Freezing prostate cancer does a man's body good

Minimally invasive 'lumpectomy' -- as effective as surgery -- preserves sexual and urinary function; related study shows 3-D mapping biopsy changed patients' management 70 percent of the time

SAN DIEGO, Calif. (March 9, 2009) - The so-called "male lumpectomy" - a minimally invasive interventional radiology treatment for prostate cancer - is as effective as surgery in destroying diseased tumors and can be considered a first-line treatment for patients of all risk levels and particularly those who have failed radiation, according to studies released at the Society of Interventional Radiology's 34th Annual Scientific Meeting. Additionally, the use of 3-D transperineal mapping biopsy for determining the extent of prostate cancer - when compared with the commonly used transrectal ultrasound (TRUS) biopsy - heavily impacted how patients' disease was managed in 70 percent of the cases.

"Our data show that focal cryoablation is as good for prostate cancer control as any other treatment - including surgery, radiation and hormone therapy - but it is less invasive and traumatic for patients, preserves sexual and urinary function and has no major complications. Interventional radiologists tailor treatment to each patient's disease. Instead of removing the entire prostate, or freezing the entire prostate or using radiation on the entire prostate, interventional radiologists can find out where the cancer is and just destroy the cancer," said study author Gary M. Onik, M.D., interventional radiologist and director of the Center for Safer Prostate Cancer Therapy in Orlando, Fla. "We've reached a tipping point: treating only the tumor instead of the whole prostate gland is a major and profound departure from the current thinking about prostate cancer," added Onik. With cryoablation, interventional radiologists insert a probe through the skin, using imaging to guide the needle to the tumor; the probe then circulates extremely cold gas to freeze and destroy the cancerous tissue. This minimally invasive treatment targets only the cancer itself, sparing healthy tissue in and around the prostate gland rather than destroying it, as traditional approaches do, noted the professor at the University of Central Florida. "You can go home on the same day of the procedure, and you can repeat the treatment, if needed, in later years," said Onik. Additionally, Onik presented results of a 3-D biopsy method that provides superior information on the extent and grade of prostate cancer as opposed to the current standard TRUS biopsy.

Calling focal cryoablation a "male lumpectomy" reflects the origins of this approach in the breast-sparing surgery that replaced radical mastectomy as the preferred treatment for breast cancer, said Onik. Unlike breast lumpectomy, a surgical lumpectomy for prostate cancer is not technically feasible; so to treat just a portion of the prostate, minimally invasive cryoablation is needed. Cryoablation (or cryo or cryotherapy) spares as much as possible of the prostate gland and its neurovascular bundles, limiting the side effects of bladder control problems (incontinence) and erectile dysfunction (impotence) that result from more radical prostate cancer treatments. It also represents an advantage over "watchful waiting," because all treatment options are preserved. "Any risks are fewer and lesser in intensity than surgery; so if you have the equivalent chance of cancer being cured with far less chance of having any complications, why wouldn't you choose it?" asked Onik.

"There is no question that we can eradicate prostate cancer (when that cancer has not spread to other parts of the body) by freezing it and that there is a better way to 'map' the disease," said Onik. He studied 120 men who had focal cryoablation over the past 12 years, including testing the levels of prostate-specific antigen (PSA) in the blood. Of those patients, 112 (93 percent) had no evidence of cancer - in spite of 72 being labeled medium to high risk for cancer recurrence. "There were no local recurrences in the areas we treated, and with the ability to re-treat the 7 percent of patients who developed a focus of cancer at a different site in the gland; cryoablation was 100 percent effective in local control of the patient's disease," said Onik. He reported that 85 percent of the men retained sexual function. Of those who did not have previous prostate surgery, all remained continent. "Incontinence becomes a big issue with many patients. For some it's a more important side effect than impotence," said Onik.

According to Onik, the 3-D transperineal biopsy complements the focal cryoablation approach because earlier detection of smaller tumors increases the likelihood that a small tumor can be treated using cryoablation. In his study, Onik restaged 180 patients who had previously undergone TRUS mapping biopsies who were considering conservative management for their cancer. The results showed that 70 percent of the men would have their management changed by the new information provided by mapping. Through mapping, more than 50 percent of men who were diagnosed with cancer on one side of the prostate gland with traditional TRUS biopsy had undetected cancer on the other side as well, he said. Management of prostate cancer is in great part determined by the Gleason score, a cancer ranking method indicating tumor grade and stage and the extent and location of a patient's disease. "When we restaged the men, we found that 22 percent of them experienced an increase in their Gleason score - meaning that they had a more aggressive cancer than was originally thought from their original biopsy. The 3-D mapping biopsy provided life-saving information," said Onik. "This biopsy

technique allows us to map the location of the tumor with tremendous precision and has the potential to greatly affect the decisions we make about treating prostate cancer," Onik said. "The data are unequivocal. If you're doing 'watchful waiting,' get mapped. If you're having radiation or hormone therapy or thinking about getting a 'nerve-sparing' radical prostatectomy, get mapped. If TRUS doesn't show all the cancer that's present, you're not going to have the proper treatment," said Onik.

With 3-D transperineal mapping, a grid placed over the perineum (the area of skin between the rectum and the scrotum) allows an interventional radiologist to accurately map the location of each biopsy core removed. The cores are taken through the skin rather than through the rectum, allowing many more cores to be removed - about 50 compared to 10-12 in a TRUS biopsy. The mapping grid also allows the location of the tumor to be known much more precisely, allowing an interventional radiologist to cryoablate (freeze) only the tumor and not the whole prostate gland.

Controversy surrounds the treatment of prostate cancer, which usually grows slowly and initially remains confined to the prostate gland, said Onik. Growing evidence of overdetection and overtreatment in many men with low-risk tumors has led to a concept in the medical community of "watchful waiting" or observing a man's disease progression prior to initiating treatment. Many patients, however, feel uncomfortable with this strategy and may proceed to radical or aggressive treatment, said Onik. "When men must choose between 'watchful waiting' and high-morbidity whole-gland treatments (like surgery and radiotherapy), a lumpectomy-type treatment, which has so markedly changed the management of breast cancer for women, is a welcome 'middle ground' addition for those with prostate cancer," said Onik.

"Interventional cryoablation for prostate cancer is not experimental. This is a treatment option that doctors should discuss with their patients early on," emphasized Onik. Most people don't realize that you can surgically remove the whole prostate and, in 20 percent of the cases, the cancer can be left (called a positive margin), said Onik, who works in consultation with urologists. Doctors should discuss cryoablation with patients early on, he advised, noting that recently the American Urological Association issued a best practice statement that indicated that cryotherapy is an option for men who have clinically organ-confined prostate cancer of any grade with negative metastatic evaluation. Since this interventional treatment is not widely known to doctors and patients, individuals will need to pursue it on their own, he added.

More information about prostate cancer, cryoablation and interventional radiology can be found online at www.SIRweb.org.

Abstract 75: "Focal Therapy for Prostate Cancer - 120 Patients With Up to 12-Year Follow-up," G. Onik, Center for Safer Prostate Cancer Therapy, Orlando, Fla., SIR 34th Annual Scientific Meeting March 7-12, 2009.

Abstract 198: "3D Prostate Mapping Biopsy Has a Potentially Significant Impact on Prostate Cancer Management," G. Onik, M. Miessau; Center for Safer Prostate Cancer Therapy, Orlando, Fla., SIR 34th Annual Scientific Meeting March 7 , 2009.

Both abstracts can be found at www.SIRmeeting.org.

Oh, my aching back: Give me a shot of ozone

Minimally invasive interventional radiology treatment relieves pain from herniated disks; pain and function outcomes similar to surgery results but with fewer complications, shorter recovery time

SAN DIEGO, Calif. (March 9, 2009) - A minimally invasive interventional radiology treatment - that safely and effectively uses oxygen/ozone to relieve the pain of herniated disks - will become standard in the United States in the next few years, predict researchers at the Society of Interventional Radiology's 34th Annual Scientific Meeting. In a related study, the interventional radiologists examined just how ozone relieves the pain associated with herniated disks.

Back pain is the most common cause of job-related disability and a leading contributor to missed work. While the pain of herniated disks can be severe, it can ease over time, and many people may no longer feel the need for medical care. However, in some, the pain from herniated (or ruptured or slipped) disks is intolerable or persists. "Having a herniated disk can affect how you perform everyday activities and can cause severe pain that influences almost everything you do; however, you don't have to undergo invasive surgery," noted Kieran J. Murphy, M.D., interventional neuroradiologist and vice chair and chief of medical imaging at the University of Toronto in Toronto, Ontario, Canada.

Oxygen/ozone therapy involves injecting a gas mixture of oxygen and ozone into a herniated disk. The treatment can limit pain and inflammation by reducing the disk's volume. Currently, open diskectomy and microdiskectomy (both involving removal of disk material through an incision) are the standards in surgical treatment for herniated disk. "Oxygen/ozone treatment of herniated disks is an effective and extremely safe procedure; interventional radiologists use imaging to guide a needle to inject oxygen/ozone into injured disks. The estimated improvement in pain and function is impressive when we looked at patients who ranged in age from 13 to 94 years with all types of disk herniations," explained Murphy. "Equally important, pain and

function outcomes are similar to the outcomes for lumbar disks treated with surgical diskectomy, but the complication rate is much less (less than 0.1 percent)," he added. "In addition, the recovery time is significantly shorter for the oxygen/ozone injection than for the diskectomy," said Murphy. "The spine is a stunningly beautiful piece of engineering, or, as our engineers say, the spine is like a complex electromechanical system. And the interventional radiology oxygen/ozone treatment takes a minimalist approach. It's all about being gentle," said Murphy.

"Ozone shrinks disk volume; this is why it provides pain relief," said Murphy, whose second study explored the mechanism of why oxygen/ozone treatment works. The bones (vertebrae) that form the spine in the back are cushioned by small, spongy disks. When these disks are healthy, they act as shock absorbers for the spine and keep the spine flexible. But when a disk is damaged, it may bulge or break open. "There are millions of people with back pain who suffer and who can't work because of their pain. Undergoing invasive surgical diskectomy puts you on a path where you may be left with too little disk. Taking out a protruding disk may lose the shock absorption that naturally resides between them in the spine," said Murphy, who predicts this procedure will become standard in the United States within the next five years.

Researchers conducted a meta-analysis of various results published for oxygen/ozone treatment in regards to pain relief, reduction of disability and risk of complications. More than 8,000 patients from multiple centers in multiple locations were included in the study. The estimated mean improvement for patients after treatment based on the 10-point visual analog scale (VAS), a standard tool for rating the disabling effects of back pain, was a change of 3.9 (with 0 being no pain and 10 representing worst pain experienced). The estimated mean improvement was 25.7 percent for the Oswestry Disability Index (ODI), which measures one's ability to manage everyday life - such as washing, dressing or standing (with 61 percent or higher representing back pain that has an impact on all aspects of daily living. The improvement scores for VAS and ODI outcomes are well above both the minimum clinically important difference and the minimum (statistically significant) detectable change, indicating that the improvement in pain and function is a real change that can be felt by the patient. Much research in oxygen/ozone treatments has been done by interventional radiologists in Italy, said Murphy, indicating that as many as 14,000 individuals have received this treatment abroad over the past five years. The mechanism of action in relieving low back pain is complex; however, the primary effect is a volume reduction due to ozone oxidation. Researchers discovered that a simple incompressible fluid model predicted that reducing disk volume by 0.6 percent results in an intradiscal pressure reduction of 1 psi (pounds per square inch). Thus a very small change in volume creates a large change in disc pressure, which reduces the applied pressure on the nerve and relieves pain. This model confirmed that a minimalistic alternative to a diskectomy, such as oxygen/ozone treatment, is capable of relieving the pain caused by a herniated disk without causing irreparable damage.

More information about interventional radiology can be found online at www.SIRweb.org.

Abstract 37: "A Meta-Analysis of the Effectiveness and Safety of Ozone Treatments for Herniated Lumbar Disks," J. Steppan and T. Meaders, ActiveO, Salt Lake City, Utah; K. Murphy, University of Toronto, Toronto, Ontario, Canada, and Johns Hopkins School of Medicine, Baltimore, Md.; M. Muto, A. Cardarelli Hospital, Naples, Italy, SIR 34th Annual Scientific Meeting March 7-12, 2009.

Abstract 38: "Ozone's Mechanisms of Action for Relieving Pain Associated With Herniated Intervertebral Disks," J. Steppan, C. Boxley and T. Meaders, ActiveO, Salt Lake City, Utah; K. Murphy, University of Toronto, Toronto, Ontario, Canada, and Johns Hopkins School of Medicine, Baltimore, Md.; M. Muto, A. Cardarelli Hospital, Naples, Italy; and K. Balagurunathan, University of Utah, Salt Lake City, Utah, SIR 34th Annual Scientific Meeting March 7, 2009. Both abstracts can be found at www.SIRmeeting.org.

Zoo chimp 'planned' stone attacks

A male chimpanzee in a Swedish zoo planned hundreds of stone-throwing attacks on zoo visitors, according to researchers.

Keepers at Furuvik Zoo found that the chimp collected and stored stones that he would later use as missiles.

Further, the chimp learned to recognise how and when parts of his concrete enclosure could be pulled apart to fashion further projectiles.

The findings are reported in the journal Current Biology.

There has been scant evidence in previous research that animals can plan for future events.

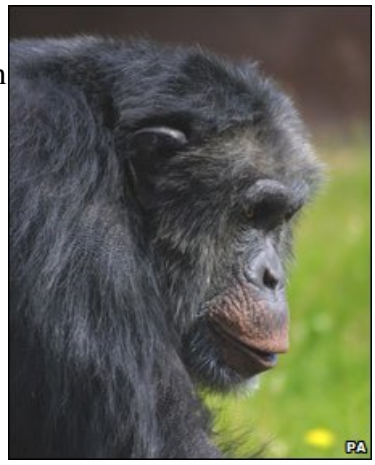
Crucial to the current study is the fact that Santino, a chimpanzee at the zoo in the city north of Stockholm, collected the stones in a calm state, prior to the zoo opening in the morning.

The launching of the stones occurred hours later - during dominance displays to zoo visitors - with Santino in an "agitated" state.

This suggests that Santino was anticipating a future mental state - an ability that has been difficult to definitively prove in animals, according to Mathias Osvath, a cognitive scientist from Lund University in Sweden and author of the new research

"We've done experimental studies, and the chimps in my mind show very clearly that they do plan for future needs, but it has been argued that perhaps this was an experimental artefact," Dr Osvath told BBC News.

"Now we have this spontaneous behaviour, which is always in some sense better evidence."



Chimpanzees have long been suspected of planning ahead

Cracking show

Dr Osvath embarked on the study after zoo staff discovered caches of stones in the section of the enclosure facing the public viewing area.

Since the initial discovery in 1997, hundreds of the caches have been removed to protect visitors, to whom the caching and the aggressive displays seem strictly related; in the off season, Santino neither hoards the projectiles nor hurls them.

Most interestingly, Santino seems to have learned how to spot weak parts of the concrete "boulders" in the centre of the enclosure. When water seeps into cracks in the concrete and freezes, portions become detached that make a hollow sound when tapped. Santino was observed gently knocking on the "boulders", hitting harder to detach bits that were loosened and adding those to his stashes of ammunition.

There are a number of examples of complex behaviour in apes that suggest forms of consciousness.

Planning behaviour like that of the current work is connected to so-called autonoetic consciousness, where information due to memory can be distinguished from that from the senses.

"I'm personally convinced that at least chimps do plan for future needs, that they do have this autonoetic consciousness," Dr Osvath said. "I hope that other zoos or those in the wild will look more closely at what is happening," he added.

"I bet there must be a lot of these kinds of behaviours out there, and I wouldn't be surprised if we find them in dolphins or other species."

Red wine vs. white? It makes no difference when it comes to breast-cancer risk

SEATTLE – The largest study of its kind to evaluate the effect of red versus white wine on breast-cancer risk concludes that both are equal offenders when it comes to increasing breast-cancer risk. The results of the study, led by researchers at Fred Hutchinson Cancer Research Center, were published in the March issue of Cancer Epidemiology, Biomarkers and Prevention.

"We were interested in teasing out red wine's effects on breast-cancer risk. There is reason to suspect that red wine might have beneficial effects based on previous studies of heart disease and prostate cancer," said lead author Polly Newcomb, Ph.D., M.P.H., head of the Cancer Prevention Program in the Public Health Sciences Division at the Hutchinson Center. "The general evidence is that alcohol consumption overall increases breast-cancer risk, but the other studies made us wonder whether red wine might in fact have some positive value."

Instead, Newcomb and colleagues found no compelling reason to choose Chianti over Chardonnay.

"We found no difference between red or white wine in relation to breast-cancer risk. Neither appears to have any benefits," Newcomb said. "If a woman drinks, she should do so in moderation – no more than one drink a day. And if a woman chooses red wine, she should do so because she likes the taste, not because she thinks it may reduce her risk of breast cancer," she said.

The researchers found that women who consumed 14 or more drinks per week, regardless of the type (wine, liquor or beer), faced a 24 percent increase in breast cancer compared with non-drinkers.

For the study, the researchers interviewed 6,327 women with breast cancer and 7,558 age-matched controls about their frequency of alcohol consumption (red wine, white wine, liquor and beer) and other breast-cancer risk factors, such as age at first pregnancy, family history of breast cancer and postmenopausal hormone use. The study participants, ages 20 to 69, were from Wisconsin, Massachusetts and New Hampshire. The frequency of alcohol consumption was similar in both groups, and equal proportions of women in both groups reported consuming red and white wine.

The National Cancer Institute, a branch of the National Institutes of Health, funded this research, which also involved investigators from Group Health Cooperative, Seattle; the University of Wisconsin; H. Lee Moffitt Cancer Center & Research Institute; and Dartmouth Medical School.

Children of older fathers perform less well in intelligence tests during infancy

Press release from PLoS Medicine

Children of older fathers perform less well in a range of cognitive tests during infancy and early childhood, according to a study published this week in the open-access journal PLoS Medicine. In contrast, the study finds that children with older mothers gain higher scores in the same tests – designed to measure the ability to think and reason, including concentration, learning, memory, speaking and reading skills.

The age at which men and women are having children is increasing in the developed world, but whilst the "biological clock" – the effect of increasing maternal age on reduced fertility – is widely-discussed, the consequences of increased paternal age are not as well known. Recent evidence demonstrates a link between older fathers and specific health problems in their children, including birth deformities and cancer, as well as neuropsychiatric conditions such as autism and schizophrenia. This new study by John McGrath, of the Queensland Brain Institute, University of Queensland in Australia, and colleagues, investigates the link between a father's age and their child's general cognitive ability, by reanalyzing an existing dataset of 33,437 children born between 1959 and 1965 in the United States. This data formed part of the US Collaborative Perinatal Project (CPP), which tested each child in the dataset at 8 months, 4 years and 7 years of age with a number of widely-used intelligence scales – including assessments of sensory discrimination and hand-eye coordination, conceptual and physical coordination, and at 7 years reading, spelling and arithmetic ability.

Crucially in their reanalysis of this dataset, McGrath and colleagues adjusted their study to take into account socio-economic factors. They used two models: one that focused on physical factors including the parents' age, and a second that indexed social factors such as maternal and paternal education and family income. They found that the older the father, the more likely the child was to have lower scores on the various tests used by the CPP – with the exception of one measure of physical coordination. The researchers also grouped the children by their mother's age and found that in contrast, the older the mother the higher the scores of the child in the cognitive tests.

Previous researchers have suggested that the children of older mothers may perform better because they experience a more nurturing home environment; if this is the case, this study suggests that children of older fathers do not necessarily experience the same benefit. The researchers advance several hypotheses as possibilities to explain the association between advanced paternal age and children's cognitive ability, including genetic and social arguments. Unlike a woman's eggs – which are formed when she herself is in the womb – a man's sperm accumulates over his lifetime, which previous studies have suggested can mean increased incidence of mutations in the sperm at an older age. However, as emphasized in an expert commentary on the findings by Mary Cannon (Royal College of Surgeons in Ireland) – who was uninvolved with the study – genetic and social factors can operate in conjunction. "New explanatory models are needed that can encompass socio-cultural and interpersonal factors as well as biological variables", she argues. Given the trend towards older maternal and paternal ages in the developing world, policy-makers may want to consider promoting an awareness of the risks to children that this study associates with delayed fatherhood.

Citation: *Saha S, Barnett AG, Foldi C, Burne TH, Eyles DW, et al. (2009) Advanced paternal age is associated with impaired neurocognitive outcomes during infancy and childhood. PLoS Med 6(3): e1000040. doi:10.1371/journal.pmed.1000040*
Available online: *http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.1000040*

'Hair blindness' likely to exist in humans

* 11:23 09 March 2009 **by Ewen Callaway**

Men have another excuse for failing to notice their wife or girlfriend's new haircut. New research hints that human brains process hairstyles distinctly from other facial features. And just as a small proportion of people have trouble recognising faces yet otherwise see normally, others probably experience hair blindness.

"I'd love to find them, but we haven't heard from anybody yet," says Brad Duchaine, a cognitive neuroscientist at University College London, who presented his preliminary findings at a recent talk at MIT in Cambridge, Massachusetts.

Duchaine, who works extensively with people with face blindness or prosopagnosia, noticed that his subjects find clever ways to spot their friends and family. "My prosopagnosics tell me that they use hair to recognise people all the time," he says. "I know I rely on hair a lot."

'Inversion effect'

To see if these anecdotes were bona fide, Duchaine modified a test he and others have used to study face recognition.

Four decades ago, researchers first noticed that people who have no trouble identifying faces often struggle to recognise upside-down faces. While they recognise other objects - cars, for instance - almost equally well

whether flipped or not. This "inversion effect" indicates that humans process faces differently than other objects, Duchaine says.

Facial feature?

To see whether inversion hinders hair recognition, his team cropped out everything but hair from a set of faces, and told about 70 volunteers to memorize the hairdos.

Next, Duchaine's team challenged volunteers to pick out familiar hairstyles amongst hair they had never seen. On average, their performance dropped by about 15 to 18% on inverted hairstyles, Duchaine says. With faces, the difference can be as high as 25%.

This suggests that our brain pays close attention to hair, yet it does not necessarily mean that the brain sees hair as a facial feature, like it does eyes and noses.

If that were the case, prosopagnosics would have trouble telling hairstyles apart. Instead, Duchaine found no such deficit. He has not tested them on inverted hairdos, but expects their performance will suffer similarly to normal subjects.

The new research hints that some human brains may blind to the characteristics of hair, however it looks **(Image: Alain Evrard/Robert Harding/Rex Features)**

Mr Potato Head

"It's an intriguing finding because hair traditionally has been an aspect of facial structure that has not received much attention," says Pawan Sinha, a neuroscientist at MIT, who attended the talk.

Researchers have traditionally thought of external facial features such as hair and jaw line as important mostly for assessing the faces of strangers from a distance. But this new research suggests that hair is critical for recognising familiar faces close-up, he says.

Yet Sinha cautions against taking a "Mr Potato Head" approach to face recognition, atomising and ranking each feature as if they were independent from one another.

"We need to think about the face as a whole, and in most natural viewing circumstances, we are looking at faces through a distance or degree, which makes it harder to parcel out individual features," he says.

Tiny brain region better part of valor

Piece of hypothalamus is key to animals' fear of territorial rivals and predators, according to a study in the Proceedings of the National Academy of Sciences

Mice lose their fear of territorial rivals when a tiny piece of their brain is neutralized, a new study reports.

The study adds to evidence that primal fear responses do not depend on the amygdala – long a favored region of fear researchers – but on an obscure corner of the primeval brain.

A group of neuroscientists led by Larry Swanson of the University of Southern California studied the brain activity of rats and mice exposed to cats, or to rival rodents defending their territory.

Both experiences activated neurons in the dorsal premammillary nucleus, part of an ancient brain region called the hypothalamus. Swanson's group then made tiny lesions in the same area. Those rodents behaved far differently. "These animals are not afraid of a predator," Swanson said. "It's almost like they go up and shake hands with a predator."

Lost fear of cats in rodents with such lesions has been observed before. More important for studies of social interaction, the study replicated the finding for male rats that wandered into another male's territory. Instead of adopting the usual passive pose, the intruder frequently stood upright and boxed with the resident male, avoided exposing his neck and back, and came back for more even when losing.

"It's amazing that these lesions appear to abolish innate fear responses," said Swanson, who added: "The same basic circuitry is found in primates and people that we find in rats and mice." The study was slated for online publication the week of March 9 in Proceedings of the National Academy of Sciences.

Swanson predicted that his group's findings would shift some research away from the amygdala, a major target of fear studies for the past 30 years. "This is a new perspective on what part of the brain controls fear," he said.

He explained that most amygdala studies have focused on a different type of fear, which might more accurately be called caution or risk aversion.

In those studies, animals receive an electric shock to their feet. When placed in the same environment a few days later, they display caution and increased activity of the amygdala. But the emotion experienced in that case may differ from the response to a physical attack. "We're not just dealing with one system that controls all fear," Swanson said.

Swanson and collaborators have been studying the role of the hypothalamus in the fear response since 1992. Because of its role in basic survival functions such as feeding, reproduction and the sleep-wake cycle, the hypothalamus seems a plausible candidate for fear studies. Yet, said Swanson, "nobody's paid any attention to it."

The PNAS study is the most recent of several by Swanson on fear and the hypothalamus. The few other researchers in the area include Newton Canteras of the University of Sao Paulo in Brazil, who collaborated with Swanson on the PNAS study, as well as Robert and Caroline Blanchard of the University of Hawaii.

The other authors on the PNAS study were Simone Motta, Marina Goto, Flavia Gouveia and Marcus Baldo, all from the University of Sao Paulo. The Brazilian government funded the study.

What drove the cow mad? Lessons from a tiny fish

Press release from PLoS Biology

For over twenty years, scientists have known that a normal protein in the brain, PrP, or prion protein, can turn harmful and cause deadly illnesses like Creutzfeldt-Jakob disease (CJD) in humans, and bovine spongiform encephalopathy (BSE) in cattle. What they could not explain is why large amounts of this normal protein are produced by our bodies in the first place. In a new study published in this week's PLoS Biology, researchers from the University of Konstanz in Germany reveal that PrP indeed plays a beneficial role for the organism – PrP helps cells communicate with one another during embryonic development.

In prion diseases, what transforms the normal PrP protein into a life-threatening substance is the abnormal alteration of its chemical structure. Moreover, prions have the treacherous ability to replicate by imprinting their abnormal structure into healthy PrPs, thereby generating new pathogenic particles. While this "conversion" process explains how prions are disseminated, "An abnormal function of the prion protein is considered to be one of the reasons for neuronal degeneration," explains Dr. Edward Málaga-Trillo, leader of the study in Konstanz. However, the normal function of PrP has remained an unsolved mystery for many years. Until now, all previous experiments in genetically modified mice had failed to provide conclusive evidence, as these animals lacking PrP seemed perfectly healthy. A dead end?

By no means. The scientists from Konstanz were able to show that the lack of PrP can cause clear physiological abnormalities in a living animal and the trick was to use the tiny zebrafish as a model.

When the researchers from Konstanz microinjected zebrafish eggs with morpholinos, DNA-like molecules that prevent the normal production of PrP, the treated zebrafish embryos were unable to develop normally and eventually died. The proteins in the fish embryos normally found at cell-to-cell contact sites disappeared, rendering these cells unable to communicate and carry out the differentiation program that shapes the major structures of the body, including the nervous system.

"We were then able to prove that PrP serves as a glue element, bringing cells together and keeping them in contact," explains co-author Dr. Gonzalo Solis, member of the team at the laboratory of Prof. Claudia Stürmer. "When two neighboring cells make contact, they become able to exchange important signals that affect the function of a tissue in the body."

Although the work by Málaga-Trillo, Solis, and colleagues does not offer an immediate cure for CJD or BSE, the team from Konstanz has fit together the first pieces of a complex puzzle, which may widen our understanding of prion diseases and provide hope for their effective treatment.

***Citation**: Málaga-Trillo E, Solis GP, Schrock Y, Geiss C, Luncz L, et al. (2009) Regulation of embryonic cell adhesion by the prion protein. PLoS Biol 7(3): e1000055. doi:10.1371/journal.pbio.1000055*

***Available online:** http://biology.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pbio.1000055*

Ecstasy could help patients with post-traumatic stress disorder

New research published in Journal of Psychopharmacology

Los Angeles, London, New Delhi, Singapore and Washington DC (March 9th, 2009) – Ecstasy may help suffers of post-traumatic stress learn to deal with their memories more effectively by encouraging a feeling of safety, according to an article in the Journal of Psychopharmacology published today by SAGE.

Studies have shown that a type of psychological treatment called exposure therapy – where the patient repeatedly recalls the traumatic experience or is repeatedly exposed to situations that are safe but still trigger their traumatic feelings – can be effective in relieving stress responses in patients with post-traumatic stress disorder (PTSD) and other anxious conditions. The therapy works by helping the patient to re-learn the appropriate response to the trigger situation, a process known as extinction learning.

But this approach can take some time, and 40% of patients continue to experience post-traumatic stress even after their treatment. To improve outcomes, scientists have been investigating the use of drug therapies to enhance the effect of exposure therapy, making the result of exposure to the fear trigger easier, faster, and more effective. MDMA (the pharmaceutical version of Ecstasy) is one such drug.

"A goal during exposure therapy for PTSD is to recall distressing experiences while at the same time remaining grounded in the present. Emotional avoidance is the most common obstacle in exposure therapy for PTSD, and high within-session emotional engagement predicts better outcome," explain authors Pål-Ørjan Johansen and Teri Krebs, who are based at the Norwegian University of Science and Technology and supported by the Research Council of Norway.

Psychiatrists that have administered MDMA to anxiety patients have noted that it promotes emotional engagement; strengthens the bond between the patient and doctor, known as the therapeutic alliance; decreases emotional avoidance; and improves tolerance for recall and processing of painful memories.

According to Johansen and Krebs, "MDMA [ecstasy] has a combination of pharmacological effects that…could provide a balance of activating emotions while feeling safe and in control." They suggest three possible biological reasons why ecstasy could help individuals with PSTD. First, ecstasy is known to increase the release of the hormone oxytocin, which is involved in trust, empathy, and social closeness.

Because people with PTSD often report feeling emotionally disconnected and unable to benefit from the supportive presence of family and friends or therapists – a situation that is likely to contribute to the development and maintenance of the disorder – use of ecstasy might also help ameliorate these symptoms, suggest the authors.

"By increasing oxytocin levels, MDMA may strengthen engagement in the therapeutic alliance and facilitate beneficial exposure to interpersonal closeness and mutual trust," they write.

The second biological explanation for ecstasy's useful effect is that it acts in two brain regions to inhibit the automatic fear response (mediated by the amygdala) and increase emotional control (mediated by the ventromedial prefrontal cortex) and therefore permits bearable revisiting of traumatic memories.

Thirdly, ecstasy increases the release of two other hormones, noradrenaline and cortisol, which are known to be essential to trigger emotional learning, including the process that leads to fear extinction, on which therapy for PTSD relies. But, caution the authors, while these compounds enhance extinction learning they may also temporarily increase anxiety in people with PTSD because the hormones are naturally released as part of the body's response to stress.

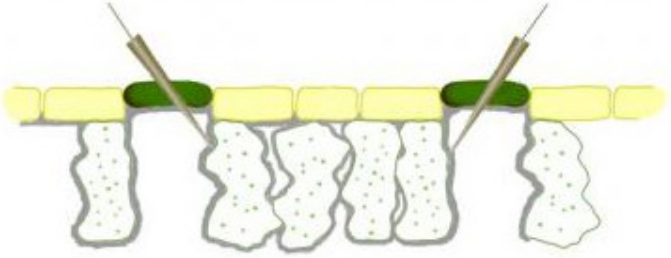
Ecstasy combined with psychotherapy is a treatment already being tested in clinical trials to help patients with PTSD. All of these trials have a similar design in which ecstasy or placebo is administered to patients a few times during their therapy sessions as part of a short term course of psychological treatment. According to the Johansen and Krebs, recent preliminary results from two of these randomized controlled trials shows that the therapy might have promise.

"Reduction of avoidance behavior linked to emotions is a common treatment target for all anxiety disorders. MDMA [ecstasy] has a combination of pharmacological effects that, in a therapeutic setting, could provide a balance of activating emotions while feeling safe and in control, as has been described in case reports of MDMA augmented psychotherapy….Future clinical trials could combine MDMA with evidence-based treatment programs for disorders of emotional regulation, such as prolonged exposure therapy for PTSD," conclude the authors.

How could MDMA (ecstasy) help anxiety disorders? A neurobiological rationale by PØ Johansen and TS Krebs is published today (Monday 9th March 2009) in the Journal of Psychopharmacology. To receive an embargoed copy of the article contact mithu.mukherjee@sagepub.co.uk, t:+44(0)207 3242223. The paper will be free to access online for a limited period from http://jop.sagepub.com/

Novel electric signals in plants

Using ion-selective micro-electrodes electrical signals in plants moving from leaf to leaf could be measured. The speed of the signals spreading as voltage changes over cell membranes ranged from 5 to 10 cm per minute. The scientists discovered this new kind of electrical signal transmission system by applying a novel method: Filamentary electrodes were inserted through open stomata directly into the inner leaf tissue and then placed onto the cell walls (see picture). Stomata are microscopically small openings in the leaf surface which plants facilitate regulating evaporation and gas exchange.



***Electrodes are inserted through stomata (small pores in the leaf surface regulating evaporation and gas exchange; dark green) into the inner leaf tissue. This way, electrical processes can be measured*. Drawing: Justus Liebig University, H. Felle**

The scientists found out that the new electrical signal they called "system potential" was induced and even modulated by wounding. If a plant leaf is wounded, the signal strength can be different and can be measured

over long distances in unwounded leaves, depending on the kind and concentration of added cations (e.g. calcium, potassium, or magnesium). It is not the transport of ions across cell membranes that causes the observed changes in voltage transmitted from leaf to shoot and then to the next leaf, but the activation of so-called proton pumps. "This is the reason why the "system potential" we measured cannot at all be compared to the classic action potential as present in nerves of animals and also in plants", says Hubert Felle from Gießen University. Action potentials follow all-or-none characteristics: they are activated if a certain stimulus threshold is reached and then spread constantly. The "system potential", however, can carry different information at the same time: The strength of the inducing stimulus (wound signal) can influence the amplitude of the systemic signal as well as the effect of different ions. "We may be on the trail of an important signal transmission system that is induced by insect herbivory. Within minutes the whole plant is alerted and the plant's defense against its enemy is activated", says Axel Mithöfer from the Max Planck Institute for Chemical Ecology in Jena.

The novel "system potential" was detected in five different plant species, among them agricultural crops like tobacco (Nicotiana tabacum), maize (Zea mays), barley (Hordeum vulgare), and field bean (Vicia faba).

Original Publication: *M. R. Zimmermann, H. Maischak, A. Mithöfer, W. Boland, H. H. Felle:*
System potentials, a novel electrical long-distance apoplastic signal in plants, induced by wounding.
Plant Physiology 149, 1593-1600 (2009).

Helium helps lung patients breathe easier

New U of C research creates innovative intervention to help people with lung disease exercise longer and harder

New research published in the international journal Chest, by Neil Eves, PhD, finds that people with chronic obstructive pulmonary disease (COPD) who breathed a mix of 60% helium and 40% oxygen during a rehabilitation program were able to exercise longer and harder than those who breathed normal air.

This innovative therapy is significant because research has shown that patients who perform more exercise and get greater improvements in fitness also get better improvements in their symptoms and health-related quality of life.

"COPD is not curable," says Eves, a researcher with the Faculties of Kinesiology and Medicine. "Our hope is that this research will help more individuals with COPD to realize the benefits of exercise."

Eves says he chose this specific gas mixture, because helium is a less dense gas that allows patients suffering with COPD to empty their damaged lungs better, while oxygen slows their breathing and further helps to reduce the shortness of breath these patients commonly suffer from. Standard air is generally made up of 78% Nitrogen and 21% Oxygen with just a trace of Helium.

In the study, individuals with COPD breathed either the helium/oxygen mix or air during cycling exercise. While both groups improved their tolerance for exercise over a six-week rehabilitation program, the group that trained with helium could exercise significantly longer following rehabilitation than the control group.

Chronic obstructive pulmonary disease is the fourth leading cause of death in Canada. It currently kills more women than breast cancer and health experts project that the disease will become more prevalent as the population ages.

Interestingly, Eves' innovative research protocol is already being used in a clinical application by Alberta Health Services Chronic Disease Management Program. "We are always interested in innovations that can help to improve the effectiveness of our health interventions," says Dr. Sandra Delon, PhD, the director of Alberta Health Services' Chronic Disease Management Program. "We've already seen some promising results in this pilot program, so we're very encouraged."

Regulate armed robots before it's too late

* 10 March 2009 **by A. C. Grayling**

IN THIS age of super-rapid technological advance, we do well to obey the Boy Scout injunction: "Be prepared". That requires nimbleness of mind, given that the ever accelerating power of computers is being applied across such a wide range of applications, making it hard to keep track of everything that is happening. The danger is that we only wake up to the need for forethought when in the midst of a storm created by innovations that have already overtaken us.

We are on the brink, and perhaps to some degree already over the edge, in one hugely important area: robotics. Robot sentries patrol the borders of South Korea and Israel. Remote-controlled aircraft mount missile attacks on enemy positions. Other military robots are already in service, and not just for defusing bombs or detecting landmines: a coming generation of autonomous combat robots capable of deep penetration into enemy territory raises questions about whether they will be able to discriminate between soldiers and innocent civilians. Police forces are looking to acquire miniature Taser-firing robot helicopters. In South Korea and Japan the development of robots for feeding and bathing the elderly and children is already advanced. Even in a robot-

backward country like the UK, some vacuum cleaners sense their autonomous way around furniture. A driverless car has already negotiated its way through Los Angeles traffic.

In the next decades, completely autonomous robots might be involved in many military, policing, transport and even caring roles. What if they malfunction? What if a programming glitch makes them kill, electrocute, demolish, drown and explode, or fail at the crucial moment? Whose insurance will pay for damage to furniture, other traffic or the baby, when things go wrong? The software company, the manufacturer, the owner?

Most thinking about the implications of robotics tends to take sci-fi forms: robots enslave humankind, or beautifully sculpted humanoid machines have sex with their owners and then post-coitally tidy the room and make coffee. But the real concern lies in the areas to which the money already flows: the military and the police.

A confused controversy arose in early 2008 over the deployment in Iraq of three SWORDS armed robotic vehicles carrying M249 machine guns. The manufacturer of these vehicles said the robots were never used in combat and that they were involved in no "uncommanded or unexpected movements". Rumours nevertheless abounded about the reason why funding for the SWORDS programme abruptly stopped. This case prompts one to prick up one's ears.

The MAARS robot is used by the US military, but who would be responsible if anything went wrong with it? **(Image: Qinetiq)**

Media stories about Predator drones mounting missile attacks in Afghanistan and Pakistan are now commonplace, and there are at least another dozen military robot projects in development. What are the rules governing their deployment? How reliable are they? One sees their advantages: they keep friendly troops out of harm's way, and can often fight more effectively than human combatants. But what are the limits, especially when these machines become autonomous?

The civil liberties implications of robot devices capable of surveillance involving listening and photographing, conducting searches, entering premises through chimneys or pipes, and overpowering suspects are obvious. Such devices are already on the way. Even more frighteningly obvious is the threat posed by military or police-type robots in the hands of criminals and terrorists.

Military robots in the hands of criminals and terrorists would pose a frightening threat

There needs to be a considered debate about the rules and requirements governing all forms of robot devices, not a panic reaction when matters have gone too far. That is how bad law is made - and on this issue time is running out. ***A. C. Grayling is a philosopher at Birkbeck, University of London***

Simple test helps predict heart attack risk

Ankle brachial index identifies peripheral arterial disease patients at high cardiovascular risk who were missed by Framingham Risk Score in 6,200-person NHANES study

SAN DIEGO, Calif. (March 10, 2009) - The use of common and readily available screening tests - like the ankle brachial index (ABI) - along with traditional risk scoring systems - such as the Framingham Risk Score - has the potential to prevent devastating heart attacks in thousands of individuals who are not originally thought to be at high risk (according to Framingham alone), say researchers at the Society of Interventional Radiology's 34th Annual Scientific Meeting. About 25 percent of all heart attacks or sudden cardiac deaths in the United States occur in individuals thought to be at low risk.

In the study, information was analyzed from the 1999-2004 National Health and Nutrition Examination Survey (NHANES) - a nationally representative cross-sectional survey of the U.S. population for 6,292 men and women ages 40 and older without known history of heart disease, stroke, diabetes or atherosclerotic vascular disease - along with available data on standard cardiovascular risk factors and screening tests (like the ABI, which is a comparative blood pressure test). For the first time, researchers determined the prevalence of peripheral arterial disease (PAD) in a large population of women and men who were not considered at high risk for cardiovascular disease. And the results are surprising: novel risk factors (those not traditionally considered in the Framingham Risk Score) are abnormal in up to 45 percent of those not considered high risk for coronary heart events.

"This is significant news that can profoundly impact public health. If novel risk factors are shown to improve risk prediction, they could be very valuable because the prevalence of abnormal values is high in populations not known to have high risk," said Timothy P. Murphy, M.D., an interventional radiologist and director of the Vascular Disease Research Center at Rhode Island Hospital in Providence. "These simple tests - like ABI

screening - have the potential to improve the accuracy of cardiovascular risk prediction and thereby have significant public health impact by helping identify people for intensive medical therapy and preventing heart attacks and strokes," said Murphy.

While 91 percent of the NHANES group was considered at low or intermediate risk of cardiovascular disease, according to Framingham criteria alone, almost 45 percent of them were found to have at least one of three conditions: an abnormal ABI or elevated plasma fibrinogen or elevated plasma C-reactive protein (CRP). "Even with abnormal ABI, which was the least prevalent of the three novel risk factors evaluated, that number translates into about 2.1 million Americans, age 40 and older, who have no known history of heart disease, stroke, diabetes or atherosclerotic vascular disease," said Murphy. "There is also a good chance that ABI, which actually detects subclinical already-established atherosclerotic disease, may actually perform better in terms of risk prediction than fibrinogen or C-reactive protein because it may be more specific," Murphy said.

About 1.1 million Americans every year have heart attacks, and almost a third of those heart attacks results in death. Another 750,000 individuals experience stroke each year. Risk factors - like smoking, diabetes, high blood pressure and obesity - increase one's risk of heart attack and are associated with 75 percent of all heart attacks. However, the other 25 percent of heart attacks or sudden cardiac deaths occur in individuals not known to have risk factors and thought to be at low risk for cardiovascular disease. "The earlier the detection of who's at risk for heart attacks is crucial. Primary prevention - such as initiating lifestyle changes and medical intervention directed at modifying risk factors (smoking cessation, blood glucose and blood pressure control, lowering cholesterol and exercise) - can be started to improve one's health before costlier and more intensive interventions are needed," said Murphy.

"Interventional radiologists often provide PAD screening tests like the ABI. Primary care doctors, who oversee medical management of the vast majority of the public at risk for cardiovascular disease, should partner with interventional radiologists in evaluating patients' risk for cardiovascular disease, as well as for managing established PAD," said Murphy. ABI, used to diagnose PAD, is a painless test that compares the blood pressure in the legs to the blood pressure in the arms to determine how well the blood is flowing and whether further tests are needed. Elevated results for plasma fibrinogen and plasma C-reactive protein, laboratory-based tests, can indicate inflammation.

More information about ABI, cardiovascular disease, and interventional radiology can be found online at www.SIRweb.org. Abstract 146: "Prevalence of Low Ankle Brachial Index, Elevated Plasma Fibrinogen and CRP Among Those Otherwise at Low-Intermediate Cardiovascular Events' Risk: Data From the National Health and Nutrition Examination Survey (NHANES) 1999- ," R. Dhangana, T.P. Murphy, M.B. Ristuccia, J.V. Cerezo and D. Tsai, all with Rhode Island Hospital/Brown University, Providence, R.I.; and M.J. Pencina, Boston University, Boston, Mass., SIR 34th Annual Scientific Meeting March 7-12, 2009. This abstract can be found at www.SIRmeeting.org.

Diagnostic errors: The new focus of patient safety experts

JAMA commentary highlights problem, suggests solutions to reduce the number of diagnoses that are missed, wrong or delayed

Johns Hopkins patient safety experts say it's high time for diagnostic errors to get the same attention from medical institutions and caregivers as drug-prescribing errors, wrong-site surgeries and hospital-acquired infections. Diagnostic misadventures represent a potentially much larger source of preventable health problems and deaths than many of the more popular targets of safety reform, they say in a commentary in the March 11 issue of the Journal of the American Medical Association.

In the article, David Newman-Toker, M.D., Ph.D., and Peter Pronovost, M.D., Ph.D., report that misdiagnosis accounts for an estimated 40,000 to 80,000 hospital deaths per year and that tort claims for diagnostic errors - defined as diagnoses that are missed, wrong or delayed - are nearly twice as common as claims for medication errors.

Typically, they note, diagnostic errors were thought to originate with individual doctors lacking the training or skill they should have, but blaming physicians hasn't produced many solutions. As with successful approaches to reducing treatment errors, they point out that reducing diagnostic errors will likely require a focus on larger "system" failures that affect medical practice overall.

"Moving away from a model that chastises individual physicians to one that focuses on improving the medical system as a whole could offer big payoffs for improving diagnostic accuracy as well as the cost effectiveness of care," says Newman-Toker, assistant professor of neurology with joint appointments in otolaryngology, health sciences informatics, epidemiology, and health policy and management at the Johns Hopkins University School of Medicine and the Johns Hopkins Bloomberg School of Public Health. "Right now," he adds, "there is often a mismatch between who gets advanced diagnostic testing and who needs it, leading to worse outcomes and higher costs. Realigning resources with needs could improve outcomes at lower cost."

Much as bloodstream infections in intensive care units have decreased through systematic solutions adopted by hospitals, such as requiring physicians to follow a procedural checklist that emphasizes sterile techniques when inserting medical catheters, Newman-Toker and Pronovost suggest that system-wide solutions could be the key for decreasing diagnostic errors.

For example, Newman-Toker notes, triage protocols in emergency departments often categorize patients with typically benign symptoms, such as isolated headache, as being at "low-risk" of having a bigger problem, even though such symptoms are sometimes indicative of dangerous conditions, such as a bleeding brain aneurysm. A systems fix that could decrease diagnostic errors might be to change the overall rules for the triage protocol so that it considers specific symptom details that help distinguish between "low-risk" and "high-risk" types of headache.

The Johns Hopkins team suggests that diagnostic errors might be reduced by systematically adopting tools such as checklists that help physicians remember critical diagnoses or by making available computer programs known as "diagnostic decision-support systems" that assist physicians in calculating the level of risk of a given patient's having certain diseases. Health systems could further decrease diagnostic errors, they say, with time-tested, low-tech tools such as independent second looks at X-rays and CT scans or rapidly directing patients with unusual symptoms to diagnostic experts.

Because diagnostic errors can be tricky to track to their roots, Pronovost, an expert on breaking down complex medical problems, says more research is needed to understand and find patterns in the origins of such errors. Pronovost, a professor of anesthesiology, critical care medicine and surgery, is medical director of Johns Hopkins' Center for Innovation in Quality Patient Care.

"The first step in addressing the diagnostic error problem is to shine a light on them so they are clearly visible," Pronovost says. "Then with wise investments, clinicians, researchers and patients can discover how to prevent them."

Brighten up! Paint study could save states millions

A new study from North Carolina State University shows that painted road markings, such as the lines separating traffic lanes, are significantly better at reflecting headlights in the direction that the paint was applied. This finding will help determine how states comply with new federal safety regulations and save money on painting their roadways.

The NC State researchers found that "retroreflectivity values" are higher in the direction of paint striping. "In other words," study co-author Dr. Joe Hummer says, "the paint reflects more light if you are following the painting truck than if you are driving from the other direction." This is a big deal, in part, because approximately 60 percent of the nation's roads are marked with paint, rather than thermoplastics or other materials. Hummer notes that paint "is expensive – two to three thousand dollars per mile of road." Hummer is a professor of civil engineering at NC State. His co-authors are fellow professor Dr. William Rasdorf and Ph.D. student Guanghua Zhang.

Hummer says the research could help state transportation departments better predict how long the painted markings will perform properly – and when they'll need to be replaced. If a state can re-paint road markings every three years instead of every two, it will save a lot of money, Hummer says.

In addition, the new research could play an important role in helping state and federal transportation authorities determine how to measure compliance with upcoming standards on pavement marking brightness. The Federal Highway Administration is expected to release the standards soon, but this new research raises the possibility that a painted line in the road could pass a new brightness standard going in one direction, but fail it if tested from the other direction. This is a question that will have to be resolved in order to ensure uniform compliance with the new standards.

The difference in retroreflectivity, depending on the direction one is driving, is equivalent to about a year of wear and tear. In other words, a painted line in the road will look one year newer if you are driving in the same direction that the paint was applied.

Hummer explains that this happens because glass beads are scattered onto freshly painted traffic markings in order to make them reflective. Because the painting truck is moving, those beads tend to bounce and roll before coming to rest. "The beads skid and build up paint on one side," Hummer says. "Therefore, they are less reflective in that direction."

The research was funded through federal aid money for statewide planning and research from the North Carolina Department of Transportation. The issue is particularly important for North Carolina because over than 80 percent of marked roads in the state are marked with paint – significantly higher than the national average. The research was published in the journal Public Works Management & Policy.

A simple balance test may predict cognitive decline in Alzheimer's disease

Amsterdam, The Netherlands, March 10, 2009 – ***A simple balance test may predict cognitive decline in Alzheimer's Disease, according to a study published in the March 2009 issue of the Journal of Alzheimer's Disease.***

This study was carried out in 16 university hospital departments of neurology, geriatrics or psychiatry in ten cities with 686 outpatients suffering from AD. This population is representative of the AD population seen by clinicians in daily practice. Patients were evaluated by a geriatrician every six months for up to two years, and their degree of cognitive impairment was measured using the Mini Mental State Examination (MMSE). At the same time, a "one-leg balance" (OLB) test was given, where a participant was asked to stand on one leg for as long as possible. The OLB test was reported as abnormal when the participant was unable to stand on one leg for 5 seconds or more.

Participants with an abnormal OLB at baseline or/and during the follow-up showed significantly more cognitive decline at 12, 18 and 24 months than the participants with a OLB test normal at baseline and normal during the follow-up. The worst condition (having an abnormal OLB at baseline and during the follow-up= no improvement) was associated with a mean adjusted cognitive decline of 9.2 points. The best condition (having a normal OLB at baseline and during the follow-up = no worsening) was associated with a mean adjusted cognitive decline of 3.8 points.

Senior Investigator Yves Rolland, Inserm and the University of Toulouse, France, states, "Our results suggested that an abnormal OLB is a marker of more advanced dementia (worst baseline characteristic) and an independent predictor of cognitive decline in AD. Our results reinforce in an AD population, the growing evidence suggesting a link between physical performances and cognitive decline. If these results are confirmed by other data, the OLB test could be adopted in clinical practice to identify AD patients at high risk of rapid cognitive decline."

The article is "An Abnormal 'One-leg Balance' Test Predicts Cognitive Decline During Alzheimer's Disease" by Yves Rolland, Gabor Abellan van Kan, Fati Nourhashemi, Sandrine Andrieu, Christelle Cantet, Sophie Guyonnet-Gillette and Bruno Vellas It is published in the Journal of Alzheimer's Disease 16:3 (March 2009).

Study of protein structures reveals key events in evolutionary history

A new study of proteins, the molecular machines that drive all life, also sheds light on the history of living organisms.

The study, in the journal Structure, reveals that after eons of gradual evolution, proteins suddenly experienced a "big bang" of innovation. The active regions of many proteins, called domains, combined with each other or split apart to produce a host of structures that had never been seen before. This explosion of new forms coincided with the rapidly increasing diversity of the three superkingdoms of life (bacteria; the microbes known as archaea; and eucarya, the group that includes animals, plants, fungi and many other organisms).

Lead author Gustavo Caetano-Anollés, a professor of bioinformatics in the department of crop sciences at the University of Illinois and an affiliate of the Institute for Genomic Biology, has spent years studying protein structures – he calls them "architectures" – which he suggests offer a reliable record of evolutionary events.

All proteins contain domains that can be identified by their structural and functional similarities to one another. These domains are the gears and motors that allow the protein machinery to work. Every protein has one or more of them, and very different proteins can contain the same, or similar, domains.

By conducting a census of all the domains that appear in different groups of organisms and comparing the protein repertoires of hundreds of different groups, the researchers were able to construct a timeline of protein evolution that relates directly to the history of life.

"The history of the protein repertoire should match the history of the entire organism because the organism is made up of all those pieces," Caetano-Anollés said.

He and his co-author, postdoctoral researcher Minglei Wang, were interested in tracing how proteins make use of their domains, or groups of domains, to accomplish various tasks. These domains or domain clusters can be thought of as "modules" which fit together in various ways to achieve different ends.

Unlike the sequence of amino acids in a protein, which is highly susceptible to change, the protein modules found today in living organisms have endured because they perform critical tasks that are beneficial to the organisms that host them, Caetano-Anollés said. “These modules are resistant to change, they are highly integrated and they are used in different contexts," he said.

By tracing the history of the modules, the researchers were able to build a rough timeline of protein evolution. It revealed that before the three superkingdoms began to emerge, most proteins contained only single domains that performed a lot of tasks. "As time progressed, these domains started to combine with others and they became very specialized," Caetano-Anollés said. This eventually led to the big bang of protein architectures.

"Exactly at the time of the big bang," he said, many of the combined domains began to split apart, creating numerous single-domain modules again. But these new modules were much more efficient and specialized than their ancient predecessors had been. "This makes a lot of sense," Caetano-Anollés said. "As you become more complex, you would want to fine-tune things, to do things in a more tailored way."

The protein modules of the three superkingdoms also began to diverge more dramatically from one another, with the eucarya (the group that includes plants and animals) hosting the greatest diversity of modules.

"This explosion of diversity allowed the eucarya to do things with their proteins that other organisms could not do," Caetano-Anollés said.

Editor's note: To reach Gustavo Caetano-Anollés, please call: 217-333-8172; e-mail: gca@illinois.edu.

Life could have survived Earth's early pounding

* 15:19 10 March 2009 **by Jeff Hecht**

Microbes living deep underground could have survived the massive barrage of impacts that blasted the Earth 3.9 billion years ago, according to a new analysis. That means that today's life might be descended from microbes that arose as far back as 4.4 billion years ago, when the oceans formed.

Around 3.9 billion years ago, shifts in the orbits of the gas giant planets are thought to have disrupted other objects in the solar system, sending many hurtling into the inner planets. Geologists call that time the Hadean Eon, and thought its fiery hell of impacts would have sterilised the Earth.

But a new study by Oleg Abramov and Steve Mojzsis of the University of Colorado in Boulder suggests hardy life-forms could have survived if they were buried underground. They will report the results on 23 March at the Lunar and Planetary Science Conference in Texas.

Sterilisation point

Using a computer model, they sent 200 million billion tonnes of mass - in rocks with the same mass distribution as those in today's asteroid belt - slamming into the planet. The biggest impacts would have done the most damage - a 500-kilometre-wide blockbuster would have spread a 350-metre-deep layer of 1200 °C ejecta over the planet.

Yet heat from the impacts would not have penetrated very deeply into the underlying solid crust. The layer heated to the sterilisation point, about 110 °C, would be only about 300 metres thick. High-temperature 'extremophile' microbes, like those in the hot springs of Yellowstone National Park, would have survived at greater depths, down to their limit of about 4 km.

Moreover, the impacts might have helped provide a refuge for these heat-loving microbes by creating cracks in the rocky crust that water could flow into.

Early oceans

So, how far back could life have originated? It's hard to say, since rocks that would have recorded evidence of any life from before the Hadean were destroyed by the "late heavy bombardment" that battered the planet at the time. The oldest isotopic evidence of life comes from rocks that formed 3.83 billion years ago, soon after the bombardment ended.

But heat-loving microbes appear to be among the Earth's earliest life-forms, and may have developed as early as 4.4 billion years ago. That's when the hot young Earth - whose top few hundred kilometres had probably been vaporised 100 million years before, in the impact that formed the Moon - would have cooled enough for seas to form.

Says Mojzsis: "For all intents and purposes, life could have started 4.4 billion years ago, and the late heavy bombardment pruned, rather than frustrated, life."

That conclusion is reasonable, says Kevin Zahnle of NASA's Ames Research Center in California.

UI study suggests salt might be 'nature's antidepressant'

Most people consume far too much salt, and a University of Iowa researcher has discovered one potential reason we crave it: it might put us in a better mood.

UI psychologist Kim Johnson and colleagues found in their research that when rats are deficient in sodium chloride, common table salt, they shy away from activities they normally enjoy, like drinking a sugary substance or pressing a bar that stimulates a pleasant sensation in their brains.

"Things that normally would be pleasurable for rats didn't elicit the same degree of relish, which leads us to believe that a salt deficit and the craving associated with it can induce one of the key symptoms associated with depression," Johnson said.

The UI researchers can't say it is full-blown depression because several criteria factor into such a diagnosis, but a loss of pleasure in normally pleasing activities is one of the most important features of psychological depression. And, the idea that salt is a natural mood-elevating substance could help explain why we're so

tempted to over-ingest it, even though it's known to contribute to high blood pressure, heart disease and other health problems.

Past research has shown that the worldwide average for salt intake per individual is about 10 grams per day, which is greater than the U.S. Food and Drug Administration recommended intake by about 4 grams, and may exceed what the body actually needs by more than 8 grams.

Johnson, who holds appointments in psychology and integrative physiology in the College of Liberal Arts and Sciences and in pharmacology in the Carver College of Medicine, published a review of these findings in the July issue of the journal "Physiology & Behavior" with Michael J. Morris and Elisa S. Na, UI graduate students. In addition to reporting their own findings, the authors reviewed others' research on the reasons behind salt appetite.

High levels of salt are contained in everything from pancakes to pasta these days, but once upon a time, it was hard to come by. Salt consumption and its price skyrocketed around 2000 B.C. when it was discovered as a food preservative. Roman soldiers were paid in salt; the word salary is derived from the Latin for salt. Even when mechanical refrigeration lessened the need for salt in the 19th century, consumption continued in excess because people liked the taste and it had become fairly inexpensive. Today, 77 percent of our salt intake comes from processed and restaurant foods, like frozen dinners and fast food.

Evolution might have played an important part in the human hankering for salt. Humans evolved from creatures that lived in salty ocean water. Once on land, the body continued to need sodium and chloride because minerals play key roles in allowing fluids to pass in and out of cells, and in helping nerve cells transfer information throughout the brain and body. But as man evolved in the hot climate of Africa, perspiration robbed the body of sodium. Salt was scarce because our early ancestors ate a veggie-rich diet and lived far from the ocean.

"Most of our biological systems require sodium to function properly, but as a species that didn't have ready access to it, our kidneys evolved to become salt misers," Johnson said.

Behavior also came to play a key role in making sure we have enough salt on board. Animals like us come equipped with a taste system designed to detect salt and a brain that remembers the location of salt sources -- like salt licks in a pasture. A pleasure mechanism in the brain is activated when salt is consumed. So the body needs salt and knows how to find it and how to conserve it. But today scientists are finding evidence that it's an abused, addictive substance -- almost like a drug.

One sign of addiction is using a substance even when it's known to be harmful. Many people are told to reduce sodium due to health concerns, but they have trouble doing so because they like the taste and find low-sodium foods bland. Another strong aspect of addiction is the development of intense cravings when drugs are withheld. Experiments by Johnson and colleagues indicate similar changes in brain activity whether rats are exposed to drugs or salt deficiency.

"This suggests that salt need and cravings may be linked to the same brain pathways as those related to drug addiction and abuse," Johnson said.

STORY SOURCE: *University of Iowa News Services, 300 Plaza Centre One, Suite 371, Iowa City, Iowa 52242-2500*

'Suspending asthma treatment a bad option for expectant mothers': Study

University of Montreal researcher studies the correlation

Pregnant women suffering from asthma run a greater risk of giving birth prematurely if they suspend their asthma treatments. According to a Université de Montréal study, published in Respiratory Medicine, the probability of suffering from hypertension during pregnancy also increases for women who interrupt their asthma treatment. "Many pregnant women cease taking their asthma medication to protect the health of their child," says Faranak Firoozi, a researcher at the Université de Montréal's Department of Pharmacy. "However, they don't know that unchecked asthma can cause greater harm to the child than the medication."

According to Firoozi, there is no correlation between taking asthma medication, such as Pulmicort or Ventolin, and any congenital birth defect. In their study, Firoozi and colleagues debunk the myth that fetal gender has an affect on maternal asthma. "Contrary to what some researchers have said, there is no difference between male and female hormones and how they impact bronchial sensitivity, which would in turn accentuate asthma symptoms when a woman carries a girl. This is good news," says Firoozi.

Firoozi used data collected by the Régie de l'assurance maladie, the Ministère de la santé et des services sociaux and the Institut de la statistique du Québec, on 13,000 pregnant women who consulted a physician for asthma between 1990 and 2002. The researcher analyzed the medication used by these women and their rate of hospitalization following their visit to the ER.

"Yes, asthma can have an important impact on pregnancy," says Firoozi. "Asthmatic women must be closely followed during pregnancy given the risks they pose to their own health and the health of their child. But the sex of the fetus has nothing to do with the asthmatic condition of pregnant women."

Is That Your Final Answer? Study Suggests Method For Improving Individual Decisions

Herd mentality. Angry mob. Mass hysteria. As these phrases suggest, we are not always confident that a large group of people will come up with the smartest decisions. So it may be surprising to learn that numerous studies have shown that a crowd of people usually gives more accurate responses to questions compared to a mere individual. Averaging the responses provided from a group increases accuracy by canceling out a number of errors made across the board (such as over- and under-estimating the answer).

What happens when we are on our own? What if there is no one else around to consult with before making a judgment - how can we be confident that we are giving a good answer? Psychologists Stefan M. Herzog and Ralph Hertwig from the University of Basel wanted to know if individuals could come up with better answers using a technique they designed and called "dialectical bootstrapping."

Dialectical bootstrapping is a method by which an individual mind averages its' own conflicting opinions, thus simulating the "wisdom of the crowd." In other words, dialectical bootstrapping enables different opinions to be created and combined in the same mind. For example, in this study, participants were asked to identify dates of various historical events. After they gave their initial answer, the participants were asked to think of reasons why the answer may be wrong and were then asked to come up with an alternative second (dialectical) answer. The results, reported in Psychological Science, a journal of the Association for Psychological Science, reveal that the average of the participants' first answer with the second answer was much closer to the correct answer, compared to the original answers on their own. In addition, the dialectical bootstrapping method (that is, thinking about why your own answer might be incorrect and then averaging across estimates) resulted in more accurate answers compared to simply making a second guess without considering why the first answer may be wrong.

These findings suggest that dialectical bootstrapping may be an effective strategy in helping us come up with better answers to many types of problems. The researchers note that while it may be frustrating going back and forth between two different answers, "as dialectical bootstrapping illustrates, being of two minds can also work to one's advantage." They conclude, "Once taught about the tool, people could make use of it to boost accuracy of their estimates across a wide range of domains."

Eight scientists who became their own guinea pigs

* 11:45 11 March 2009 **by Eleanor Harris**

Olivier Ameisen, a French cardiologist, found his own cure for alcoholism through a bout of pharmacological self-experimentation - a story related in his book, The End of My Addiction. While editing our review of Ameisen's book, I started thinking about other scientists who've become their own test subjects - and my colleagues were quick to chime in.

Many of the stories we turned up proved hard to verify, and others too scurrilous to publish - but here are eight extraordinary (and occasionally disgusting) stories of medical self-experimentation.

Experimenting on yourself very rarely leads to scientific glory - it's much more likely to result in swift admission to the casualty ward, or even to the morgue. So New Scientist doesn't recommend you try these experiments on yourself, or anyone else for that matter.

The vomit sauna

A special place must be reserved in the annals of self-experimentation for medical student Stubbins Ffirth, who conducted a series of increasingly revolting experiments in the early 19th century to prove that yellow fever was not contagious.

Ffirth started off by pouring "fresh black vomit" from a patient with yellow fever into cuts in his arm. He didn't get yellow fever.

Emboldened by this success, Ffirth graduated to dribbling the vomit into his eyes and smearing assorted other bodily fluids from yellow-fever sufferers over his person - including blood, spit, sweat and urine (see Top 10 bizarre experiments, if you really want to). He even sat in a "vomit sauna" full of heated regurgitation vapours, which caused him "great pain in [his] head", but left him in rude health.

Finally, he took to actually ingesting the vomit - first in pill form, then straight from a patient's mouth. Since he still didn't get ill, he considered the case proven. Presumably others did too, since he was in due course awarded his medical doctorate.

But they were wrong: yellow fever is contagious, albeit only if directly transmitted into the bloodstream. That was proven by another self-experimenter, US army surgeon Jesse Lazear, who allowed himself to be bitten by yellow fever-infected mosquitoes in the early 1900s. Ironically, the mosquito whose bite proved fatal to Lazear was reportedly not one of his experimental specimens, but a wild specimen.

August Bier's leaking spine

In 1898, German surgeon August Bier invented spinal anaesthesia, which involved a small dose of cocaine being injected into the cerebrospinal fluid surrounding the spinal cord. That was a great improvement on existing methods of general anaesthesia, but how effective was it?

To find out, Bier decided to be anaesthetised himself. But things didn't go as planned for Bier - or for his hapless assistant, Augustus Hildebrandt.

Hildebrandt was supposed to administer the cocaine but, thanks to a mix-up with the equipment, Bier was left with a hole in his neck from which cerebrospinal fluid began to flow.

Rather than abandon the effort, however, the two men switched places. Once Hildebrandt had been anaesthetized, Bier stabbed, hammered and burned his assistant, pulled out his pubic hairs and - presumably eager to leave no stone unturned in testing the new method's efficiency - squashed his testicles.
Once the cocaine had worn off, the pair went out for a boozy dinner, despite their injuries. Both suffered terribly in subsequent days but, while Bier took it easy as he recovered, Hildebrandt had to stand in for his boss at work.

Perhaps unsurprisingly, he subsequently fell out with Bier, becoming one of his fiercest critics and denying his discovery of spinal anaesthesia - which rapidly caught on.

Pierre Curie's arm

In June 1903, physicist Pierre Curie rolled up his sleeve and revealed a burn-like wound on his arm to a packed audience at the UK's Royal Institution. The wound had been caused by a sample of radium salts, which he had taped to the skin of his arm for just 10 hours, more than 50 days earlier. During the course of his demonstration, Curie dropped some radium on the desk. The resulting contamination was still detectable, and in need of cleaning up, half a century later.

Curie and his wife, Marie, hoped that radium's burning effect might prove useful in the treatment of cancer. But ironically, the radiation that the sample gave off - which was also emitted by various other chemicals to which the Curies routinely exposed themselves in the course of their work - were actually having a catastrophic effect on their health.

Both Pierre and Marie were constantly ill, tired and in pain, but their experiments did pave the way for the use of radium in medicine. Later in 1903, they shared the Nobel Prize in Physics for their research on radiation.

JBS Haldane's smoking ear

One self-experimenter whose work had long-term personal consequences was the polymath JBS Haldane.

Haldane wanted to build on work done by his father, John Scott Haldane, on the physiology of working Navy divers in the early 20th century. But whereas Haldane senior restricted himself to observation and measurement, his son took a more direct approach, repeatedly putting himself in a decompression chamber to investigate the physiological effects of various levels of gases.

Haldane was motivated by concern for the welfare of sailors in disabled submarines, and his work led to a greatly improved understanding of nitrogen narcosis, as well as the safe use of various gases in breathing equipment. But he paid a high price, regularly experiencing seizures as a result of oxygen poisoning - one resulting in several crushed vertebrae.

He also suffered from burst eardrums, but he was sanguine about the damage. "The drum generally heals up," he said, adding, "if a hole remains in it, although one is somewhat deaf, one can blow tobacco smoke out of the ear in question, which is a social accomplishment."

Nathaniel Kleitman's cave

In 1938, the eminent sleep researcher Nathanial Kleitman, accompanied by his research assistant Bruce Richardson, moved into Mammoth Cave, Kentucky. Kleitman wanted to find out if humans could adapt to a longer, 28-hour day. The cave, 120 feet underground, offered a perfect environment to test the idea out: there was no natural light and the temperature remained constant, so there were no clues as to when it was day and night.

It was not a comfortable environment, however: as well as being isolated and claustrophobic, the researchers found themselves sharing their beds with rats.

A month later, they emerged, having discovered that while Kleitman had struggled to change his sleeping patterns, Richardson had adapted to the 28-hour cycle. Their studies helped to advance knowledge of human circadian rhythms, and spawned practical recommendations for shift-workers.

Kleitman didn't confine himself to caves: he later spent two weeks on board a submarine and a spell in the Arctic, with its long periods of darkness and daylight, in both cases studying sleep patterns.

Albert Hofmann's bicycle ride

Swiss chemist Albert Hofmann, who discovered the drug lysergic acid diethylamide (LSD) while looking for medically useful derivatives of the ergot fungus, is also credited as the first to experience an acid trip.

Hofmann took his first trip, in 1943, by accident, apparently as a result of accidentally spilling the chemical on his fingertips in his Basel laboratory. He went home and "sank into a not-unpleasant condition", a dreamy state in which he saw psychedelic images.

His second experience was less agreeable: he deliberately took a dose that he believed to be light, but which led to intense effects while riding home on his bicycle - an episode that has become notorious in recreational pharmaceutical circles.

While the chemical may have uses in psychiatry, its impact to date has arguably been more cultural than medical. Hofmann himself continued to take LSD, and advocate its careful use, for the rest of his life.

Hofmann wasn't alone in testing out psychedelic drugs on himself: US chemist Alexander Shulgin ingested many chemicals, including MDMA (ecstasy), leading to its use in psychotherapy, and Harvard psychologist Timothy Leary experimented with LSD on himself, to test, among other things, whether it could be used to treat alcoholism.

Leary eventually lost his job after he began touting psychedelics as a hotline to spiritual enlightenment.

Barry Marshall's bad breath

Junior doctor Barry Marshall was sure the medical establishment was wrong about the cause of stomach ulcers. The received wisdom was that they were caused primarily by lifestyle factors, but Marshall and pathologist Robin Warren were sure that the bacterium Helicobacter pylori was to blame.

To prove their hypothesis, they needed to examine how the bacteria affected a healthy human volunteer - but as Marshall explained to New Scientist in a 2006 interview, "I was the only person informed enough to consent".

Marshall didn't tell the hospital's ethics committee what he had in mind, for fear of being turned down, or even his own wife, until after he had swallowed the bacteria. He was fine for three days, but then began vomiting; his wife complained that he had "putrid breath". A biopsy taken 10 days later confirmed the bacteria had infected his stomach and that he had gastritis, which can eventually lead to ulcers.

It still took another eight years for Marshall and Warren's theory to be widely accepted, but their work eventually earned them the 2005 Nobel Prize for Physiology or Medicine.

David Pritchard's itchy skin

Various researchers have infected themselves with parasites. One such is biologist David Pritchard, who in 2004 allowed fifty hookworm larvae to burrow through his skin.

Hookworms seem able to modify the body's immune response in ways that may be useful in treating immune system disorders, such as asthma and Crohn's disease. Such disorders are comparatively rare in places where hookworm infestation is common. Other members of Pritchard's lab also infected themselves with the hookworms, which can survive for up to a decade but are easy to kill off with drugs. "They itch quite a bit when they go through the skin," said Pritchard, but become really troublesome only when they reached his stomach.

Fifty turned out to be too many: ten was a safer number. Trials are continuing to evaluate the treatment, including a test to see if the hookworms can help multiple sclerosis sufferers.

Are there any notable medical self-experimenters you think we should have included? Tell us about them in the comments.

18 and Under

Distractions May Shift, but Sleep Needs Don't

By PERRI KLASS, M.D.

For a long time, children used to go to bed early, and not just in Proust. Think of Robert Louis Stevenson:

In winter I get up at night
And dress by yellow candle-light.
In summer, quite the other way,
I have to go to bed by day.
I have to go to bed and see
The birds still hopping on the tree.

Well, not my children. Clearly, I did this wrong.

When I read that Barack and Michelle Obama had set their daughters' bedtime for 8 p.m., I asked my oldest (now 25) if he remembered having a bedtime when he was little. He just laughed at me.

When he was a preschooler, I was a pediatric resident (before the limits on work hours), and evenings tended to start around 7 p.m. And mind you, these were 1980s evenings, free of e-mail and cellphones and texting and

all the other distractions that make it harder and harder for a child — or an adult — to say goodnight. I'm not sure any of my three children ever had a regular bedtime before 9:30 or 10.

Even at that, I'm afraid, we were pretty ad hoc: oh my, it's almost 11 and the kid is still awake! Time to read him a story and put him to bed.

There's nothing I care about more fervently than reading to children, and I have long been an advocate - both in public and as a parent — for books at bedtime. Ah yes, but what is bedtime, and who decides? My youngest, who is 13, has to get up pretty early, and we try to persuade him to go to bed by 10:30 or so on school nights - unless he still has homework, or we're all out at a movie, or there's an important baseball game on the West Coast.

In other words, I'm still getting it wrong, and I'm only now coming to understand why it matters.

"The literature really strongly suggests the average early to mid-adolescent needs 9 to 9.25 hours a night," said Dr. Judith Owens, an associate professor of pediatrics at the Alpert Medical School of Brown University, who directs the Pediatric Sleep Disorders Clinic at Hasbro Children's Hospital.

She quickly headed off my question about children — or adults — who don't need that much sleep. "It's a bell-shaped curve," she said, with just 2.5 percent of the population needing significantly less sleep than average.

"The problem," she went on, "is that 95 percent of us think we're in that 2.5 percent. You should assume until proven otherwise that your kid needs that much sleep."

What is the bedtime recommendation for an 8- or 9-year-old? The experts sensibly suggest that you work backward from wake-up time, trying for 10 hours of sleep, and testing your routine by checking whether the child wakes spontaneously, alert and cheerful and ready for the day (no, mine generally did not).

In part, the idea of fixed and early bedtimes for children is part of a larger parental vision of the protected life of the child, moving along on a very distinct daily schedule, and also, of course, protecting some time for the parents. But it's also redolent of nursery hours and nursery comfort.

"Can anything harm us, mother, after the night-lights are lit?" asks Michael in "Peter Pan," and Mrs. Darling reassures him (not realizing that he is about to fly away to Never-Never Land). "So long, farewell," sing the von Trapp children in "The Sound of Music." And of course, "When the Children Are Asleep," plan the couple in "Carousel."

As children move into middle school, Dr. Owens said, they still need plenty of sleep, but it gets harder for them to follow the schedule that the world demands.

"Sleep needs don't change all that dramatically from late elementary through middle school into high school," she said. "What changes is the circadian rhythm of sleep and wake, and typically as you go into and through puberty your sleep and wake time shifts by as much as two hours. They simply can't fall asleep as early as they did when they were 7 or 8 years old." That is why many experts say the high school day should start later.

Mary Carskadon, a professor of psychiatry and human behavior at Brown and the director of chronobiology research at E. P. Bradley Hospital, says that in the sleep lab, researchers can assess a child's sleep drive by looking at EEG recordings of the brain, and monitor circadian rhythm by testing saliva.

"We assess the amount of melatonin that's produced, an excellent marker of brain timing: when we see the melatonin signal turn on, that's telling us it's nighttime for the brain. We've measured that signal at different developmental stages," she said, and "as kids are passing through puberty, we see this push for nighttime to be later."

Even as we've come to understand more and more about the importance of sleep, for brain function and learning, for mental and physical health, the world has gotten to be a harder and harder place for a child to go to sleep. The basic advice pediatricians give to parents of young children about bedtime routines — turn off the television, take her on your lap, read a book — is important for older children, too: spend time together, wind down, turn off electronic devices, read a book.

Let's face it, even if you keep the television out of the bedroom (which you should absolutely do), the nursery is now pretty fully wired in many families, and most children are aware of entertainment and communication possibilities that go on all evening long. I may have let my children stay up too late (O.K., I did let my children stay up too late), but at least I pushed hard for reading, being read to and just plain hanging out.

And as we try to take account of the new research on the importance of sleep, the bedtime routine may remain every bit as important as the bedtime.

Really?

The Claim: Daylight Saving Time Can Affect Your Health

By ANAHAD O'CONNOR

Leif Parsons

THE FACTS Daylight saving time, which began this week in most of the United States, has long been promoted as a way to save energy. Whether it does is still a matter of debate. But it does seem clear from studies that a one-hour time adjustment can have unintended health consequences.

It seems that when the clock is moved forward or back one hour, the body's internal clock — its circadian rhythm, which uses daylight to stay in tune with its environment — does not adjust. In a study of 55,000 people, for example, scientists found that on days off from work, subjects tended to sleep on standard time, not daylight time: their waking hour followed the seasonal progression of dawn.

In other studies, scientists tracked large groups of people for eight weeks at a time as they made the transitions to daylight time in spring and to standard time in autumn. They found that in spring, people's peak activity levels were more in tune with their body clock than with the actual clock. Studies suggest that this disconnect between body time and clock time can result in restlessness, sleep disruption and shorter sleep duration. Other studies have suggested links between time change and increases in heart attacks, suicides and accidents, though scientists say more study is needed.

THE BOTTOM LINE Daylight saving time is associated with sleep disruptions and possibly more serious consequences.

Genetic Tests May Reveal Source of Mystery Tumors

By ANDREW POLLACK

When Jo Symons was found to have cancer, there was an extra complication: doctors could not tell what type of cancer she had.

Tumors were found in her neck, chest and lymph nodes. But those tumors had spread there from someplace else, and her doctors could not determine whether the original site was the breast, the colon, the ovary or some other organ. Without that knowledge, they could not offer optimal treatment.

Such mystery tumors are estimated to account for 2 percent to 5 percent of all cancer, or at least 30,000 new cases a year in the United States, making them more common than brain, liver or stomach cancers. For patients, such a diagnosis can amount to a double agony - not only do they have cancer, but doctors cannot treat it properly.

"You don't believe that in the 21st century it is possible for the medical profession not to know where the cancer is coming from," said Ms. Symons's husband, John.

But now 21st-century medicine may help. New genetic tests may pinpoint the origin of the mystery tumors. The tests, which cost more than $3,000 each, still need to prove their worth better, experts say, though some of them are hopeful.

"I can tell you there have been several patients I've had where their therapy was altered" based on the test results, said Dr. F. Anthony Greco, director of the Sarah Cannon Cancer Center in Nashville and a leading expert on cancer of unknown primary, or CUP, as the mysterious disease is formally known.

Dr. Greco said it appeared that in many cases the primary tumor was too small to be detected, and in other cases it may have disappeared. "Why the primary tumor didn't grow and get bigger we have no idea," he said.

Such tumors are typically found in the liver, the lymph nodes or the bones, but can be in other places as well. But when tumor samples, taken either from a biopsy or from surgical removal, are examined under a microscope, they do not resemble cancers that would originate in the places they are found. Nor do the cells clearly resemble those from breast, colon or other types of cancer.

The problem is that cancers are treated based on their origin. If a cancer that originated in the breast is found in the liver, it is still classified as breast cancer and treated with breast cancer drugs.

Lacking such a classification, doctors can use drugs that work for a variety of cancers. But such treatment presumably is less effective than one using drugs matched to the type of cancer.

So the discovery of an unclassified cancer often sets off a frantic search for the original tumor.

"I had every test out there — PET scan, M.R.I., colonoscopy, mammogram — I even swallowed a pill with a camera on it" to take pictures of the digestive tract, Lori Young of Huntsville, Ala., wrote on a Web site for people with cancer of unknown primary. But her original tumor could not be found.

Ms. Young, 39 and a mother of two, was found to have tumors that had spread to her liver in October 2007. She is being treated with drugs typically used for lung cancer.

Patients say the inability to find the original tumor adds to their anxiety.

"You're always in limbo," said Susan Droman of Akron, Ohio, who discovered she had cancer of unknown primary after it had spread to her vertebrae a year ago, causing excruciating pain. "We would have been happier if it had been an actual tumor you see so they could get it out of there."

Mark Kargul, a former airline pilot from San Clemente, Calif., who has mystery tumors in his liver, likened the experience to being unable to find the source of a leak in one's home. "You can mop up the floor," Mr. Kargul said, "but the next day the flood will be back."

It is even hard for patients to explain their situation to friends and family, or to get advice from them. The new tests may solve some mysteries. Already there are four such tests on the market, and at least one other is being developed.

Generally the tests analyze which genes are active or inactive in a tumor sample. They compare that genetic fingerprint with the fingerprints from known tumor types, trying to come up with the best match.

The Tissue of Origin test from Pathwork Diagnostics of Sunnyvale, Calif., measures the activity of 1,500 genes. The CancerType ID, from BioTheranostics, based in San Diego, looks at 92 genes. The CupPrint test from Agendia, which is based in the Netherlands, looks at about 500 genes. That test is not available yet in the United States.

The MiRview Mets test from Israel-based Rosetta Genomics takes a different approach, analyzing microRNAs, which are tiny snippets of genetic material that help control the activity of genes.

Only the Pathwork test has been approved by the Food and Drug Administration, although the approved version has been superseded by a more practical version that is not approved. Tests can be offered by laboratories without F.D.A. permission, even as they are still being validated.

The tests are generally 80 to 90 percent accurate, according to published studies.

But that is when they are used on tumors whose origin is known. In practice, the tests would be used on tumors whose origin is unknown. And those may by their very nature be harder to classify, said Dr. Lawrence Weiss, chief of pathology at the City of Hope cancer center in Duarte, Calif.

A study published last September in The Journal of Clinical Oncology reported that the Agendia test correctly classified 83 percent of known tumor samples. But the test could classify only 64 percent of unknown tumors.

And of course, if the tumor origins are truly unknown, how does one even know if the genetic test is coming up with the correct answer?

One way, Dr. Greco said, is that there are rare cases in which the primary site becomes known months later, like when a patient suddenly starts feeling pain at that site.

Dr. Greco collected the original biopsy samples from some of these patients and found the BioTheranostics test to be about 70 percent accurate in classifying the tumors, compared with only 10 percent to 20 percent for the most advanced pathology techniques.

How valuable the tests will be still remains to be seen. Some biopsies do not provide enough genetic material for analysis. Ms. Droman, for instance, could not get any answer from the Rosetta test, and Mr. Kargul could not get one from the BioTheranostics test.

Dr. Weiss of City of Hope said that pathologists now used antibodies that can latch onto telltale proteins in the tumor. That technique, called immunostaining, can classify about two-thirds of tumors that would have been considered unknown primaries about 30 years ago, Dr. Weiss said. That leaves only one-third, or about 1 percent of all cancers, that might benefit from the newer genetic tests.

Still, for those patients, however many there are, any clue could be helpful. Dr. Martin A. Martino, a gynecologic oncologist at Lehigh Valley Health Network in Allentown, Pa., said he recently used the Pathwork test to classify a patient's tumor as ovarian. That allowed her to enroll in a clinical trial testing a new drug for ovarian cancer.

The real proof of the value of the tests would be to show that patients live longer after undergoing the tests, presumably because they would then receive treatment better matched to their tumors.

"That's really the major question now," said Dr. James Abbruzzese, chairman of gastrointestinal oncology at the University of Texas M.D. Anderson Cancer Center in Houston. "Do patients have better outcomes from having a hopefully better handle on where the cancer came from?"

M.D. Anderson treats 250 to 350 patients a year with cancer of unknown primary. It is using the genetic tests in selected circumstances. "We try to ask ourselves, 'Is this information going to change the treatment we recommend for the patient?' " Dr. Abbruzzese said.

Jo Symons took the Agendia test, but not before being treated with two different chemotherapy regimes, both unsuccessful. The test showed that she had pancreatic cancer, so she was given chemotherapy for that cancer.

But pancreatic cancer is notoriously difficult to treat, and she died in September 2006, only seven months after her initial diagnosis. To help other patients, Mr. Symons set up the Cancer of Unknown Primary Foundation, also known as Jo's Friends, after his late wife (www.cupfoundjo.org).

"It may have made more a difference psychologically than it did in terms of time," Mr. Symons, who lives near Oxford, England, said of the genetic test. "It gave us comfort to identify where the cancer had come from. It's very uncomfortable not knowing where a problem has arisen in your body."

Consuming a little less salt could mean fewer deaths

Study highlights:

· A moderate decrease in daily salt intake could benefit the U.S. population and reduce the rates of heart disease and deaths.

· All segments of the U.S. population would be expected to benefit, with the largest health benefits experienced by African Americans who are more likely to have hypertension and whose blood pressure may be more sensitive to salt.

PALM HARBOR, Fla., March 11, 2009 - For every gram of salt that Americans reduce in their diets daily, a quarter of a million fewer new heart disease cases and over 200,000 fewer deaths would occur over a decade, researchers said at the American Heart Association's 49th Annual Conference on Cardiovascular Disease Epidemiology and Prevention. These results were derived from a validated computer-simulation of heart disease among U.S. adults.

"A very modest decrease in the amount of salt - hardly detectable in the taste of food - can have dramatic health benefits for the U.S.," said Kirsten Bibbins-Domingo, Ph.D., M.D., M.A.S., lead author of the study and an assistant professor of Medicine and of Epidemiology at the University of California, San Francisco. "It was a surprise to see the magnitude of the impact on the population, given the very small reductions in salt that we were modeling."

A 3-gram–a-day reduction in salt intake (about 1200 mg of sodium) would result in 6 percent fewer cases of new heart disease, 8 percent fewer heart attacks, and 3 percent fewer deaths. Even larger health benefits are projected for African Americans, who are more likely to have high blood pressure and whose blood pressure may be more sensitive to salt. Among African Americans, new heart disease cases would be reduced by 10 percent, heart attacks by 13 percent and deaths by 6 percent.

For years, ample evidence has linked salt intake to high blood pressure and heart disease. Yet, salt consumption among Americans has risen by 50 percent and blood pressure has risen by nearly the same amount since the 1970s, according to researchers. Currently, Americans eat 9-12 grams of salt per day (or 3600-4800 mg of sodium. This amount is far in excess than recommended by most health organizations (5-6 grams/day of salt or 2000-2400 mg sodium). Each gram of salt contains 0.4 grams of sodium.

"It's clear that we need to lower salt intake, but individuals find it hard to make substantial cuts because most salt comes from processed foods, not from the salt shaker," Bibbins-Domingo said. "Our study suggests that the food industry and those who regulate it could contribute substantially to the health of the nation by achieving even small reductions in the amount of salt in these processed foods."

To estimate the benefit of making small reductions in salt intake, the investigators used the Coronary Heart Disease Policy Model, a computer simulation of heart disease in the U.S. adult population. The model can be used to evaluate the impact of policy changes on the health of the nation, and has previously been used to project the future of heart disease in the United States given the current rate of childhood obesity, Bibbins-Domingo said.

The researchers used the model to estimate the impact of an immediate reduction of daily salt intake by 0–6 grams on the incidence of cardiovascular disease and deaths between 2010–2019. In that period, the model suggests that more than 800,000 life-years could be saved for each gram of salt lowered. Larger reductions would have greater benefits, with a 6 gram reduction resulting in 1.4 million fewer heart disease cases, 1.1 million fewer deaths and over 4 million life-years saved.

Because the majority of salt in the diet comes from prepared and packaged foods, the results of the study reveal the need for regulatory changes or voluntary actions by the food industry to make achievable changes in heart health, Bibbins-Domingo said.

The researchers are planning to assess the cost-effectiveness of various interventions already being used to reduce salt consumption in other countries, including industry collaborations, regulations and labeling changes.

Co-authors are: Glenn M. Chertow, M.D., M.P.H.; Andrew E. Moran, M.D., M.A.S.; Pamela G. Coxson, Ph.D.; and Lee Goldman, M.D., M.P.H. Individual author disclosures are available on the abstract.

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MIT battery material could lead to rapid recharging of many devices

Beltway for electrical energy solves long-standing problem

CAMBRIDGE, Mass.--MIT engineers have created a kind of beltway that allows for the rapid transit of electrical energy through a well-known battery material, an advance that could usher in smaller, lighter batteries — for cell phones and other devices — that could recharge in seconds rather than hours.

The work could also allow for the quick recharging of batteries in electric cars, although that particular application would be limited by the amount of power available to a homeowner through the electric grid.

The work, led by Gerbrand Ceder, the Richard P. Simmons Professor of Materials Science and Engineering, is reported in the March 12 issue of Nature. Because the material involved is not new — the researchers have simply changed the way they make it — Ceder believes the work could make it into the marketplace within two to three years.

State-of-the-art lithium rechargeable batteries have very high energy densities — they are good at storing large amounts of charge. The tradeoff is that they have relatively slow power rates — they are sluggish at gaining and discharging that energy. Consider current batteries for electric cars. "They have a lot of energy, so you can drive at 55 mph for a long time, but the power is low. You can't accelerate quickly," Ceder said.

Why the slow power rates? Traditionally, scientists have thought that the lithium ions responsible, along with electrons, for carrying charge across the battery simply move too slowly through the material.

About five years ago, however, Ceder and colleagues made a surprising discovery. Computer calculations of a well-known battery material, lithium iron phosphate, predicted that the material's lithium ions should actually be moving extremely quickly.

"If transport of the lithium ions was so fast, something else had to be the problem," Ceder said.

Further calculations showed that lithium ions can indeed move very quickly into the material but only through tunnels accessed from the surface. If a lithium ion at the surface is directly in front of a tunnel entrance, there's no problem: it proceeds efficiently into the tunnel. But if the ion isn't directly in front, it is prevented from reaching the tunnel entrance because it cannot move to access that entrance.

Ceder and Byoungwoo Kang, a graduate student in materials science and engineering, devised a way around the problem by creating a new surface structure that does allow the lithium ions to move quickly around the outside of the material, much like a beltway around a city. When an ion traveling along this beltway reaches a tunnel, it is instantly diverted into it. Kang is a coauthor of the Nature paper.

Using their new processing technique, the two went on to make a small battery that could be fully charged or discharged in 10 to 20 seconds (it takes six minutes to fully charge or discharge a cell made from the unprocessed material).

Ceder notes that further tests showed that unlike other battery materials, the new material does not degrade as much when repeatedly charged and recharged. This could lead to smaller, lighter batteries, because less material is needed for the same result.

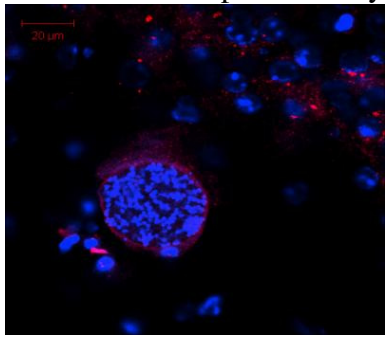
"The ability to charge and discharge batteries in a matter of seconds rather than hours may open up new technological applications and induce lifestyle changes," Ceder and Kang conclude in their Nature paper.

This work was supported by the National Science Foundation through the Materials Research Science and Engineering Centers program and the Batteries for Advanced Transportation Program of the U.S. Department of Energy. It has been licensed by two companies.

Research supports toxoplasmosis link to schizophrenia

Scientists have discovered how the toxoplasmosis parasite may trigger the development of schizophrenia and other bipolar disorders.

The team from the University of Leeds' Faculty of Biological Sciences (UK) has shown that the parasite may play a role in the development of these disorders by affecting the production of dopamine - the chemical that relays messages in the brain controlling aspects of movement, cognition and behaviour.



Toxoplasmosis, which is transmitted via cat faeces (found on unwashed vegetables) and raw or undercooked infected meat, is relatively common, with 10-20% of the UK population and 22% of the US population estimated to carry the parasite as cysts. Most people with the parasite are healthy, but for those who are immune-suppressed - and particularly for pregnant women - there are significant health risks that can occasionally be fatal.

This is a toxoplasma cyst outlined in red fluorescent cyst dye in mouse brain section. Hundreds of parasites are visible in the cyst as blue dots (nuclei stained blue) and in surrounding brain tissue. **image courtesy of E. Prandovszky**

Dr Glenn McConkey, lead researcher on the project, says: "Toxoplasmosis changes some of the chemical messages in the brain, and these changes can have an enormous effect on behaviour. Studies have shown there is a direct statistical link between incidences of schizophrenia and toxoplasmosis infection and our study is the first step in discovering why there is this link."

The parasite infects the brain by forming a cyst within its cells and produces an enzyme called tyrosine hydroxylase, which is needed to make dopamine. Dopamine's role in mood, sociability, attention, motivation and sleep patterns are well documented and schizophrenia has long been associated with dopamine, which is the target of all schizophrenia drugs on the market.

The team has recently received $250,000 (£160,000) to progress its research from the US-based Stanley Medical Research Institute, which focuses on mental health conditions and has a particular emphasis on bipolar illnesses.

Dr McConkey says: "It's highly unlikely that we will find one definitive trigger for schizophrenia as there are many factors involved, but our studies will provide a clue to how toxoplasmosis infection - which is more common than you might think – can impact on the development of the condition in some individuals.

"In addition, the ability of the parasite to make dopamine implies a potential link with other neurological conditions such as Parkinson's Disease, Tourette's syndrome and attention deficit disorders, says Dr McConkey. "We'd like to extend our research to look at this possibility more closely."

Iron induces death in tumor cells

Rapid growth of cancer cells and their frequent divisions have their price: Cancer cells need considerably more energy than healthy cells. Their metabolism runs at full speed and requires large amounts of micronutrients, particularly iron. However, high levels of iron in the cell lead to the production of extremely harmful free radicals. To protect itself from these, the cell inactivates free iron by binding it to what are called iron storage proteins.

Collaborating with physicians of the Dermatology Department of Mannheim University Hospitals, Dr. Karsten Gülow and Professor Dr. Peter Krammer, head of the Division of Immunogenetics at DKFZ, investigated Sézary's disease (also called Sézary syndrome), an extremely aggressive type of cutaneous T cell lymphoma. The majority of currently available treatments are not really effective against this fatal type of cancer.

Using a molecular-biological trick, Gülow and colleagues succeeded in blocking the production of one of the iron storage proteins in lymphoma cells. This leads to a rise in the level of free, non-bound iron in these cells. The iron boosts the production of free oxygen radicals which cause oxidative stress and, thus, cause damage to the cancer cells and induce their death. Healthy cells with their low iron level, however, survive the treatment unharmed.

The DKFZ researchers have already found evidence that this iron effect also works in other lymphomas. They are now investigating whether selective release of iron may be a suitable approach for developing a novel cancer treatment.

Michael K. Kiessling, Claus D. Klemke, Marcin M. Kamiński, Ioanna E. Galani, Peter H. Krammer, and Karsten Gülow: Inhibition of constitutively activated NF-κB induces ROS- and iron dependent cell death in cutaneous T cell lymphoma. Cancer Research 2009; DOI:10.1158/0008-5472.CAN-08-3221

BMC researchers find that single question can identify unhealthy alcohol use in patients

(Boston) Researchers at Boston Medical Center (BMC) have found that a single-screening question recommended by the National Institute of Alcohol Abuse and Alcoholism (NIAAA) accurately identifies unhealthy alcohol use in primary-care patients. This research supports the use of the brief screen in the primary-care setting. The BMC study appears online in the Journal of General Internal Medicine.

Unhealthy alcohol use, the spectrum from risky consumption to alcohol use disorders, alcohol abuse and dependence, is prevalent but under-diagnosed in primary-care settings. Commonly used alcohol screening instruments are comprised of multiple questions, often do not cover the full spectrum of unhealthy use, and can be time consuming to administer. Consequently, many patients are not screened.

The NIAAA recommends a single-question screen for unhealthy alcohol use. The recommended question asks, ***"How many times in the past year have you had X or more drinks in a day?" (where X is 5 for men and 4 for women).*** While similar single-question screens have been validated in various settings, the NIAAA recommended screening test had not been validated in the primary-care setting. BMC researchers attempted to validate this version of the screening question in a sample of primary-care patients.

Of the 286 study participants reviewed, unhealthy alcohol use was reported by 31 percent of participants. Six percent consumed risky amounts but did not have alcohol-related problems or a disorder, 13 percent consumed risky amounts and had problems but no current disorder and 12 percent had a current alcohol use disorder. The

single-question screen was 81.8 percent sensitive and 79.3 percent specific for the detection of unhealthy alcohol use. It was slightly more sensitive and less specific for the detection of a current alcohol use disorder.

"The single-question screening recommended by the NIAAA appears to have favorable characteristics," said lead author Peter Smith, MD, attending physician in the section of General Internal Medicine at Boston Medical Center. "Single-question screening tests for unhealthy alcohol use may help to increase the frequency of screening in primary-care."

Researchers further state that screening and brief intervention by primary-care physicians for those with unhealthy alcohol use reduces risky consumption among those without dependence and improves patient outcomes.

This study was funded by the National Institute of Alcohol Abuse and Alcoholism. The National Institute of Alcohol Abuse and Alcoholism had no role in the design and conduct of the study, the collection, management, analysis and interpretation of the data, or the preparation, review and approval of the manuscript.

Researchers discover a new pathway that regulates inflammation

CHAMPAIGN, Ill. — Inflammation, the body's earliest response to damage or infection, can aid the healing process and trigger an immune response against invading pathogens. But inflammation gone awry can also undermine health, as in diseases such as rheumatoid arthritis or asthma.

Researchers at the University of Illinois have identified a novel pathway that controls the activity of a key protein involved in inflammation. Their findings could have important implications for the treatment of diseases or conditions linked to chronic inflammation.

At the heart of the cell's inflammatory response is a protein complex called NF-kappa B. In the new study, biochemistry professor Lin-Feng Chen and his colleagues deciphered a molecular code that controls its function. Their results appear in the European Molecular Biology Organization (EMBO) Journal.

The NF-kappa B protein complex consists of two subunits that can bind to DNA and regulate the expression of particular genes. The complex acts like a molecular switch that can be turned on when the cell is under attack and then off when the attack has been cleared. Upon activation, it rapidly moves into the nucleus and sets in motion an army of proteins that cause inflammation. Often referred to as the master regulator of the immune system, NF-kappa B belongs to a large family of proteins called transcription factors that control which genes are turned on or off.

"Inflammation is like a chemical storm during which many special chemicals that signal the immune system are released at the site of infection," Chen said. "NF-kappa B, the protein which is central to the inflammatory response, has to be tightly controlled; otherwise things could go crazy within the body."

Normally, a second protein inactivates NF-kappa B by directly binding to it. But when the cell is under stress (for example, during infection), this inhibitory protein is dismantled. NF-kappa B, now relieved of inhibition, rushes into the nucleus and activates gene expression. Once it finishes its job, NF-kappa B stimulates the production of its inhibitory partner and is itself inhibited again.

Recent studies found that NF-Kappa B also was being degraded in the nucleus, indicating an alternate means by which NF-kappa B activity is regulated in the cell. "Every step of NF-kappa B activation is tightly controlled," Chen said. He and his colleagues hunted for the signals that could control its degradation and inactivation.

Chen's earlier work gave him important clues about how protein activity can be modified when small chemical groups are added to the protein after it is assembled. This process, called post-translational modification, tags the proteins. Like the sign on the front of a bus declaring its destination, the tags direct proteins to different fates. "One of the goals of our lab is to study how post-translational modifications affect NF-kappa B activity under normal and diseased conditions," Chen said.

To identify whether a particular molecular tag, called a methyl group, could be added to NF-kappa B to regulate its activity, Xiao-Dong Yang, a postdoctoral researcher in Chen's lab and lead author on the new study, performed a simple experiment. He mixed the NF-kappa B protein with a protein whose function is to add a methyl group to certain other proteins. He discovered that a subunit of NF-kappa B was, in fact, being labeled with a methyl group.

Adding a methyl group increases the weight of the protein by a very small amount. In collaboration with chemistry professor Neil Kelleher, the researchers used an ultrasensitive molecular scale, called mass spectrometry, and identified two amino acids in the protein that had been modified with the methyl group.

In a series of experiments, Chen and his colleagues found that the presence of the methyl group signaled that NF-kappa B was to be degraded in the nucleus. This showed, for the first time, how NF-kappa B could be degraded and regulated independent of its inhibitor protein.

Chen said that understanding the role of different post-translational tags on NF-kappa B could lead to the discovery of a "transcription factor code" or "NF-kappa B code," similar to the "histone code." Like the genetic

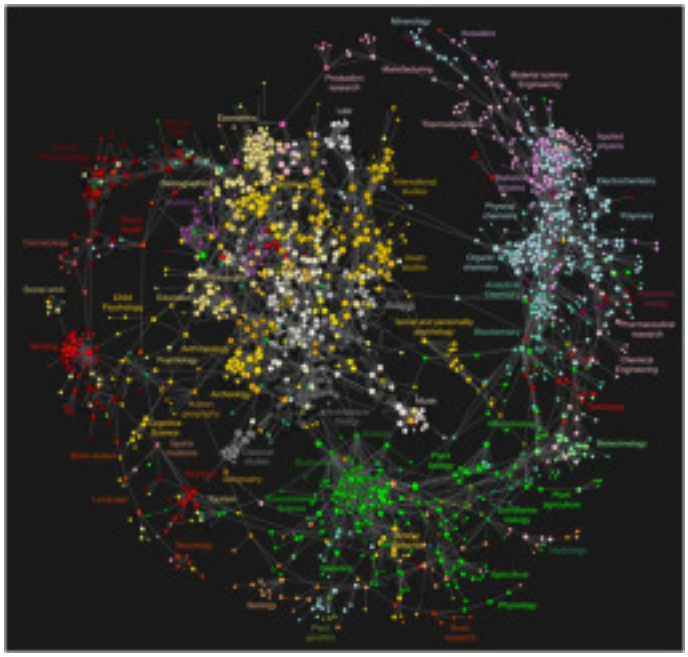
code, which spells out the sequence of amino acids in a protein, the transcription factor code stores information about how various post-translational modifications signal different biological fates.

"In some cancers and inflammatory diseases NF-kappa B is permanently active. The turn-off mechanism has been inactivated," Chen said. He hopes that the discovery of this pathway could lead to the development of new drugs to influence the methylation – and hence the activity – of this transcription factor and the inflammatory response.

Los Alamos Researchers Create 'Map of Science'

LOS ALAMOS, N.M., March 11, 2009 — Data provides high-resolution picture of scientists' information retrieval habits

Los Alamos National Laboratory scientists have produced the world's first Map of Science—a high-resolution graphic depiction of the virtual trails scientists leave behind when they retrieve information from online services. The research, led by Johan Bollen, appears this week in PLoS ONE (the Public Library of Science).



"This research will be a crucial component of future efforts to study and predict scientific innovation, as well novel methods to determine the true impact of articles and journals," Bollen said.

While science is of tremendous societal importance, it is difficult to probe the often hidden world of scientific creativity. Most studies of scientific activity rely on citation data, which takes a while to become available because both the cited publication and the publication of a particular citation can take years to appear. In other words, citation data observes science as it existed years in the past, not the present.

This "Map of Science" illustrates the online behavior of Scientists accessing different scientific journals, publications, aggregators, etc. Colors represent the scientific discipline of each journal, based on disciplines classified by the Getty Research Institute's Art and Architecture Thesaurus, while lines reflect the navigation of users from one journal to another when interacting with scholarly web portals. enlarge image

Credit: Los Alamos National Laboratory

Bollen and colleagues from LANL and the Santa Fe Institute collected usage-log data gathered from a variety of publishers, aggregators, and universities spanning a period from 2006 to 2008. Their collection totaled nearly 1 billion online information requests. Because scientists typically read articles online well before they can be cited in subsequent publications, usage data reveal scientific activity nearly in real-time. Moreover, because log data reflect the interactions of all users—such as authors, science practitioners, and the informed public—they do not merely reflect the activities of scholarly authors.

Whenever a scientist accesses a paper online from a publisher, aggregator, university, or similar publishing service, the action is recorded by the servers of these Web portals. The resulting usage data contains a detailed record of the sequences of articles that scientists download as they explore their present interests. After counting the number of times that scientists, across hundreds of millions of requests, download one article after another, the research team calculated the probability that an article or journal accessed by a scientist would be followed by a subsequent article or journal as part of the scientists' online behavior. Based on such behavior, the researchers created a map that graphically portrays a network of connected articles and journals.

Bollen and colleagues were surprised by the map's scope and detail. Whereas maps based on citations favor the natural sciences, the team's maps of science showed a prominent and central position for the humanities and social sciences, which, in many places, acted like interdisciplinary bridges connecting various other scientific domains. Sections of the maps were shaped by the activities of practitioners who read the scientific literature but do not frequently publish in its journals.

The maps furthermore revealed unexpected relations between scientific domains that point to emerging relationships that are capturing the collective interest of the scientific community—for instance a connection between ecology and architecture.

"We were surprised by the fine-grained structure of scientific activity that emerges from our maps," said Bollen.

According to Bollen, future work will focus on issues involved in the sustainable management of large-scale usage data, as well the production of models that explain the online behavior of scientists and how it relates to

the emergence of scientific innovation. This information will help funding agencies, policy makers, and the public to better understand how best to tap the ebb and flow of scientific inquiry and discovery.
The research team includes Bollen, Herbert Van de Sompel, Ryan Chute, and Lyudmila Balakireva of LANL's Digital Library Research and Prototyping Team and Aric Hagberg, Luis Bettencourt and Marko A Rodriguez of LANL's Mathematical Modeling and Analysis Group, and LANL's Center for Nonlinear Studies. Bettencourt also is part of the Santa Fe Institute. Bollen and colleagues received funding from the Andrew W. Mellon foundation to examine the potential of large-scale usage data. The study is part of the MESUR (Metrics from Scholarly Usage of Resources) project of which Bollen is the principal investigator. The MESUR usage database is now considered the largest of its kind.

'Mind-reading' experiment highlights how brain records memories

It may be possible to "read" a person's memories just by looking at brain activity, according to research carried out by Wellcome Trust scientists. In a study published today in the journal Current Biology, they show that our memories are recorded in regular patterns, a finding which challenges current scientific thinking.

Demis Hassabis and Professor Eleanor Maguire at the Wellcome Trust Centre for Neuroimaging at UCL (University College London) have previously studied the role of a small area of the brain known as the hippocampus which is crucial for navigation, memory recall and imagining future events. Now, the researchers have shown how the hippocampus records memory.

When we move around, nerve cells (neurons) known as "place cells", which are located in the hippocampus, activate to tell us where we are. Hassabis, Maguire and colleagues used an fMRI scanner, which measures changes in blood flow within the brain, to examine the activity of these places cells as a volunteer navigated around a virtual reality environment. The data were then analysed by a computer algorithm developed by Demis Hassabis.

"We asked whether we could see any interesting patterns in the neural activity that could tell us what the participants were thinking, or in this case where they were," explains Professor Maguire, a Wellcome Trust Senior Research Fellow. "Surprisingly, just by looking at the brain data we could predict exactly where they were in the virtual reality environment. In other words, we could 'read' their spatial memories."

Earlier studies in rats have shown that spatial memories – how we remember where we are – are recorded in the hippocampus. However, these animal studies, which measured activity at the level of individual or dozens of neurons at most, implied that there was no structure to the way that these memories are recorded. Hassabis and Maguire's work appears to overturn this school of thought.
"fMRI scanners enable us to see the bigger picture of what is happening in people's brains," she says. "By looking at activity over tens of thousands of neurons, we can see that there must be a functional structure - a pattern - to how these memories are encoded. Otherwise, our experiment simply would not have been possible to do."

Professor Maguire believes that this research opens up a range of possibilities of seeing how actual memories are encoded across the neurons, looking beyond spatial memories to more enriched memories of the past or visualisations of the future. "Understanding how we as humans record our memories is critical to helping us learn how information is processed in the hippocampus and how our memories are eroded by diseases such as Alzheimer's," added Demis Hassabis.

"It's also a small step towards the idea of mind reading, because just by looking at neural activity, we are able to say what someone is thinking."

Professor Maguire led a study a number of years ago which examined the brains of London taxi drivers, who spend years learning "The Knowledge" (the maze of London streets). She showed that in these cabbies, an area to the rear of the hippocampus was enlarged, suggesting that this was the area involved in learning location and direction. In the new study, Hassabis, Maguire and colleagues found that the patterns relating to spatial memory were located in this same area, suggesting that the rear of the hippocampus plays a key role in representing the layout of spatial environments.

Estrogen activates critical lung genes to improve lung function following preterm birth

DALLAS - Estrogen may be a new postnatal therapy to improve lung function and other outcomes in preterm infants, researchers at UT Southwestern Medical Center have found in an animal study.

"Ironically, a hormone that has received great attention as a potential means to optimize the health of older women may be a beneficial treatment for humans during the earliest stages of life," said Dr. Philip Shaul, professor of pediatrics at UT Southwestern and the study's senior author.

The study, conducted in preterm primates, appears in the March issue of the American Journal of Respiratory and Critical Care Medicine. The study was performed at the Southwest Foundation for Biomedical Research Primate Center in San Antonio as part of a National Institutes of Health-funded consortium

investigating causes and treatments for bronchopulmonary dysplasia (BPD), a devastating primary complication of premature birth that develops in the preterm lung following ventilation and oxygen support.

Sufficient production of nitric oxide in fetal and newborn lungs is necessary for the lungs to develop and function properly. During the latter part of pregnancy the placenta produces large amounts of estrogen that enters the fetal circulation. Another spike of estrogen occurs during labor. In prior studies in cultured cells the investigators found that estrogen activates the genes in lung cells encoding nitric oxide synthases, enzymes that produce nitric oxide. That research suggested treatment with the hormone may achieve the same results in the intact lung. Premature infants — nearly 50,000 are born in the U.S. each year — miss out on this exposure to estrogen in the womb and, as a consequence, may experience respiratory problems because they lack nitric oxide.

Dr. Shaul and his colleagues found that administering estrogen to premature primates accomplished several things. First, the treated animals had greater abundance of nitric oxide synthases in their lungs, resulting in markedly enhanced lung function and a significantly reduced need for ventilation support. This represents an important step in lessening the lung injury that causes BPD in humans, Dr. Shaul said. It also prevented low blood pressure, which is a common problem in preterm infants.

Estrogen also caused the closure of the ductus arteriosus, a shunt that connects the pulmonary artery to the aorta during the primates' fetal development to allow blood flow to bypass the fetus' fluid-filled lungs. In the case of full-term infants, the ductus arteriosus normally closes at the time of birth once breathing is established. In premature infants, however, it frequently fails to close resulting in further impairment in lung and heart function.

"With just one therapeutic intervention multiple benefits occurred in the lungs and the circulation," Dr. Shaul said. "Estrogen-based therapies to prevent BPD and other complications of prematurity should be further developed, and it is our hope to begin clinical trials in the near future."

Dr. Shaul said that future studies also would need to evaluate other potential targets of estrogen in the lung in addition to nitric oxide synthases and possible effects of postnatal estrogen treatment on nonpulmonary development, including those related to the later reproductive health of the child.

Other UT Southwestern researchers involved in the study were the lead author Dr. Donald McCurnin, professor of pediatrics and medical director of the neonatal intensive care unit at Children's Medical Center Dallas; Dr. Brigham Willis, a former assistant professor of pediatrics; and Ivan Yuhanna, senior research associate in pediatrics.

Also participating were researchers from UT Health Science Center at San Antonio; the Southwest Foundation for Biomedical Research; Washington University School of Medicine; National Jewish Medical and Research Center, the University of Utah School of Medicine, the University of California, San Francisco, School of Medicine; SRI International, the University of Rochester School of Medicine and Dentistry; and Vanderbilt University School of Medicine.

First-in-class compound proves safe, tolerable in preventing blood clots

DURHAM, NC – A new drug derived from magnolia trees appears to be able to uncouple two important functions of thrombin in blood clot formation and may offer a way to better control the potentially dangerous complications of bleeding and clot formation during procedures to open blocked coronary arteries, say researchers at the Duke Clinical Research Institute (DCRI).

Results of the Phase II study of the drug, known as SCH 530348, appear online in the journal The Lancet and will appear in the publication's Mar. 14 issue. An international, Phase III study is already under way.

Thrombin is a protein in the blood that performs two key functions in clot formation: It activates platelets, particles that clump together to form the scaffolding of a clot, and it helps produce fibrin, a protein necessary in repairing damaged tissue.

"One of the intriguing things about this new investigational compound is that it blocks the thrombin receptor that activates platelet formation yet preserves the beneficial activity of fibrin formation," said Richard Becker, M.D., a cardiologist at DCRI and the lead author of the study. "And the data to date indicated the compound does this even when patients are taking aspirin and clopidogrel."

Blood clots are a big issue for patients facing percutaneous coronary intervention (PCI) the process of clearing clogged arteries with a balloon and then propping them open with stents. Patients who undergo PCI are usually prescribed anti-clotting agents like aspirin or clopidgrel (Plavix). Becker said while those drugs are effective, they can sometimes lead to bleeding, and with current therapy, the rate of additional cardiovascular events remains quite high. "So there is a very aggressive search going on for better and safer agents," he said.

In the current study, researchers randomly assigned 1030 patients 45 years or older scheduled to undergo non-urgent PCI or angiography with planned PCI to a group that would receive one of three escalating doses of SCH 530348 (10 mg, 20 mg or 40 mg), or to a control group, which took a placebo. Both researchers and patients were both blinded to who was taking which drug.

Aspirin and clopidogrel were not prescribed as part of the study – investigators followed standard practice at each study site and found that 95 percent of the patients were given both aspirin and clopidogrel.

Two hundred and twenty-seven patients were assigned to placebo; 773 took the experimental drug. Researchers measured responses across all four groups with special focus on the primary clinical endpoint, which was the amount of bleeding according to the thrombolysis in myocardial infarction (TIMI) scale.

They found that SCH 530348 was generally tolerable at all dosing levels and did not increase bleeding, even when taken along with aspirin and clopidogrel. Bleeding occurred in 2 percent of 129, 3 percent of 120, and 4 percent of 173 patients in the 10 mg, 20 mg, and 40 mg drug groups, respectively; compared with 3 percent of the 151 patients in the placebo group (p = .5786).

Patients were also randomized to a daily maintenance dose of the drug (.5 mg, 1 mg, or 2.5 mg). Investigators found that bleeding occurred in 2 percent of 136, 4 percent of 139 and 3 percent of 138 patients in those groups, respectively, compared with 2 percent in the placebo group (p = .7561).

"The uncoupling of benefit and bleeding risk among patients with acute coronary syndromes is an important objective in drug development," Becker said. "We will need to see if Phase III clinical trials can confirm these findings."

Co-authors from Duke on the study include senior author Robert Harrington, Karen Pieper and Diane Joseph. Additional co-authors include David Moliterno and Khaled Ziada, from the University of Kentucky; Lisa Jennings, from the University of Tennessee Health Sciences Center; Alan Niederman, from The Jim Moran Heart and Vascular Research Institute; Frans Van de Werf, from University Hospitals Leuven, Belgium; and Jinglan Pei, Gail Berman, John Strony and Enrico Veltri, from Schering-Plough.

Pieper, Joseph, Ziada and Joseph report no interest or support from Schering-Plough. All other authors report research support, consulting fees or stock in the company. Schering-Plough funded the study.

Weighing the options after life-altering stroke

Choosing to have aggressive brain surgery after suffering a severe stroke generally improves the patients' lives and allows them to live longer, according to research by neurologists at the University of Rochester Medical Center.

The findings should help patients and families put into perspective a decision that is nearly always painful and difficult to make - whether putting a patient through aggressive surgery after a catastrophic stroke is worth it.

"For families facing this difficult choice, the more information we can provide, the better for their decision-making," said neurologist Adam G. Kelly, M.D., who has helped hundreds of families chart a course after severe stroke. Kelly presented the findings last month at the International Stroke Conference in San Diego.

Kelly and colleague Robert Holloway, M.D., studied three separate analyses of patients who had had a serious type of stroke known as a malignant middle cerebral artery infarction, in which blood flow to a large part of the brain is cut off. Further damage occurs when the damaged brain swells in the days immediately following the initial stroke, as delicate brain tissue is pushed up against the hard inner skull. Increased swelling and pressure in the brain diminish blood flow even further.

Even under the best circumstances, patients who have suffered such strokes face at least moderate disability, and often their challenges are severe, no matter what type of treatment is chosen. A patient might be paralyzed on one side of the body. They may have lost their ability to speak or even to comprehend what is said to them. They may need a breathing or feeding tube. At the very least, they'll likely need help each day with tasks like bathing, cooking, and taking care of themselves.

Kelly and Holloway looked at patients who were treated with medical options alone and compared their outcomes to those of patients who had a surgical procedure known as a hemicraniectomy. In that procedure, doctors remove a piece of the skull temporarily, limiting further damage by giving the brain room to swell. The portion of the skull that is removed is put back in place a few months later.

Typically the decision whether or not to go ahead with the surgery is made by families grappling with the catastrophic effects of severe stroke on their loved one. In the face of great uncertainty and under great duress and time pressures, families have to make the decision.

"There is no reliable early predictor of how most people will do after a stroke," said Kelly, an instructor and fellow in the Department of Neurology.

"Some people have a small stroke, with few effects, and we can predict that outcome fairly well. Others have strokes that are immediately catastrophic. But the vast majority of patients are in the middle, and we have a hard time predicting what the outcome will be. There is a lot we don't know about how the brain responds to injury, and how it recovers," Kelly said.

Kelly and Holloway studied data from three studies in Europe that looked at the outcomes of 93 people after stroke. The studies demonstrated that patients who didn't have the surgery were about three times more likely to

die within a year than patients who did have the surgery, though many of the surgical patients were left with considerable disability.

Using a technique called decision analysis, Kelly and Holloway re-evaluated the outcomes of these trials to incorporate quality-of-life ratings for surviving patients. The authors found that even in the face of significant stroke-related disability, as a whole, patients who had undergone the surgical procedure had an improvement in their quality of life. The physicians then used a related method called sensitivity analysis to determine situations in which surgery might not be the preferred treatment. Only under circumstances where patients valued the outcome after stroke extremely poorly - almost as a fate worse than death - was surgery not the preferred option.

"There has been debate for a long time about the effects of this surgery for patients. It definitely saves lives, but we're asking whether the surgery really paid off for these patients. Did the patients value their health state? Was it worth it to them?" asks Kelly. "The answer most often is 'yes.'"

The authors say there are several types of patients for whom surgery clearly isn't a good option. These include people who were already in poor health before the stroke, people whose chances of surviving the surgery are questionable, and patients who have clearly stated that they would not want such measures to be taken.

For those who do opt for surgery, Kelly and Holloway found that living longer due to the surgery was only part of the benefit. Those patients also valued their health. That might seem difficult to understand for people who are healthy, but it does not surprise Holloway, who has worked with hundreds of patients severely limited by stroke.

"For years I've witnessed families wrestle with these decisions," said Holloway. "If the families make the decision based on what they imagine the future to be, they may decide it's a surgery the patient wouldn't want. But nearly always, when they've made the decision to go ahead with the surgery, the families are subsequently happy they made that decision.

"People who survive devastating stroke often do much better than people think they will do. People who haven't experienced a health condition, such as stroke, almost always provide a lower estimate of their quality of life compared to people who are actually living with that condition or disease," Holloway added.

Kelly has witnessed the same dynamics himself.

"People have a remarkable ability to compensate for whatever problems they face," said Kelly, whose fellowship is supported by the National Institute of Neurological Disorders and Stroke. "Oftentimes, the fear of the unknown, and the anxiety it causes, is worse than the actual situation. Over time, people adapt to their deficits, and as they do, they value their quality of life more highly."

Why Should Iowa Remain the First Presidential Primary? Because it is More Representative Than You Might Think.

Washington, DC - A new study finds that Iowa reflects the diversity of America more than most other U.S. states and is well-placed to deserve its status as the first presidential nomination primary. In particular, Iowa was found to be particularly typical of the U.S. in economic and social terms.

The research was presented in an article by political scientists Michael Lewis-Beck (University of Iowa) and Peverill Squire (University of Missouri) entitled “Iowa: The Most Representative State?” appearing in the January issue of PS: Political Science & Politics, a journal of the American Political Science Association. The article is available online at http://www.apsanet.org/media/PDFs/PSJan09LewisBeckSquire.pdf.

The authors set out to answer the question of whether or not Iowa is truly as unrepresentative of the U.S. as is widely assumed, especially the idea that its “heavily rural, northern European-descended population make it far from demographically representative of contemporary America.” They note initially that in terms of size, location, and accession to the Union (1846), Iowa is about at the midpoint for all states—but that investigating the characteristics of the inhabitants of the state is the necessary crucial step. To do so, they examine “an extensive battery of state-level socioeconomic and political measures…[and] uncover their underlying patterns.”

Their measures include 51 different indicators of social, cultural, economic, political, and policy activities in each of the 50 states that are further weighted and compiled into 3 main factors: Economics, Diversity, and Social Problems. The results for each state on each indicator and factor were then scored and ranked. Their findings show that the overwhelming majority (39) of Iowa’s indicators was typical of the broader U.S. population, or within one standard deviation of the average. The findings show that not only is “Iowa a reasonably representative state,” but that Iowa’s standing of 12th overall outperforms New Hampshire—its longstanding national rival for the first-in-the-nation primary.

Diversity was a drag on Iowa’s overall ranking, where “in a nutshell, the population of Iowa is too old and white to represent the nation” but the authors observe that “this is not the only factor that counts….Nor is it arguably the most important….in terms of distinguishing one state from another, the economics dimension is

about three times as important as the [social] problems dimension, and almost twice as important as the diversity dimension."

Elaborating on that point, the authors underscore their finding that Iowa is the most representative state in the Union on economic conditions. They conclude by noting that "all things considered, there seems to be no cause to take away Iowa's first-in-the-nation presidential selection status. If one state must hold this position then it is hard to make a better pick."

Multiple route bone marrow stem cell injections show promise to treat spinal cord injury

Tampa, Fla. (Mar. 12, 2009) – Researchers from DaVinci Biosciences, Costa Mesa, California, in collaboration with Hospital Luis Vernaza in Ecuador, have determined that injecting a patient's own bone marrow-derived stem cells (autologous BMCs) directly into the spinal column using multiple routes can be an effective treatment for spinal cord injury (SCI) that returns some quality of life for SCI patients without serious adverse events.

Publishing in the current issue of Cell Transplantation (Vol. 17 No.12), the researchers reported on eight patients with SCI (four acute and four chronic) to whom they administered BMCs directly into the spinal column, spinal canal and intravenously for each patient and followed for two years using MRI imaging to assess morphological changes in the spinal cord.

"Our objective in this study was to demonstrate that multiple route administration of BMCs for SCI is safe and feasible," said corresponding author Dr. Francisco Silva. "To date, we have administered BMCs into 52 patients with SCI and have had no tumor formations, no cases of infection or increased pain, and few instances of minor adverse events. We also found that patient quality of life improved."

According to Dr. Silva, presently there is no cure or effective treatment for spinal cord injury, a disorder affecting millions globally. Tissue loss from the primary injury and the complexity of cell types required for functional recovery lead the list of considerations. Once more, to be considered successful, any treatment should ultimately help to improve patient quality of life and demonstrate functional improvements.

"Autologous stem cell transplantation of BMCs can promote the growth of blood vessels and, therefore, represent an alternative therapy," said Dr. Silva.

Following primary trauma to the adult spinal cord there is evidence of hemorrhage and blood flow is attenuated, he explained. The disruption of blood flow leads to spinal cord infarction, the disruption of the blood-spinal cord injury barrier, swelling and the release of molecules influencing spinal cord perfusion and ischemia, a restriction in blood supply.

"BMCs are well known for their ability to grow blood vessels," explained Dr. Silva. "This angiogenesis is necessary for wound healing and establishing a growth permissive environment. We hypothesized that improved blood flow and oxygen supply could contribute to functional improvements for SCI transplanted with autologous BMCs."

In eight patients who received BMC transplants through various routes and followed for two years, the scientists reported several functional improvements, perhaps the most important of which was improved bladder control.

Finally, the researchers noted that one of their cases suffered a gunshot wound and that their study marked the first time a gunshot wound victim had received BMC transplants through multiple routes.

"It is important to note," concluded Dr. Silva," that all of our patients with acute injuries improved significantly with no signs of deterioration or impediment of presumed spontaneous recovery."

According to Dr. Svitlana Garbuzova-Davis, a spinal cord researcher at the University of South Florida, the study highlights the value of using several different simultaneous routes for the administration of stem cells, as well as the benefit of the cells themselves.

"While it would be interesting to know the respective contribution of each route of administration, this study does appear to support the need to move to carry out double blind clinical trials of BMCs in SCI, especially if a non-invasive route could be used."

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Crab chemical could give cars a self-healing 'shell'

* 18:00 12 March 2009 **by Kurt Kleiner**

You might never have to fear for your car's paintwork again if a new kind of polyurethane that is able to heal its own surface scratches makes it to market.

Small scratches to the surface of the material close up in only a few minutes when the material is exposed to the ultraviolet light in sunlight. This life-like healing occurs because the damaged polymer molecules around the edges of a scratch use the energy from the UV to form new cross-links and recreate the network that makes up the material.

The material could make a good top coat for an automobile, says Marek Urban, a polymer scientist at the University of Southern Mississippi, Hattiesburg, who led the study.

Crab chemical

Previous self-healing materials have mostly used some form of liquid epoxy that is encapsulated in spheres or fibres, or delivered by an engineered vascular system. When the material is damaged, the epoxy is released into the fissure and sets when it contacts a hardening agent in the material.

Taking a different approach with their new self-healing polymer, Urban and his team combined polyurethane with a molecule made up of chitosan, a carbohydrate found in the shells of crustaceans like crabs and lobsters. The researchers modified the chitosan slightly with the addition of the structures composed of four carbon atoms called oxetane rings.

Video: ***A material that heals its own scratches could make perfect paint***

It is the oxetane rings that give the material its ability to heal, says Urban. When a scratch is made, some of the rings are broken, leaving chemically reactive free ends. However, while he has worked out which bonds are involved in the reaction, the exact details of the chemical process are so far unknown.

Exposure to UV light creates reactive spots on sections of the chitosan molecules which then combine with the broken oxetane rings to form new chemical cross links that close up the damage. The process appears to begin at the bottom of a scratch, pulling it closed like a zipper.

Deep healing?

Urban says that scratches about 10 micrometers wide and 50 deep – just visible with the naked eye – heal over after 30 minutes of exposure to UV light. The fact the process starts at the bottom the two sides of a scratch are closest together suggests it will work for larger scratches, too, he adds.

Urban says that the material could be useful for a number of applications, including vehicles and furniture, or electronic devices like cellphones. "Anything you can think of," he told New Scientist, "If you scratch it, let it sit in Sun for some time and it's cured."

"I think this is a great new technology," says Michael Kessler, a materials scientist at Iowa State University. But he said it isn't clear how thoroughly the material would heal from deeper and wider scratches. "It's a first step," he says, pointing out that the material needs to have other desirable characteristics for different applications, such as heat tolerance or hardness. *Journal reference: Science (DOI: 10.1126/science.1167391)*

Paradoxical gene causes and protects against Alzheimer's

* 18:00 12 March 2009 **by Ewen Callaway**

A newly discovered gene mutation found to cause Alzheimer's disease when inherited from both parents may give protection from the disease when only one copy is inherited. The discovery may lead to a new treatment for the neurodegenerative condition.

A 44-year-old man with two copies of a mutation in a gene called APP first showed signs of Alzheimer's in his mid-thirties. Yet his relatives with a single copy of the mutation – including an 88-year-old aunt – seem to be protected from the disease, new research suggests.

Mimicking this single-copy condition with a drug could offer a new way of treating Alzheimer's, says Fabrizio Tagliavini, a neurologist at Carlo Besta National Neurological Institute in Milan.

Tagliavini's team uncovered the mutation in a person who showed signs of early-onset Alzheimer's but who lacked mutations in other genes associated with this inherited form of the disease.

Stark contrast

Only a small percentage of Alzheimer's cases are linked to a single, inherited mutation, yet researchers have made great strides in understanding the more common late-onset form of the disease by studying these mutations.

The gene in question, APP, makes a protein called A-beta, which sticks together in the brain and blocks neurons from communicating with one another. Many researchers argue that such clumps underlie the symptoms of Alzheimer's, such as memory and speech difficulties.

Six of the patient's relatives with one copy of this mutation show no sign of Alzheimer's disease, while a younger sister with two copies has some cognitive problems, but not full-blown Alzheimer's, Tagliavini says. This stands in stark contrast to other mutations known to cause early-onset Alzheimer's, where a single copy is enough to cause the disease.

Clump resistant

In a bid to explain this difference, Tagliavini's team analysed cells taken from the 44-year-old man. His cells developed far more A-beta clumps than cells extracted from people without normal APP.

When the team mixed normal and mutant forms of the protein, the mixture clumped far less often than mutant protein or normal protein alone. This could be why the patient's relatives with one copy of the mutation seem able to stave off Alzheimer's, he says.

Recreating this situation with a synthetic protein could offer a new way of treating the disease in people with two copies of the APP mutation, Tagliavini says. Indeed, his team found that a mutant protein just six units long (proteins are usually much longer) is enough to keep the proteins from aggregating into clumps.

This kind of smaller protein has a better chance of travelling from blood vessels, across the blood-brain barrier and into the brain, but Tagliavini admits the potential therapy will need much more tinkering – not to mention testing. "We are very far from this point, but we can work on this," he says.

New perspective

"There are other anti-aggregation therapies that are much further along," notes Rudolph Tanzi, an Alzheimer's expert at Harvard Medical School in Boston, who was not involved in the study.

Tanzi founded a company called Prana Biotechnology that is now testing one such therapy in patients, but Tanzi says the more Alzheimer's drugs that are in development, the better.

Whatever happens, the newly discovered APP mutation will change how researchers think about the genetics of the disease, he says. All previously identified mutations causing inherited Alzheimer's are dominant, meaning that only one copy of the mutation is enough to cause the disease.

"It's pretty exciting from a genetic standpoint because it's the first recessive mutation we've seen in Alzheimer's to date," Tanzi says. *Journal reference: Science (DOI: 10.1126/science.1168979)*

Device turns pink before you do

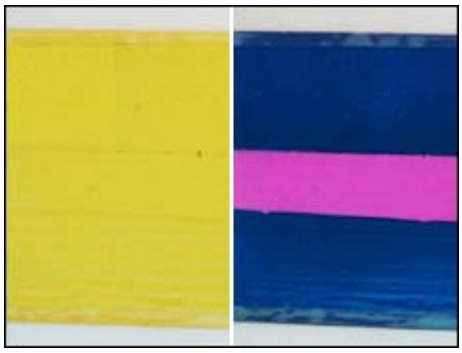
By Victoria Gill Science reporter, BBC News

Researchers have developed an indicator that turns an appropriate shade of pink to alert wearers of sunburn.

The thin film device could be worn as a wrist band to warn wearers they risk receiving a potentially harmful dose of ultraviolet rays.

UV rays drive a chemical reaction in the indicator, releasing an acid into a dye, and causing it to change colour.

The research team from the University of Strathclyde report their work in the journal Chemical Communications.



When the line turns pink, it's time to get out of the sun

Professor of chemistry, Andrew Mills, who led the team, describes this combination of a UV-driven reaction with an acid-sensitive dye as "intelligent ink".

"People think of chemical reactions as happening in test tubes," he said. "But here you have a reaction in a very thin layer of ink film that produces a colour change."

Other indicators are already available that detect and measure UV. But what's special about this one, said Professor Mills, is that it can be adjusted to give an instant signal at the point when sun exposure is about to cause damage.

Don't feel the burn

Professor Mills has made a prototype of the film, combining a dye that gradually changes colour from yellow to blue, and a central strip of dye that turns pink.

"This delayed reaction is the novel feature," Professor Mills explained. As soon as the indicator turns pink, he says "you should get out of the sun because if you stay you'll burn".

The device could also be adapted to different skin types; adding an alkali to the dye would increase the delay before the colour change.

"Our plan is to start a company that will make products out of this technology, such as wrist bands or clothing labels," Professor Mills said.

"We've already been approached by a number of skincare product manufacturers who are interested in the technology."

Jodie Moffat, health information officer from Cancer Research UK, said that anything highlighting the damage that UV exposure can cause would be of value.

According to the charity, more than 2,300 people die from skin cancer each year in the UK.

Ms Moffat said she could imagine "this sort of device being used to encourage people to protect their skin".

But, she added, it would need to be thoroughly tested to ensure it reflected exposure levels in real life situations.

'Fridges and washing machines liberated women': researcher

Université de Montréal professor studies impact of household technology

The advent of modern appliances such as washing machines and refrigerators had a profound impact on 20th Century society, according to a new Université de Montréal study. Plug-in conveniences transformed women's lives and enabled them to enter the workforce, says Professor Emanuela Cardia, from the Department of Economics.

Within a short time-span, household technology became accessible to the majority. In the late 1910s, a refrigerator sold for $1,600 and 26 years later such appliances could be purchased for $170. Access to electric stoves, washing machines and vacuum cleaners was also generalized.

"These innovations changed the lives of women," says Professor Cardia. "Although it wasn't a revolution per se, the arrival of this technology in households had an important impact on the workforce and the economy." Professor Cardia based her research on more than 3,000 censuses conducted between 1940 and 1950, from thousands of American households, across urban and rural areas. "We calculated that women who loaded their stove with coal saved 30 minutes everyday with an electric stove," says Cardia. "The result is that women flooded the workforce. In 1900, five percent of married women had jobs. In 1980, that number jumped to 51 percent."

In 1913, the vacuum cleaner became available, in 1916 it was the washing machine, in 1918 it was the refrigerator, in 1947 the freezer, and in 1973 the microwave was on the market. All of these technologies had an impact on home life, but none had a stronger impact than running water.

"We often forget that running water is a century-old innovation in North America, and it is even more recent in Europe. Of all innovations, it's the one with the most important impact," says Cardia.

In 1890, 25 percent of American households had running water and eight percent had electricity. In 1950, 83 percent had running water and 94% had electricity. According to Cardia, in 1900, a woman spent 58 hours per week on household chores. In 1975, it was 18 hours.

While there have been several studies on the industrial revolution and different aspects of technology, says Cardia, very few investigations have focused on the household revolution. "Yet, women play a very important role in the economy whether they hold a job or work at home."

On the Web: Read the complete study, "Household Technology: Was it the Engine of Liberation?" at http://www.cireq.umontreal.ca/personnel/cardia_household_technology.pdf.

Rabies deaths from dog bites could be eliminated

Hamilton, ON (March 11, 2009) - Someone in the developing world – particularly in rural Africa - dies from a rabid dog bite every 10 minutes.

But global elimination of this horrific disease appears to be possible, according to a team which includes scientists from McMaster University, Britain and the United States.

In a paper in the current issue of PLoS Biology, they report their analysis of data on rabies transmission in two districts of rural Tanzania (Serengeti and Ngorongoro) and suggest that with "sustained, international commitment, global elimination of rabies from domestic dog populations, the most dangerous vector to humans, is a realistic goal."

Jonathan Dushoff, an assistant professor of biology at McMaster University, and a member of the Michael G. DeGroote Institute for Infectious Disease Research, analyzed the data. "The paper provides important evidence that the elimination of canine rabies may be possible."

Rabies is an acute viral encephalitis that is spread through the saliva of infected animals. Human rabies deaths from domestic dogs are rare in North America, but the disease causes over 24,000 deaths a year in Africa, mostly in poor rural communities and, most often, in children. Globally, 55,000 people die annually from canine rabies.

During a rabies outbreak in northern Tanzania, the team of scientists was able to directly trace case-to-case transmission of rabies. From this data, they generated a detailed analysis of rabies transmission biology and found evidence for surprisingly low levels of transmission.

The scientists also analysed outbreak data from around the world and found the transmission of canine rabies has been inherently low throughout its global historic range, explaining the success of control efforts in developed countries.

"Achieving vaccination coverage of 60 per cent or more in dog populations in Africa is both logistically and economically feasible through annual vaccination campaigns," the scientists said in the PLoS paper.

Given the success of the current research, Dushoff said a larger study is planned. "If the (larger study) works, we hope that the World Health Organization and the Gates Foundation will decide to tackle rabies world-wide. Canine rabies may well be a disease we can get rid of."

The cost of rabies both in terms of the 55,000 deaths a year and post exposure vaccination treatments is very significant, Dushoff said. "If it really is a disease that can be eliminated, our group believes we should go and get it. This paper is one step along the route of trying to figure out whether canine rabies is controllable, how it can best be controlled and promoting the idea it's a disease we can eliminate."

Dushoff's theoretical biology lab at McMaster is a "dry" lab – with no laboratory benches, chemical reagents or biological specimens. Its main tools are computers, pencils and chalkboards. Scientists working there use statistical, computational and mathematical techniques to engage a broad range of biological questions.

The lab's main focus is on a broad range of questions surrounding the evolution and spread of infectious diseases of humans – including rabies, influenza, malaria and HIV.

Fledgling mantle plume may be cause of African volcano's unique lava

Nyiragongo, an active African volcano, possesses lava unlike any other in the world, which may point toward its source being a new mantle plume says a University of Rochester geochemist. The lava composition indicates that a mantle plume—an upwelling of intense heat from near the core of the Earth—may be bubbling to life beneath the soil of the Democratic Republic of the Congo. The findings are presented in the current issue of the journal Chemical Geology.

"This is the most fluid lava anyone has seen in the world," says Asish Basu, professor of earth science at the University of Rochester. "It's unlike anything coming out of any other volcano. We believe we're seeing the beginning of a plume that is pushing up the entire area and contributing to volcanism and earthquakes."

Basu analyzed the lava, which resides in the world's largest lava lake—more than 600 feet wide inside the summit of Nyiragongo—and found that the isotopic compositions of neodymium and strontium are identical to ancient asteroids. This suggests, says Basu, that the lava is coming from a place deep inside the Earth where the source of molten rock is in its pristine condition.

Because the Earth's crust is undergoing constant change via tectonic motion, weathering, and resurfacing, its chemical composition has been dramatically altered over its 4-billion-year lifespan, but the Nyiragongo magma source in the deep mantle has not, says Basu. That magma source is thought to retain some of the solar system's original make-up of elements, and this is what Basu and his colleagues believe they have detected in Nyiragongo's lava lake.

Scientists believe mantle plumes can last hundreds of millions of years, and that their heat can create phenomena such as Yellowstone National Park or the string of Hawaiian Islands. Basu says Nyiragongo's frequent eruptions may be the birthing pains of a similar plume and the possible beginning of new large-scale geological formations in the region.

Basu says other well known features of the region also point toward the idea of a growing plume. Nyiragongo lies on a vast ring of volcanoes and fissures that wrap around Uganda and the United Republic of Tanzania, and inside this ring the land is domed upward more than a mile above sea level. Basu believes the head of the plume is pooling in this region, pushing it upward like a 500-mile-wide air bubble in a pie crust.

But it is Nyiragongo, says Basu, that is being fed directly from the plume. Another volcano, Nyamuragira, just 15 miles to the north of Nyiragongo displays much more conventional lava compositions. Basu says this is because Nyamuragira is being fed from the edge of where the plume's head is pooling, mixing in elements of melted crust and upper mantle, whereas Nyiragongo is being fed directly from the plume's main body. Together the two mountains are responsible for approximately 40 percent of all of Africa's volcanic eruptions.

"This is a very troubled region of the world, and we hope to be able to help better understand the conditions under which the people of that area must live," says Basu. Nyiragongo last erupted in 2002, sending its super-fluid lava down its slopes at more than 60 miles per hour toward the nearby town of Goma, destroying 4,500 buildings and leaving 120,000 homeless. Basu and other scientists hope that understanding the composition of the lava that feeds Nyiragongo may help ongoing worldwide scientific efforts to understand the hazards of the region.

Basu's analysis was funded by the National Science Foundation. His colleagues were Ramananda Chakrabarti, research fellow at Harvard University, Alba Santo and Orlando Vaselli of the University of Florence, Italy, and Dario Tedesco of the University of Naples, Italy.

University of Pennsylvania Researchers Find that the Unexpected Is a Key to Human Learning

PHILADELPHIA – The human brain's sensitivity to unexpected outcomes plays a fundamental role in the ability to adapt and learn new behaviors, according to a new study by a team of psychologists and neuroscientists from the University of Pennsylvania.

Using a computer-based card game and microelectrodes to observe neuronal activity of the brain, the Penn study, published this week in the journal Science, suggests that neurons in the human substantia nigra, or SN,

play a central role in reward-based learning, modulating learning based on the discrepancy between the expected and the realized outcome.

"This is the first study to directly record neural activity underlying this learning process in humans, confirming the hypothesized role of the basal ganglia, which includes the SN, in models of reinforcement including learning, addiction and other disorders involving reward-seeking behavior," said lead author Kareem Zaghloul, postdoctoral fellow in neurosurgery at Penn's School off Medicine. "By responding to unexpected financial rewards, these cells encode information that seems to help participants maximize reward in the probabilistic learning task."

Learning, previously studied in animal models, seems to occur when dopaminergic neurons, which drive a larger basal ganglia circuit, are activated in response to unexpected rewards and depressed after the unexpected omission of reward. Put simply, a lucky win seems to be retained better than a probable loss.

Similar to an economic theory, where efficient markets respond to unexpected events and expected events have no effect, we found that the dopaminergic system of the human brain seems to be wired in a similar rational manner -- tuned to learn whenever anything unexpected happens but not when things are predictable," said Michael J. Kahana, senior author and professor of psychology at Penn's School of Arts and Sciences.

Zaghloul worked with Kahana and Gordon Baltuch, associate professor of neurosurgery, in a unique collaboration among departments of psychology, neurosurgery and bioengineering. They used microelectrode recordings obtained during deep brain stimulation surgery of Parkinson's patients to study neuronal activity in the SN, the midbrain structure that plays an important role in movement, as well as reward and addiction. Patients with Parkinson's disease show impaired learning from both positive and negative feedback in cognitive tasks due to the degenerative nature of their disease and the decreased number of dopaminergic neurons.

The recordings were analyzed to determine whether responses were affected by reward expectation. Participants were asked to choose between red and blue decks of cards presented on a computer screen, one of which carried a higher probability of yielding a financial reward than the other. If the draw of a card yielded a reward, a stack of gold coins was displayed along with an audible ring of a cash register and a counter showing accumulated virtual earnings. If the draw did not yield a reward or if no choice was made, the screen turned blank and participants heard a buzz.

"This new way to measure dopaminergic neuron activity has helped us gain a greater understanding of fundamental cognitive activity," said Baltuch, director of the Penn Medicine Center for Functional and Restorative Neurosurgery.

The work is supported by grants from the National Institutes of Health, the Conte Center and the Dana Foundation.

Studies show children can complete treatment for peanut allergies and achieve long-term tolerance

DURHAM, NC -- A carefully administered daily dose of peanuts has been so successful as a therapy for peanut allergies that a select group of children is now off treatment and eating peanuts daily, report doctors at Duke University Medical Center and Arkansas Children's Hospital.

"It appears these children have lost their allergies," says Wesley Burks, MD, Chief of the Division of Pediatric Allergy and Immunology at Duke. "This gives other parents and children hope that we'll soon have a safe, effective treatment that will halt allergies to certain foods."

Long-term tolerance in children with peanut allergies was documented for the first time by the presence of key immunologic changes, according to researchers at Duke and Arkansas Children's Hospital who presented their findings at the American Academy of Asthma and Immunology meeting in Washington, DC today.

Tests of several immunologic indicators suggest the body builds tolerance quickly.

"At the start of the study, these participants couldn't tolerate one-sixth of a peanut," Burks said. "Six months into it, they were ingesting 13 to 15 peanuts before they had a reaction."

About four million Americans have food allergies, and allergies to tree nuts and peanuts are the most common. Life-threatening reactions can occur from exposure to even a trace amount of peanuts, and nearly half of the 150 deaths attributed to food allergies each year are caused by peanut allergies.

Duke and Arkansas Children's Hospital began enrolling patients in studies five years ago to determine if incremental doses of peanut protein could change how the body's immune system responds to its presence. The doses start as small as 1/1000 of a peanut. Eight to 10 months later, the children are ingesting the equivalent of up to 15 peanuts per day. The children stay on that daily therapy for several years and are monitored closely.

Nine of the 33 children participating in the study have been on maintenance therapy for more than 2.5 years. After a series of food challenges, four of those children were taken off the treatment and continue to eat peanuts.

Some have been off treatment for more than a year. Doctors keep tabs on any potential changes in their immune system via skin, blood and immune studies.

One of the tests used in the study looks at immunoglobulin E (IgE), a protein the body makes in response to peanut allergens. "If you have it, you're likely allergic, if you don't, you aren't," explained Burks. Children in this study generally started with IgE levels greater than 25. "At the end of the study, their peanut IgEs were less than 2 and have remained that way since we stopped the treatment," he said.

Because the pool of children now off treatment is so small, Burks says it's hard to say whether these children simply outgrew their allergies or if the therapy did something to enhance that outcome. The next step is a blinded study in which children on treatment are compared to a control group. First year results were presented at the meeting by Stacie M. Jones, MD, a pediatric allergist at Arkansas Children's Hospital. So far, the oral immune therapy appears to be working.

"We see initial desensitization effects of the treatment are real," Burks says. "Those children are now able to eat up to 15 peanuts with no reaction, but the children not on treatment have symptoms early on in the study."

Despite the news, Burks insists this research is still ongoing and cautions parents and professionals against trying any version on their own. "In my clinic, I would do the same things I've always done. Once diagnosed with a food allergy, I would recommend they avoid the food. We have to wait for the studies to show the treatment is safe, and to see desensitization start to work. We also want to know the therapy works long term."

Burks also cautions that some people are too sensitive to peanut allergens to be able to undergo the therapy.

The studies were funded by the National institute of Health, the Food Allergy and Anaphylaxis Network, Food Allergy Project, Gerber Foundation and the Robins Family Foundation.

A natural approach for HIV vaccine

Research suggests scientists should follow the body's lead to prevent HIV from taking root

For 25 years, researchers have tried and failed to develop an HIV vaccine, primarily by focusing on a small number of engineered "super antibodies" to fend off the virus before it takes hold. So far, these magic bullet antibodies have proved impossible to produce in people. Now, in research to be published March 15 online by Nature, scientists at The Rockefeller University have laid out a new approach. They have identified a diverse team of antibodies in "slow-progressing" HIV patients whose coordinated pack hunting knocks down the virus just as well as their super-antibody cousins fighting solo.

By showcasing the dynamic, natural immune response in these exceptional patients, the research, led by Michel C. Nussenzweig, Sherman Fairchild Professor and head of the Laboratory of Molecular Immunology, suggests that an effective HIV vaccine may come from a shotgun approach using of a wide range of natural antibodies rather than an engineered magic bullet.

"We wanted to try something different, so we tried to reproduce what's in the patient. And what's in the patient is many different antibodies that individually have limited neutralizing abilities but together are quite powerful," says Nussenzweig, who also is a Howard Hughes Medical Institute investigator. "This should make people think about what an effective vaccine should look like."

HIV strains mutate rapidly, making them especially wily adversaries of the immune system. But one element is shared almost universally among the diverging strains — a protein on the envelope of the virus called gp140 that HIV needs to infect immune cells. Prior research has shown that four randomly engineered antibodies that block the activity of that protein prevent the virus from infecting immune cells in culture, but all attempts to coax the human body into producing those four have failed.

So Johannes Scheid, a visiting student in Nussenzweig's lab who is now a doctoral candidate, turned his attention to the antibodies produced by six people infected with HIV whose immune systems put up an exceptionally strong fight. The patients represent the roughly 10 to 20 percent of HIV patients who are able to control the virus and are very slow to progress to disease. Their immune systems' memory B cells produce high levels of antivirus antibodies, but until now, researchers have known little about the antibodies or how effective they are.

With help from Rockefeller's Center for Clinical and Translational Science and Rockefeller scientists David D. Ho and Jeffrey V. Ravetch, Scheid and colleagues isolated 433 antibodies from these individuals' blood serum that specifically targeted the envelope protein - the chink in HIV's protean armor. He cloned the antibodies and produced them in bulk, mapped which part of the envelope protein each targeted, and gauged how effective each was in neutralizing the virus. In the process, he identified a new structure within the envelope protein - called the gp120 core - that had never been recognized as a potential target for antibodies. "It's the first time that anyone has defined what is really happening in the B cell response in these patients," says Scheid.

Scheid's work shows that it's common for these antibodies to have neutralizing activity, says Nussenzweig. But each antibody alone has limited ability to fight the virus. "Individually, they're not as strong as the Famous

Four," says Nussenzweig, referring to the high-profile super antibodies on which several vaccine attempts have been based. But in high concentrations, a combination of the sets of antibodies cloned from the individual patients seemed to act as teams to knock down the virus in cell culture as well as any single antibody studied to date. These natural antibodies were also able to recognize a range of HIV strains, indicating that their diversity may be an advantage over a single super antibody that focuses on only one part of the virus, which can mutate. The findings suggest that research into vaccines that mimic this natural antibody response could pay off.

Young dinosaurs roamed together, died together

A herd of young birdlike dinosaurs met their death on the muddy margins of a lake some 90 million years ago, according to a team of Chinese and American paleontologists that excavated the site in the Gobi Desert in western Inner Mongolia.

The sudden death of the herd in a mud trap provides a rare snapshot of social behavior. Composed entirely of juveniles of a single species of ornithomimid dinosaur (Sinornithomimus dongi), the herd suggests that immature individuals were left to fend for themselves when adults were preoccupied with nesting or brooding.

"There were no adults or hatchlings," said Paul Sereno, professor at the University of Chicago and National Geographic Explorer-in-Residence. "These youngsters were roaming around on their own," remarked Tan Lin, from the Department of Land and Resources of Inner Mongolia.

This is a map of Inner Mongolia in northern China showing the site of the discovery of a herd of young Sinornithomimus dinosaurs, a place near the outpost Suhongtu. **Courtesy of Project Exploration**

Within an exquisite pair of the skeletons, prepared for display in Sereno's lab and airlifted back to China in late February, preserve stomach stones and the animal's' last meals are preserved.

Sereno, Tan and Zhao Xijin, professor in the Chinese Academy of Sciences, led the 2001 expedition that found the fossils. Team members also included David Varricchio of Montana State University (MSU), Jeffrey Wilson of the University of Michigan and Gabrielle Lyon of Project Exploration. The findings are published in the December 2008 issue of Acta Palaeontologica Polonica, and the work was funded by the National Geographic Society and the David and Lucile Packard Foundation.

"Finding a mired herd is exceedingly rare among living animals," said Varricchio, an assistant professor of paleontology at MSU. "The best examples are from hoofed mammals," such as water buffalo in Australia or feral horses in the American West, he said.

The first bones from the dinosaur herd were spotted by a Chinese geologist in 1978 at the base of a small hill in a desolate, windswept region of the Gobi Desert. Some 20 years later, a Sino-Japanese team excavated the first skeletons, naming the dinosaur Sinornithomimus ("Chinese bird mimic").

Sereno and associates then opened an expansive quarry, following one skeleton after another deep into the base of the hill. In sum, more than 25 individuals were excavated from the site. They range in age from one to seven years, as determined by the annual growth rings in their bones.

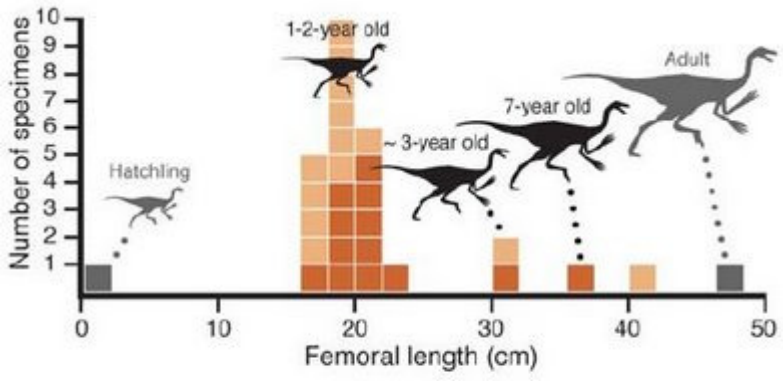
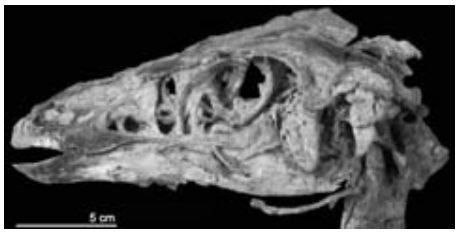


Fig. 5. Size distribution of individuals from the Suhongtu quarry representing a juvenile to subadult herd. Missing hatchling and adult sizes shown in gray. Colors in plot differentiate skeletons from this study (rust) from those excavated previously (orange) (Kobayashi and Lü 2001).

The team meticulously recorded the position of all of the bones and the details of the rock layers to try to understand how so many animals of the same species perished in one place. The skeletons showed similar exquisite preservation and were mostly facing the same direction, suggesting that they died together and over a short interval.

The details provided key evidence of an ancient tragedy. Two of the skeletons fell one right over the other. Although most of their skeletons lay on a flat horizontal plane, their hind legs were stuck deeply in the mud below. Only their hip bones were missing, which was likely the handiwork of a scavenger working over the meatiest part of the body bodies shortly after the animals died.

"These animals died a slow death in a mud trap, their flailing only serving to attract a nearby scavenger or predator," Sereno said. Usually, weathering, scavenging or transport of bone have long erased all direct evidence of the cause of death. The site provides some of the best evidence to date of the cause of death of a dinosaur.



Sinornithomimus dongi

Plunging marks in mud surrounding the skeletons recorded their failed attempts to escape. Varricchio said he was both excited and saddened by what the excavation revealed. "I was saddened because I knew how the animals had perished. It was a strange sensation and the only time I had felt that way at a dig," he said.

In addition to herd composition and behavior, the site also provides encyclopedic knowledge of even the tiniest bones in the skull and skeleton. "We even know the size of its eyeball," Sereno said. "Sinornithomimus is destined to become one of the best- understood dinosaurs in the world."

Click here to view a video featuring Paul Sereno discussing his research.

The scientific paper on the herd site is published in Acta Palaeontologica Polonica available at http://www.app.pan.pl/article/item/app53-567.html. More information about team members and the expedition is available at http://www.projectexploration.org/mongolia.

Monkeys 'teach infants to floss'

Making sure your offspring know how to clean their teeth appears to be as important to monkeys as to humans.

Mother monkey teaches her young to floss

Female monkeys in Thailand have been observed showing their young how to floss their teeth - using human hair.

Researchers from Japan said they watched seven long-tailed macaques cleaning the spaces between their teeth in the same manner as humans.

They spent double the amount of time flossing when they were being watched by their infants, the team said.

This suggests the mothers were deliberately teaching their young how to floss, Professor Nobuo Masataka of Kyoto University's Primate Research Institute said.

"I was surprised because teaching techniques on using tools properly to a third party are said to be an activity carried out only by humans," he told the AFP news agency.

He said the study, carried out in Lopburi, north of Bangkok, is still in the hypothesis stage.

"We would like to shift our focus to the baby monkeys to check whether the mothers' actions are effectively helping them learn how to clean their teeth," he added.