend they have the answer to mass extinction of animals and plants 93 million years ago. The answer, research has uncovered, has been found at the bottom of the sea floor where lava fountains erupted, altering the chemistry of the sea and possibly of the atmosphere.

Earth and Atmospheric Science researchers Steven Turgeon and Robert Creaser found specific isotope levels of the element osmium, an indicator of volcanism in seawater, in black shale—rocks containing high amounts of organic matter—drilled off the coast of South America and in the mountains of central Italy.

According to their research, the eruptions preceded the mass extinction by a geological blink of the eye. The event occurred within 23 thousand years and the underwater volcanic eruption had two consequences: first, nutrients were released, which allowed mass feeding and growth of plants and animals. When these organisms died, their decomposition and fall towards the sea floor caused further oxygen depletion, thereby compounding the effects of the volcanic eruption and release of clouds of carbon dioxide in to the oceans and atmosphere. The result was a global oceanic anoxic event, where the ocean is completely depleted of oxygen, Anoxic events—while extremely rare—occur in periods of very warm climate, which means that this research could not only help prove a mass-extinction theory, but also help scientists studying the effects of global warming.

## Asthma and other allergies tied to absence of specialized cells

### *NYU researchers identify immune cells that block allergic reactions*

NEW YORK July, 16, 2008 – When it comes to allergies, both the problem and the solution are found within us. Our immune systems respond to foreign substances with an arsenal of cells. Some are programmed to "remember" invaders they've encountered in the past. Normally, anything previously identified as harmless is allowed to pass. Sometimes, however, the immune response goes awry, triggering an allergic reaction.

Now, researchers at NYU School of Medicine have zeroed in on a class of custom-made immune cells that block allergic reactions. These regulatory T cells are manufactured according to instructions from a gene called Foxp3 whenever we eat or inhale a potential allergen for the first time, ensuring that the next time we encounter that substance, we will not mount an allergic response.

"We don't become allergic to lots of things—we eat all kinds of things, we breathe all kinds of things, and what prevents us from developing allergies is that we make regulatory T cells, which specifically recognize this allergen," says Maria A. Curotto de Lafaille, Ph.D., Associate Research Scientist at NYU Langone Medical Center. "Every time we don't react to something or don't become allergic, it's not because nothing is happening," Dr. de Lafaille explains. "It's because something very important is happening: We're making these cells,"

Mucosal tissue, which lines both the respiratory and digestive tracts, has long been known as an effective barrier against allergens, which are always protein molecules. The NYU research shows that Foxp3-directed regulatory T cells (Treg) are produced in the mucosal tissue and remain there to prevent allergic reactions. New ones are tailor-made every time an unknown protein is inhaled or ingested. The inability to make Treg cells results in high susceptibility to becoming allergic.

The NYU researchers induced allergic reactions in mice with a Foxp3 mutation that prevented formation of Treg cells. Exposure to the same allergen—in this case egg protein—did not elicit an allergic response in mice that were able to make Treg cells. The findings are reported in the July 18, 2008, issue of the journal Immunity.

The formation of Foxp3-positive Treg cells occurs in response to any potential allergen, so the findings are applicable to a broad range of allergic reactions and autoimmune diseases, says Dr. de Lafaille. When people suffer from allergies, including life-threatening ones such as asthma, something goes wrong in the process by

which Foxp3 signals Treg cell formation. The problem is not necessarily a mutation in the Foxp3 gene, which is known to cause severe autoimmune disease. Rather, something occurs, or fails to occur, in the lungs or the gut that interferes with the production or activity of allergen-specific Treg cells.

The NYU researchers also determined that Treg cells control damage from long-term inflammation. They found high concentrations of Treg cells in inflamed lung tissue of mice without the Foxp3 defect. "The question arose about what these cells are doing in the tissue—are they beneficial or not?" Dr. de Lafaille says. It turns out that even though the Treg cells did not prevent inflammation in an ongoing allergic reaction, they kept it under control, ensuring it did not worsen or spread to other areas of the body. "We think that over time these regulatory T cells become more important than the inflammatory cells and end up completely shutting off the inflammation. But it's not overnight and it's not black and white," Dr. de Lafaille emphasizes.

This finding provides a key to one of the most serious consequences of asthma. In addition to breathing problems during an acute attack, people with asthma have chronic inflammation, which can permanently damage their airways. If a means could be found to increase the number of Treg cells in inflamed tissue, this might be prevented. Allergic asthma, the most common and best-understood type, affects more than 10 million people in the US, many of them children. Acute asthma attacks are responsible for nearly 4000 deaths in the United States each year.

Dr. Yi Ding, Dr. de Lafaille, and other members of Dr. Juan Lafaille's laboratory have been investigating ways to grow allergen-specific Treg cells in the lab and inject them into people who cannot make their own. The group published a paper in Nature Medicine in February 2008 describing a method of making the cells. "The big challenge is how to isolate the cells that will recognize the right allergens that the person is allergic to," Dr. de Lafaille says. Another approach is to stimulate the body to manufacture the cells itself, an area of ongoing research.

This work represents an important step in understanding the genetic and cellular mechanisms underlying the allergic response, which may lead to more effective therapies. Current treatment is aimed at suppressing symptoms and reducing inflammation after an allergic reaction has already occurred. Having identified the cell type that must be present to prevent allergies, Dr. de Lafaille and her colleagues are now looking for the glitch that blocks formation of those cells.

*The study published in the journal Immunity was supported by grants from the National Institutes of Health, the National Multiple Sclerosis Society, and the Sandler Foundation. The co-authors of the study include: Nino Kutchukhidze and Shiqian Shen, former postdoctoral students in pathology, Yi Ding, a graduate student in pathology, and Herman Yee, M.D., Ph.D., associate professor of pathology, and Juan J. Lafaille, Ph.D., associate professor of pathology and Medicine at NYU Langone Medical Center.*

## Yale researchers discover remnant of an ancient 'RNA world'

Some bacterial cells can swim, morph into new forms and even become dangerously virulent - all without initial involvement of DNA. Yale University researchers describe Friday in the journal Science how bacteria accomplish this amazing feat - and in doing so provide a glimpse of what the earliest forms of life on Earth may have looked like.

To initiate many important functions, bacteria sometimes depend entirely upon ancient forms of RNA, once viewed simply as the chemical intermediary between DNA's instruction manual and the creation of proteins, said Ronald Breaker http://www.biology.yale.edu/facultystaff/breaker.html , the Henry Ford II Professor of Molecular, Cellular and Developmental Biology at Yale and senior author of the study.

Proteins carry out almost all of life's cellular functions today, but many scientists like Breaker believe this was not always the case and have found many examples in which RNA plays a surprisingly large role in regulating cellular activity. The Science study illustrates that - in bacteria, at least - proteins are not always necessary to spur a host of fundamental cellular changes, a process Breaker believes was common on Earth some 4 billion years ago, well before DNA existed.

"How could RNA trigger changes in ancient cells without all the proteins present in modern cells? Well, in this case, no proteins, no problem," said Breaker, who is also a Howard Hughes Medical Institute investigator.

Breaker's lab solved a decades-old mystery by describing how tiny circular RNA molecules called cyclic di-GMP are able to turn genes on and off. This process determines whether the bacterium swims or stays stationary, and whether it remains solitary or joins with other bacteria to form organic masses called biofilms. For example, in Vibrio cholerae, the bacterium that causes cholera, cyclic di-GMP turns off production of a protein the bacterium needs to attach to human intestines.

The tiny RNA molecule, comprised of only two nucleotides, activates a larger RNA structure called a riboswitch. Breaker's lab discovered riboswitches in bacteria six years ago and has since shown that they can regulate a surprising amount of biological activity. Riboswitches, located within single strands of messenger

RNA that transmit a copy of DNA's genetic instructions, can independently "decide" which genes in the cell to activate, an ability once thought to rest exclusively with proteins.

Breaker had chemically created riboswitches in his own lab and - given their efficiency at regulating gene expressions - predicted such RNA structures would be found in nature. Since 2002, almost 20 classes of riboswitches, including the one described in today's paper, have been discovered, mostly hidden in non-gene-coding regions on DNA. "We predicted that there would be an ancient 'RNA city' out there in the jungle, and we went out and found it," Breaker said.

Bacterial use of RNA to trigger major changes without the involvement of proteins resolves one of the questions about the origin of life: If proteins are needed to carry out life's functions and DNA is needed to make proteins, how did DNA arise?

The answer is what Breaker and other researchers call the RNA World. They believe that billions of years ago, single strands of nucleotides that comprise RNA were the first forms of life and carried out some of the complicated cellular functions now done by proteins. The riboswitches are highly conserved in bacteria, illustrating their importance and ancient ancestry, Breaker said.

Understanding how these RNA mechanisms work could lead to medical treatments as well, Breaker noted. For instance, a molecule that mimics cyclic di-GMP could be used to disable or disarm bacterial infections such as cholera, he said.

## Suckling infants trigger surges of trust hormone in mothers' brains

Researchers from the University of Warwick, in collaboration with other universities and institutes in Edinburgh, France and Italy, have for the first time been able to show exactly how, when a baby suckles at a mother's breast, it starts a chain of events that leads to surges of the "trust" hormone oxytocin being released in their mothers brains.

The study, published on 18th July in the journal PLoS Computational Biology, focuses on the role of oxytocin, a very important hormone recently found be involved in the enhancement of "trust" and love in humans and animals. Oxytocin has long been known to be the trigger that, when released into the blood, causes milk to be let down from the mammary gland. When oxytocin is released within the brain, it also helps to strengthen the bond between mother and child, but to have these effects, a very large amount must be released abruptly to cause a wave of the hormone that can spread through the brain.

What was not known before this study is exactly how the few thousand neurones, which are specialized to release oxytocin, are marshalled together to produce a sufficiently intense burst of activity to do all of that. In fact, even when a child is not suckling these neurons are continually producing oxytocin but in small amounts and in a much more uncoordinated way. Previous studies on individual neurons have found no obvious way of modifying their behaviour to get the coordinated response needed to produce the large, regular pulses of oxytocin that are needed.

Now this University of Warwick led team of experimental neuroscientists and theoreticians have found a likely answer. The neuroscientists have found that in response to suckling the neurons start releasing oxytocin from their "dendrites" as well as from their nerve endings – this was unexpected because dendrites are usually thought as the part of a neurone which receive, rather than transmit information.

The dendrites usually create a weak network of connections between neurons. However the researchers have now shown that the release of oxytocin from the dendrites allows a massive increase in communication between the neurons. This co-ordinates a "swarm" of oxytocin factories, producing massive intense bursts of oxytocin release at intervals of around 5 minutes or so.

The synchronous activation of the few thousand oxytocin producing neurons is an example of "emergent" process. It develops in just the same way as a flock of birds or insects - closely coordinated action developing without a single leader.

University of Warwick computational biology researcher Professor Jianfeng Feng said: "We knew that these pulses arise because, during suckling, oxytocin neurons fire together in dramatic synchronized bursts. But exactly how these bursts arise has been a major problem that has until now eluded explanation. This research has allowed us to incorporate all the latest research in a large computational model of the whole population of oxytocin cells."

"In this model we have shown that the dendritic interactions are enhanced enough to trigger a massive positive-feedback on activity. The model gives us a possible explanation of an important event in the brain that could be used to study and explain many other similar brain activities."

*Note for editors: The research paper is entitled "Emergent synchronous bursting of oxytocin neuronal Network" by Professor Jianfeng Feng and Enrico Rossoni (the University of Warwick), , Brunello Tirozzi (University of Rome,) David Brown of*

*(Babraham Institute Cambridge), Gareth Leng (Centre for Integrative Physiology in Edinburgh), and Françoise Moos (Biologie des Neurones Endocrines, CNRS-Universite)*

## Researchers discover primary sensor that detects stomach viruses

Scientists at Washington University School of Medicine in St. Louis have identified the primary immune sensor that detects the presence of stomach viruses in the body. They show that the sensor – a protein called MDA-5 – triggers an immune response that revs up the body's defenses to fight off the infection. This knowledge may help develop a treatment that prevents or reduces infection, the researchers suggest in their study, published July 18th in the open-access journal PLoS Pathogens.

The stomach flu is technically not the flu at all: the flu virus only affects the respiratory tract. The stomach flu is known scientifically as a norovirus. Norovirus outbreaks are common in locations where people live close together, such as cruise ships, nursing homes, military bases and schools. Antibiotics are ineffective, because they fight bacteria, not viruses. Only recently have scientists been able to grow noroviruses in the laboratory and study them.

"Our research strongly indicates that MDA-5 is the primary sensor for norovirus infection, but the body's ability to detect the virus is so important that it doesn't just rely on one sensor," says senior investigator Marco Colonna, M.D., professor of pathology and immunology. "We found that another protein sensor – TLR3 – serves as a back-up and there may be others that have not yet been discovered."

The team demonstrated their work in mice but says the same proteins are likely responsible for detecting norovirus infection in humans. MDA-5, and to a lesser extent, TLR3, respond by causing other cells to release interferon, which shuts down production of the virus and initiates a full-scale immune attack. MDA-5 and TLR3 are both intracellular proteins. The researchers suspected that these two proteins may be important in detecting noroviruses because they are known to be important in recognizing similar types of viral infections.

Lead author Stephen McCartney, a graduate student in Colonna's lab, first found that cells in the test tube that lack the MDA-5 protein don't mount an appropriate immune response against norovirus infection.

The team then investigated two groups of mice – one group was bred without the ability to produce MDA-5 and the other was bred to lack TLR3. Again, both groups of mice had a defective immune response against noroviruses. In particular, mice without MDA-5 had higher levels of norovirus in their bodies and a defect in the ability to signal other immune cells to respond. Mice that lacked TLR3 also had a decreased response to norovirus infection, the researchers noted.

Interestingly, some people have common variations of the MDA-5 gene that could make them more susceptible to norovirus infection, the researchers say. A norovirus treatment could be especially helpful to people who are more prone to the infection.

*http://www.plospathogens.org/doi/ppat.1000108 (link will go live on Friday, July 18)*
*CITATION: McCartney SA, Thackray LB, Gitlin L, Gilfillan S, Virgin IV HW, et al. (2008) MDA-5 Recognition of a Murine Norovirus. PLoS Pathog 4(7): e1000108. doi:10.1371/journal.ppat.1000108*

## Early study reveals promising Alzheimer's disease treatment

A drug once approved as an antihistamine in Russia improved thinking processes and ability to function in patients with Alzheimer's disease in a study conducted there, said an expert at Baylor College of Medicine in Houston. The findings are published in the current issue of the journal The Lancet.

"More research is needed, but we are encouraged by the effect the drug Dimebon had on Alzheimer's patients" said Dr. Rachelle Doody, professor of neurology at BCM and lead author of the study.

In the study, the authors noted that Dimebon is the first drug for Alzheimer's disease that demonstrated continued improvement in patients over a 12 month period. Other approved drugs do not have this effect.

Half of the 183 patients in the Russian study received Dimebon; the other half were given a placebo or an inactive pill. Clinicians at the study sites then monitored the patients' progress over the next year on five different outcomes. All of those in the study had mild to moderate Alzheimer's disease.

"What we saw in the clinical trial is that people on the medication continued to improve over time," Doody said. "Those on placebo continued to decline."

Researchers believe the medication works by stabilizing mitochondria, the cellular components that produce energy, and possibly by inhibiting brain cell death. Researchers evaluated patients' thinking and memory ability, overall function, psychiatric and behavioral symptoms, and ability to perform daily activities.

"Usually at this point in a drug's development, we are happy to see improvement in one of the outcome measures," Doody said. "We saw improvement in all five."

Some participants complained of occasional dry mouth, but no one opted out of the study because of the side effects.

"As we continue research, we hope to replicate these results," Doody said. "My belief is that this drug will turn out to be useful for Alzheimer's disease, regardless of the stage of the disease."

Doody said this is only the first study looking into the effects of Dimebon on Alzheimer's disease. She also noted that it involved only a relatively small population from one specific region of the world. The ongoing Phase 3 study will include several international locations including the United States.

*Other researchers who contributed to this study include: Dr. Svetlana I. Gavrilova, Russian Academy of Medical Sciences, Moscow, Russia; Dr. Mary Sano, Mount Sinai School of Medicine, New York City, NY; Dr. Ronald G. Thomas, University of California, San Diego, La Jolla, CA; Dr. Paul S. Aisen, formerly with Georgetown University School of Medicine, Washington, DC and now at the University of California, San Diego; ; Dr. Sergey O. Bachurin, Russian Academy of Sciences, Institute of Physiologically Active Compounds, Chernogolovka, Russia; Drs. Lynn Seely and David Hung, Medivation, Inc., San Francisco, CA.*

*Funding for this study came from Medivation, Inc., the company developing the drug worldwide. Doody is also a member of the Scientific and Clinical Advisory board for Medivation, Inc.*

*After the embargo lifts, the full report can be found at www.thelancet.com*

## Vaccine for koala chlamydia close

### *Researchers at QUT have had good results with a trial vaccine for chlamydia, a disease which is decimating koala populations in the wild*

Professors Peter Timms and Ken Beagley from Queensland University of Technology's Institute of Health and Biomedical Innovation (IHBI) said the vaccinated koalas, which are at Brisbane's Lone Pine Koala Sanctuary, were mounting a good response to the vaccine.

"A good T-cell immune response is essential if the vaccine is to be effective," Professor Timms said.

"This initial trial will measure only the animals' immune response and will not involve any live chlamydial infections.

"If all goes well with this trial our future studies will evaluate the vaccine on sick and injured koalas brought in for care, relocated animals, and koalas in other sanctuaries.

"As many as 25-50 per cent of koalas coming into care in both Queensland and NSW are showing clinical signs of the disease and it seems to be getting worse."

The researchers have been working on developing a vaccine for the sexually transmitted disease chlamydia trachomatis in humans for many years.

"We've been able to develop the vaccine for koalas as a result of our studies on the development of human chlamydial vaccines done in the mouse model. We identified several novel vaccine proteins that we are trialling to protect koalas as well," Professor Beagley said.

He said chlamydia in koalas was a significant cause of infertility, urinary tract infections, and inflammation in the lining of the eye that often led to blindness.

"The number of koalas with chlamydia seems to be increasing and when combined with habitat destruction, chlamydial disease continues to be a major threat to koalas' survival," he said.

Professors Timms and Beagley said that despite the importance of developing a vaccine against chlamydia for koalas the team is struggling to raise enough funds to continue their work.

## Researchers find a partially shared genetic profile between schizophrenia and bipolar disorder

Philadelphia, PA, July 17, 2008 – Both schizophrenia and bipolar disorder can be disabling conditions, and both present clinically with significant mood and psychotic symptoms. These two illnesses also share genetic variants that might be involved in the predisposition to both disorders. A new study scheduled for publication in the July 15th issue of Biological Psychiatry sought to analyze the patterns of gene expression in the brains of individuals diagnosed with one of these disorders to search for a common "characteristic [genetic] signature."

Using microarray gene expression, Drs. Ling Shao and Marquis Vawter tested whether there was a core set of genes shared in the predisposition or long term consequences of both illnesses. The researchers found 78 dysregulated genes, representing genes involved in nervous system development and cell death, which displayed differential expression compared to control subjects. As Dr. Vawter further explains, "the pattern of dysregulation was similar in the prefrontal cortex for both illnesses and pointed to key processes. Part of the set of core genes could be explained by medication responses; however most of these core genes did not appear to be correlated to medication response."

John H. Krystal, M.D., Editor of Biological Psychiatry and affiliated with both Yale University School of Medicine and the VA Connecticut Healthcare System, adds: "The new findings by Drs. Shao and Vawter provide evidence that there are a large number of genes that show a similar pattern of abnormal regulation in their sample of post-mortem brain tissue from individuals who had been diagnosed with schizophrenia or bipolar disorder. This overlap could provide insight into the neurobiology of both disorders." Better

understanding of the neurobiology related to the shared genes may offer a window into discovery of common brain mechanism(s) that could guide the identification of new and more effective treatments.

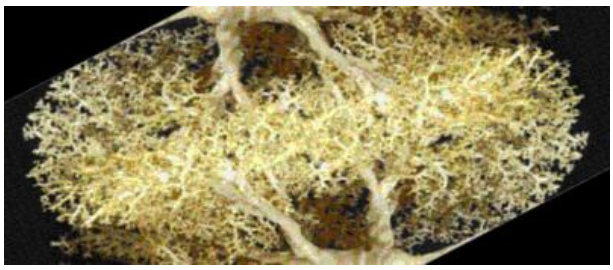
The authors also mention in their article recent discussions that have focused on considering schizophrenia and bipolar disorder as a single illness viewed along a continuum of mood and psychotic symptoms. Dr. Krystal concurs, noting that "we have traditionally treated these diagnoses as unrelated conditions even though many of the same medications, such as antipsychotic medications, are used to treat both conditions." Thus, there may be a need for our understanding of psychiatric diagnoses to evolve to fit the growing support of some common disease-related mechanisms that cross diagnostic boundaries, as evidenced by the findings in this study.

***Notes to Editors:*** *The article is "Shared Gene Expression Alterations in Schizophrenia and Bipolar Disorder" by Ling Shao and Marquis P. Vawter. Drs. Shao and Vawter are affiliated with the Department of Psychiatry and Human Behavior, Functional Genomics Laboratory, School of Medicine, University of California, Irvine, California. The article appears in Biological Psychiatry, Volume 64, Issue 2 (July 15, 2008), published by Elsevier.*

*The authors' disclosures of financial and conflicts of interests are available in the article. Dr. Krystal's disclosures of financial and conflicts of interests are available at http://journals.elsevierhealth.com/webfiles/images/journals/bps/Biological_Psychiatry_Editorial_Disclosures_02_22_08.pdf. Full text of the article mentioned above is available upon request. Contact Jayne M. Dawkins at (215) 239-3674 or ja.dawkins@elsevier.com to obtain a copy or to schedule an interview.*

## Tree branching key to efficient flow in nature and novel materials

DURHAM, N.C. – Nature, in the simple form of a tree canopy, appears to provide keen insights into the best way to design complex systems to move substances from one place to another, an essential ingredient in the development of novel "smart" materials.



***Canopy-to-Canopy*** **Adrian Bejan**

Duke University engineers believe that an image of two tree canopies touching top-to-top can guide their efforts to most efficiently control the flow of liquids in new materials, including the next generation of aircraft and rocket "skins" that can self-repair when damaged, or self-cool when overheated.

"Examples of this branching design tendency are everywhere in nature, from the channels making up river deltas to the architecture of the human lung, where cascading pathways of air tubes deliver oxygen to tissues," said Adrian Bejan, J.A. Jones Professor of Mechanical Engineering at Duke's Pratt School of Engineering.

Developing the most efficient and effective manner of controlling flow is becoming increasingly important, as engineers strive to create the next generation of nanodevices and "smart" materials. The goal of this research is to create materials that act like human skin by delivering liquid healing agents through a network much like blood vessels. Materials such as these will need efficient delivery systems, Bejan said.

Working with Sylvie Lorente, professor of civil engineering at the University of Toulouse, France, Bejan found that the laws of constructal theory (http://www.constructal.org/), which he first described in 1996, could guide the creation of these novel "smart" materials.

The constructal theory is based on the principle that flow systems evolve to minimize imperfections, reducing friction or other forms of resistance, so that the least amount of useful energy is lost. The theory applies to virtually everything that moves, Bejan said.

"We examined a flow system that looks more like the canopy-to-canopy model and found it to be more efficient than models in use now that are made up of parallel flow channels," said Bejan, whose analysis was published early online in the Journal of Applied Physics. The research was supported by the Air Force Office of Scientific Research and Lawrence Livermore National Laboratory. "We believe that this strategy will allow for the design of progressively more complex vascular flow systems."

In addition to finding that flow is maximized by these branching larger-to-smaller-to-larger systems, the researchers discovered that to maintain this gain in efficiency, the tree vasculature needs to become more complex as the flow increases. This is an important insight, Bejan said, because as new "smart" components become smaller, the efficiency of the flow systems will need to increase.

"Constructal design concepts serve the vascularization needs of these new 'smart' structures ideally, because trees have evolved a natural architecture for maximally delivering water throughout the tree volume," Bejan said. "If a single stream is to touch a structure at every point, then that stream must serve that structure much like a tree, or much in way the bronchial tree supplies air to the total lung volume."

Earlier, the constructal law was used to explain traffic flows, the cooling of small-scale electronics and river currents. Bejan recently reported that the theory can explain basic characteristics of locomotion for every creature, whether they run, swim or fly. The physics principle also explains many essential features of global

circulation and climate, including the boundaries between different climate zones, average wind speed and the average temperature difference between night and day.

Most recently, Bejan demonstrated that the constructal theory also helps explain why annual college rankings tend not to undergo major changes year-to-year.

## UNC, Caltech research finds further evidence for genetic contribution to autism

Some parents of children with autism evaluate facial expressions differently than the rest of us – and in a way that is strikingly similar to autistic patients themselves, according to new research by psychiatrist Dr. Joe Piven of the University of North Carolina at Chapel Hill and neuroscientist Ralph Adolphs, Ph.D., of the California Institute of Technology.

Piven, Adolphs and colleague Michael Spezio, Ph.D., formerly of Caltech but now at Scripps College in Claremont, Calif., collaborated to study 42 parents of children with autism, a complex developmental disability that affects an individual's ability to interact socially and communicate with others. Based on psychological testing, 15 of the parents were classified as being socially aloof.

"This manifests as a tendency not to prefer interactions with others, not to enjoy 'small talk' for the sake of the social experience and to have few close friendships involving sharing and mutual support," said Piven, senior author of the study, Sarah Graham Kenan professor of psychiatry in the UNC School of Medicine and director of the newly established Carolina Institute for Developmental Disabilities. "This characteristic is really a variation of normal and not associated with any functional impairment."

The parents participated in an experiment that measured how they make use of the face to judge emotions. The subjects were shown images depicting facial expressions of emotion that were digitally filtered so that only certain regions of the face were discernible – the left eye, for example, or the mouth. The subjects were then asked to decide as quickly as possible if the emotion depicted was "happy" or "fear." The part of the face shown and the size of the revealed area randomly varied from trial to trial.

An analysis of the subjects' correct responses revealed that "aloof" parents relied much more heavily on the mouth to recognize emotion than they did on the eyes, as compared to non-aloof parents and, to a greater extent, to a group of parents of children without autism. Prior studies by Adolphs and his colleagues have shown that humans normally evaluate emotions by looking at the eyes – but studies by Adolphs and Piven have shown that individuals with autism do not.

"We found that some parents who have a child with autism process face information in a subtly but clearly different way from other parents," Adolphs said. "This is evidence for the hypothesis that the parents with the autistic child have brains that function somewhat differently as well."

He and other researchers are currently investigating that idea through brain imaging studies. One area of interest is the amygdala, a region located on either side of the brain in the medial temporal lobe that is known to process information about facial emotions and may have abnormal volume in both autistic individuals and their nonautistic siblings.

The finding indicates that certain aspects of autism do run in families. Although such a genetic link was noted in the 1940s in the earliest descriptions of autism, "our study adds considerable specific detail to the story," Adolphs said.

"Our data strongly suggest that genetic factors make a substantial contribution to autism, but that does not mean that all of the cause of autism is genetic. Together with many other studies, our study argues that genetic factors play a very important role in autism, while leaving open a role for other, environmental factors," he said.

UNC and Caltech are currently working together to follow up on the finding by looking at the neural circuitry of face processing in parents of autistic individuals, using functional MRI in a National Institutes of Health-funded study.

"We hope that this research contributes towards a cure for autism, even if only indirectly," Adolphs said. "Once we understand better how people with autism – and their relatives – process social information like information about the faces of other people they look at, we will be in a better position to teach them strategies for social interaction and will be able to explain to them how they differ from neurotypical people."

Piven said that this approach may disaggregate the phenotype in autism and provide new targets for genetic studies. "In other words, it may lead us to finding genes that are responsible for the face-processing component in autism," he said.

The researchers noted that an important part of the paper is that it is not claiming all people with autism – or their parents – are 'impaired'. Instead, they said the study shows that parents who have children with autism – like the autistic subjects themselves – are different and do things differently.

*The paper, "Selective face processing abnormalities in parents of autistic children," is published in the journal Current Biology, and is available at http://www.current-biology.com .*

*The research was funded by grants from the National Institutes of Health and the Simons Foundation.*

# 'Ten Commandments' of race and genetics issued

* Updated 18:13 18 July 2008
* NewScientist.com news service

*** Devin Powell**

Even with the human genome in hand, geneticists are split about how to deal with issues of race, genetics and medicine.

Some favor using genetic markers to sort humans into groups based on ancestral origin – groups that may show meaningful health differences. Others argue that genetic variations across the human species are too gradual to support such divisions and that any categorisation based on genetic differences is arbitrary.

These issues have been discussed in depth by a multidisciplinary group – ranging from geneticists and psychologists to historians and philosophers – led by Sandra Soo-Jin Lee of Stanford University, California.

Now the group has released a set of 10 guiding principles for the scientific community, published as an open letter in this week's Genome Biology.

1. All races are created equal

No genetic data has ever shown that one group of people is inherently superior to another. Equality is a moral value central to the idea of human rights; discrimination against any group should never be tolerated.

2. An Argentinian and an Australian are more likely to have differences in their DNA than two Argentinians

Groups of human beings have moved around throughout history. Those that share the same culture, language or location tend to have different genetic variations than other groups. This is becoming less true, though, as populations mix.

3. A person's history isn't written only in his or her genes

Everyone's genetic material carries a useful, though incomplete, map of his or her ancestors' travels. Studies looking for health disparities between individuals shouldn't rely solely on this identity. They should also consider a person's cultural background.

4: Members of the same race may have different underlying genetics

Social definitions of what it means to be "Hispanic" or "black" have changed over time. People who claim the same race may actually have very different genetic histories.

5. Both nature and nurture play important parts in our behaviors and abilities

Trying to use genetic differences between groups to show differences in intelligence, violent behaviors or the ability to throw a ball is an oversimplification of much more complicated interactions between genetics and environment.

6. Researchers should be careful about using racial groups when designing experiments

When scientists decide to divide their subjects into groups based on ethnicity, they need to be clear about why and how these divisions are made to avoid contributing to stereotypes.

7. Medicine should focus on the individual, not the race

Although some diseases are connected to genetic markers, these markers tend to be found in many different racial groups. Overemphasising genetics may promote racist views or focus attention on a group when it should be on the individual.

8. The study of genetics requires cooperation between experts in many different fields

Human disease is the product of a mishmash of factors: genetic, cultural, economic and behavioral. Interdisciplinary efforts that involve the social sciences are more likely to be successful.

9. Oversimplified science feeds popular misconceptions

Policy makers should be careful about simplifying and politicising scientific data. When presenting science to the public, the media should address the limitations of race-related research.

10. Genetics 101 should include a history of racism

Any high school or college student learning about genetics should also learn about misguided attempts in the past to use science to justify racism. New textbooks should be developed for this purpose.

The Stanford group didn't always agree when coming up with these ideas. Predictably enough, the biomedical scientists tended to think of race in neutral, clinical terms; the social scientists and scholars of the humanities argued that concepts of race cannot be washed clean of their cultural and historical legacies.

But both groups, according to the letter, recognise the power of the gene in the public imagination and the historical dangers of its misrepresentation as deterministic and immutable.

*Journal reference: Genome Biology (DOI: 10.1186/gb-2007-9-7-404)*

## As rates rise, researchers find better way to identify melanoma

University of Rochester Medical Center researchers found a new protein produced excessively in malignant melanoma, a discovery that is particularly relevant as skin cancer rates climb dramatically among young women.

The protein, IMP-3, is not over-expressed in harmless moles but is increased in the most dangerous types of skin cancer, and in a subset of lesions that can be difficult to predict called thin melanomas. The finding offers a potential target for treatment - but perhaps most importantly might give doctors a new, objective way to distinguish melanoma from some benign moles that look like melanoma but are not cancerous.

"We are very excited about our finding that IMP-3 is an important progression marker in malignant melanoma," said first author Jennifer G. Pryor, M.D., a third-year resident in the URMC Department of Pathology and Laboratory Medicine. "Although we have learned a lot about melanoma in recent years, it has unique biologic properties that sometimes make it difficult to diagnose and to plan for the proper treatment. This protein may have a key role in helping us to understand and distinguish between various types of melanocytic lesions." The research is published in the journal Modern Pathology. http://www.nature.com/modpathol/journal/v21/n4/full/3801016a.html

This summer the National Cancer Institute warned that new cases of melanoma among young women jumped 50 percent since 1980. Possible explanations, medical experts said, include increased use of tanning beds and more time spent outdoors. Overall rates of melanoma have also been rising among older adults.

The pilot study investigated samples of 56 biopsied lesions from 48 adults. The lesions fell into the category of cutaneous melanocytic neoplasms, a diverse group that includes benign moles; Spitz nevi, a type of mole seen in younger people that can be easily mistaken for melanoma but is not cancerous; and malignant melanoma, which has several phases of growth.

Pathologists play a major role in diagnosing and staging skin cancers, by sorting through neoplasms and identifying features. They analyze cells within the lesions and apply chemical stains and other tools to measure the depth and predict future behavior of the growths.

This study by Pryor and co-authors showed why IMP-3 might be an important tool for pathologists. None of the benign moles or the benign moles with irregular features and some abnormal cells over-expressed the IMP-3 protein. However, the protein was produced excessively in most melanomas, and overly expressed more often in metastatic melanomas.

IMP-3 was also over-expressed in rare cases of invasive thin melanomas. This is significant because most thin melanomas have a good prognosis, but some act more aggressively and currently there is no accurate way to distinguish between the types of thin lesions.

IMP-3 is an insulin-like growth factor-II mRNA binding protein. It is involved in cell proliferation and appears to play a role in tumor formation in a number of cancers.

In previous studies expression of the IMP-3 protein has been linked to pancreas, kidney, ovary and lung cancers, but this is the first published study to demonstrate a connection to melanoma, Pryor said.

Additional research is needed to compare IMP-3 expression with long-term survival data from thin melanoma patients, to find out if patients whose tumors express IMP-3 might benefit from more careful monitoring and aggressive treatment, the study noted.

The antibody used in this research was obtained from the Dako Corporation of California, through a collaborative arrangement initiated by the corresponding author, Haodong Xu, M.D., Ph.D., associate professor of Pathology and Laboratory Medicine at URMC. Xu and his colleagues have previously published studies of IMP-3 as a potential therapeutic target for high grade neuroendocrine carcinomas.

*The URMC Department of Pathology and Laboratory Medicine funded the research. Additional co-authors on the paper include Patricia A Bourne, former laboratory supervisor; Qi Yang, laboratory technologist; Glynis Scott, M.D., professor, URMC Department of Dermatology; and Betsy O. Spaulding, of the Dako Corporation.*

## Research Publications Online: Too Much of A Good Thing?

### *New research shows that as more scholarly and research journals are available online, researchers cite fewer, newer papers*

The Internet gives scientists and researchers instant access to an astonishing number of academic journals. So what is the impact of having such a wealth of information at their fingertips? The answer, according to new research released today in the journal Science, is surprising--scholars are actually citing fewer papers in their own work, and the papers they do cite tend to be more recent publications. This trend may be limiting the creation of new ideas and theories.

James Evans is an assistant professor of sociology at the University of Chicago, who focuses on the nature of scholarly research. During a lecture on the influence of private industry money on research, a student instead

asked how the growth of the Internet has shaped science. "I didn't have an immediate answer," Evans said in an interview last week.

When he reviewed the research on the Internet and science, Evans discovered that most of it focused on much faster and broader the Internet allows scholars to search for information, but not how the medium itself was impacting their work. "That's where this idea came from. I wanted to know how electronic provision changed science, not how much better it made it," he said.

After receiving support from the National Science Foundation to pursue this question, Evans analyzed a database of over 34 million articles and compared their online availability from 1998 to 2005 to the number of times they were cited from1945 to 2005. The results showed that as more journal issues came online, few articles were cited, and the ones that were cited tended to be more recent publications. Scholars also seemed to concentrate their citations more on specific journals and articles. "More is available," Evans said, "but less is sampled, and what is sampled is more recent and located in the most prominent journals."

***Having research papers and other scholarly writing available online gives researchers access to a great deal of materials without having to enter a library. But how does this impact the new research that they produce? James Evans at the University of Chicago has studied this question and his conclusion is surprising--despite having greater access to scholarly materials, researchers are actually citing fewer papers. The papers they do cite tend to be newer and are likely to be cited by other researchers.*** **Credit: Jupiter Images**

Evans's research also found that this trend was not evenly distributed across academic disciplines. Scientists and scholars in the life sciences showed the greatest propensity for referencing fewer articles, but the trend is less noticeable in business and legal scholarship. Social scientists and scholars in the humanities are more likely to cite newer works than other disciplines.

So what is it about doing research online versus in a bricks-and-mortar library that changes the literature review so critical to research? Evans has identified a few possible explanations. Studies into how research is conducted show that people browse and peruse material in a library, but they tend to search for articles online Online searches tend to organize results by date and relevance, which leads allows scholars and scientists to pick recent research from the most high profile journals. Some search tools like Google factor the frequency with which other users select an item during similar searchers to determine relevance. Online, researchers are also more likely to follow hyper-linked references and links to similar work within an online archive. Because of this, as more scholars choose to read and reference a given article, future researchers more quickly follow.

Does this phenomenon spell the end of the literature review? Evans doesn't think so, but he does believe that it makes scholars and scientists more likely to come to a consensus and establish a conventional wisdom on a given topic faster. "Online access facilitates a convergence on what science is picked up and built upon in subsequent research." The danger in this, he believes, is that if new productive ideas and theories aren't picked up quickly by the research community, they may fade before their useful impact is evaluated. "It's like new movies. If movies don't get watched the first weekend, they're dropped silently," Evans said.

Evans plans to work with linguists and computer scientists to explore how ideas are expressed in articles to better understand what the consequences of losing old ideas are and how they can be retrieved and resurrected, a challenge he sees as being important in the pursuit of knowledge. "With science and scholarship increasing online, findings and ideas that don't receive attention very soon will be forgotten more quickly than ever before." -**NSF-** ***View a video interview with sociologist James Evans of the University of Chicago.***
*http://nsfgov.httpsvc.vitalstreamcdn.com/nsfgov_vitalstream_com/internet_citation.swf*

## When Fish Talk, Scientists Listen

### *MBL Visiting Investigators Explore the Evolution of Social Communication*

MBL, WOODS HOLE, MA—A male midshipman, a close relative of the toadfish, doesn't need good looks to attract a mate – just a nice voice. After building a nest for his potential partner, he calls to nearby females by contracting his swim bladder, the air-filled sac fish use to maintain buoyancy. The sound he makes is not a song or a whistle, but a hum; more reminiscent of a long-winded foghorn than a ballad. Female midshipman find it very alluring, and they only approach a male's nest if he makes this call.

In a paper published this week in Science, three Marine Biological Laboratory (MBL) visiting investigators show that the sophisticated neural circuitry that midshipman use to vocalize develops in a similar region of the central nervous system as the circuitry that allows a human to laugh or a frog to croak, evidence that the ability to make and respond to sound is an ancient part of the vertebrate success story. The research is presented by

Andrew Bass of Cornell University, Edwin Gilland of Howard University College of Medicine, and Robert Baker of New York University Medical Center.

"Fish have all the same parts of the brain that you do," says Bass, the paper's lead author. The way our brains work is also similar. Just as we have neurons that coordinate when our larynx and tongue change shape to produce words, toadfish and midshipman orchestrate the movement of muscles attached to their swim bladder to produce grunts and hums.

***Closeup of the head of a male Gulf toadfish, Opsanus beta. Toadfish are close relatives of midshipman (same family of teleost fish) that also vocalizes to attract females to his nest (there is no evidence of two male morphs in this species). Gulf toadfish build their nests in shallow waters along the southeastern and Gulf coasts of the United States.***

Using larval toadfish and midshipman, the group traced the development of the connection from the animal's vocal muscles to a cluster of neurons located in a compartment between the back of its brain and the front of its spinal cord. The same part of the brain in more complex vertebrates, such as humans, has a similar function, indicating that it was highly selected for during the course of evolution.

Scientists have known for decades that these fish make sounds, but they are not the only species whose hums, growls, and grunts have meaning. "There's reason to suggest that the use of sound in social communication is widespread among fishes," Bass says.

This research is an example of the growing field of evolutionary neurobiology, which aims to understand the evolution of behavior through neurobiology. According to Bass, fish are an incredibly successful group, making up nearly half of the living species of vertebrates, and vocal communication may be partly responsible. "The kind of work we're doing contributes to answering questions as to why these animals are so successful," Bass says. "We're only touching the tip of the iceberg here."

The majority of this research was completed at the MBL over the past five years, although the question of how fish communicate through sound first came to Bass as a graduate student studying the neurobiology of fish at the University of Michigan. In the summer of 1986, Bass, then a summer instructor at the MBL, met Robert Baker, who was also researching the neurobiology of fish calling. For years they discussed fish social behavior with the roots of the hypothesis tested in the Science paper first published in 1997 and the research to test that hypothesis beginning in 2003. "The whole project began at the MBL," Bass says. "It's where collaborations happen."

## Coffee and cigarette consumption are high among AA attendees

* More than one million Americans currently participate in the Alcoholics Anonymous (AA) program.

* Recent findings confirm that coffee and cigarette use among AA members is greater than among the general U.S. population.

* Most AA members drink coffee for its stimulatory effects; more than half smoke to reduce feelings of depression, anxiety and irritability.

More than one million Americans currently participate in the Alcoholics Anonymous (AA) program. While AA participants are reportedly notorious for their coffee drinking and cigarette smoking, very little research has quantified their consumption of these two products. Recent findings confirm that coffee and cigarette use among this population is greater than among the general U.S. population: most AA members drink coffee and more than half smoke.

Results will be published in the October issue of Alcoholism: Clinical & Experimental Research and are currently available at Early View.

"Drinking coffee and smoking cigarettes are part of the culture of AA, but we knew little about the degree to which this occurred, how much more prevalent these behaviors were compared to the general American population, or why AA participants actually drank coffee or smoked cigarettes," said Peter R. Martin, professor of psychiatry and pharmacology, director of the Vanderbilt Addiction Center at the Vanderbilt University School of Medicine, and corresponding author for the study.

Martin added that many questions remain about the effects of coffee and cigarettes on recovering alcoholics. "What do cigarettes or coffee do for them; how do they believe that they are affected by smoking and drinking coffee?," he asked. "Is this behavior simply a way to bond or connect in AA meetings, analogous to the peace pipe among North American Indians, or do constituents of these natural compounds result in pharmacological actions that affect the brain? Perhaps most interesting, how do these consummatory behaviors affect the brain and what is their role in recovery?"

While the most common cause of death in long-term recovering alcoholics is related to the health consequences of cigarette smoking, Martin noted, recent epidemiological studies have shown that coffee consumption is not harmful to health and may, in fact, reduce the risk of death from suicide, certain cancers, and other diseases.

While that may be true, noted Robert Swift, professor of psychiatry and human behavior at Brown University Medical School, little is known about coffee's role vis-à-vis abstinence, whether drinking coffee makes it easier or harder to stay sober. "It's possible that coffee is even a gateway drug, with coffee drinking beginning at about the time persons begin using alcohol. In addition, a potential negative interaction is coffee's known negative effects on sleep. Many alcoholics in long-term recovery frequently have trouble with sleep, and coffee consumption could make sleep problems worse."

A strength of this study, Swift added, is that relatively little is known about AA, why some persons are helped by it while others are not. "The authors have been successful in gaining the confidence of AA groups and incorporating them into a research study," he said.

Martin and his colleagues asked participants (n=289) in all open AA meetings during the summer of 2007 in Nashville, TN to self-report a variety of information: a "timeline followback" for coffee, cigarette and alcohol consumption, the AA Affiliation Scale, coffee consumption and effects questions, the Fagerstrom Test for Nicotine Dependence, and the Smoking Effects Questionnaire.

"The most important finding was that not all recovering alcoholics smoke cigarettes while almost all drink coffee," said Martin.

More specifically, most individuals (88.5%) consumed coffee and approximately 33 percent drank more than four cups per day. The most common self-reported reasons were because of coffee's stimulatory effects: feeling better, better concentration, greater alertness. More than half of the respondents (56.9%) smoked cigarettes; of those, 78.7 percent smoked at least half a pack per day, and more than 60 percent were considered highly or very highly dependent. The most common self-reported reasons were because of smoking's reduction of "negative affect," which refers to depression, anxiety and irritability. "Many of these negative affective states are described by patients as contributors or triggers to relapse after periods of sobriety," said Martin.

"I think that it is important for alcohol researchers and clinicians to know that alcoholics, even those who do not use other illicit drugs, are not just addicted to alcohol, but use other psychotropic drugs like caffeine and nicotine," said Swift. "I found it interesting that coffee contains a lot of psychoactive substances, in addition to caffeine. A second important aspect is the finding that rates of smoking are much higher in alcoholics in recovery than in the general population. Smoking kills and is at least as harmful for alcoholics as is alcohol. Yet, AA tolerates or otherwise does not address smoking in its members."

"Yet, if coffee is beneficial and cigarettes are harmful to health, AA members seem to be going in the right direction by reducing smoking and perhaps increasing their coffee drinking," observed Martin. "We are now working on more detailed analyses of results to examine whether these changes in coffee and cigarette use are predictive of recovery from alcoholism per se."

*Alcoholism: Clinical & Experimental Research (ACER) is the official journal of the Research Society on Alcoholism and the International Society for Biomedical Research on Alcoholism. Co-authors of the ACER paper, "Coffee and Cigarette Consumption and Perceived Effects in Recovering Alcoholics Participating in Alcoholics Anonymous in Nashville, TN," were: Michael S. Reich and A.J. Reid Finlayson in the Vanderbilt Addiction Center in the Department of Psychiatry at Vanderbilt University School of Medicine; Mary S. Dietrich in the Department of Biostatistics at the Vanderbilt University School of Medicine; and Edward F. Fischer in the Department of Anthropology at Vanderbilt University. The study was funded by the National Institute on Alcohol Abuse and Alcoholism, and the National Institute on Drug Abuse.*

## Loud music can make you drink more, in less time, in a bar

Commercial venues are very aware of the effects that the environment – in this case, music – can have on in-store traffic flow, sales volumes, product choices, and consumer time spent in the immediate vicinity. A study of the effects of music levels on drinking in a bar setting has found that loud music leads to more drinking in less time.

Results will be published in the October issue of Alcoholism: Clinical & Experimental Research and are currently available at Early View.

"Previous research had shown that fast music can cause fast drinking, and that music versus no music can cause a person to spend more time in a bar," said Nicolas Guéguen, a professor of behavioral sciences at the Université de Bretagne-Sud in France, and corresponding author for the study. "This is the first time that an experimental approach in a real context found the effects of loud music on alcohol consumption."

Researchers discretely visited two bars for three Saturday evenings in a medium-size city located in the west of France. The study subjects, 40 males 18 to 25 years of age, were unaware that they were being observed;

only those who ordered a glass of draft beer (25 cl. or 8 oz.) were included. With permission from the bar owners, observers would randomly manipulate the sound levels (either 72 dB, considered normal, or 88 dB, considered high) of the music in the bar (Top 40 songs) before choosing a participant. After the observed participant left the bar, sound levels were again randomly selected and a new participant was chosen.

Results showed that high sound levels led to increased drinking, within a decreased amount of time.

Guéguen and his colleagues offered two hypotheses for why this may have occurred. "One, in agreement with previous research on music, food and drink, high sound levels may have caused higher arousal, which led the subjects to drink faster and to order more drinks,"" said Guéguen. "Two, loud music may have had a negative effect on social interaction in the bar, so that patrons drank more because they talked less."

In France, observed Guéguen, more than 70,000 persons per year die because of chronic alcohol consumption, and alcohol is associated with the majority of fatal car accidents. "We have shown that environmental music played in a bar is associated with an increase in drinking," he said. "We need to encourage bar owners to play music at more of a moderate level ... and make consumers aware that loud music can influence their alcohol consumption."

*Alcoholism: Clinical & Experimental Research (ACER) is the official journal of the Research Society on Alcoholism and the International Society for Biomedical Research on Alcoholism. Co-authors of the ACER paper, "Sound Level of Environmental Music and Drinking Behavior: A Field Experiment with Beer Drinkers," were: C. Jacob, H. Le Guellec, and T. Morineau of the Université de Bretagne-Sud; and M. Lourel of the Université de Rouen. The study was funded by the Centre de Recherches en Psychologie, Cognition & Communication through the Université de Bretagne-Sud.*

## Saharan dust storms sustain life in Atlantic Ocean

***Research at the University of Liverpool has found how Saharan dust storms help sustain life over extensive regions of the North Atlantic Ocean***

Research at the University of Liverpool has found how Saharan dust storms help sustain life over extensive regions of the North Atlantic Ocean.

Working aboard research vessels in the Atlantic, scientists mapped the distribution of nutrients including phosphorous and nitrogen and investigated how organisms such as phytoplankton are sustained in areas with low nutrient levels.

They found that plants are able to grow in these regions because they are able to take advantage of iron minerals in Saharan dust storms. This allows them to use organic or 'recycled' material from dead or decaying plants when nutrients such as phosphorous – an essential component of DNA – in the ocean are low.

Professor George Wolff, from the University's Department of Earth and Ocean Sciences, explains: "We found that cyanobacteria – a type of ancient phytoplankton – are significant to the understanding of how ocean deserts can support plant growth. Cyanobacteria need nitrogen, phosphorous and iron in order to grow. They get nitrogen from the atmosphere, but phosphorous is a highly reactive chemical that is scarce in sea water and is not found in the Earth's atmosphere. Iron is present only in tiny amounts in sea water, even though it is one of the most abundant elements on earth.

"Our findings suggest that Saharan dust storms are largely responsible for the significant difference between the numbers of cyanobacteria in the North and South Atlantic. The dust fertilises the North Atlantic and allows phytoplankton to use organic phosphorous, but it doesn't reach the southern regions and so without enough iron, phytoplankton are unable to use the organic material and don't grow as successfully."

Professor Ric Williams, co-author of the research, added: "The Atlantic is often referred to as an 'ocean desert' because many nutrients, which are essential in plant life cycles, are either scarce or are only accessible in the darker depths of the ocean. Plants, however, need some sunlight in order to absorb these important nutrients and so can't always access them from the ocean depths. They therefore need to find the nutrients from elsewhere. Now that we are able to show how cyanobacteria make use of organic material we can understand more clearly how life is sustained in the ocean and why it isn't an 'ocean desert.'

"These findings are important because plant life cycles are essential in maintaining the balance of gases in our atmosphere. In looking at how plants survive in this area, we have shown how the Atlantic is able to draw down carbon dioxide from the atmosphere through the growth of photosynthesising plants."

*The research is published in Nature GeoScience.*

## HIV conquers immune system faster than previously realized

DURHAM, N.C. – New research into the earliest events occurring immediately upon infection with HIV-I shows that the virus deals a stunning blow to the immune system earlier than was previously understood. According to scientists at Duke University Medical Center, this suggests the window of opportunity for successful intervention may be only a matter of days – not weeks – after transmission, as researchers had previously believed.

Appearing in the August issue of the Journal of Virology, the finding may make the challenge of designing an effective HIV/AIDS vaccine appear daunting. But researchers say the study has also yielded a blueprint for what a successful vaccine should look like, and moreover, when such a vaccine would need to work.

Until now, scientists believed that the window of opportunity to intervene in the process of HIV-1 infection lay in the three to four weeks between transmission and the development of an established pool of infected CD4 T cells. HIV-1 cripples the immune system by invading and killing CD4 T cells, key infection-fighters in the body.

"But this new study shows that HIV-I does a lot of damage to the immune system very early in that time frame, and now we feel that the opportunity to intervene most effectively may range from about five to seven days after infection," said Barton Haynes, M.D., the senior author of the study and director of the Center for HIV/AIDS Vaccine Immunology (CHAVI) at Duke University Medical Center.

Haynes said the findings suggest that an optimal vaccine strategy would have to pack a double punch: First, establishing as much immunity as possible before infection, much as classic vaccines do, and then following a few days later with a mechanism to provoke a strong, secondary, broad-based antibody response. "Vaccine candidates to date have pretty much followed a single strategy. Now we know that we need to activate multiple arms of the immune system and we have a better idea of when to do it."

The conclusion comes from the study of 30 people who were newly-infected with HIV-1. Plasma from these individuals was sampled every three days for several months – before, during, and after the "ramp-up" phase of infection, when HIV-1 is multiplying rapidly and heading toward its peak viral load. In measuring the levels of four products of CD4 T cell death during this period in these samples, they were able to track and establish a timetable of the virus's destructive path.

The four byproducts of CD4 T cell death include TRAIL (tumor necrosis factor-related apoptosis-inducing ligand), Fas ligand, TNF receptor type 2 and plasma microparticles, tiny bits of cell membrane that are broken up and left floating around in the plasma when the cell dies and breaks apart.

The researchers found that TRAIL levels increased significantly a full week (7.2. days) before peak viral load, which is approximately 17 days after HIV-1 transmission, suggesting that during the earliest period of infection, called the eclipse phase, TRAIL may actually initiate or hasten HIV-1's destruction of CD4 T cells. In contrast, they found that the levels of the other three cell death products were most significantly elevated during peak viral load.

"What this demonstrates is that significant T cell death is occurring much earlier during this period than we previously believed, and that TRAIL itself may be a co-conspirator in enhancing cell death," Haynes said. "This leads us to believe that the time frame for successful intervention has to move even close to the point of infection."

Researchers also examined the effects of cell death products upon B cells, another arm of the immune system responsible for the creation of antibodies. Previous studies have shown that the antibody response to HIV-1 is "too little, too late" – appearing after the virus has peaked and after the reservoir of infected T cells has already been established.

Through a series of in vitro laboratory experiments with peripheral blood cells, scientists found that microparticles suppressed levels of IgG and IgA, two classes of antibodies that normally would protect a person against infection. "This is important because many scientists believe that a fast-acting memory B cell response as well as a T cell response will be necessary to fight HIV-1" said Nancy Gasper-Smith, PhD, the lead author of the study.

Daniel Douek, M.D., PhD, chief of the Human Immunology Section of the National Institutes of Health, said the study sheds new light on key events in the earliest phase of infection. "The cohort is a gem. It is clear from the raised levels of TRAIL that the body senses the virus before plasma viral loads have peaked. This suggests that the virus begins to cause damage in ways that may be unrelated to the well-described massive depletion of gut CD4 T cells that becomes apparent around peak viral load. For clinical practice, this means the window of opportunity in which antiviral therapies and vaccines must act is becoming ever narrower."

"These and other studies that recently revealed more about the singular nature of HIV-1 have given us valuable information that is helping us move closer to establishing a basic science foundation that can lead to novel technologies for vaccine design, Haynes said. Haynes. "It is becoming clearer why we have failed in our efforts to date, and what we need to confront to succeed in the future."

*The study was supported by grants from the National Institutes of Health*

*Colleagues from Duke who contributed to the research include Deanna Crossman, John Whitesides, Nadia Mensali, Janet Ottinger, Steven Plonk, M. Anthony Moody, Guido Ferrari, Kent Weinhold, Sara Miller and Thomas Denny. Additional co-authors are David Pisetsky and Charles Reich, from the Durham Veterans Administration Hospital; Li Qin and Stephen Self,*

*from Fred Hutchinson Cancer Research Center and the Statistical Center for HIV-AIDS Research and Prevention; George Shaw from the*

## Averting postsurgical infections in kids: Give antibiotics within hour before first incision

Giving children preventive antibiotics within one hour before they undergo spinal surgery greatly reduces the risk for serious infections after the surgery, suggests a Johns Hopkins study to be published in the August issue of Pediatric Infectious Disease Journal (also available online ahead of print). Children who received antibiotics outside of the golden one-hour window were three and half times more likely to develop serious infections at the surgery site, researchers report, pointing out that something as simple as ensuring that a child gets timely prophylaxis can prevent serious complications and reduce the length of hospital stay.

"When it comes to preventing infections, when a child gets antibiotics appears to be one of the most critical yet most easily modifiable risk factors, and may matter just as much as the type and dosage of the medication ,"says lead researcher Aaron Milstone, M.D., infectious disease specialist at the Johns Hopkins Children's Center. "The moral of this is that an ounce of timely prevention is indeed worth a pound of treatment."

Nearly 780,000 postsurgical infections occur in the United States each year, according to estimates from the Institute for Healthcare Improvement. An infection after surgery nearly doubles a patient's risk of death, doubles a patient's hospital stay and adds up to $50,000 to treatment costs per patient, researchers say.

While preoperative antibiotic prophylaxis is standard in adults, there are no standard guidelines on how to administer antibiotics in children undergoing surgery.

Reviewing nearly 1,000 spinal fusion surgeries performed in children over a six-year period at Hopkins, investigators found 36 deep surgical site infections. More serious than superficial skin infections, these can cause serious complications and require aggressive treatment including additional surgeries and long-term antibiotics. Of the 36 cases, 28 percent received medication outside the one-hour window, either more than an hour before incision or after the surgery began. Other factors affecting infection risk included underlying medical conditions and previous spinal surgeries, researchers found.

Even though spinal fusion surgeries are complex procedures and thus carry higher risk for deep-site infections, the findings are likely relevant to many types of surgical procedures, the researchers say, because timing is always critical when administering antibiotics, either as treatment or prevention.

*Other Hopkins investigators in the study: Lisa Maragakis, M.D., Timothy Townsend, M.D., Kathleen Speck, M.P.H., Paul Sponseller, M.D., Xiaoyan Song, Ph.D., and Trish Perl, M.D., M.Sc. The research was funded by grants from the Centers for Disease Control and the Pediatric Infectious Diseases Society.*

*Full text of the Hopkins study: http://www.pidj.com/pt/re/pidj/pdfhandler.00006454-900000000-99856.pdf;jsessionid=L2QTt0vvxQQ5HyQgCd7LfpRH15s2N7GDJvhS1RJ0bWLLtzr4WC4j!-406629960!181195629!8091!-1*

## Analysis of Quickly Stopped Rx Orders Provides New Tool for Reducing Medical Errors

### *Penn Study Shows 66% of Medication Orders Stopped Within 45 Minutes are Bad Orders.*

PHILADELPHIA –By studying medication orders that are withdrawn ("discontinued") by physicians within 45 minutes of their origination, researchers at The University of Pennsylvania School of Medicine have demonstrated a systematic and efficient method of identifying prescribing errors. The method, they say, has value to screen for medication errors and as a teaching tool for physicians and physicians-in-training. The report is published in the July/August 2008 issue of the Journal of the American Medical Informatics Association.

Dr. Ross Koppel and colleagues at Penn's Department of Biostatistics and Epidemiology used a hospital's computerized physician order entry (CPOE) system to track prescriptions that were discontinued within 45 minutes. They found the rate of errors among the quickly stopped orders was 66%. The Rx problem may have been detected by the ordering physician, another physician, a pharmacist, or a nurse, but the prescribing physician issues the stop order.

The University of Pennsylvania team examined each order stopped within a two-hour time period, and when relevant, each subsequent order. Then they interviewed the prescribing physicians, asking about why they stopped the orders–looking at both who caught the error and the doctor's own explanation for the change. Often the reason for the change was obvious, e.g., a medication for the wrong eye, or a dose that was far too large. Sometimes the reasons were more subtle, e.g., a more appropriate antibiotic. Dr. Koppel notes the classes of drugs most likely to be quickly discontinued made sense because they were often among the most difficult-to-prescribe: low therapeutic index drugs, insulin, antiretrovirals, antineoplastics, and immunosuppressive drugs.

Prof. Koppel (a sociologist by training) said that although they originally focused on the two-hour period, they found that 45 minutes was the most efficient time cut for the measure. "Because this type of analysis is so new, we didn't know how long the post-ordering timeframe should be until we did it." By analyzing the

discontinued orders within 15-minute time blocks, we were able to glean insights into the most efficacious time parameter to maximize ratios of inappropriate-to-appropriate medication orders.

"Also, we did not count orders that were stopped within the first minute. That's so we didn't include typos and the kind of errors that would be the equivalent to tearing up a flawed paper prescription when writing it," said Koppel.

The researchers had a live transmission of every medication order as it was written, and were able to interview the ordering physicians within hours, often within minutes. The team conducted the research over the course of two months, selecting times and days that reflected the physicians' ordering patterns at the hospital.

Currently, methods of identifying prescribing errors are plagued with inaccuracies stemming from several systematic biases. Self-report and reports by colleagues are known to substantially under-represent reality. Examining medical records misses errors linked to undocumented diagnoses, as well as being time-consuming and expensive. Other manifestations of medication error go unrecognized, write the authors, because symptoms are often complex, patients have multiple problems and polypharmacy may obscure causes and outcomes. The paper identifies eight methods of detecting medication error and summarizes their shortcomings. Koppel added that "prescription errors are often obscured by the messy reality of illness, multi-faceted treatments, and the rapid pace and complexity of an acute care hospital"

The measure proposed here, while preliminary, indicates that 66% of prescriptions discontinued within 45 minutes after their origination are inappropriate. Even beyond the ratio comparisons, the value of this measure is several-fold: When linked to a CPOE system, it is rapid, constant (24/7), and does not depend on possibly biased evaluators, self-report, or others' reports. Data collection is also cost-free as part of a CPOE system.

Moreover, suggested one of the study's co-authors, Brian L. Strom, MD, MPH, Chairman and Professor of the Center for Clinical Epidemiology & Biostatistics at Penn, "although the remaining proportion of rapidly stopped orders could not be substantiated as inappropriate, it could be argued that almost all of these orders were perceived as problematic by their authors—that is why they stopped them."

Difficulties identifying and measuring medication errors are a constant theme of the hospital patient safety literature. Many scholars indicate such difficulties are critical barriers to addressing medication errors. Koppel added that "Our method does not replace the others, but may add a technique that appears both efficient and objective. It can identify and help physicians who are having problems with a particular group of medications or patient types and can help post-graduate medical educators focus on areas requiring additional training."

## PCI preference -- will that be an arm or a leg?

DURHAM, N.C. – When it comes to stenting – using metal tubes to prop open blocked arteries – physicians are continuing to choose to gain entry to the circulatory system through an opening in the leg instead of the arm, even though the latter option appears to be safer, with fewer side effects, say researchers at Duke Clinical Research Institute.

"Bleeding complications are reduced by 70 percent when interventional cardiologists go in through a radial artery in the wrist," says Dr. Sunil Rao, a cardiologist at Duke and the lead author of the study. "But our research shows that only a tiny fraction of stenting procedures are done this way. The study suggests that maybe it's time to change the way we practice."

Researchers reviewed data from 593,094 cases of percutaneous coronary intervention (PCI) in 606 hospitals across the U.S. included in the National Cardiovascular Data Registry from 2004 to 2007. They tracked the incidence of radial PCI (r-PCI) versus leg or femoral PCI (f-PCI) during that period and calculated which patients were more likely to get which option.

They found that the arm approach had gained favor over the four-year period, but still comprised only 1.3 percent of the total number of procedures. They also found that 40 percent of radial PCI was performed in only seven centers. Academic medical centers were more likely to be sites of higher r-PCI use than centers not affiliated with a college or university.

The data further revealed that r-PCI was more likely to be chosen as an approach for younger patients, those with significantly higher body mass index and patients with a higher prevalence of peripheral vascular disease

The study appears in the August issue of Journal of the American College of Cardiology: Cardiovascular Intervention. The study was funded by the National Cardiovascular Data Registry and the American College of Cardiology.

"The findings are somewhat surprising, given that numerous studies have shown that r-PCI is similarly successful to f-PCI, and that r-PCI can significantly lower risk of bleeding, especially among women, patients younger than 75 and people undergoing PCI for acute coronary syndrome," says Rao. He says previous studies have also shown that r-PCI may cost less because it can mean shorter time in the hospital for some patients.

A decade's worth of skilled training and technical advances in stent design has contributed to an increased safety profile for most stenting procedures. But Rao says bleeding can be a complication in about 10 percent of some procedures. While most bleeding is minor, such bleeding can be life-threatening in a small number of cases. PCI also carries a slight risk of death from blood clots or ruptured arterial walls.

Rao uses r-PCI himself almost exclusively, reserving f-PCI for three types of cases: where the catheter is too big to fit inside the radial artery; in cases where the patient has had coronary bypass surgery, which can complicate access from the left wrist; or in cases where there is no alternate blood flow to the hand.

Rao notes that r-PCI is the preferred option in Europe. He says slower acceptance of the technique in the United States may be due to normal resistance to change, resistance to having to master a new learning curve and a lack of industry effort to market new devices specially designed for r-PCI.

*Colleagues contributing to the study include senior author Eric Peterson, M.D., Fang-Shu Ou, M.S., Tracy Wang, M.D., and Matthew Roe, M.D., from the Duke Clinical Research Institute; Ralph Brindis, M.D., from the Oakland Kaiser Hospital and John Rumsfeld, M.D., from the Denver VA Medical Center.*

## Still puzzling: Best care for the frail and elderly with coronary artery disease

DURHAM, N.C. – A new study from Duke University Medical Center finds that patients treated solely with medications after suffering from chest pain, heart attack or coronary artery disease are more likely to die during the first year following their initial hospitalization.

"Patients managed medically without stenting or bypass surgery tend to be elderly and frail, and in some sense we feel they have been overlooked," says Matthew Roe, a cardiologist at Duke and the senior author of the study appearing in the August issue of the Journal of the American College of Cardiology: Cardiovascular Intervention. "We wanted to find out what clinical factors were funneling them into a medicine-only group and what happened to them, when compared to patients who received stents and bypass procedures."

Roe led a team of researchers in examining a subset of 8,225 patients from a previous study (the SYNERGY trial) which compared the effects of two different anti-clotting drugs in heart patients. For the current study, researchers included only patients who had undergone cardiac catheterization and who had been found to have at least one significant blockage in a coronary artery. A majority of these patients (52 percent) underwent coronary stent implantation to open their arteries, while 32 percent were medically managed, and 16 percent underwent coronary bypass surgery.

Investigators discovered that patients in the medical management group were more likely to be elderly women with low body weight, and more likely to have had peripheral artery disease, high blood pressure, diabetes or a history of stroke or a previous bypass surgery.

Researchers found that with all else being equal, the risk of death was highest for the medically managed group and lowest for patients who underwent stenting. Death rates among medically managed patients increased rapidly during the first three months following release from the hospital, and stayed higher than those in the other two groups. At one year, the mortality rate among the medically managed group was 7.7 percent, 3.6 percent for patients who underwent stenting, and 6.2 percent among those who underwent bypass procedures.

"It is important to know that the patients in the medically managed group had a higher death rate despite receiving most of the currently recommended medications for this condition from clinical practice guidelines," says Roe. "There are often very good reasons why stenting or bypass are not viable options for some patients. What this study tells us is that for these patients who are medically managed, we need to come up with better treatment approaches that lessen their risk of death."

Roe says possible solutions may arise from a new trial that is just getting under way. The new study, called TRILOGY will compare clopidogrel (Plavix) with the experimental drug prasugrel, another anti-clotting agent, among elderly and frail medically-managed patients with chest pain and coronary artery disease. An earlier trial found that prasugrel was effective in reducing the risk of clotting, but it also brought about a higher risk of bleeding. The TRILOGY trial will compare the two drugs again, but will study a lower dose of prasugrel than in the earlier study. The Duke Clinical Research Institute will manage TRILOGY, which is expected to enroll approximately 10,000 patients in hundreds of hospitals world-wide.

*Colleagues from the Duke Clinical Research Institute who contributed to the published study include Mark Chan, Kenneth Mahaffey, Lena Sun, Karen Pieper and Robert Califf. Co-authors from other institutions include Harvey White, from Aukland City Hospital, New Zealand; and Philip Aylward and James Ferguson from the Texas Heart Institute.*

*The SYNERGY trial was funded by Sanofi-Aventis.*

## What would Earth look like to alien astronomers?

* 00:40 18 July 2008
* NewScientist.com news service
*** Maggie McKee**

What would Earth look like to alien astronomers? If they had access to telescopes far more powerful than our own, it might look a lot like what the Deep Impact spacecraft recently saw from its vantage point 50 million kilometres away.

Over the course of one Earth day in May, the spacecraft snapped images every 15 minutes to produce a movie of the Moon gliding in front of our home planet, whose swirling clouds and continents rotated in and out of view.

"Making a video of Earth from so far away helps the search for other life-bearing planets in the universe by giving insights into how a distant, Earth-like alien world would appear to us," says Michael A'Hearn of the University of Maryland, College Park. ***Video**: http://www.youtube.com/watch?v=vXd-VIf0zwQ*

**Point of light**

A'Hearn is the principal investigator for an extension of the Deep Impact mission, which sent an impactor into Comet Tempel 1 on 4 July 2005 and watched the debris fly. Now, in an extended mission called EPOXI, the spacecraft will search for extrasolar planets on its way to a flyby of a comet called Hartley 2.

The Moon has been seen 'transiting' the Earth previously by other spacecraft, but never in such good detail. "To image Earth in a similar fashion, an alien civilisation would need technology far beyond what Earthlings can even dream of building," says EPOXI team member Sara Seager of MIT.

Alien astronomers around the nearest stars, which lie a few light years away, would glimpse just a single point of light if they wielded telescopes like the ones terrestrial researchers are now planning.

**Alien oceans**

But even that single point of light could yield valuable data. Previous research has shown that it would be possible to tell how fast the Earth is rotating, and make a rough map of its continents and oceans, by observing how that point of light changes over time.

"The video will help us connect a varying point of planetary light with underlying oceans, continents and clouds – and finding oceans on extrasolar planets means identifying potentially habitable worlds," Seager said in a statement.

Team member Drake Deming of NASA's Goddard Space Flight Center in Greenbelt, Maryland, agrees. "A 'Sun glint' can be seen in the movie, caused by light reflected from Earth's oceans, and similar glints to be observed from extrasolar planets could indicate alien oceans."

Also, the team used a near-infrared filter to make the video, which made the continents stand out more clearly from the bodies of water.

That's because plants and some microbes reflect near-infrared light – apparently because absorbing it would cause them to overheat during photosynthesis – and that causes land masses to appear bright at these wavelengths.

## Smell of fresh earth traced to bacteria genes

* 18:45 18 July 2008
* NewScientist.com news service
*** Catherine Brahic**

Everybody recognises the earthy smell of a field that's been freshly tilled, but how this smell forms has so far remained a mystery. A team at Brown University has now identified the bacterial genes responsible for the scent.

The smell of earth comes from a combination of two harmless chemicals called geosmin and methylisoborneol. Both belong to a class of compounds called terpenes and are synthesised by soil bacteria.

Last year, David Cane discovered the gene that helps make geosmin, but methylisoborneol remained elusive. Unlike the other terpenes, which all contain either 10 or 15 carbons, it contains 11.

Cane and his colleague Chieh-Mieh Wang scanned a database containing all 8000 genes from a soil bacterium called Streptomyces. They came across one that looked like it coded for a terpene catalyst, but when they inserted the gene into another bacterium, nothing happened – no terpenes were formed.

Double gene trouble

"We then noticed another gene, right next to the first one, which looked like it might code for a catalyst that adds a single carbon to chemical compounds," says Cane.

That was the "eureka" moment. Cane realised that, together, the two genes could theoretically produce an 11-carbon terpene – the elusive methylisoborneol. And indeed, when they genetically engineered an E. coli bacterium to express both genes, they obtained the scented compound.

Methylisoborneol is also responsible for the muddy smell that tap water sometimes takes on when reservoirs are invaded by blooms of blue-green algae. Cane believes these algae probably have both genes as well, and says that knowing their sequence could make it possible to detect the early signs of blooming, saving the millions of dollars that are sometimes spent on treating full-blown blooms.

*Journal reference: Journal of the American Chemical Society (DOI: 10.1021/ja80803639g)*

## Vestigial Vocal Organ Muffles Human Speech

**Jennifer Viegas**, Discovery News

All four great apes -- humans, chimps, gorillas and orangutans -- have vocal tract air sacs evolved for calling out to others over long distances. In humans, new research suggests, the anatomical structures have shrunk, leaving us with the vestiges of the sacs and much quieter voices as a result. The find highlights how human evolution sacrificed volume for a better ability to speak with others, one on one.

***All Over But the Shouting...***

Such "private talk" allows an individual to exclude unwanted listeners, such as eavesdropping prey in the wild or business rivals in modern life.

For many animals, explained lead author Tobias Riede, "an amplifying device is helpful."

"Unfortunately, it comes with a cost," added Riede, who is a researcher at the National Center for Voice and Speech in Denver. "You have to fine-tune it in order to keep the voice from breaking."

He and his colleagues came to that conclusion after studying models of mammalian air sacs, made "Myth Busters"-style out of PVC pipe, an inflatable urinary bladder from a pig, and other items. All experiments were conducted at the Japan Institute of Science and Technology, where Riede was a visiting researcher.

The scientists found that the larger air sacs in our ape ancestors, as well as certain other mammals, accomplish three things when an individual vocalizes. First, they make sounds louder.

"This happens if the acoustic resonance frequency of the air sacs meets the vibration frequency of the vocal folds," explained Riede.

Second, they change the spectral characteristics of sounds, meaning that the timbre or pitch can vary among individuals.

Finally, the air sacs cause vocalizations to break at times, giving the voice a hoarse, uncontrolled quality, not unlike a singer trying to reach a high note whose voice instead cracks.

The findings are published in this month's Journal of the Acoustical Society of America.

If humans had maintained a large vocal sac, our voices would be particularly prone to cracking, said Reide. Men's voices tend to fall within the 80 to 120 hertz spectrum, while women's voices fall between 180 to 250 hertz.

"These numbers are identical to the frequency of vocal fold vibrations," he said, adding that air sacs would be a disadvantage since "our voices would break all of the time if the air sac resonance [would] come near the frequency of the vocal fold vibrations."

Humans instead have what appear to be relics of the larger air sacs. These are the laryngeal ventricles, located in the voice box.

Chuck Brown, a professor of psychology at the University of South Alabama who specializes in the biology of acoustic communication, told Discovery News that prior to the research, he did not know that other primates may use the air sac effect "to heighten the possibility of communication in some settings."

"In speech, instabilities in voicing are usually regarded as undesirable phenomena that tend to impair communication," Brown said. "Yet, in many of our closest primate relatives, the presence of air sacs and other features of their vocal anatomy appear to be designed to expand the opportunities" for communication.

Riede and his team have already confirmed their findings by studying how air sacs work in Siamang gibbons, but they hope to conduct more studies on animals with air sacs -- big and small -- in the future.