

New MRI technique developed at UT Southwestern detects subtle but serious brain injury

DALLAS — May 12, 2008 — A new technique for analyzing magnetic resonance imaging data, developed by researchers at UT Southwestern Medical Center, can reveal serious brain injury missed by current tests and help predict a patient's degree of recovery.

In brain injuries sustained when the head suddenly stops moving — during a motor vehicle accident, for instance — the force can shear and damage nerve cells. This kind of injury does not show up on computerized tomography scans, the researchers said, and magnetic resonance imaging does not yet reliably detect this type of injury.

“This is a new way of measuring a common injury that has been overlooked,” said Dr. Ramón Díaz-Arrastia, professor of neurology and senior author of the paper, which appears in the May issue of the journal *Archives of Neurology*.

“No matter how many seat belts and airbags there are, if you hit a tree at 50 miles an hour, you're going to have this kind of injury,” Dr. Díaz-Arrastia said. “It may account for up to half of the traumatic brain injuries from car accidents.”

The injury typically affects the portions of nerve cells in the brain called the axons, the long, thin extensions of nerve cells that reach from one area to another. When the brain is subjected to powerful, inertial forces, axons can be deformed and damaged. This type of trauma, called diffuse axonal injury, or DAI, is often difficult to diagnose, Dr. Díaz-Arrastia said.

In the study, the researchers performed MRI analysis on 12 people, ranging in age from 16 to 37, who had severe closed-head brain injury, who were either able to give consent or whose legal guardians gave consent.

From the patients' point of view, the test was the same as undergoing an ordinary MRI. The difference was that the researchers used a new mathematical analysis, called diffusion tensor tractography, to detect diffuse axonal injury. They also analyzed the MRI data using an existing method called FLAIR, for fluid attenuation and inversion recovery.

The new analysis tested for how easily water could move around in the brain in the areas surrounding cells. When the axons are damaged, they swell, absorbing the water around them and leaving less that can move around between cells. As the axons die, they release the water, resulting in more water surrounding the cells.

By comparing multiple MRI images over time, the researchers could detect this change in water motion. Their analysis focused on three areas of the brain — the corpus callosum, the fornix and the peduncular projections — that consist largely of axons that project from one part of the brain to another.

The researchers tested the patients' degree of consciousness and ability to care for themselves immediately after their injuries, as well as six to 11 months later. One patient died, and one had fully recovered, with the rest showing partial recovery. One patient could not be located for the follow-up.

In most of the brain areas studied, the degree of diffuse axonal injury, which is reflected by a reduction of the motion of water around the nerve cells, was significantly linked to how much the patients improved over time, the researchers found. In contrast, FLAIR analysis did not show a statistically significant link with the degree of recovery.

Further studies are under way to include more patients, which will provide more power to the analysis. The researchers will also study other areas of the brain that are at risk for diffuse axonal injury to see whether MRI analysis can be useful in those regions as well.

Other UT Southwestern researchers involved in the study were Dr. Michael Devous, professor of radiology; Dr. Roddy McColl, associate professor of radiology; Dr. Christopher Madden, assistant professor of neurological surgery; Dr. Carlos Marquez de la Plata, assistant professor of psychiatry; Drs. Anthony Whittlemore and Evelyn Babcock, both assistant professors of radiology; Carol Moore and Kan Ding, both clinical research coordinators in neurology; and medical students Tiffany Rickbeil, Julia Dobervich, David Kroll, Bao Dao and Nisha Mohindra.

Lead author Jun-Yi Wang; Dr. Khamid Bakhadirov; and Dr. Herve Abdi from the department of cognition and neuroscience at UT Dallas also participated in the study.

The work was supported by the National Institute on Disability and Rehabilitation Research and the National Institutes of Health.

Anti-inflammatory drugs do not improve cognitive function in older adults

The anti-inflammatory drugs naproxen and celecoxib do not appear to improve cognitive function in older adults with a family history of Alzheimer's disease, and naproxen may have a slightly detrimental effect, according to an article posted online today that will appear in the July 2008 print issue of *Archives of Neurology*, one of the JAMA/Archives journals.

Inflammatory processes may play a role in Alzheimer's disease and other neurodegenerative disorders, as well as in the decline of cognitive (thinking, learning and memory) function in older adults, according to background information in the article. “Consistent with this hypothesis, observational studies have shown an association between the use of non-steroidal anti-inflammatory drugs (NSAIDs) and a lower risk of Alzheimer's disease,” the authors write.

The ADAPT (Alzheimer's Disease Anti-Inflammatory Prevention Trial) Research Group conducted a randomized clinical trial involving 2,117 individuals age 70 and older with a family history of Alzheimer's disease. From March 2001 to December 2004, 617 took 200 milligrams of the NSAID celecoxib twice daily, 596 took 220 milligrams of naproxen sodium twice daily and 904 took placebo. Each year, the study participants took seven tests assessing cognitive function that were added into one global summary score. Treatments were halted in December 2004 because another study found increased cardiovascular risks associated with celecoxib.

“The ADAPT cognitive function results through six months after study treatment cessation do not show a protective effect with the use of NSAIDs and may suggest that cognitive scores are lower,” the authors write. “The global summary scores, which combine the results from seven individual tests in the cognitive assessment battery, were significantly lower over time for naproxen, but not for celecoxib, compared with placebo.”

There are several explanations for the difference between these findings and those of previous observational trials, the authors note. Because observational trials do not assign participants to treatment groups but analyze existing behavior, additional factors that were not measured may have confounded or affected the results. In addition, the findings of this trial may apply only to celecoxib and naproxen and not to other anti-inflammatories, such as ibuprofen. Finally, NSAIDs may be protective only when given several years before the time when cognitive function would have begun to decline.

“Continued follow-up of trial participants, even after cessation of treatment, appears warranted to investigate treatment effects with respect to the timing of exposure,” the authors write. “However, for now we suggest that naproxen and celecoxib should not be used for the prevention of Alzheimer’s disease.”

(Arch Neurol. 2008;65[7]:(doi:10.1001/archneur.2008.65.7.nct70006). Available pre-embargo to the media at www.jamamedia.org.)

Editor’s Note: This study was supported by a grant from the National Institute on Aging. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Texting costs are 'out of this world'

University of Leicester space scientist says texting is at least four times more expensive than receiving scientific data from space

A University of Leicester space scientist has worked out that sending texts via mobile phones works out to be far more expensive than downloading data from the Hubble Space Telescope!

Dr Nigel Bannister’s calculations were used for the Channel 4 Dispatches programme “The Mobile Phone Rip-Off”.

He worked out the cost of obtaining a megabyte of data from Hubble – and compared that with the 5p cost of sending a text.

He said: “The bottom line is texting is at least 4 times more expensive than transmitting data from Hubble, and is likely to be substantially more than that.

“The maximum size for a text message is 160 characters, which takes 140 bytes because there are only 7 bits per character in the text messaging system, and we assume the average price for a text message is 5p. There are 1,048,576 bytes in a megabyte, so that's 1 million/140 = 7490 text messages to transmit one megabyte. At 5p each, that's £374.49 per MB - or about 4.4 times more expensive than the ‘most pessimistic’ estimate for Hubble Space Telescope transmission costs.”

Dr Bannister said it had been difficult to work out exactly how much Hubble data transmission costs. So he contacted NASA who gave him a firm figure of £8.85 per megabyte (MB) for the transmission of data from HST to the Earth.

“This doesn't include the cost of the ground stations and the time of the personnel along the way, but it is an unambiguous number for that part of the process. So that's £8.85 to get each MB from Hubble, to the first point of contact on the ground, but no further. Hence we need to go a little bit further to estimate exactly how much it costs to transmit data from Hubble to the end user - i.e. to the data archive which scientists can access. This is difficult, so I had to make some conservative assumptions.”

Dr Bannister estimated the cost of the data from Hubble could vary between £8.85 and £85 per MB- much cheaper than the £374.49 per MB cost of transmitting one MB of text.

He concludes: “Hubble is by no means a cheap mission – but the mobile phone text costs were pretty astronomical!”

Ancient protein offers clues to killer condition

More than 600 million years of evolution has taken two unlikely distant cousins – turkeys and scallops - down very different physical paths from a common ancestor. But University of Leeds researchers have found that a motor protein, myosin 2, remains structurally identical in both creatures.

The discovery suggests that the tiny motor protein is much more important than previously thought – and for humans it may even hold a key to understanding potentially fatal conditions such as aneurisms.

Says Professor Knight of the University’s Faculty of Biological Sciences: “This is an astonishing discovery. Myosin 2’s function is to make the smooth muscle in internal organs tense and relax involuntarily. These creatures have completely different regulatory mechanisms: the myosin in a turkey’s gizzards allows it to ‘chew’ food in the absence of teeth, while that in a scallop enables it to swim. Yet they have exactly the same structure.”

Myosin molecules generate tension in smooth muscle by adhering to form a filament, which grabs hold of a neighbouring filament, and relaxes by letting go. When the muscle is in a relaxed state, myosin molecule folds itself up into a compact structure.

This folded structure allows the smooth muscles to adjust to being different lengths so they can operate over a large distance, such as the bladder or the uterus expanding and contracting. In contrast, skeletal muscles operate over a narrow range, defined by how much joints can move.

Professor Knight says: “We were puzzled to find that the scallop’s myosin 2 had retained its ability to fold and unfold, as they don’t need to accommodate a large range of movement. After all, the scallop only moves its shell a little when it swims.

“In evolution, if something is not essential to the survival of an organism, it is not conserved. The fact that the scallop has retained all the functions of its myosin 2 over hundreds of millions of years tells us that this folding is of fundamental functional importance in muscle and that we don’t know as much about it as we need to know.”

In humans, any changes in the composition of myosin within the muscles can be fatal. For example, a swelling in the walls of an artery can cause a brain aneurism, while an enlarged heart can lead to cardiac arrest in a young, fit person.

Says Professor Knight: “Because these malfunctions occur in our internal organs, we are often unaware of what is going wrong until it’s too late. Learning how to control myosin, how to move it around without disturbing the delicate balance between filaments and individual molecules, is an emerging area and one we are only just beginning to tackle.” The research, funded by BBSRC, is published in the US journal *Proceedings of the National Academy of Sciences (PNAS)*.

When following the leader can lead into the jaws of death

International study of animal behaviour has important implications for human decision-making

For animals that live in social groups, and that includes humans, blindly following a leader could place them in danger.

To avoid this, animals have developed simple but effective behaviour to follow where at least a few of them dare to tread – rather than follow a single group member.

This pattern of behaviour reduces the risk of imitating maverick behaviour of an individual as the group recognise that consensus is better than following someone that goes it alone.

The study was carried out at the University of Leicester, by Ashley J. W. Ward now at the University of Sydney and in collaboration with David J. T. Sumpter of Uppsala University; Iain D. Couzin of Princeton University; Paul J. B. Hart of the University of Leicester and Jens Krause of the University of Leeds. It is published in the *Proceedings of the National Academy of Sciences (PNAS)*. The research was funded by the Natural Environment Research Council.

Dr Ward, formerly of the University of Leicester, led the study. He said: “Social conformity and the desire to follow a leader, regardless of cost, exert extremely powerful influences on the behaviour of social animals, from fish to sheep to humans.

“The decision of whether to follow the lead of another individual is a fundamental problem for grouping animals - leadership in an animal social group may be assumed by an individual (or individuals) which exhibit a directional preference according to the habitat information it holds. This may be information about, for example, the location of food or a predator’s whereabouts. In such cases, the benefits to followers of acquiring this information may be significant, but whilst information is a valuable commodity, simple acceptance or ‘blind copying’ could result in a string of ill-informed decisions. Thus group members should exercise a degree of discrimination with regards to whom they follow.”

The team investigated how animals use the behaviour of others to make more accurate movement decisions, especially when it isn’t possible to identify which individuals possess pertinent information? One plausible answer is that animals in groups only respond when they see a threshold number of fellow group members perform a particular behaviour.

Dr Ward added: “Our experiments examined whether groups of fish could be led by replica individuals of the same species. We explored following behaviour both in a neutral situation and in a potentially dangerous situation where the subject fish had to be persuaded to swim past a model of a predatory fish. That the test fish regarded the model predator as a threat was confirmed by our control experiments, where fish showed a strong aversion to the predator model. Despite this, solitary test fish were prepared to follow a replica leader towards the predator model, suggesting that an isolated member of a social species will pay almost any cost to stick close to a ‘friend’. When test fish were in larger groups of 4 and of 8 fish, however, the picture was very different: a solitary replica leader was ignored. Instead, it required 2-3 replica leaders to influence these larger groups.

“By adopting this ‘quorum response’, where subjects are prepared to follow a leader only when a threshold number of individuals behave in a particular way, animals can reduce the likelihood of spreading non-adaptive following behaviour. Whereas a single, maverick individual may act irrationally in a given situation, it is far less likely that two individuals will act so strangely.”

The researchers say that in order to benefit fully from information transfer, animals - and this would include humans - may have to follow quorum rules to filter out maverick behaviour.

The researchers conclude: “The reason why this study is important is that while quorum responses have been shown in invertebrates, like ants, bees and cockroaches, this is the first time (as far as we know) that it has been shown in so-called higher animals with relatively complex brains. The quorum decision rule is simple, but extremely effective, and it has important implications for human decision-making. In fact some of the group who have worked on the fish research have recently shown that groups of humans can be persuaded to take group decision guided by just one informed individual.

“We chose to test quorum decision-making with fish because they’re easier to work with, but although we tend to think that we are more complex than fish in our decision-making, the reality is that we’re more similar to them than we may choose to admit!

“Much human action is driven by simple decision rules and our work illustrates how those rules are common throughout the animal kingdom. A better understanding of this decision-making mechanism in humans and other animals helps us understand how people behave in crowds and shows why sometimes people in groups do apparently stupid things, such as stand in the street and stare skyward when there’s nothing to see, just because someone else is doing it.”

Full pdf preprints of the articles that accompany these titles and include these authors are available at:
<http://www.eurekalert.org/pio/pnas.php>

Arsenic-based therapy shown to help eradicate leukemia-initiating cells

Unexpected discovery demonstrates key role for PML tumor suppressor gene

BOSTON -- In both leukemia and solid tumors, there exists among the multitude of warrior cancer cells a small subgroup that work undercover, patiently lying in wait to launch their attacks. Known as either cancer initiating cells (CICs) or leukemia initiating cells (LICs), these stealth populations are impervious to conventional chemotherapy and undaunted by targeted cancer therapies. When a leukemia patient relapses following a period of remission, it is the LICs that bear responsibility for the disease's reemergence.

The secret to the survival abilities of these cells has been unclear. But in a paradoxical discovery, a research team led by investigators at Beth Israel Deaconess Medical Center (BIDMC) has found that a tumor suppressor protein known as PML appears to be the factor that enables LICs to maintain their quiescence – the inert state that protects them from being destroyed by cancer therapies – and suggests that inhibition of PML is a promising target for new therapeutics.

Their findings, which appear in today's advance on-line issue of the journal *Nature*, additionally demonstrate that PML can be degraded with an arsenic-based agent used in traditional Chinese medicine. Importantly, when combined with chemotherapy, the arsenic-based therapy -- already proven safe and non-toxic in clinical trials -- can successfully treat chronic myeloid leukemia.

"Leukemia initiating cells share many properties of normal hematopoietic stem cells," explains senior author Pier Paolo Pandolfi, MD, PhD, Director of the Cancer Genetics Program in BIDMC's Cancer Center and Professor of Medicine and of Pathology at Harvard Medical School. "They are pluripotent, they readily replicate and they can indefinitely remain in a dormant state of quiescence."

Consequently, while the majority of leukemic cells are vulnerable to any cancer therapies – including chemotherapy and targeted cancer treatments – that destroy cells during active DNA replication, LICs, with their unique quiescent properties, resemble an automobile with an endless supply of fuel and a sturdy set of brakes: They sit quietly idling in place, waiting to reinitiate malignancy after a period of remission.

Pandolfi's laboratory has been working to develop new therapeutic approaches to target LICs and thereby treat chronic myeloid leukemia (CML), one of the most extensively investigated of stem cell disorders. CML is typically treated with the targeted therapy imatinib (Gleevec), a tyrosine kinase inhibitor.

"Gleevec does dramatically improve prognosis of CML patients," notes Pandolfi. "But, unfortunately, Gleevec is not curative in most cases. Because it targets only dividing cells, the pool of quiescent LICs are able to remain intact." As a result, when Gleevec therapy is discontinued, the cancer almost inevitably relapses.

The investigators set out to analyze expression of PML, a tumor suppressor protein that controls fundamental processes such as apoptosis, cellular proliferation and senescence. PML is commonly associated with acute promyelocytic leukemia (APL), in which it leads to the formation of a fusion protein that blocks cell differentiation.

After ascertaining that PML was highly expressed in the LICs of a CML mouse model, Pandolfi's team also determined that PML is highly expressed in blasts from CML patients and that low PML levels corresponded with patients' increased response to therapy and overall survival rates.

"We then analyzed LIC function in the absence of PML and revealed that PML has an indispensable role in maintaining LIC quiescence," he adds. "As a result, PML-deficient LICs grow exhausted over time, becoming incapable of generating CML in the transplanted animals."

Lastly, the investigators examined the impact of As₂O₃, an arsenic-based therapy that targets PML for degradation and is currently used for the treatment of acute promyelocytic leukemia. As predicted, inhibition of PML by As₂O₃ successfully disrupted LICs, increasing the efficacy of the anti-cancer therapy by sensitizing the LICs to pro-apoptotic stimuli.

"It's actually a very simple concept," says Pandolfi. "Ninety percent of existing cancer treatments are antiproliferative agents – they target the pool of proliferative cells, leaving behind the dormant LICs.

"But in determining that PML serves to guard the LICs that have been left behind, we also discovered that if we knock out PML [through pharmacologic means], the LICs will lose their braking abilities and run out of gas, thereby committing the fatal error of proliferation -- and exposing themselves to the deadly effects of cancer therapies."

Pandolfi's laboratory is now trying to determine whether PML exerts a similar role in the stem cells of other tissues, as well as in the cancer initiating cells of solid tumors.

"If this turn out to be the case," he adds, "the transient use of As₂O₃ may represent a more global strategy to target CICs in other forms of cancer."

This study was supported by grants from the National Institutes of Health.

Study coauthors include BIDMC Cancer Genetics investigators Keisuke Ito (first author), Rosa Bernardi, and Alessandro Morotti; Sahoko Matsuoka and Yasuo Ikeda of Keio University School of Medicine, Tokyo, Japan; Giuseppe Saglio of the University of Turin, Turin, Italy; Julie Teruya-Feldstein of Memorial Sloan-Kettering Cancer Center, New York, NY; and Jacalyn Rosenblatt and David Avigan of BIDMC's Division of Hematology and Oncology.

Human vision inadequate for research on bird vision

The most attractive male birds attract more females and as a result are most successful in terms of reproduction. This is the starting point of many studies looking for factors that influence sexual selection in birds. However, is it reasonable to assume that birds see what we see? In a study published in the latest issue of *American Naturalist*, Uppsala researchers show that our human vision is not an adequate instrument.

“The results mean that many studies on sexual selection may need to be re-evaluated,” says Anders Odeen, research assistant at the Department of Animal Ecology at Uppsala University, who carried out this study with his colleague Olle Håstad.

The significance of birds’ plumage, both in terms of richness of colour and particular signals, has been shown to be a major factor in birds’ choice of partner. In order to assess the colours of birds, everything from binoculars to RGB image analyses are used. However, most studies are based on the hypothesis that human colour vision can be used to assess what birds see.

“It’s a bit like a colour blind person describing the colours of clothes – it’s often quite accurate but sometimes it can go badly wrong.”

This problem has been discussed in the research arena, but so far no study has been able to show its extent. The Uppsala researchers used a mathematical model to investigate how bird and human retina work. Using the model combined with information on differences in the colour-sensitive cones of the eye, they have been able to figure out how colour contrasts are perceived. Greater colour contrast can be translated as ‘richness of colour’ or more ‘brightly coloured’.

“We show that the colours are perceived differently in over 39 percent of cases, which means that it is possible that more than one third of previous studies have been based on inaccurate information.”

The differences were partly due to the fact that human vision cannot perceive UV light, while avian vision can. There are several differences between human and avian perception of colour, which show that certain shades that can be seen clearly by birds are not perceived at all by humans. Through evolution, our colour vision has developed from a more primitive version. This means that we have gone from having two types of colour sensitive cones in our eyes to having three. Birds have four.

“Most other animal species only have two, which means that their colour vision is rudimentary. It is human colour vision that differs from the norm, so in reality it’s ridiculous to use our colour vision to assess the colours of other animals.

The results are not only significant for basic research on sexual selection. They also illustrate the risks of making certain decisions on the basis of human vision, for example, in designing and legislating on lighting systems for domestic fowl.

Anti-scar bandage

[Keloid scars](#) are angry red lesions that sometimes form after surgery or injury when the skin "overheals" creating an extra tough region of new skin. Dermatologists believe that one factor in their formation is stretching during healing caused by the patient moving, or by the tissue beneath swelling.

So [Geoff Gurtner](#) and colleagues at the Stanford University Medical Center in California have developed bandages that can prevent this kind of stretching.

Their bandages are made of "shape memory" polymers that set into a rigid shape after being applied to the wound. They are fixed into place using powerful adhesives, or sewn or stapled over the wound during surgery. The team has tested the idea on mice and says it can significantly reduce the amount of scarring by holding the healing tissue firm.

Read the full [anti-scar bandage](#) patent application.

High-pressure tooth spray

Cars have been cleaned for years using high-pressure hoses that rely on water droplets moving at high speed to displace dirt. A number of people have thought of trying the same idea with teeth to remove food, bacteria and plaque from the teeth.

But treading the line between damaging the mouth and having no effect at all relies on the distance between the spray head and the teeth, says consumer electronics company [Philips](#).

The company has designed a spray head with a couple of probes that project out in front of it. The user simply places these against their teeth to ensure that the head is the optimum distance away.

The company seems to be planning toothbrushes with the sprays built in. A separate Philips patent describes a sensor for a spray toothbrush that reflects a light beam off tooth enamel to measure how clean, allowing the user to be told exactly when to stop. Another patent describes a version of the spray that can have its temperature controlled by the user. *Read the full [high-pressure spray toothbrush](#), [clean tooth detector](#) and [temperature-controlled tooth spray](#) patent applications.*

Mind-mapping light pulses

In recent years, neuroscientists have begun to explore the connection between mind and brain using techniques including [functional MRI](#) and [magnetoencephalography](#) to show how specific brain regions "light up" during particular activities.

But these techniques have limited spatial resolution and result in images that lack detail. Also, fMRI – which measures the oxygenation of blood rather than the activation of neurons directly – is rather slow.

Injecting neurons with voltage-sensitive dyes that change colour when the brain cells "fire" provides a faster read-out. But the dyes can only be injected into small regions, and the process often damages the tissue.

Now [Martin Fischer](#) at Duke University in Durham, North Carolina, US, has developed a new imaging technique. It exploits the fact that the passage of a light pulse through neurons is altered when the neurons fire.

By zapping the brain with carefully chosen light pulses, and observing how they are changed by the tissue, it is possible to read out the neuronal activity. Fischer says that this entirely new form of imaging has a spatial resolution on the submicron scale and takes snapshots just milliseconds apart.

However, light will likely only be able to penetrate at best a few millimetres into a brain. Fischer says this is enough to investigate much of the [cerebral cortex](#) where the brain's higher function lies. It should also be enough to image entire mouse or rat brains.

Read the full [mind-mapping light pulses](#) patent application.

PET imaging may not improve diagnostic accuracy in early head and neck cancer

Positron emission tomography with a radioactive tracer (18F-FDG PET) may not improve the detection of small metastases in patients with head and neck cancer who have no clinical evidence of disease in neighboring lymph nodes, according to a meta-analysis published online May 13 in the Journal of the National Cancer Institute.

A key prognostic factor for head and neck squamous cell cancer patients is whether their disease has spread to the nearby lymph nodes. Unfortunately, some patients who appear clinically to be free of such metastases, referred to as cN0, actually have small metastases. Clinicians use magnetic resonance imaging (MRI), computed tomography (CT), and FDG-PET to try to detect these lesions, but strong data supporting the use of FDG-PET are lacking.

To systematically examine the value of FDG-PET for diagnosing clinically node-negative patients, John P. A. Ioannidis, M.D., of the University of Ioannina School of Medicine in Greece and colleagues performed a meta-analysis of 32 previously published studies that tested FDG-PET in head and neck cancer patients with one or fewer nodal metastases.

FDG-PET failed to identify 50 percent of the occult lesions in clinically node-negative patients and incorrectly identified normal tissue as being cancerous 13 percent of the time. When the researchers compared the sensitivity and specificity of FDG-PET with MRI and CT, they found that there was a trend for a small improvement in detection with FDG-PET, but the differences were not statistically significant. The false positive rate was similar for all three imaging techniques.

“Thus, there is little evidence to support the routine use of 18F-FDG-PET to evaluate possible lymph node metastasis among patients with [head and neck squamous cell cancer] and a clinically negative neck,” the authors write.

In an accompanying editorial, David L. Schwartz, M.D., of the University of Texas M. D. Anderson Cancer Center in Houston and colleagues commend the authors for their efforts to systematically analyze the value of FDG-PET in diagnosing clinically node-negative head and neck cancer patients. They note that single institutions studies have provided most data thus far, as no large randomized trials have addressed the question.

The editorialists contend, however, that clinicians typically use one or more diagnostic imaging techniques, as well as clinical examinations, to assemble an overall picture of their patient's disease and do not rely on a single test. Therefore, comparing one imaging technique against another may not adequately capture the possible benefit gained from an approach. “Prospective data remain a critical necessity to translate imaging improvements with FDG-PET into proven treatment improvements,” the editorialists write.

Adding ultrasound to mammography may improve breast cancer detection in high-risk women

The addition of an ultrasound examination to mammography for women at high-risk of breast cancer resulted in a higher rate of cancer detection, but also increased the number of false-positive results, according to a study in the May 14 issue of JAMA.

Supplemental screening ultrasound has the potential of depicting small, node-negative breast cancers (when there is no cancer in the lymph nodes) not seen on mammography, according to background information in the article.

Wendie A. Berg, M.D., Ph.D., of the American Radiology Services Inc., Johns Hopkins Green Spring, Lutherville, Md., and colleagues conducted a study to compare the diagnostic effectiveness of screening breast mammography plus ultrasound vs. mammography alone in women at increased risk of breast cancer. The study included 2,809 women with dense breast tissue who were randomized to undergo mammographic and ultrasonographic examinations.

Forty participants (41 breast lesions) were diagnosed with cancer: 8 suspicious on both ultrasound and mammography; 12 on ultrasound alone; 12 on mammography alone; and 8 participants (involving 9 breast lesions) on neither.

The diagnostic yield for mammography was 7.6 cancers per 1,000 women screened (20/2,637); 31 cancers were diagnosed in 2,637 participants by the combination of mammography plus ultrasound, producing a yield of 11.8 per 1,000 women, and an increased yield due to ultrasound of 4.2 per 1,000 over mammography alone (or an additional 1.1 to 7.2 cancers per 1,000 high-risk women).

The diagnostic accuracy of mammography was 0.78; for ultrasound, 0.80; and for combined mammography plus ultrasound, 0.91. The positive predictive value of biopsy recommendation after full diagnostic workup was 19 of 84 for mammography (22.6 percent), 21 of 235 for ultrasound (8.9 percent), and 31 of 276 for combined mammography plus ultrasound (11.2 percent).

The false-positive rate for mammography was 4.4 percent; for ultrasound, 8.1 percent; and for combined mammography plus ultrasound, 10.4 percent.

“The detection benefit of a single screening ultrasound in women at elevated risk of breast cancer is now well validated. However, it comes with a substantial risk of false-positive results (i.e., biopsy with benign results and/or short interval follow-up). Our results should be interpreted in the context of recent guidelines recommending annual magnetic resonance imaging [MRI] in women at very high risk of breast cancer,” the authors conclude. (*JAMA*. 2008;299[18]:2151-2163. Available pre-embargo to the media at www.jamamedia.org)

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

Editorial: *The 'Coming of Age' of Nonmammographic Screening for Breast Cancer*

In an accompanying editorial, Christiane K. Kuhl, M.D., of the University of Bonn, Germany, comments on the findings of Berg and colleagues.

"Mammography will probably remain the basis for breast cancer screening for the foreseeable future. However, increasing evidence suggests that for many women, mammography does not provide the best possible accuracy. Early diagnosis is important and has been the single major reason for improved breast cancer survival rates. Notwithstanding this success, a success mainly credited to mammographic screening, there is good reason to move on. As long as breast cancer remains the most common cause of cancer death in women, the search for techniques that can help cover the limitations of screening mammography must continue." "The concept of mammographic screening has been in use for more than 40 years. It may now be time to carefully reconsider. Individualized screening schemes tailored to the individual risk and to the personal preferences of a woman may be the way to consider how to screen for breast cancer. Whether in the long run, ultrasound or breast MRI will be more appropriate for this purpose remains to be seen."

(JAMA. 2008;299[17]:2086-2087. Available pre-embargo to the media at www.jamamedia.org)

Girls, young women can cut risk of early breast cancer through regular exercise

St. Louis, May 13, 2008 — Mothers, here's another reason to encourage your daughters to be physically active: Girls and young women who exercise regularly between the ages of 12 and 35 have a substantially lower risk of breast cancer before menopause compared to those who are less active, new research shows.

In the largest and most detailed analysis to date of the effects of exercise on premenopausal breast cancer, the study of nearly 65,000 women found that those who were physically active had a 23 percent lower risk of breast cancer before menopause. In particular, high levels of physical activity from ages 12 to 22 contributed most strongly to the lower breast cancer risk.

The study, by researchers at Washington University School of Medicine in St. Louis and Harvard University in Boston, will be available online May 13 in the *Journal of the National Cancer Institute*.

"We don't have a lot of prevention strategies for premenopausal breast cancer, but our findings clearly show that physical activity during adolescence and young adulthood can pay off in the long run by reducing a woman's risk of early breast cancer," says lead investigator Graham Colditz, M.D., Dr.P.H., the Niess-Gain Professor and associate director of Prevention and Control at the Siteman Cancer Center at Washington University School of Medicine and Barnes-Jewish Hospital. "This is just one more reason to encourage young girls and women to exercise regularly."

One-fourth of all breast cancers are diagnosed in women before menopause. Numerous studies have shown that physical activity reduces the risk of postmenopausal breast cancer, but the few studies that have looked at the influence of exercise on breast cancer risk before menopause have produced conflicting results.

For the current analysis, researchers examined data on a subset of women enrolled in the Nurses' Health Study II, a prospective study of registered nurses ages 24 to 42. These 64,777 women had filled out detailed annual questionnaires about their levels of physical activity from age 12 on. After six years of follow-up, 550 women had been diagnosed with breast cancer.

The researchers found the age-adjusted incidence rates for invasive breast cancer dropped from 194 cases per 100,000 person-years in the least active women to 136 cases in the most active. The levels of physical activity reported by the most active women were the equivalent of running 3.25 hours a week or walking 13 hours a week. The benefit of exercise was not linked to a particular sport or intensity but related to total activity.

"You don't have to be a marathon runner to get the risk-reducing benefits of exercise," Colditz adds.

One leading theory to explain the lower risk of breast cancer among active young women is that exercise reduces their exposure to estrogens. Numerous studies have shown that the more estrogen a woman is exposed to, the greater her risk for breast cancer. Thus, women who begin menstruating later or enter menopause early have a lower risk of breast cancer. And young women who are physically active are more likely to start their periods later and less likely to have regular cycles when they begin their periods.

Maruit SS, Willett WC, Feskanich D, Rosner B, Colditz GA. A prospective study of age-specific physical activity and premenopausal breast cancer. Journal of the National Cancer Institute. May 13, 2008 (advance online publication). The research was funded by grants from the National Cancer Institute and the American Cancer Society.

Shrimps see beyond the rainbow

A Swiss marine biologist and an Australian quantum physicist have found that a species of shrimp from the Great Barrier Reef, Australia, can see a world invisible to all other animals.

Dr Sonja Kleinlogel and Professor Andrew White have shown that mantis shrimp not only have the ability to see colours from the ultraviolet through to the infrared, but have optimal polarisation vision — a first for any animal and a capability that humanity has only achieved in the last decade using fast computer technology. The findings are published in the journal *PLoS ONE*.

"The mantis shrimp is a delightfully weird beastie," said Professor White, of the University of Queensland. "They're multi-coloured, their genus and species names mean 'mouth-feet' and 'genital-fingers'; they can move each eye independently, they see the world in 11 or 12 primary colours as opposed to our humble three, and now we find that this species can see a world invisible to the rest of us."

Dr Kleinlogel, is based at the Max Planck Institute for Biophysics in Frankfurt, and collected the shrimp from the reef. She notes that, "...scuba divers know them as 'thumb-splitters', they've got wickedly strong claws and are very aggressive!"

Most animals can tell how fast the electric field in a light wave is oscillating, which is perceived as colour. (Blue light oscillates faster than green, which is faster than red). The direction of the oscillation is known as polarisation: many animals, from budgerigars to ants have some form of polarisation vision. Since the 1950s, animals have been shown to use linear polarisation vision for navigation, for finding food, for evading hunters, and for sex, or as Professor White says, "...for the four fs: feeding, fighting, fleeing and...flirting."

Commonly, polarisation vision is quite restricted: in its simplest form, different directions of polarisation show up as lighter or darker patches — you can see this yourself by looking at clear blue sky with polarising sunglasses. But polarisation is more subtle than this: the electric field of the light can oscillate back and forth in a line or around and around in a circle, or anywhere in between.

The two scientists have shown that shrimp of the species *Gonodactylus smithii* have eyes that simultaneously measure four linear and two circular polarisations, enabling them to determine both the direction of the oscillation, as well as how polarised the light is.

"This is very useful because natural light can vary from strongly polarised, like the glare off snow or water, to unpolarised, like the sun," Professor White said.

"Any changes to the amount of polarisation instantly tells the animal that something is going on."

Colleagues at The University of Queensland have recently found a related species where the males reflect circular polarisation from their bodies, and hypothesized that circular polarisation vision is used for sexual signalling. Professor White smiles and says, "I think of that as the 'prawnographic' hypothesis."

He continues, "It can't be the whole story in our case, though. We found the same structures in the eyes of both boy and girl mantis shrimps, and yet neither have circularly polarised markings on their bodies. Each eye measures the six polarisation components that are precisely required for optimal polarisation vision. In fact, the physics we used to understand what was going on is the same physics that we use in quantum computing for optimal storage of information."

"It is this unique talent — to measure linear and circular polarisation simultaneously — which presents a completely new concept of polarisation vision," Dr Kleinlogel continues. "There wouldn't be much point in only being able to see circular polarisation as it is extremely rare in nature. Even the polarized light reflected from some shrimp's bodies is only weakly circular polarised and often contains more linear polarisation."

"We doubt that circular polarisation is used exclusively as a secret shrimp sex signal! It makes more sense that mantis shrimp evolved both circular and linear polarisation receptors to work together so they can detect tiniest changes in any polarisation."

Prof. White notes, "Some of the animals they like to eat are transparent, and quite hard to see in sea-water - except they're packed full of polarising sugars - I suspect they light up like Christmas trees as far as these shrimp are concerned." "And of course," Dr Kleinlogel concludes, "they can still flirt with each other using fancy polarisation cues!"

See <http://quantum.info/shrimp> for further information.

Mayo Clinic study shows acupuncture and myofascial trigger therapy treat same pain areas

Acupuncture and myofascial trigger therapy treat same pain areas, Mayo specialist says

JACKSONVILLE, Fla. – Ancient acupuncture and modern myofascial pain therapy each focus on hundreds of similar points on the body to treat pain, although they do it differently, says a physician at Mayo Clinic in Jacksonville who analyzed the two techniques.

Results of the study, published May 10 in the *Journal of Complementary and Alternative Medicine*, suggest that people who want relief from chronic musculoskeletal pain may benefit from either therapy, says chronic pain specialist Dr. Peter Dorsher of the Department of Physical Medicine and Rehabilitation at Mayo Clinic.

"This may come as a surprise to those who perform the two different techniques, because the notion has been that these are exclusive therapies separated by thousands of years," he says. "But this study shows that in the treatment of pain disorders, acupuncture and myofascial techniques are fundamentally similar – and this is good news for anyone looking for relief."

Classic Chinese acupuncture treats pain and a variety of health disorders using fine needles to "reset" nerve transmission, Dorsher says. Needles are inserted in one or several of 361 classical acupoints to target specific organs or pain problems. "This is a very safe and effective technique," he says.

Myofascial trigger-point therapy, which has evolved since the mid-1800s, focuses on tender muscle or "trigger point" regions. There are about 255 such regions described by the *Trigger Point Manual*, the seminal textbook on myofascial pain. These are believed to be sensitive and painful areas of muscle and fascia, the web of soft tissue that surrounds muscle, bones, organs and other body structures. To relieve pain at these trigger points, practitioners use injections, deep pressure, massage, mechanical vibration, electrical stimulation and stretching, among other techniques.

In the study, Dorsher analyzed studies published on both techniques and demonstrated that acupuncture points and trigger points are anatomically and clinically similar in their uses for treatment of pain disorders.

In another recent study, he found that at least 92 percent of common trigger points anatomically corresponded with acupoints, and that their clinical correspondence in treating pain was more than 95 percent. "That means that the classical acupoint was in the same body region as the trigger point, was used for the same type of pain problem, and the trigger point referred pain pattern followed the meridian pathway of that acupoint described by the Chinese more than 2,000 years before," Dorsher says. Myofascial pain therapy has lately incorporated the use of acupuncture needles in a treatment called "dry needling" to treat muscle trigger points. "I think it is fair to say that the myofascial pain tradition represents an independent rediscovery of the healing principles of traditional Chinese medicine," Dorsher says. "What likely unites these two disciplines is the nervous system, which transmits pain."

The study was funded by Mayo Clinic.

Rensselaer student invents alternative to silicon chip

Troy, N.Y. — Even before Weixiao Huang received his doctorate from Rensselaer Polytechnic Institute, his new transistor captured the attention of some of the biggest American and Japanese automobile companies. The 2008 graduate's invention could replace one of the most common pieces of technology in the world—the silicon transistor for high-power and high-temperature electronics.

Huang, who comes from humble roots as the son of farmers in rural China, has invented a new transistor that uses a compound material known as gallium nitride (GaN), which has remarkable material properties. The new GaN transistor could reduce the power consumption and improve the efficiency of power electronics systems in everything from motor drives and hybrid vehicles to house appliances and defense equipment.

"Silicon has been the workhorse in the semiconductor industry for last two decades," Huang said. "But as power electronics get more sophisticated and require higher performing transistors, engineers have been seeking an alternative like gallium nitride-based transistors that can perform better than silicon and in extreme conditions."

Each household likely contains dozens of silicon-based electronics. An important component of each of those electronics is usually a silicon-based transistor known as a silicon metal/oxide semiconductor field-effect transistor (silicon MOSFET). To convert the electric energy to other forms as required, the transistor acts as a switch, allowing or disallowing the flow of current through the device.

Huang first developed a new process that demonstrates an excellent GaN MOS (metal/oxide/GaN) interface. Engineers have known that GaN and other gallium-based materials have some extremely good electrical properties, much better than silicon. However, no useful GaN MOS transistor has been developed. Huang's innovation, the first GaN MOSFET of its kind in the world, has already shown world-record performance according to Huang. In addition, Huang has shown that his innovation can integrate several important electronic functions onto one chip like never before. "This will significantly simplify entire electronic systems," Huang said. Huang has also designed and experimentally demonstrated several new novel high-voltage MOS-gated FETs which have shown superior performance compared to silicon MOSFET in terms of lower power consumption, smaller chip size, and higher power density.

The new transistors can greatly reduce energy loss, making energy conversion more efficient. "If these new GaN transistors replaced many existing silicon MOSFETs in power electronics systems, there would be global reduction in fossil fuel consumption and pollution," Huang said.

The new GaN transistors can also allow the electronics system to operate in extremely hot, harsh, and high-power environments and even those that produce radiation. "Because it is so resilient, the device could open up the field of electronic engineering in ways that were not previously possible due to the limitations imposed by less tolerant silicon transistors," he said.

Huang has published more than 15 papers during his time as doctoral student in the Department of Electrical, Computer, and Systems Engineering at Rensselaer. Despite obvious difficulties, his parents worked tirelessly to give Huang the best possible educational opportunities according to Huang. And when school wasn't enough, Huang's father woke him up early every morning to practice mathematical calculations without a calculator, instilling in Huang a lifelong appreciation for basic, theoretical mathematics and sciences.

He received a bachelor's in electronics from Peking University in Beijing in 2001 and a master's in physics from Rensselaer in 2003. He will receive his doctorate from Rensselaer on May 17, 2008 and plans to work as a device engineer in the semiconductor industry.

OHSU Cancer Institute researchers pinpoint how smoking causes cancer

Although it has been known that smoking causes cancer new research shows how it happens

PORTLAND, Ore. – Oregon Health & Science University Cancer Institute researchers have pinpointed the protein that can lead to genetic changes that cause lung cancer.

The research will be published Tuesday, May 12, in the British Journal of Cancer.

Researchers discovered that the production of a protein called FANCD2 is slowed when lung cells are exposed to cigarette smoke. Low levels of FANCD2 leads to DNA damage, triggering cancer. Cigarette smoke curbs the production of 'caretaker' proteins, like FANCD2, which normally prevent cancer by fixing damages in DNA and causing faulty cells to commit suicide.

Research has shown that smoking is strongly linked to lung cancer, but this discovery may help scientists improve treatments for lung disease in the future.

“These findings show the important role FANCD2 plays in protecting lung cells against cigarette smoke, and may explain why cigarette smoke is so toxic to these cells,” said lead author Laura Hays, Ph.D., research assistant professor of medicine (hematology/medical oncology) and member of the OHSU Cancer Institute.

Senior author, Grover Bagby, M.D., further stated that: “Dr. Hays’ work shows that FANCD2 is an important protein in protecting against cancer, and cigarette smoke knocks out its production. Although there are probably other proteins involved in this process, we know this is a key one because cells with very high levels of FANCD2 were resistant to the toxic effects of the smoke.” Bagby is the founding and past director of the OHSU Cancer Institute and professor at the Northwest Cancer Veterans Affairs Research Center at the Portland Veterans Affairs Medical Center.

The authors created an artificial windpipe in the lab to replicate the environment of a smoker’s lung. They then studied the effects of cigarette smoke on different proteins in cells and found that FANCD2 levels were low enough to allow DNA damage.

FANCD2 is part of a family of proteins involved in an inherited condition called Fanconi anemia. People with the condition are more likely to develop cancers at a young age and have low levels of these proteins.

Lesley Walker, Ph.D., director of cancer information at Cancer Research UK, said: “This interesting piece of science adds to our understanding of why smoking is so deadly. Smoking is the single biggest preventable cause of cancer and causes nine out of 10 cases of lung cancer.

“But the good news is that quitting works – after five years without smoking, your risk of a heart attack will have fallen to half that of a smoker. And after 10 years, your risk of lung cancer will have halved too.”

Lung cancer is the most common cancer in the world, with 1.3 million people diagnosed every year.

Particulars: Cigarette smoke induces genetic instability in airway epithelial cells by suppressing FANCD2 expression. Hays et al. 2008. British Journal of Cancer.

This research was supported by Michael J Dowd, Regina M Dowd, Patrick J Coughlin, Steve T Huff, Cooley Family Fund for Critical Research of the Oregon Community Foundation, Medical Research Foundation of Oregon, Oregon Opportunity Program, NIH RO1-HL61013, NIH RO1-HL71795, NIH RO1-HL659, NIH/NHLBI 5PO1 HL48546, and VA Merit Review.

Chemical Compound Prevents Cancer In Lab

Researchers study several compounds to stop or prevent cancer

Oklahoma City, OK -- While researching new ways to stop the progression of cancer, researchers at the University of Oklahoma Health Sciences Center, have discovered a compound that has shown to prevent cancer in the laboratory.

The compound, which still faces several rounds of clinical trials, successfully stopped normal cells from turning into cancer cells and inhibited the ability of tumors to grow and form blood vessels. If successful tests continue, researchers eventually hope to create a daily pill that would be taken as a cancer preventive.

“This compound was effective against the 12 types of cancers that it was tested on,” said Doris Benbrook, Ph.D., principle investigator and researcher at the OU Cancer Institute. “Even more promising for health care is that it prevents the transformation of normal cells into cancer cells and is therefore now being developed by the National Cancer Institute as a cancer prevention drug.”

The synthetic compound, SHetA2, a Flex-Het drug, directly targets abnormalities in cancer cell components without damaging normal cells. The disruption causes cancer cells to die and keeps tumors from forming.

Flex-Hets or flexible heteroarotinoids are synthetic compounds that can change certain parts of a cell and affect its growth. Among the diseases and conditions being studied for treatment with Flex-Hets are polycystic kidney disease, kidney cancer and ovarian cancer.

Benbrook and her research team have patented the Flex-Het discovery and hope to start clinical trials for the compound within 5 years. If the compound is found to be safe, it would be developed into a pill to be taken daily like a multi-vitamin to prevent cancer.

The compound also could be used to prevent cancer from returning after traditional radiation and chemotherapy treatments, especially in cancers that are caught in later stages such as ovarian cancer where life expectancy can be as short as 6 months after treatment.

“It would be a significant advancement in health care if this pill is effective in preventing cancer, and we could avoid the severe toxicity and suffering that late stage cancer patients have to experience,” Benbrook said.

Virtual telescope brings the cosmos to your desktop

* 16:01 13 May 2008

* NewScientist.com news service

* **New Scientist Space and Reuters**

Any Star Trek fan knows that space travel is not always easy, but Microsoft wants to make travelling the "final frontier" as simple as turning on your computer.

The world's largest software maker launched a free software application called WorldWide Telescope on Monday that allows everyone from space novices to astronomy professors easily explore galaxies, star systems and distant planets.

The WorldWide Telescope stitches together 12 terabytes – the data equivalent of 2.6 billion pages of text – of pictures from sources including the Hubble Space Telescope, the Chandra X-Ray Observatory and the Spitzer Space Telescope.

The experience is similar to playing a video game, allowing users to zoom in and out of galaxies that are thousands of light years away. It allows seamless viewing of far-away star systems and rarely-seen space dust in breathtaking clarity.

A test version of the software is available for download here.

Microsoft archrival Google also has its eyes to the skies. Google Sky started as an add-on to Google Earth but was later upgraded to a version that could be used through a Web browser. Google's version is also free.

Science careers

Microsoft said it will release the WorldWide Telescope free of charge as a tribute to Jim Gray, a Microsoft researcher who went missing off the coast of California while sailing in 2007. Gray worked with astronomers to organise the vast amounts of data and images being pulled from spacecraft.

Microsoft expects the technology used in the WorldWide Telescope to help the company in future software applications, but the program's goal is to spark children's interest in space and encourage them to pursue careers in science and engineering.

"My idea of success is if WorldWide Telescope changes how people see the universe and for a generation of kids to have a degree of knowledge about space that they are just not getting now," said Curtis Wong, manager of Microsoft's Next Media Research Group.

"Contextualising astronomy is missing right now. You see all of these Hubble images and they're amazing, but you have no idea about how big they are, how far away it is."

The software allows users to develop their own guided tours of the universe to share with others or take part a guided tour created by astronomy experts.

Inca Skull Surgeons Were "Highly Skilled," Study Finds

Scott Norris for *National Geographic News* May 12, 2008

Inca surgeons in ancient Peru commonly and successfully removed small portions of patients' skulls to treat head injuries, according to a new study.

The surgical procedure—known as trepanation—was most often performed on adult men, likely to treat injuries suffered during combat, researchers say.

A similar procedure is performed today to relieve pressure caused by fluid buildup following severe head trauma.

Around the ancient Inca capital of Cuzco (see Peru map), remains dating back to A.D. 1000 show that surgical techniques were standardized and perfected over time, according to the report.

Many of the oldest skulls showed no evidence of bone healing following the operation, suggesting that the procedure was probably fatal.

But by the 1400s, survival rates approached 90 percent, and infection levels were very low, researchers say.

The new findings show that Inca surgeons had developed a detailed knowledge of cranial anatomy, said lead author Valerie Andrushko, of Southern Connecticut State University in New Haven.

"These people were skilled surgeons," she said.

Beer, Plants Aided Patients

Inca healers carefully avoided areas of the skull where cutting would be more likely to cause brain injury, bleeding, or infection, Andrushko noted.

The operations were conducted without the modern benefits of anesthesia and antibiotics, but medicinal plants were probably used, she said.

"They were aware of the medicinal properties of many wild plants, including coca and wild tobacco," Andrushko said.

"These, along with maize beer, may have been used to alleviate some of the pain.

"Natural antiseptics such as balsam and saponins [plants with soaplike properties] may have reduced the likelihood of infection following trepanation," she added.

The new study was recently published online in *The American Journal of Physical Anthropology*.

"Skull Was Slowly Scraped Away"

Andrushko and study co-author John Verano of Tulane University in New Orleans studied remains from 11 burial sites in Cuzco and the surrounding region.

(See related photos: "Frozen Inca Mummy Goes On Display" [September 11, 2007].)

Their survey found that trepanation was a remarkably common practice in the Inca capital. Of 411 skulls that were sufficiently well preserved to study, 66 had holes cut through the bone.

In one location, 21 of 59 skulls—over a third—had received trepanation.

While methods of trepanation varied over time, Inca surgeons eventually settled on a scraping technique to penetrate the skull without causing wider injury.

"The skull was slowly scraped away, resulting in a circular hole surrounded by a wider area of scraped bone," Andrushko said.

Some of the skulls had been perforated more than once, including one individual who had undergone the operation seven times.

In another unusual case, in which the patient did not survive the operation, a rectangular section of bone that had been removed was set back in place prior to burial.



Tiffany Tung is an archaeologist at Vanderbilt University in Nashville, Tennessee, and was not part of the research. She said that the new study is the first to compare the frequency and success rate of trepanation over time and in different communities.

"This is the kind of richly detailed study that really gives us a sense of what life was like for ancient Andean populations," Tung said.

"It's astounding that [such a large percentage] of the population underwent skull surgery and that so many survived."

War Wounds

Trepanation was practiced as early as 400 B.C. in South America and is known from other parts of the world as well. Archaeologists have long debated whether the skull perforations were conducted as a medical procedure or for ritual or cultural reasons.

With regard to the Inca, Tung said, the new study should settle the debate.

"I think the authors are spot on when they suggest that cranial surgery was performed primarily to treat head injuries," she said.

Those injuries may have most often been sustained during warfare, according to the new study's authors.

Nearly all of the surgeries were performed either near the middle of the skull or on the left side—the regions most likely to be injured during combat with a right-handed opponent, Andrushko noted.

In addition, some of the skulls showed signs of previous injury in the area where the operation was performed.

The fact that 19 of the surgical patients were women, however, suggests that the operation may have sometimes been performed for other reasons—possibly as an attempted cure for epilepsy or chronic bone infection, the authors note.

Really?

The Claim: If You're Hyperventilating, Breathe Into a Paper Bag

By ANAHAD O'CONNOR

THE FACTS Like a bandage for a cut or a crutch for a broken leg, the brown paper bag is a symbol for hyperventilation.

Grabbing a bag and breathing into it repeatedly, known in medical literature as "rebreathing," has long been recommended to ease rapid, uncontrolled breathing. Some doctors even keep bags in the office for that reason. But most medical studies and experts suggest that the method, though accepted, is dangerous and should be retired.

The idea behind it is to increase carbon dioxide levels. Hyperventilation causes the body to expel too much carbon dioxide, and "rebreathing" exhaled air helps restore that lost gas.

The problem is that several medical conditions, like asthma and heart attacks, can be confused with hyperventilation. In such cases reducing oxygen and increasing carbon dioxide can be deadly. One study in *The Annals of Emergency Medicine* described three cases in which people having heart attacks thought, wrongly, that they were hyperventilating and died after losing oxygen while breathing into bags.

Another study said using a bag was no better at easing hyperventilation than using an open tube. For better results, experts say, stay calm and practice breathing slowly and deliberately.

THE BOTTOM LINE Most studies advise against paper bags to treat hyperventilation.

Global Update

Fake Malaria Drugs Emerging in Vulnerable Countries in Africa

By DONALD G. McNEIL Jr.

Until recently, fake malaria drugs have been a problem largely confined to Southeast Asia, where a sampling two years ago found 53 percent of the drugs substandard, and drug experts said Asia was facing "an epidemic of counterfeits."

A study released last week suggests that the epidemic is spreading to Africa, where the malaria burden is even greater, and the regulatory agencies are even weaker.

Tests on 195 packs of malaria drugs bought at private pharmacies found that 35 percent either did not contain enough active ingredient or did not dissolve quickly enough to work.

"The results are not happy reading for people taking these drugs," said Richard Tren, director of Africa Fighting Malaria, a health advocacy group that sponsored the tests.

The samples were bought in six cities: Accra, Ghana; Dar es Salaam, Tanzania; Kampala, Uganda; Kigali, Rwanda; Lagos, Nigeria; and Nairobi, Kenya. The study was published in *The Public Library of Science*.

Moreover, a third of the packets tested contained just artemisinin, the newest antimalarial from China. Last year, to prevent artemisinin-resistant strains of malaria from developing, the World Health Organization asked all the world's drug companies to stop selling it except in multidrug cocktails.

Nearly half the drugs that were made in Africa — assuming that their packaging was legitimate — failed the tests. So did a third of those made in Asia. None of the three samples of CoArtem, a multidrug cocktail made in Switzerland for global health agencies, failed.

Oral Cancer in Men Associated With HPV

By NICHOLAS BAKALAR

The sexually transmitted virus called HPV, for human papillomavirus, is well known to lead to cervical cancer in women — which is why the federal government recommends that all girls be vaccinated for HPV at 11 or 12, before they become sexually active.

Now researchers are finding that many oral cancers in men are also associated with the virus.

A clinical trial testing therapies for advanced tongue and tonsil cancers has found that more than 40 percent of the tumors in men were infected with HPV. If there is good news in the finding, it is that these HPV-associated tumors were among the most responsive to treatment.

Of an estimated 28,900 cases of oral cancer a year, 18,550 are in men.

“The high risk of HPV-associated cancers in men suggests that vaccinating all adolescents is something that should strongly be considered,” said the lead researcher, Dr. Francis P. Worden, a clinical assistant professor of medicine at the University of Michigan.

HPV can enter the mouth during oral sex. A study published in February by researchers at Johns Hopkins estimated that 38 percent of oral squamous-cell cancers are HPV related, and suggested that their increasing number might be a result of changing sexual behaviors.

The new study, published in two papers in *The Journal of Clinical Oncology*, included 51 men and 15 women with cancers of the tonsils or the base of tongue. The researchers were able to examine biopsies of 42 of the subjects before treatment. After tests for HPV, the researchers found that 27 tumors, nearly two-thirds, were positive for the virus. Of the 51 men, researchers found 22 with HPV.

Other experts found the results interesting, but said it was unclear what they would mean for treatment. Finding the answer to that question is the next step, said Dr. Maura L. Gillison, an associate professor of oncology at Johns Hopkins who was not involved in the study.

“Clearly,” Dr. Gillison added, “it should give people optimism that the vaccine that was approved largely for women and for cervical cancer could have broader implications, and also for other cancers that occur in both men and women. All of our clinical trials now will be designed for either HPV-positive or HPV-negative patients. Right now, these patients are treated the same way.”

All the patients in the study were initially treated with induction chemotherapy, that is, an initial course to shrink the tumor. Those whose tumors did not shrink by at least 50 percent, 12 patients, were then treated with surgery. Most of those did not survive their illness.

Of the remaining group, 49 of 54 responded to the next step, combined chemotherapy and radiation. In that group, 78 percent needed no surgery, and 70 percent survived more than four years. Of the 49, almost half, 24, were positive for HPV, and all but 3 of those were men.

People with tumors with high HPV levels were significantly more likely to respond to treatment. They were also more likely to survive their cancer and to survive over all.

The researchers also tested these tumors for the presence of four genetic markers: EGFR, a cell receptor associated with various cancers; BCLXL, a repressor of cell death; and the tumor-suppressor proteins p53 and p16. The scientists found that these were also accurate predictors of the success or failure of the treatment. Women and smokers were less likely to be treated successfully.

“Patients who have HPV infections are at higher risk for these cancers,” Dr. Worden said. “But the good news is that if that’s the cause of their cancer, they’re more likely to survive treatment. We still don’t know what the ideal treatment regimens are. For example, these patients may benefit from less intense chemotherapy and radiation.”

Although the researchers acknowledge that the number of patients in their study was small, they conclude that especially in patients with HPV-positive tumors, chemotherapy followed by combined chemotherapy and radiation appears to be an effective treatment.

An author of the papers has an interest in a company that is developing an HPV detection method.

Researchers fine-tune clot-busting treatment for bleeding in brain ***Treatment dramatically increases survival for deadly condition***

A multicenter study led by Johns Hopkins doctors has fine-tuned the dosage and timing for administering clot-busting tissue plasminogen activator (tPA) to patients with strokes caused by bleeding within the brain. The treatment, as reported this week at the European Stroke Conference in Nice, France, has been shown to dramatically decrease death and disability in patients with this typically lethal subset of stroke.

“We’ve gone from what’s usually an 80 percent death rate in patients with this condition to an 80 percent survival rate,” says study leader Daniel Hanley, M.D., professor of neurology at the Johns Hopkins University School of Medicine.

This condition, known as intracerebral hemorrhage (ICH), causes blood to clot inside the brain’s interior cavities, building up pressure within the brain. The higher pressure, along with inflammation caused by chemicals in the trapped blood, can irreversibly damage the brain, usually leading to death or extreme disability. Until recently, Hanley notes, no treatment existed for this subset of stroke.

The new research builds on a series of previous studies designed to test the safety and efficacy of clot-busting drugs in patients with ICH. This treatment, developed by Hanley and his colleagues, clears the trapped blood out of the brain by bathing-and dissolving-the clot directly in tPA. This drug normally isn’t recommended for conditions that involve bleeding, such as ICH, because it can increase the risk of further hemorrhage. However, since high-dose (80 to 100 mg) tPA is effective at breaking up clots in other conditions, such as heart attacks and other types of strokes, Hanley and his colleagues wondered whether very low doses of the drug might be a safe and effective way to treat ICH.

The previous studies showed that giving tPA to ICH patients hadn’t significantly increased bleeding or death, so in the latest study, Hanley and his colleagues sought to determine the safest and most effective treatment regimen using this drug.

At 20 hospitals located across the United States, Canada, Great Britain, and Germany, the researchers recruited 52 patients recently diagnosed with ICH. All of the patients had received the usual treatment for this condition, placing a catheter inside the brain to release the trapped blood. Using the same catheter as a conduit for flooding tPA directly onto the clot, the researchers put each patient on one of three treatment regimens: 0.3 milligrams of the drug every 12 hours, 1 milligram of the drug every 12 hours, or 1 milligram of the drug every 8 hours.

Tracking patients' progress with daily CT scans, the researchers found that the clots dissolved within three to four days on average, with patients on 1 milligram of tPA every 8 hours dissolving their clots about a day faster than those on the other treatment regimens. This timing is about two to three times faster than that of previous patients who didn't receive tPA. Hanley notes that additional bleeding among all the patients was minimal; those treated with tPA weren't any more likely to have additional hemorrhaging than those past patients who didn't receive the drug.

One month after treatment, more than 80 percent of the patients were alive, and 10 percent of these had recovered enough to return to their jobs, the researchers report.

"We think that this treatment is the most promising story in brain hemorrhage in many years," says Hanley. "We've taken a condition that used to have an extremely high rate of death and disability and turned it around."

The researchers plan to launch a definitive trial to test this treatment in 500 patients in the near future.

Other Hopkins researchers who participated in this study include Wendy Ziai, M.D.; Ricardo Carhuapoma, M.D.; Neal Naff, M.D.; Becky Sullivan, M.B.A.; Timothy Morgan, B.S.; Eric Melnychuk, B.A., E.M.T.-B; Susan Rice, R.N., M.P.H., C.C.R.P.; Amber Stahl, B.A.; Alison Kwon, B.A., C.C.R.C.; Shannon LeDroux, B.S.; Amanda Bistran, B.S.; Sofia Syed and Karen Lane, C.M.A., C.C.R.P.

*This study was funded by the FDA Orphan Drug Program and partially supported by a sponsored research agreement and drug from Genentech. For more information, go to: <http://clearivh.com/default.aspx>
http://www.hopkinsmedicine.org/Press_releases/2006/02_17_06.html*

Tooth loss strongly linked to risk of esophageal, head and neck, and lung cancer

PHILADELPHIA – Studying thousands of patients, Japanese researchers have found a strong link between tooth loss and increased risk of three cancers – esophageal, head and neck, and lung. They suggest that preservation of teeth may decrease risk of developing these diseases.

In the May issue of *Cancer Epidemiology, Biomarkers and Prevention*, a journal of the American Association for Cancer Research, scientists from Aichi Cancer Center in Nagoya and Nagoya University Graduate School of Medicine speculate that bacterial infection and inflammation resulting from poor oral care that leads to tooth loss could also be driving development of these cancers. Periodontal disease is known to increase risk for stroke and heart disease.

"Tooth loss is a common consequence of chronic bacterial infection and may, therefore, serve as a surrogate for chronic infection and inflammation, which in turn may be important to the pathogenesis of cancer," said the study's lead author, Akio Hiraki, Ph.D., a researcher at the Aichi Cancer Center.

Researchers measured rates of 14 different cancers and rates of tooth loss in 5,240 cancer patients in Japan, and compared those rates among 10,480 matched cancer-free participants. The researchers specifically found that people with tooth loss were 136 percent more likely to develop esophageal cancer, had a 68 percent increased risk of developing head and neck cancer and a 54 percent greater chance of developing lung cancer. The researchers also found that the rate of cancer increased proportionally to the number of teeth a patient had lost.

These increased risks were seen after researchers took into account a patient's history of smoking and alcohol use.

Smaller studies have linked tooth loss to different cancers, but this is the largest study to date, and the first conducted within an Asian population, the researchers say. This is also the first study to show a link to lung cancer, they add.

The researchers noted that age and gender affected the associations between tooth loss and cancer risk. For head and neck and esophageal cancers, there were clear associations between tooth loss and cancer risk in women and patients younger than 70 years old, but a less clear link in men and older patients.

The researchers say that while widespread inflammation could explain the link between tooth loss and cancer risk, they also note that tooth loss in the cancer patients may simply reflect unhealthy behaviors that contribute to cancer risk. Furthermore, people who have lost teeth may not be able to eat a healthy diet, and diet is also a factor in cancer development.

Whatever the mechanism, the researchers stress that oral care is critical to good health.

"The oral cavity is a gateway between the external environment and the gastrointestinal tract and acts in both food ingestion and digestion," the researchers wrote. "Oral hygiene potentially affects gastrointestinal flora and nutritional status and may thus have implications for the development of chronic disease."

Wild sloths are no sleepyheads after all

* 00:01 14 May 2008

* NewScientist.com news service

* **Jo Marchant**

Far from deserving their lazy reputation, wild sloths sleep far less than biologists had thought.

The first study to measure the sleep patterns of animals in the wild has found that three-toed sloths doze for less than 10 hours a day, compared to the rather more somnolent 16 hours a day recorded in captivity.

As well as helping repair the sloth's reputation, the result could have profound implications for research into the function of sleep in both animals and humans.

Previous studies of sleep in animals have all been carried out in captivity, because measuring the electrical activity of the brain involved an invasive surgical procedure. Also, the equipment needed for recording the resulting data was too bulky to place on an animal moving about in the wild.

Wild three-toed sloths were fitted with state-of-the-art EEG caps that provided the researchers with several days' readout of brain activity. The result? They are much less sleepy than assumed (Image: Roland Kays)



Not bothered

But two new technological developments have allowed Niels Rattenborg of the Max Planck Institute for Ornithology in Sarnberg, Germany, and his colleagues to overcome these obstacles.

The first is a "black box" made by Alexei Vyssotski at the University of Zurich, Switzerland. Originally designed to monitor the brain activity of homing pigeons, it can record and store several days' worth of data, but is small enough to be carried by a small animal or bird.

The second is an EEG cap designed for use in humans. Rather than implanting large electrodes into the brain as with older equipment, Rattenborg's team inserted fine wires just beneath the skin of the animals' scalps.

Rattenborg decided to test the equipment on sloths because, as well as their reputation for sleeping a lot, they don't move too fast, and they are relatively calm. "They don't seem to be bothered by us putting things on their heads," he says.

'Persistent concern'

The researchers snared three female three-toed sloths (*Bradypus variegates*) from high in the treetops of Barro Colorado Island (BCI) in the middle of the Panama Canal.

After being fitted with radio tracking collars and EEG caps, the animals were released and monitored for 3 to 5 days each. Two more sloths were followed for a further 7 months using just radio collars.

The idea that wild animals might have different sleep patterns from captive ones has been "a persistent concern" since sleep studies began 40 years ago, says Rattenborg. Even so, he was surprised how big the difference was.

The sloths at BCI slept an average of only 9.63 hours per day, compared to 15.85 hours per day in a previous study of captive animals. Sloths in captivity may sleep more because they don't need to forage for food or watch for predators, or just because they are bored.

The result is important because many of the theories for why sleep evolved are based on studies that compare sleep in different species.

Human implications

John Lesku who works at the Max Planck Institute for Ornithology with Rattenborg has recently found, for example, that bigger-brained species have more REM sleep, suggesting that it has a neurophysiological role, such as memory consolidation.

Lesku admits that if wild animals have different sleeping patterns to captive ones, all of the previous research may need to be reassessed.

"What is the significance of the relationships we have found?" he says. "We need to explore sleep in the wild in more species."

Rattenborg agrees. "If we study animals in their natural environment where sleep patterns evolved, we may discover new patterns that may give us new ideas about the evolutionary function of sleep," he says. "And that may have implications for understanding sleep in humans."

He now plans to repeat the study in ostriches, which belong to an early evolutionary branch of birds, to see how their sleep patterns compare to those of more modern groups.

Journal references: Biology Letters (DOI: 10.1098/rsbl.2008.0203); Sleep Medicine Reviews (DOI: 10.1016/j.smrv.2007.10.1003)

Researchers Find New Treatment for Hepatitis C

"New" drug is already approved for lowering cholesterol

Oklahoma City, OK -- Researchers at the OU Health Sciences Center have found a new use for an old drug. Their findings appear online Friday in the American Journal of Gastroenterology.

The drug, Fluvastatin, has been approved since 1993 by the U.S. Food and Drug Administration for the treatment of elevated cholesterol in adults. Millions of patients have taken Fluvastatin for cholesterol without difficulty.

In a study of 31 veterans at the Veteran's Administration Medical Center in Oklahoma City, researchers found that Fluvastatin significantly lowered the viral load, or levels of hepatitis C virus, for up to six weeks when used alone. Hepatitis C is the disease that claimed the life of Oklahoman Mickey Mantle.

"This research is the first to demonstrate the antiviral activity of Fluvastatin in human beings infected with hepatitis C, most of whom were non-responders to the standard of care treatment," said Ted Bader, M.D., the principle investigator on the project and the director of liver diseases at the OU Health Sciences Center.

Since Fluvastatin will not completely clear the hepatitis C virus by itself, researchers have started a phase II randomized, controlled trial that combines Fluvastatin with the standard treatment of peg-interferon and ribavirin. They hope to use the combination of medicines to significantly improve the cure rate for hepatitis C. After further required testing and approval, the drug could be available as a new treatment for hepatitis C far sooner than any other anti-hepatitis C drug currently under research and development.

"We need additional drugs to add to this regimen to improve the cure rate," Bader said. "When patients are cured, they feel dramatically better, their health care costs plummet, their risk of liver cancer drops dramatically, and if they do not have cirrhosis, they will not need a liver transplant. Moreover, they are no longer infectious."

In the initial investigative study funded by the VA Research Foundation of Oklahoma City and Dr. Michael Bronze at the OU College of Medicine, veterans with chronic HCV were given oral doses of Fluvastatin daily for two to 12 weeks. Within a month, half of the patients showed a reduction of the virus. One patient's viral load was about 50 times lower than before taking Fluvastatin.

Hepatitis C is a significant problem for Oklahoma. More than 80,000 Oklahomans have chronic hepatitis C (HCV), but less than 5 percent have been treated. HCV is the leading cause of liver-related deaths in our state and also is the cause for the majority of the 70 liver transplants performed in Oklahoma each year.

Nationwide, 2 percent of Americans (about 4 million) are infected with chronic hepatitis C, which is four times the number of patients infected with HIV. Chronic hepatitis C is often asymptomatic and can lead to progressive liver disease.

Most people with hepatitis C contracted the disease through blood transfusions before 1992 when a test was implemented to screen for the disease. You also can get the virus by injecting drugs with contaminated needles and, less commonly, from contaminated needles used in tattooing and body piercing.

Researchers find first conclusive evidence of Alzheimer's-like brain tangles in nonhuman primates

Finding could shed light on why humans develop neurodegenerative diseases and pave the way for new treatments

Researchers at the Yerkes National Primate Research Center, Emory University, have discovered the first conclusive evidence of Alzheimer's-like neurofibrillary brain tangles in an aged nonhuman primate. The unprecedented finding, described in the online issue of the *Journal of Comparative Neurology*, has the potential to move the scientific community one step closer to understanding why age-related neurodegenerative diseases, such as Alzheimer's disease, are uniquely human and seem to never fully manifest in other species--including our closest evolutionary relative, the chimpanzee.

Lead researchers Rebecca Rosen, a doctoral student who is conducting her research at Yerkes, and Lary Walker, PhD, a neuroscientist and research professor at Yerkes, in collaboration with colleagues at UCLA, made the unanticipated finding during a routine post-mortem study of an aged, female chimpanzee that died of natural causes. The researchers also discovered deposits of beta-amyloid protein in plaques and blood vessels of the chimp's brain tissue, although these changes were infrequent compared to Alzheimer's disease in humans.

"We've seen these plaques in aged chimpanzees before, but this is the first time researchers have found both hallmark features of Alzheimer's disease--plaques and neurofibrillary tangles--in a nonhuman primate," explains Walker.

As many as five million Americans are living with Alzheimer's disease, the most common form of dementia. A cure has eluded researchers, and the disease is considered progressive and fatal. Brain plaques and tangles associated with the disease are prime suspects in damaging and killing nerve cells that cause memory loss and dementia.

"Alzheimer's disease has a huge number of potential causes," says Rosen. "By studying the development of human features of the disease that occur naturally in nonhuman primates, we may be able to isolate what makes people so susceptible to neurodegenerative disease and identify targets for therapeutics."

The research reported in the *Journal of Comparative Neurology* is just one of the projects at Yerkes aimed at uncovering underlying mechanisms and pathogenesis of Alzheimer's disease. Walker is evaluating the immune response of squirrel monkeys to a vaccine targeting beta-amyloid protein. The goal is to see if the vaccine prompts the immune system to make antibodies against the protein without side effects. In another study, Rosen is looking at the structure of beta-amyloid protein in multiple primate species with the hope of identifying the correct target for new drugs and immunotherapy.

Rosen noted Yerkes has provided her with unparalleled access to resources for graduate-level research and training. Added Walker, "Yerkes is one of the only facilities in the world that offers researchers the resources to study chimpanzees across the entire lifespan, including behavior, biochemistry, physiology, molecular biology and disease pathology."

For more than seven decades, the Yerkes National Primate Research Center, Emory University, has been dedicated to conducting essential basic science and translational research to advance scientific understanding and to improve the

health and well-being of humans and nonhuman primates. Today, the center, as one of only eight National Institutes of Health-funded national primate research centers, provides leadership, training and resources to foster scientific creativity, collaboration and discoveries. Yerkes-based research is grounded in scientific integrity, expert knowledge, respect for colleagues, an open exchange of ideas and compassionate, quality animal care.

Within the fields of microbiology and immunology, neuroscience, psychobiology and sensory-motor systems, the center's research programs are seeking ways to: develop vaccines for infectious and noninfectious diseases, such as AIDS and Alzheimer's disease; treat cocaine addiction; interpret brain activity through imaging; increase understanding of progressive illnesses such as Parkinson's and Alzheimer's; unlock the secrets of memory; determine behavioral effects of hormone replacement therapy; address vision disorders; and advance knowledge about the evolutionary links between biology and behavior.

In addition to Rosen and Walker, study authors were Aaron Farberg, Marla Gearing, Jeromy Dooyema, Patrick Long, Daniel Anderson, Jean-Francois Pare, Timothy Duong, William Hopkins and Todd Preuss of Emory University, and Jeremy Davis-Turak, Giovanni Coppola and Daniel Geschwind of the David Geffen School of Medicine at UCLA.

Funding for the study was from the National Institutes of Health and the James S. McDonnell Foundation.

Reference: "Tauopathy with paired helical filaments in an aged chimpanzee." *The Journal of Comparative Neurology*, Vol. 509, Issue 3, July 20, 2008, pp. 259-270. Published online May 14, 2008.

Green tea compounds beat OSA-related brain deficits

Chemicals found in green tea may be able to stave off the cognitive deficits that occur with obstructive sleep apnea (OSA), according to a new study published in the second issue for May of the American Thoracic Society's American Journal of Respiratory and Critical Care Medicine.

Researchers examined the effects green tea polyphenols (GTP), administered through drinking water, on rats who were intermittently deprived of oxygen during 12-hour "night" cycles, mimicking the intermittent hypoxia (IH) that humans with OSA experience.

People with OSA have been reported to have increased markers of oxidative stress and exhibit architectural changes in their brain tissue in areas involved in learning and memory. Chronic IH in rats produce similar neurological deficit patterns.

"OSA has been increasingly recognized as a serious and frequent health condition with potential long-term morbidities that include learning and psychological disabilities [...]," wrote David Gozal, M.D., professor and director of Kosair Children's Hospital Research Institute at the University of Louisville, lead author of the article. "A growing body of evidence suggests that the adverse neurobehavioral consequences imposed by IH stem, at least in part, from oxidative stress and inflammatory signaling cascades."

GTPs are known to possess anti-oxidant properties, acting as a free radical scavengers, and research has shown that the compounds may reduce the risk of a variety of different diseases.

"Recent studies have demonstrated the neuroprotective activity of GTP in animal models of neurodegenerative conditions such as Parkinson's and Alzheimer's disease," wrote Dr. Gozal.

In this study, the researchers divided 106 male rats into two groups that underwent intermittent oxygen depletion during the 12-hour "night" cycle for 14 days. One group received drinking water treated with GTP; the other received plain drinking water.

They were then tested for markers of inflammation and oxidative stress, as well as for performance in spatial learning and memory tasks—namely a water "maze" in which the rat had to memorize the location of a hidden platform.

The IH-rats that received the green tea-treated water performed significantly better in a water maze than the rats that drank plain water. "GTP-treated rats exposed to IH displayed significantly greater spatial bias for the previous hidden platform position, indicating that GTPs are capable of attenuating IH-induced spatial learning deficits," wrote Dr. Gozal, adding that GTPs "may represent a potential interventional strategy for patients" with sleep-disordered breathing.

Crystal (Eye) Ball: Study Says Visual System Equipped With "Future Seeing Powers"

New research categorizes more than 50 types of illusions that help us perceive the present

Troy, N.Y. — Catching a football. Maneuvering through a room full of people. Jumping out of the way when a golfer yells "fore." Most would agree these seemingly simple actions require us to perceive and quickly respond to a situation. Assistant Professor of Cognitive Science at Rensselaer Polytechnic Institute Mark Changizi argues they require something more — our ability to foresee the future.

It takes our brain nearly one-tenth of a second to translate the light that hits our retina into a visual perception of the world around us. While a neural delay of that magnitude may seem minuscule, imagine trying to catch a ball or wade through a store full of people while always perceiving the very recent (one-tenth of a second prior) past. A ball passing within one meter of you and traveling at one meter per second in reality would be roughly six degrees displaced from where you perceive it, and even the slowest forward-moving person can travel at least ten centimeters in a tenth of a second.

Changizi claims the visual system has evolved to compensate for neural delays, allowing it to generate perceptions of what will occur one-tenth of a second into the future, so that when an observer actually perceives something, it is the present rather than what happened one-tenth of a second ago. Using his hypothesis, called "perceiving-the-present," he

was able to systematically organize and explain more than 50 types of visual illusions that occur because our brains are trying to perceive the near future. His findings are described in May-June issue of the journal *Cognitive Science*.

“Illusions occur when our brains attempt to perceive the future, and those perceptions don’t match reality. There has been great success at discovering and documenting countless visual illusions. There has been considerably less success in organizing them,” says Changizi, who is lead author on the paper. “My research focused on systematizing these known incidents of failed future seeing into a ‘periodic table’ of illusion classes that can predict a broad pattern of the illusions we might be subject to.”

More than meets the eye

We experience countless illusions in our lifetime. The most famous being geometrical illusions — those with converging lines and a vanishing point we often see in Psychology 101 classes or in entertaining optical illusion books.

The Hering illusion is exemplified by the perceived curvature of the straight lines near the vanishing point in the center of the drawing. The optical illusion occurs because our brains are predicting the way the underlying scene would project in the next moment if we were moving in the direction of the vanishing point.

To picture one, think of the Hering illusion, which looks like a bike spoke with two vertical lines drawn on either side of the center vanishing point. Although the lines are straight, they seem to bow out away from the vanishing point. The optical illusion occurs because our brains are predicting the way the underlying scene would project in the next moment if we were moving in the direction of the vanishing point.

“Evolution has seen to it that geometric drawings like this elicit in us premonitions of the near future,” says Changizi. “The converging lines toward a vanishing point are cues that trick our brains into thinking we are moving forward — as we would in the real world, where the door frame seems to bow out as we move through it — and we try to perceive what that world will look like in the next instant.”

Beyond geometric, Changizi was able to identify 27 other classes of illusions. He organized them into 28 predictable categories classified on a matrix that distributes them among four columns based on the type of visual feature that is misperceived (size, speed, luminance, and distance) and among seven rows based on the different optical features that occur when an observer is moving forward.

He then culled hundreds of previously documented illusions to test whether they would follow the appropriate prediction as determined by the table, and found that they did, indeed, follow the patterns he laid out in the matrix.

This new organization of illusions presents a range of potential applications, including more effective visual displays and enhanced visual arts. It especially may help constrain neuroscientists aiming to understand the mechanisms underlying vision, according to Changizi.

Changizi conducted his research during a fellowship in the Sloan-Swartz Center for Theoretical Neurobiology at the California Institute of Technology. Coauthors on the paper include: Caltech Biology Professor Shinsuke Shimojo, former Caltech undergraduate student Andrew Hsieh, and former Caltech postdoctoral researcher Ryota Kanai, as well as Romi Nijhawan, a psychologist at the University of Sussex in England.

The research was supported by a grant from the National Institutes of Health.

New Study Casts Further Doubt on Risk of Death from Higher Salt Intake

BRONX, NY — Contrary to long-held assumptions, high-salt diets may not increase the risk of death, according to investigators from the Albert Einstein College of Medicine of Yeshiva University. They reached their conclusion after examining dietary intake among a nationally representative sample of adults in the U.S. The Einstein researchers actually observed a significantly increased risk of death from cardiovascular disease (CVD) associated with lower sodium diets. They report their findings in the advance online edition of the *Journal of General Internal Medicine*.

The researchers analyzed data from the Third National Health and Nutrition Examination Survey (NHANES III), which was conducted by the federal government among a nationally representative sample of U.S. adults. These data were then compared against death records that had been collected by the government through the year 2000. The sample of approximately 8,700 represented American adults who were over 30 years of age at the time of the baseline survey (1988-1994) and were not on a special low-salt diet.

After adjusting for known CVD risk factors, such as smoking, diabetes and blood pressure, the one-fourth of the sample who reported consuming the lowest amount of sodium were found to be 80% more likely to die from CVD compared to the one-fourth of the sample consuming the highest level of sodium. The risk for death from any cause appeared 24% greater for those consuming lower salt, but this latter difference was not quite large enough to dismiss the role of chance.

"Our findings suggest that for the general adult population, higher sodium is very unlikely to be independently associated with higher risk of death from CVD or all other causes of death," says Dr. Hillel W. Cohen, lead author of the study and associate professor of epidemiology and population health at Einstein.

Since the first NHANES survey in the early 1970s, data from NHANES have been used extensively to describe patterns of nutrition and health in the U.S. The results from this current study are consistent with findings reported



previously from two earlier NHANES surveys. While the federal government currently repeats NHANES surveys every two years, NHANES III is the latest available survey that can be compared with later death records.

Since NHANES III was an observational study and not a clinical trial, no definite conclusions about cause and effect were possible, says Dr. Cohen. "However, our findings do again raise questions about the usefulness or even safety of universal recommendations for lower salt diets for all individuals, regardless of their blood pressure status or other health characteristics," he cautions.

Other Einstein researchers on the study were Dr. Susan M. Hailpern and Dr. Michael H. Alderman.

How small molecule can take apart Alzheimer's disease protein fibers

Implications for host of neurodegenerative diseases

PHILADELPHIA – Researchers from the University of Pennsylvania School of Medicine have shown, in unprecedented detail, how a small molecule is able to selectively take apart abnormally folded protein fibers connected to Alzheimer's disease and prion diseases. The findings appear online this week in the Proceedings of the National Academy of Sciences. Finding a way to dismantle misfolded proteins has implications for new treatments for a host of neurodegenerative diseases.

Abnormal accumulation of amyloid fibers and other misfolded forms in the brain cause neurodegenerative diseases. Similarly, build-up of abnormally folded prion proteins between neurons causes the human version of mad cow disease, Creutzfeldt-Jakob disease.

Alzheimer's fibers without DAPH (left). Note uniform fibers. Alzheimer's proteins with DAPH (right). Note fibers have broken up. James Shorter, PhD, University of Pennsylvania School of Medicine

"Surprisingly, a small molecule called DAPH selectively targets the areas that hold fibers together, and converts fibers to a form that is unable to grow. Normally fibers grow from their ends, but the drug stops this activity," says senior author James Shorter, PhD, Assistant Professor of Biochemistry and Biophysics. "Our data suggest that it is possible to generate effective small molecules that can attack amyloid fibers, which are associated with so many devastating diseases."

The researchers are now working on how DAPH acts as a wedge to stop the fibers from growing. "Presumably DAPH fits very neatly into the crevices between fiber subunits," explains Shorter. "When we grow yeast cells with the prion in the presence of DAPH, they begin to lose the prion. We also saw this in the test tube using pure fibers. The small molecule directly remodels fiber architecture. We've really been able to get at the mechanism by which DAPH, or any small molecule, works for the first time." DAPH was originally found in a screen of small molecules that reduce amyloid-beta toxicity in the lab of co-author Vernon Ingram, Shorter's collaborator at the Massachusetts Institute of Technology (MIT).

In a test tube, if a small amount of amyloid or prion fiber is added to the normal form of the protein, it converts it to the fiber form. But when DPAH is added to the mix, the yeast prion protein does not aggregate into fibers. "It's essentially stopping fiber formation in its tracks," says Huan Wang, first author and research specialist in Shorter's lab. "We were surprised to see two very different proteins, amyloid-beta and Sup35, sensitive to this same small molecule."

The next step is to identify more potent DAPH variants with greater selectivity for deleterious amyloids. Since some amyloids may turn out to be beneficial – for example, one form may be involved in long-term memory formation – it will be necessary to find a drug that does not hit all amyloids indiscriminately. "We'd need one that hits only problem amyloids, and DAPH gives us a hint that such selectivity is possible" says Shorter.

This work was initiated in Susan Lindquist's lab at MIT and completed at Penn. The study was funded by the National Institute of General Medical Sciences, the Alzheimer's Association, the Kurt and Johanna Immerwahr Fund for Alzheimer Research, a DuPont-MIT alliance, the American Heart Association, and pilot grants from the University of Pennsylvania Alzheimer's Disease Core Center and Institute on Aging.

Insecticides in pet shampoo may trigger autism

* 12:17 15 May 2008

* NewScientist.com news service

* **Linda Geddes**

Could insecticides in pet shampoos trigger autism spectrum disorders? That's the suggestion of one of the first large-scale population-based studies to look how environmental factors and their interactions with genes contribute to the condition.

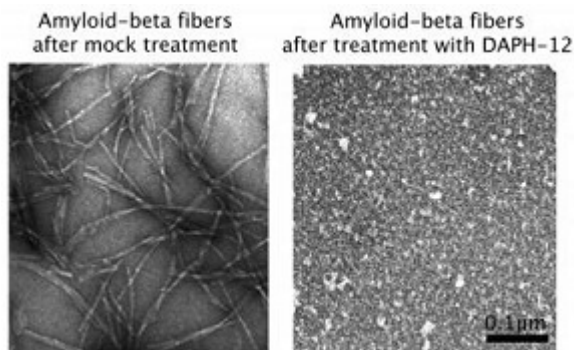
Mothers of children with an autism spectrum disorder (ASD) were twice as likely to have reported using pet shampoos containing a class of insecticide called pyrethrins as those of healthy children, according to survey results presented Thursday at the International Meeting for Autism Research in London. The risk was greatest if the shampoo was used during the second trimester of pregnancy.

Meanwhile, another study suggests that exposure to organophosphate insecticides double the risk of developmental disorders, including autism. Organophosphates have previously been linked to Gulf War syndrome.

While many chemicals have previously been blamed for triggering autism, there have been very few rigorous studies designed to investigate the link.

Neuronal damage

2008/05/19



To remedy this, Irva Hertz-Picciotto and her colleagues at the University of California in Davis, US, studied 333 children with ASD and 198 healthy children, and their families.

They collected blood and urine samples, as well as conducting in-depth questionnaires on medical history and any possible exposure to medications, household products or metals that could have occurred around the time of conception, during pregnancy, or after birth. They also collected information on lifestyle, and whether the children were breast-fed, for example.

Previous studies in insects and rodents have suggested that pyrethrins could damage the blood-brain barrier during early life, and cause neuronal damage. They may also interfere with the transmission of signals along nerve fibres.

"Autism is associated with an imbalance between excitatory and inhibitory neurotransmitters within the brain, and one could hypothesise that children with an imbalance in this system may be more sensitive to the effects of pyrethrins," says Isaac Pessah at UC Davis, who was also involved in the study.

'No single answer'

However, Hertz-Picciotto and other experts caution that pyrethrins were unlikely to be the only cause of autism, which is increasingly recognised as being caused by a complex interplay of both genetic and environmental factors.

"This is a candidate, but there is unlikely to be a single answer to what causes autism," says Tony Charman of University College London, UK, and chairman of IMFAR.

"The findings now need to be replicated and more studies need to be done to understand how this toxin affects development," he says.

Neither are pyrethrins likely to be the only chemicals that increase the risk of ASD.

Genetic susceptibility

For example, in a separate study, Brenda Eskenazi and her colleagues at the University of California in Berkeley, measured levels of metabolites from organophosphates in urine samples taken from 400 women during pregnancy, and their children. Such metabolites were associated with a two-fold risk of developmental disorders in the children.

As well as being used in agricultural products like sheep dip, organophosphates are used in head-lice treatments, pet shampoos and other household products.

Pessah says that chemicals like pyrethrins and organophosphates are likely to increase the risk of autism in children who already have an underlying genetic susceptibility.

"ASD is a spectrum of disorders, some of which are very mild, and chemical or environmental factors may shift that profile so that children who would otherwise not receive a diagnosis of ASD will receive one."

Geri Dawson, chief scientific officer at research charity Autism Speaks, agrees.

"Probably in the majority of cases autism is a complex disorder involving multiple genes and multiple environmental factors," she says. "However, at least if we can identify the environmental factors, there is something we can do about them."

New drug combination brings 1-2 punch against acute leukemia

CINCINNATI, OHIO - Researchers at The University of Texas M. D. Anderson Cancer Center have discovered a drug combination that kills leukemia cells by shutting down their energy source and hastening cell starvation.

In a preclinical study, Lauren Akers, D.O., postdoctoral fellow from the Children's Cancer Hospital at M. D. Anderson, found that combining a novel glycolysis inhibitor, 3-BrOP, with mTOR inhibitor, rapamycin, induced more than 90 percent cell death in human tissue cultures of acute lymphocytic leukemia. She presented her study at the American Society of Pediatric Hematology/Oncology annual conference on May 16.

"We already knew that 3-BrOP was effective in preclinical research of glioblastoma, colon cancer and lymphoma, and most recently acute leukemias" says Akers, lead investigator on the study. "We also knew that mTOR inhibitors intensify cellular starvation. This study showed that the two together have a more powerful impact on treating acute lymphocytic leukemia, which is the most common childhood cancer."

Glycolysis is a process that turns glucose into energy for cells. Unlike healthy cells that get their energy for growth from both glycolysis and respiration, cancer cells are highly dependent on glycolysis. Using the M. D. Anderson-developed drug, 3-BrOP, researchers inhibited glycolysis, thus starving the leukemia cells from their energy source while leaving healthy cells free to get their energy from respiration.

Rapamycin is an mTOR inhibitor that keeps cancer cells from coping with stress, thus resulting in cell death. When researchers on the study combined the two drugs, they discovered a synergistic effect.

"We found that a lower dosage of 3-BrOP with rapamycin created the same results of more than 90 percent tumor cell death," says Akers. "Theoretically, we believe that patients will better tolerate the therapy by lowering the dosage of 3-BrOP and combining it with rapamycin."

Other researchers on the study include senior investigator Patrick Zweidler-McKay, M.D., Ph.D., Anna Franklin, M.D. and Wendy Fang, M.D., all from the Children's Cancer Hospital at M. D. Anderson. Peng Huang, M.D., Ph.D., from the Department of Molecular Pathology at M. D. Anderson was also an investigator and was responsible for the development of 3-BrOP.

The team of researchers plans to conduct additional mouse studies, which could lead to a Phase I clinical trial some time in the future.

Experts Tackle Shipment Issues for Beneficial Radiation Sources

Mediterranean Workshop Focuses on Radioactive Materials for Medicine, Industry

 Listen to this story

Delays and denials of shipments involving regulated radioactive materials used in medicine and industry are of growing concern to safety and industry experts. Meeting in Rome this week at an IAEA workshop, they agreed on an action plan for the Mediterranean region that seeks to ease hardships for hospitals, research centres and organizations that rely on timely delivery of beneficial radiation sources.

The shipment issues have surfaced over the past several years, with international dimensions. Data reported to the IAEA over a recent six-month period indicate more delays than denials are taking place. Denials block shipments entirely, and delays can virtually render a radioisotope useless because of its short radioactive half-life.

Between September 2007 and March 2008, a total of 69 reports of delays and denials of shipments (42 delays, 19 denials and 8 unspecified) were reported to the IAEA. Of these, 46 reports concerned air transport, while the remaining 23 cases concerned sea, rail and road transport modes. In terms of the most common types of radioactive sources involved, 23 reports concerned iodine-131 (which has a half-life of eight days and is used in medical diagnosis), 14 fluorodeoxyglucose (a solution used for medical imaging incorporating fluorene-18, which has a half-life of just under 110 minutes); and 13 cobalt-60 (which has a half-life of 5.27 years and is used in radiotherapy for cancer care, among other applications).

The main outputs of the Rome workshop are the establishment of:

- * A regional action plan focusing on six areas (i.e. awareness, training, communication, lobbying, economic, and harmonization);
- * A regional network that would allow participants to share their experience and lessons learned, as well as identify and disseminate best practices; and
- * A regional database of denial of shipments instances that will help identify issues and trends in a consistent and reliable manner.

The participants also stressed that successful communication and strong cooperation between a range of partners is essential for eventually resolving problems. Partners include the International Steering Committee on Denial of Shipments, the IAEA, the UN and International Modal Organizations, trade associations, regional networks, and national focal points in each country will lead to a better understanding and, eventually, a resolution of this problem. The workshop was hosted by the Government of Italy through the National Agency for Environmental Protection and Technical Services (APAT).

At the workshop, the IAEA's Khammar Mrabit, Head of the Regulatory Infrastructure and Transport Safety Section, highlighted the importance of tackling the issue of denial of shipments of radioactive material, emphasizing the importance of international safety standards and practices.

"There has been no significant accident from transport of radioactive material over the past half century," he said. "Denial of shipments potentially increases the risks to safety and security. We should not let the issue of denial of shipments of radioactive material render ineffective the good work that has been done for over 50 years of establishing a strong safety record."

In his welcome remarks, Roberto Mezzanotte, Director of APAT's Department of Nuclear, Technological and Industrial Risk, also emphasized the urgency of the problem. "The issue of denial of shipments is not just for specialists but affects the lives of millions of people around the world. The majority of the radioactive material shipped every day is used in hospitals for diagnostics and treatment of several illnesses," he said.

The three-day *Regional Workshop on Denial of Shipment of Radioactive Material for Countries in the Mediterranean Basin* was held in Rome, Italy, from 14-16 May. More than 80 participants from 15 countries of the Mediterranean Basin and eight international organizations and associations attended. The workshop was part of the IAEA's response to reports of increasing numbers of instances of radioactive material being denied shipment by carriers, and followed a similar meeting in Montevideo, Uruguay, in July 2007 for the Latin American region. Three more workshops are scheduled for June 2008 in Africa, Asia and the Pacific.

Background

Production of isotopes is limited to a few countries, which underscores the importance of timely, efficient and safe international shipments to hospitals and industries. Some radioisotopes, such as iodine-123 - used for heart and thyroid imaging - have a half-life of only hours. Consequently, any interruption to their delivery can threaten the medical care of patients.

According to industry statistics 85,000 nuclear medicine procedures are carried out around the world every day. Additionally, radioactive material shipped every day all over the world is also used in a multitude of industrial applications, research and development, and in the generation of electricity and power.

Story Resources

- [Info on Regional Workshops on Denials of Shipment of Radioactive Material](#) [pdf]
- [International Steering Group on Denial of Shipments](#)
- [Lifesaving Medical Isotopes Being Denied Shipment](#)
- [IAEA Division of Radiation, Transport & Waste Safety](#)
- [IAEA Department of Nuclear Safety and Security](#)

- [Italian National Agency for Environmental Protection and Technical Services \(APAT\)](#)

Global biodiversity slumps 27% in 35 years

* 00:01 16 May 2008

* NewScientist.com news service

* **Michael Marshall**

The latest data on the global biodiversity of vertebrates shows that it has fallen by almost one-third in the last 35 years. But experts say it may still underestimate the effect humans have had on global species counts.

The Living Planet Index (LPI) follows trends in nearly 4,000 populations of 1,477 vertebrate species and is said to reflect the impact humans have on the planet. It is based on a wide range of population datasets, such as commercial data on fish stocks and projects such as the Pan-European Common Bird Monitoring scheme.

New figures show that between 1970 and 2005, the global LPI has fallen by 27%. This suggests that the world will fail to meet the target of reducing the rate of biodiversity loss set by the 2002 Convention on Biological Diversity.

The results were released as part of a WWF report entitled *2010 and Beyond: Rising to the biodiversity challenge*.

"Governments have signally failed to deliver on their biodiversity commitments, and biodiversity declines are continuing," Jonathan Loh, a researcher at the Institute of Zoology and the editor of the report, told New Scientist.

Global picture

Ground-living vertebrates have declined by 25%, with most of the slump occurring since 1980. Marine species held fairly steady until the late 1990s before falling sharply to give an overall drop of 28%. Freshwater species have decreased by 25%, primarily since the late 1980s.

Loh says the most dramatic declines have been observed in the tropics. Tropical ground-living species have seen an average population drop of 46%, while their temperate cousins have shown no overall change.

Freshwater vertebrates show different trends in different regions, leading to "no obvious signal", says Loh. European and North American populations show no overall change, but Asian-Pacific populations have declined steeply since the late 1980s.

In the world's oceans, northern vertebrate populations have held fairly steady over the entire period, but may have entered a downward trend since 1990. By contrast, southern populations have fallen precipitously, although because less data is collected there the trend is less certain.

Rose-tinted view

The LPI focuses exclusively on vertebrates, which are relatively well-monitored. Loh says, "We started collecting data on invertebrates, but it's very patchy and not good enough as yet."

The survey may be "bird-biased", he adds, because their populations are well-monitored. The LPI tracks 811 bird species but just 241 fish and 302 mammals.

Fish should actually comprise the bulk of the Index. The world's 30,000 species of fish compare to just 10,000 bird species and 5,400 mammals.

Loh says this suggests that the situation is worse than the data shows. "Birds are doing better than fish," he says, "so if anything, by biasing the survey towards them we're underestimating the global decline."

Incomplete picture

There is also a lack of good data for Latin America and Africa. Loh says that, frustratingly, "the more species there are in an area, often the less data there are on how they're doing. For instance the UK is well-monitored, but has relatively few species. It's a priority for us to find out what's happening in areas like the Amazon Basin."

The WWF report was published ahead of a worldwide conference on biodiversity, the ninth meeting of the Conference of the Parties on 19-30 May. The conference will assess what has been achieved by the Convention on Biological Diversity.

Man-made 'defensin' rips resistant bacteria apart

* 17:15 16 May 2008

* NewScientist.com news service

* **Colin Barras**

A mimic of the potent proteins used by white blood cells to punch holes in bacteria is to begin clinical trials in Canada. It could be a valuable new weapon against the growing threat of antibiotic-resistant "superbugs".

Phagocyte immune cells that engulf bacteria use defensins to digest their prey. These small molecules are electrically attracted to the bacterium's outer membrane, and fuse with it to create gaping holes that destroy invaders.

The complexity of bacterial cells's outer membranes means they cannot easily evolve to become resistant to defensins. But attempts to harness them for medicine have struggled. Defensins are difficult and expensive to produce, and are typically destroyed by the host's immune system before they can reach an area of infection.

Local effect

"They are not optimised to circulate around the body," Bill DeGrado, a biochemist at the University of Pennsylvania, Philadelphia, US, told New Scientist. He decided that building his own defensin was the only solution.

His research team stripped down the structure of natural defensins to just the essential membrane-busting components, making one small enough to go undetected by the immune system.

They focussed on the split chemical personality that makes the molecules deadly to bacteria. They have one water-soluble end, and one water-repellent end with a positive charge. This draws the defensin to bacterial membranes like a targeted torpedo.

After settling on a simple ribbon-like structure, they enlisted the help of theoretical chemist Michael Klein at the University of Pennsylvania to check whether the proposed molecule could be stable.

Staying power

The simulated results were good enough to encourage DeGrado to build the molecule and set up a company, Polymedix, to develop it.

In a standard measure of the risk of bacteria evolving resistance to a new treatment, the defensin outstripped conventional antibiotics.

In the test, a sample of bacteria was given enough compound to kill 90% of the culture, with the survivors used to found a new one. The process was repeated, which drives the bacteria to evolve resistance.

"For conventional antibiotics, you generally find it takes 100 times more of the antibiotic to kill the bacteria after 9 repeats," says Nick Landekic, Polymedix's chief executive. "We've done 14 repeats with PMX-30063 and there is no change in its potency."

"Really exciting"

Michael Zasloff at Georgetown University, Washington DC, US, was not involved with the work but plans to follow its progress.

"Their compounds are really exciting and look great, but the value of this class will be based on safety." He says there is a chance that PMX-30063 may punch holes in human cells as well as bacterial ones.

"My concerns are with how it interacts with sites in the body known to be sensitive to damage by positively-charged peptides – areas such as the kidney and middle ear," says Zasloff.

DeGrado and colleagues think the risk is low, saying their molecule is several thousand times more likely to target bacterial cells than it is to attack mammalian ones.

After a programme of animal testing the Canadian government's regulator, Health Canada, this month gave the go-ahead to human clinical trials.

Houston Journal

A Pest Without a Name, Becoming Known to Ever More

By RALPH BLUMENTHAL

HOUSTON — Look out, Texas Gulf Coast, here comes *Paratrechina pubens*, or something like that.

Scientists do not quite know what to call them, they are so new. But folks in the damp coastal belt south of Houston have their own names (some of them printable) for the little invaders now seemingly everywhere: on the move underfoot; infesting woodlands, yards and gardens; nesting in electrical boxes and causing shorts; and even raising anxiety at Hobby Airport and the Johnson Space Center.

"We call them running ants," said Diane Yeo, a homeowner in suburban Pearland, turning over a planter by her swimming pool to reveal a seething carpet of ants, yes, running, each about the size of the letter "i" on this page.

That was not the worst of it. "Looks like they're carrying eggs," said her husband, Bob.

The ant is a previously unknown variety with a staggering propensity to reproduce and no known enemies. The species, which bites but does not sting, was first identified here in 2002 by a Pearland exterminator, Tom Rasberry, who quickly lent his name to the find: the crazy rasberry ant.

"I sprayed some pesticide just to knock them down," Mr. Rasberry recalled on Thursday. "But the next year I went from seeing a couple thousand to millions of them."

Mr. Rasberry demonstrated in a patch of woods not far from his business, Budget Pest Control, that the ants were swarming under every clod of grass and over every tree branch and limb.

And the ants' seasonal gestation period, which reaches its peak in the summer, is just beginning, said Paul Nester, a program specialist for the Texas AgriLife Extension Service of Texas A&M University.

"They're the ant of all ants," said Dr. Nester, who said they had infested five coastal counties, "and are moving about half a mile a year." But he said broad areas of Texas and beyond were probably not threatened because the ants preferred the warmth and moistness of the coast.

Variants of the species found in Colombia have been known to asphyxiate chickens and even attack cattle by swarming over their eyes, nasal passages and hooves, according to the Center for Urban and Structural Entomology at Texas A&M, which is conducting much of the research on the ants. It lists some of the findings on its Web site: urbanentomology.tamu.edu/ants/exotic_tx.cfm.

Jason Meyers, a doctoral student in urban entomology at Texas A&M who is writing his dissertation on the ants, described them as enigmatic and confirmed that they were discovered by Mr. Rasberry. They belong to the genus *Paratrechina*, like others seen in Colombia, the Caribbean and Florida, Mr. Meyers said, but are different enough for entomologists to only guess at their species, listing them for now as "near" *pubens*.

"It's a very fecund species, with multiple queens," Mr. Meyers said.

The ants often eat fire ants, with which they are sometimes compared, and they "outcompete" fire ants for the food supply and reproduce far faster, Mr. Meyers said.

They are vulnerable to some pest control poisons — Mr. Rasberry uses products containing the chemicals fipronil and chlorfenapyr — but given the ants' staggering proliferation and environmental restrictions on the products, not enough of the chemicals can be put down to make a difference, Mr. Meyers said.

Some might think the infestation an exterminator's dream, but it is not so, said Mr. Rasberry. While an ordinary treatment might cost \$85 every three months, treating for the raspberry ants costs up to \$600, he said. Yet the efforts are so arduous and ineffective and have left customers so dissatisfied "they are actually costing me money," Mr. Rasberry said.

Downtown Houston seems to have been spared, though the ants have been spotted scurrying thickly across suburban roads. But news accounts of the scourge have spread widely, said Frank Michel, spokesman for Mayor Bill White.

"The Russians are concerned," Mr. Michel said. "I got a call from Moscow wanting to know if NASA was safe."
"I reassured the Russians we're O.K.," he said.

Galaxies Twice as Bright as They Seem, Study Finds

By DENNIS OVERBYE

The universe, it seems, has been operating with a dimmer switch.

The galaxies are actually twice as luminous as they appear to us in the sky, according to a new study by an international team of astronomers led by Simon Driver, of the University of St. Andrews in Scotland. Dust, however, blocks half the light from getting out.

The results, which have just been published in *The Astrophysical Journal Letters*, resolve a longstanding problem with the energy budget of the cosmos.

Interstellar dust absorbs the visible light emitted by stars and then re-radiates it as infrared, or heat, radiation. But when astronomers measured this heat glow from distant galaxies, the dust appeared to be putting out more energy than the stars.

"You can't get more energy out than you put in, so we knew something was very wrong," said Dr. Driver, in a press release issued by the Science and Facilities Council in the United Kingdom.

He and his colleagues embarked on a program of comparing a model of galactic dust with measurements of the light from 10,000 nearby galaxies using the Isaac Newton Telescope in the Canary Islands and other instruments. That allowed them to calculate by color what percentage of starlight was escaping the galaxies and getting to telescopes: 20 percent of short-wavelength ultraviolet light, 45 percent of green light, 75 percent of the red light, and so on.

The end result, that the stars in galaxies are actually pumping out twice as much energy as previously thought, was still a shock, Dr. Driver said. For the universe as a whole, they calculated, that amounts to 5 quadrillion watts per cubic light-year from thermonuclear fusion, a nice new number for those concerned about their cosmic carbon footprints.

The results also mean that there is about 20 percent more mass in stars than previously thought. But since stars make up such a small percentage of the universe to begin with — dark matter and dark energy account for 95 percent or so — it is a small adjustment over all.

"Basically increasing the stellar mass in the nearby universe by 20 percent has little impact," Dr. Driver said in an e-mail message from Scotland.

The results will have more impact, he said, on comparative observations of nearby and faraway galaxies, where, he said, dust has not previously been taken into account.

Whales are 'cheetahs of the deep'

By Matt Walker BBC

Super-fast pilot whales have been observed sprinting after prey, likely to include giant squid.

The rapid pursuit has brought comparisons with the fleet-footed land predator, the cheetah.

The cetaceans even use the same, highly specialised hunting strategy that cheetahs use, scientists report in the *Journal of Animal Ecology*.

They say it gives the lie to our perception that deep sea whales are slow, energy-saving creatures.

It is the first time such remarkable behaviour - occurring hundreds of metres underwater, in complete darkness - has been recorded.

"As far as we know, no other whale has been recorded to swim nearly as fast at depth," says marine biologist Natacha Aguilar Soto, of La Laguna University in Tenerife, Spain.

"Short-finned pilot whales seem to be the greatest burst-speed athletes of the deep-diving mammals."

Energetic sprint

Aguilar Soto is a member of an international team of researchers drawn from La Laguna University, Woods Hole Oceanographic Institution in Massachusetts, US, and Aarhus University, Denmark.

The team tagged and studied 23 short-finned pilot whales (*Globicephala macrorhynchus*) living off the coast of the Canary Islands, one of only three places in the world that these whales permanently reside.

The tags, designed by co-author Mark Johnson of Woods Hole, recorded the speed, depth and direction of the whales' dives, and also the sounds made and heard by the whales.

During the day, the whales are frequently seen lazing on the surface, often in social groups (see video). That led scientists to previously think the whales only hunt at night. But the tags demonstrate the whales also hunt during the day. And when they do, they dive deep, and they dive fast.

Tags showed the whales take just 15 minutes to dive to depths of 800m to 1,000m (0.6 mile), and more.

And when they pinpoint their prey, the whales surge after it, reaching speeds of nine metres per second, or 32 kilometres per hour (20mph). What's more, they may keep up the sprint for 200m (650ft), before either catching the prey or giving up the chase.

The discovery fundamentally challenges our perceptions of how deep-sea creatures behave, says Aguilar Soto.

Until now, researchers assumed that deep-diving whales moved relatively slowly, due to the need to conserve oxygen whilst holding their breath.

"It was completely unexpected that short-finned pilot whales sprint at depth with limited oxygen reserves. Cheetahs, for example, more than double their breathing rate during chases," says Aguilar Soto.

So like cheetahs, pilot whales must therefore follow a high-risk, high-gain hunting strategy based on high-speed, energetically expensive sprints. But somehow, the whales do it while still holding their breath. And that may explain why they are spotted lazing on the surface - the whales may be actually recovering from the exertion of the hunt.

Deep battle

There is also tantalising, indirect evidence that the whales may sometimes chase down giant squid.

During the dives, the acoustic tags revealed that the whales switched from slower echolocation clicks to a fast series of clicks, or buzz.

That allows them to "see with sound" with greater resolution in the darkness, says co-author Peter Madsen of Aarhus University.

"The analogy is like going from snap-shots to video," he says, indicating the whales are trying to capture prey after the sprints.

But "the prey must be large or calorific to reward the deep dives, and they must be able to move rapidly given the top speeds we clocked for the whales," says Aguilar Soto.

One animal fits the bill, the giant squid *Architeuthis*. "We found a piece of fresh *Architeuthis* arm floating in the vicinity of diving pilot whales and findings of bitten *Architeuthis* are common in the area where the whales live," Aguilar Soto explains.

Also, colleague Pablo Aspas recently took a photo of a pilot whale half-breaching with a piece of large squid in its mouth (pictured above).

"Its colour and the shape of the cups indicate it may well belong to *Architeuthis* and the size of the piece indicates that the full length of the tentacle would be more than two metres, corresponding to a squid 4-5 metres long and some 180kg in weight," says cephalopod expert Angel Guerra of the Institute for Marine Investigations in Vigo, Spain.

"We have imagined battles between sperm whale and giant squid. But it may turn out that it is pilot whales, one-third the size of sperm whales, which are sprinting for the giant squid!" says Aguilar Soto.

Ancestors had leg-up to trees

The ancestors of humans, apes and monkeys may have taken to the trees because of their small body size.

Scientists have long wondered why early primates inhabited forest canopies, given that climbing appears to consume more energy than walking.

US researchers studied primates climbing and walking on treadmills.

They say there was no difference in energy consumption for small primates, giving clues to how their ancestors entered the trees 65 million years ago.

Dr Jandy Hanna of Duke University, Durham, North Carolina, said the data suggested that the earliest primates were able to exploit a new environment without added cost if they remained small.

"The earliest primates differentiated from other mammals partly due to their exploitation of a new arboreal niche - that of the terminal branches of trees," she told BBC News.



A number of primates were studied, including the mongoose lemur

Early primates, which would have been about the size of large rats, then underwent a number of evolutionary changes as they adapted to their new environment.

These changes included nails rather than claws and grasping hands and feet.

"The benefit/payoff of invading this new environment (and the appearance of these anatomical changes) was an insect- and fruit-rich environment," said Dr Hanna.

Professor Robin Crompton, of the Primate Evolution and Morphology group at the University of Liverpool, UK, said it had been observed in the wild that small animals such as the mouse lemur and dwarf bushbaby move in much the same manner on verticals as horizontals.

"For the first time, [the US researchers] show that for primates of up to 4kg or so, at least, the energetic efficiency of vertical motion increases very little with size, while previous work has shown that the efficiency of walking increases sharply," he said.

Full details of the study are published in the journal *Science*.

New data show benefit of finasteride in preventing prostate cancer ***Link between finasteride and high grade prostate cancer questioned***

PHILADELPHIA – A comprehensive re-evaluation of the largest prostate cancer prevention study ever completed produced new findings suggesting that men and their doctors should consider a more aggressive approach that includes finasteride to prevent the development of prostate cancer.

A pathologic analysis of that same study sheds light on the significance of the cancers found in that study. Additionally, this study highlights the role of prostate specific antigen (PSA) scores in treatment decision-making. Researchers found that even those men who have a low PSA screening value can have cancer that is difficult to cure.

The two studies will be published online in advanced of the June 2008 issue of *Cancer Prevention Research*, a journal of the American Association for Cancer Research.

The original study, the Prostate Cancer Prevention Trial (PCPT), had randomized 18,822 men to receive either a placebo or an agent known as finasteride, currently approved to control prostate growth, for seven years. Results showed that while finasteride reduced prostate cancer risk by 25 percent, it appeared to increase development of more aggressive prostate cancer in some men. Because of this finding and concerns that tumors detected had low PSA values and might be of little risk to patients, since the study's original publication in 2003, few doctors have recommended finasteride for prostate cancer prevention.

From a new analysis of PCPT data using advanced statistical modeling techniques and a complete assessment of prostate tissue biopsies, they concluded that these concerns are now resolved: finasteride actually reduced the risk of developing prostate cancer more than researchers had originally thought, did not increase development of more aggressive cancers, and the majority of tumors prevented were those that could spread and cause death.

These new findings suggest that men should take an "individualized" approach to prostate cancer prevention, said Ian M. Thompson, M.D., Chair of the Department of Urology at the University of Texas Health Sciences Center at San Antonio, who is senior author on both studies, and was also lead author for the Southwest Oncology Group (SWOG) on the original PCPT results paper, which was published in July 2003.

"Because we now know that men with even low PSAs can develop prostate tumors, if a man is worried about his risk, regardless of PSA score, he can take an agent that is now proven to be effective in lowering that risk," Thompson said.

Researchers looked at whether finasteride actually increased aggressive cancers in some men, and by studying biopsies and prostate gland tissue that had been removed, concluding that it did not. "Finasteride actually shrank the prostate gland, so it appeared in initial studies that more cancer was being found in biopsies of men who took the drug," said Mary Redman, Ph.D., a biostatistician at the Fred Hutchinson Cancer Research Center.

"What that means is that the cancer took up more prostate tissue in men who were treated, and that is why it was easier to find in a biopsy. Cancer was probably missed more often in biopsies of men on a placebo drug because the prostate gland itself was larger," Redman said.

Redman found that in addition to a 25 to 30 percent reduction in prostate cancer development overall in men taking finasteride, there was no evidence that the drug increased the rate of aggressive tumors and likely decreased their rate by 27 percent.

"We think men should not be concerned about finasteride increasing their risk of these aggressive tumors" she said.

The second study examined whether the cancers detected in the men in the trial who had a low PSA level had clinically significant disease. With about 75 percent of the tumors detected on the study were classified as those which could potentially take a man's life, researchers concluded that there is no clear-cut PSA threshold that can be considered normal.

All patients in PCPT were to have a biopsy of their prostate gland at some point during the seven-year trial, so investigators evaluated characteristics of the biopsy in relation to each man's PSA score. Current practice is to consider a PSA score of below four as normal and above four as abnormal.

What they found, according to lead author Scott Lucia, M.D., a pathologist at the University of Colorado, Denver, was that while a large majority of the participants diagnosed with prostate cancer had a PSA that was considered normal, 72 percent of all tumors diagnosed from biopsies in both treated and untreated men were considered significant. In short, the finding of significant disease couldn't be predicted by the PSA score, he said. Most patients in the study who had a PSA score of four or less and then had prostate cancer diagnosed by a routine biopsy were found to have significant prostate cancer, while some men who had a high PSA were found to have insignificant cancer.

That doesn't mean that the researchers support reducing the level by which PSA scoring should trigger therapeutic intervention, Lucia said. "Over 90 percent of men in the country diagnosed with prostate cancer opt for treatment, yet we also found that even at higher PSA levels, men are being treated for tumors that would not have threatened their health," he said. "This is the dilemma of PSA screening. While lower cut-off levels, those below four, increase risk of detection of insignificant disease, cure is more likely; conversely, more significant disease is detected with higher levels but at a greater risk of incurable disease."

It does mean that men need to speak with their physicians about their PSA, when they should be biopsied, and about potential use of finasteride, which can reduce their risk, so that they will make a decision that is right for them, researchers say. For example, Lucia says, a man whose family members have been diagnosed with the disease may decide to have a biopsy even though his PSA is below four. If cancer is found then may opt to undergo treatment; if cancer is not

found, he may choose to use finasteride to prevent the cancer from developing. Another man may decide to put off a biopsy, regardless of PSA score, if he is worried about side effects of treatment.

"These are not easy decisions, especially when we know now that we cannot rely on what the PSA looks like it is telling us," Lucia said.

Emphasizing the importance of prevention, "if given the option of having my prostate cancer found early, getting it treated and then getting over the side effects of treatment or never getting cancer in the first place, I'd choose prevention any day," said Thompson.

Men experience domestic violence, with health impact **Group Health study debunks five myths about abuse of men**

SEATTLE—Domestic violence can happen to men, not only to women, according to Group Health research in the June American Journal of Preventive Medicine. "Domestic violence in men is under-studied and often hidden—much as it was in women 10 years ago," said study leader Robert J. Reid, MD, PhD, an associate investigator at the Group Health Center for Health Studies. "We want abused men to know they're not alone." His findings confirm some common beliefs but also debunk five myths about abuse in men:

Myth 1: Few men experience domestic violence. Many do. In-depth phone interviews with over 400 randomly sampled adult male Group Health patients surprised Dr. Reid and his colleagues: 5% had experienced domestic violence in the past year, 10% in the past five years, and 29% over their lifetimes. The researchers defined domestic violence to include nonphysical abuse—threats, chronic disparaging remarks, or controlling behavior—as well as physical abuse: slapping, hitting, kicking, or forced sex.

Myth 2: Abuse of men has no serious effects. The researchers found domestic violence is associated with serious, long-term effects on men's mental health. Women are more likely than men to experience more severe physical abuse, said Dr. Reid. "But even nonphysical abuse—can do lasting damage." Depressive symptoms were nearly three times as common in older men who had experienced abuse than in those who hadn't, with much more severe depression in the men who had been abused physically.

Myth 3: Abused men don't stay, because they're free to leave. In fact, men may stay for years with their abusive partners. "We know that many women may have trouble leaving abusive relationships, especially if they're caring for young children and not working outside the home," said Dr. Reid. "We were surprised to find that most men in abusive relationships also stay, through multiple episodes, for years."

Myth 4: Domestic violence affects only poor people. The study actually showed it to be an equal-opportunity scourge. "As we found in our previous research with women experiencing domestic violence, this is a common problem affecting people in all walks of life," said Dr. Reid. "Our patients at Group Health have health insurance and easy access to health care, and their employment rate and average income, education level, and age are higher than those of the rest of the U.S. population."

Myth 5: Ignoring it will make it go away. Not so. "We doctors hardly ever ask our male patients about being abused—and they seldom tell us," said Dr. Reid. "Many abused men feel ashamed because of societal expectations for men to be tough and in control." Younger men were twice as likely as men age 55 or older to report recent abuse. "That may be because older men are even more reluctant to talk about it," he added.

This study extends Group Health's research on domestic violence, a.k.a. intimate partner violence. The team's previous publications have documented the prevalence, persistence, and health effects of domestic violence on women. In the current study, they asked men the same questions that they had asked of women. "Our team is concerned about abuse of people: of women as well as men," Dr. Reid added. "We do not want to downplay the seriousness of domestic violence as experienced by women."

Dr. Reid said more research is needed to determine the best ways for doctors to ask men if they have experienced domestic violence—and how best to help them into couples counseling, leaving their partners, or getting protection orders. The National Domestic Violence Hotline is toll-free 1-800-799-SAFE (7233).

The Agency for Healthcare Research and Quality and the Group Health Center for Health Studies funded this work, co-authored by Melissa Anderson, MS, Paul Fishman, PhD, David Carrell, PhD, and Robert Thompson, MD of the Group Health Center for Health Studies; Amy Bonomi, PhD, MPH, now an Ohio State University associate professor of human development & family science in Columbus; and Group Health Center for Health Studies affiliate scientific investigator Frederick Rivara, MD, MPH, of Harborview Injury Prevention and Research Center and the University of Washington.

Monkey made to treat Huntington's disease

* 18:00 18 May 2008

* NewScientist.com news service

* **Ewen Callaway**

Monkeys genetically engineered to get the deadly neurological disease Huntington's could provide a unique way to test potential treatments because of their cognitive and genetic similarities to humans.

"Monkey models may have a privilege over other animal models," says Anthony Chan, a biologist at Yerkes National Primate Center in Atlanta, Georgia, whose team engineered five rhesus macaque monkeys to churn out the mutant protein that causes Huntington's.

Researchers routinely splice human genes in and out of mice to give them diabetes, cancer, and heart disease. But mice are of limited use when investigating brain diseases such as Huntington's: people who have it can't control their

movement, speech or swallowing and their cognitive abilities deteriorate. But mice engineered to express the Huntington's protein don't jerk their muscles like humans do and it can be tough to gauge their cognitive decline.

To see if primates might offer more insight, Chan's team used a virus to insert the Huntington's gene into the DNA of 130 macaque eggs, along with a gene that makes a fluorescent green jellyfish protein. The researchers then fertilised the eggs and implanted them into eight mothers.

All the monkeys born expressed the green protein, indicating that gene transfer was successful (see picture), and some already appear to have the monkey equivalent of Huntington's. The brains of one set of twins, who died a day after birth, were littered with clumps of a mutant protein found in humans with Huntington's, while the lone animal, who died a month after birth, jerked involuntarily.

Testing ground

Meanwhile, Chan's team is watching two surviving twins for symptoms, which can strike swiftly and unpredictably in humans. They will also analyse the monkeys' blood for early predictors of the disease.

"I think this is amazing," says Chris Ross, a neuroscientist at Johns Hopkins University in Baltimore. He studies mouse forms of Huntington's but says that monkeys will help test several potential drug treatments, he says. Huntington's affects 1 in 10,000 people of European descent.

Transgenic monkeys with other human diseases, such as early onset Alzheimer's or fragile X syndrome, are sure to follow, says Gerald Schatten, a biologist at the University of Pittsburgh in Pennsylvania.

Yet even researchers accustomed to animal work say working with transgenic monkeys should always be a last resort. "There should be higher levels of scrutiny in working with our closest animal cousins," Schatten says.

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Women 'face raised whiplash risk'

Women drivers are three times more likely than men to suffer whiplash injuries if their car is hit from behind, Swedish researchers say.

Women's risk is increased because they generally sit closer to the steering wheel, the Umea University team said having studied data on 400 injuries.

They said crash-test dummies should better reflect women's figures and help influence seat design.

But UK accident experts said there were already a range of dummies used.

Dummy difference

The researchers looked at insurance company data on more than 400 whiplash injuries claimed for during the 1990s.

They also carried out their own studies into how more than 200 men and women adjusted their car seats and then how they sat as they drove and as they were stationary.

They then compared the results from the human test with those from tests of a commonly used crash-test dummy, the BioRID, which is the same size as the average man or a large woman.

They concluded women's increased risk was partially due to them tending to sit higher and closer to the steering wheel and to have the seat back more upright.

For both women and men, sitting in the driver's seat entails twice the risk compared with the front passenger seat.

And when the data from dummy testing was examined, the researchers found it differed significantly in seat adjustments used and positioning.

They said: "Current crash dummies used to develop vehicle seats and neck supports, for instance, are geared to men of normal size, but not to women.

"This is especially true in regard to height.

"Nor does testing methodology take into consideration differences between the sexes, or differences in sitting position between the driver's seat and the front passenger seat."

The researchers, led by Bertil Jonsson, are also calling for a new test dummy to be designed to replicate an average-sized woman.

Head support

Mira, based in Nuneaton, Warwickshire, carries out safety tests for cars sold across the world.

It said a range of dummies were already used, including one which was used to represent both a small man and an average-sized woman.

"There are lots of different dummies out there," a spokesman said. "No-one thinks they have got the definitive dummy.

"Which one is used depends on what part of the world you want to sell a car in and what specific tests you want to carry out."

A spokesman for the UK's Royal Society for the Prevention of Accidents said: "A properly adjusted head restraint will help prevent whiplash by reducing the distance between the back of the head and head restraint, stopping the neck from bending back.

"It will also reduce the amount of time it takes your head to initially contact the head restraint, and increase the amount of time that your head is supported during an accident."

He added: "It's important everyone adjusts the head rest as necessary - every time the car is used if there are different drivers using it."