Elastography reduces unnecessary breast biopsies

CHICAGO – Elastography is an effective, convenient technique that, when added to breast ultrasound, helps distinguish cancerous breast lesions from benign results, according to an ongoing study presented today at the annual meeting of the Radiological Society of North America (RSNA).

When mammography yields suspicious findings, physicians often use ultrasound to obtain additional information. However, ultrasound has the potential to result in more biopsies because of its relatively low specificity, or inability to accurately distinguish cancerous lesions from benign ones. Approximately 80 percent of breast lesions biopsied turn out to be benign, according to the American Cancer Society.

"There's a lot of room to improve specificity with ultrasound, and elastography can help us do that," said the study's lead author, Stamatia V. Destounis, M.D., a diagnostic radiologist at Elizabeth Wende Breast Care, a large, community-based breast imaging center in Rochester, N.Y. "It's an easy way to eliminate needle biopsy for something that's probably benign."

Elastography improves ultrasound's specificity by utilizing conventional ultrasound imaging to measure the compressibility and mechanical properties of a lesion. Since cancerous tumors tend to be stiffer than surrounding healthy tissue or cysts, a more compressible lesion on elastography is less likely to be malignant.

"You can perform elastography at the same time as handheld ultrasound and view the images on a split screen, with the two-dimensional ultrasound image on the left and the elastography image on the right," Dr. Destounis said.

As part of the ongoing study, 179 patients underwent breast ultrasound and elastography. The research team obtained 184 elastograms and performed biopsies on all solid lesions. Of 134 biopsies, 56 revealed cancer. Elastography properly identified 98 percent of lesions that had malignant findings on biopsy, and 82 percent of lesions that turned out to be benign. Elastography was also more accurate than ultrasound in gauging the size of the lesions.

"Ultrasound can underestimate the true size of lesions, as it only sees the actual mass and not the surrounding changes the mass may cause," Dr. Destounis said.

In 2009, there will be an estimated 192,370 new cases of invasive breast cancer among women in the United States, according to the American Cancer Society, along with about 62,280 new cases of ductal carcinoma in situ, a noninvasive, early form of breast cancer.

Coauthors are Andrea L. Arieno, B.S., Melissa N. Skolny, M.S., Renee Morgan, R.T., Patricia Somerville, M.D., and Philip F. Murphy, M.D.

Also at RSNA 2009, Dr. Smitha Putturaya, M.D., F.R.C.R., presented findings from an ongoing, seven-year study on breast elastography conducted at the Charing Cross Hospital Breast Unit in London, U.K. Dr. Putturaya and colleagues found that using elastography as an adjunct to routine breast ultrasound safely decreases the number of biopsies of benign lesions and offers the potential to map tumors more precisely.

Note: Copies of RSNA 2009 news releases and electronic images will be available online at RSNA.org/press09 beginning Monday, Nov. 30.

Chicken capsules good for aching joints

Chicken collagen can provide relief from rheumatoid arthritis (RA) symptoms. A randomised, controlled trial, published in BioMed Central's open access journal Arthritis Research & Therapy, has found that Chicken type II collagen (CCII), a protein extracted from the cartilage of chicken breast, is a safe and effective treatment for RA.

Wei Wei, from Anhui Medical University, China, worked with a team of researchers to test the novel treatment by comparing it to the established antirheumatic drug methotrextate, in 503 RA patients. Patients who received a 12-week course of CCII capsules showed significantly improved joint function, with fewer and milder adverse effects than those taking methotrexate. According to Wei, "We've shown that CCII is a promising alternative therapeutic strategy that may be used as a nutritional supplement against rheumatoid arthritis".

RA is an autoimmune disease caused by the body mounting a response against its own cartilage – the rubbery tissue, composed mainly of collagen, which cushions and lubricates joints. By dosing patients with collagen in the form of CCII capsules, the researchers believe that 'oral tolerance' can be developed. Wei said "Oral tolerance is a reduction in autoimmune activity caused by repeated dietary exposure to the offending substance. Treatment of autoimmune diseases by induction of oral tolerance is attractive because of the few side effects and easy clinical implementation of this approach. Indeed, our work confirms that treatment with oral CCII leads to improvement in arthritis with no significant side effects".

Notes to Editors:

1. A multicenter, double-blind, randomized, controlled phase III clinical trial of chicken type II collagen in rheumatoid arthritis

Wei Wei, Ling-Ling Zhang, Jian-Hua Xu, Feng Xiao, Chun-De Bao, Li-Qing Ni, Xing-Fu Li, Yu-Qiong Wu, Ling-Yun Sun, Rong-Hua Zhang, Bao-Liang Sun, Sheng-Qian Xu, Shuang Liu, Wei Zhang, Jie Shen, Hua-Xiang Liu and Ren-Cheng Wang
Arthritis Research & Therapy (in press)
During embargo, article available here: http://arthritis-research.com/imedia/1257409752874094_article.pdf?random=613049
After the embargo, article available at journal website: http://arthritis-research.com/

Scientists reveal malaria parasites' tactics for outwitting our immune systems

Malaria parasites are able to disguise themselves to avoid the host's immune system, according to research funded by the Wellcome Trust and published today in the journal Proceedings of the National Academy of Sciences.

Malaria is one of the world's biggest killers, responsible for over a million deaths every year, mainly in children and pregnant women in Africa and South-east Asia. It is caused by the malaria parasite, which is injected into the bloodstream from the salivary glands of infected mosquitoes. There are a number of different species of parasite, but the deadliest is the Plasmodium falciparum parasite, which accounts for 90 per cent of deaths from malaria.

The malaria parasite infects healthy red blood cells, where it reproduces. The P. falciparum parasite generates a family of molecules, known as PfEMP1, that are inserted into the surface of the infected red blood cells. The cells become sticky and adhere to the walls of blood vessels in tissues such as the brain. This prevents the cells being flushed through the spleen, where the parasites would be destroyed by the body's immune system, but also restricts blood supply to vital organs.

Symptoms can differ greatly between young and older children depending on previous exposure to the parasite. In young children, the disease can be extremely serious and potentially fatal if untreated; older children and adults who have grown up in endemic areas are resistant to severe malaria but rarely develop the ability to rid their bodies of the parasite.

Each parasite has 'recipes' for around sixty different types of PfEMP1 molecule written into its genes. However, the exact recipes differ from parasite to parasite, so every new infection may carry a set of molecules that the immune system has not previously encountered. This has meant that in the past, researchers have ruled out the molecules as vaccine candidates. However there appear to be at least two main classes of PfEMP1 types within every parasite, suggesting different broad tactical approaches to infecting the host. The most efficient tactic or combination of tactics to use may depend on the host's immunity.

Now, Dr George Warimwe and colleagues from the Kenya Medical Research Institute (KEMRI)-Wellcome Trust Programme and the Wellcome Trust Sanger Institute, have shown that the parasites adapt their molecules depending on which antibodies it encounters in the host's immune response. They have also found evidence to suggest that there may be a limit to the number of molecular types that are actually associated with severe disease.

"The malaria parasite is very complex, so our immune system mounts many different responses, some more effective than others and many not effective at all," explains Dr Peter Bull from the KEMRI-Wellcome Trust Programme and the University of Oxford, who led the research. "We know that our bodies have great difficulty in completely clearing infections, which begs the question: how does the parasite manage to outwit our immune response? We have shown that, as children begin to develop antibodies to parasites, the malaria parasite changes its tactics to adapt to our defences."

The researchers at the KEMRI-Wellcome Trust Programme studied malaria parasites in blood samples from 217 Kenyan children with malaria. They found that a group of genes coding for a particular class of PfEMP1 molecule called Cys-2 tended to be switched on when the children had a low immunity to the parasite; as immunity develops, the parasite switches on a different set of genes, effectively disguising it so that immune system cannot clear the infection

Dr Warimwe and colleagues also found an independent association between activity in Cys-2 genes and severe malaria in the children, suggesting that specific forms of the molecule may be more likely to trigger specific disease symptoms. This supports a previous study in Mali which suggested that the same class of PfEMP1 molecule was associated with cerebral malaria.

The findings could suggest a new approach to tackling malaria, in terms of both vaccine development and drug interventions, argues Dr Bull.

"If there exists a limited class of severe disease-causing variants that naturally-exposed children learn to recognise readily, this opens up the possibility of designing a vaccine against severe malaria that mimics an adult's immune response, making the infections less dangerous. But this would still be an enormous task.

"Similarly, if we can establish what the particular class of molecules are doing, then we may be able to develop a drug to modify this function and relieve symptoms of severe disease."

Stroke and heart disease trigger revealed in new research

Scientists have identified the trigger that leads to the arteries becoming damaged in the disease atherosclerosis, which causes heart attacks and strokes, in research published today in the journal Circulation. The authors of the study, from Imperial College London, say their findings suggest that the condition could potentially be treated by blocking the molecule that triggers the damage. The research also suggests that bacteria may be playing a part in the disease.

In atherosclerosis, 'plaques' form in arteries that feed the brain and heart, obstructing the blood flow. The plaques are made of substances like fatty deposits and cholesterol. Immune cells are attracted into these plaques, which form inside the wall of the artery, leading to the artery becoming inflamed and to the artery wall being damaged. Sometimes, the plaque can burst as a result of this damage, causing a stroke or a heart attack.

Today's research, which was funded by the British Heart Foundation and the European Commission, reveals the trigger that leads to the inflammation and damage to the artery wall. The researchers hope they can block this trigger in order to prevent damage to the artery and, ultimately, heart attacks and strokes.

The trigger identified in the research is a molecule called TLR-2. This 'receptor' molecule lives on the surface of an immune cell and when it recognises harmful molecules and cells, including bacteria, it switches the immune cell into attack mode, to protect the body. It can also switch on the immune cells when the body is under stress.

Today's research shows that TLR-2 is unusually active in plaques in the carotid artery in the neck. In lab tests, the researchers showed that blocking the TLR-2 receptor stopped cells from making the molecules that cause inflammation and damage to the artery. This, they say, suggests that the molecule is triggering the damage to the artery. It also suggests that 'danger molecules,' which kick into action when the body is under stress, and bacteria, may be triggering damage to the arteries by switching on the TLR-2 molecules, increasing the risk of plaques bursting and causing strokes and heart attacks.

If a drug could be developed that would block TLR-2 molecules, the researchers believe this would potentially treat atherosclerosis and prevent damage to the artery. They say this would ultimately reduce people's risk of strokes and heart attacks.

Dr Claudia Monaco, one of the corresponding authors of the study from the Kennedy Institute of Rheumatology and Vascular Surgery at Imperial College London, said: "Heart attack and stroke are the two most common causes of death in the Western world, and strokes account for an estimated ten per cent of all deaths. When a person suffers a heart attack, their heart can't function properly as a pump and this can have a severe impact on their ability to perform everyday activities. For survivors, strokes can also be extremely debilitating, often impairing a person's movement, vision or memory. Developing new ways to prevent heart attacks and strokes, by treating atherosclerosis, will help improve people's quality of life.

"Our new study reveals the trigger for inflammation and tissue breakdown in artery plaques. We have also shown that this trigger mechanism can be blocked using antibodies. If we can find a way to successfully block these receptors in people, without reducing their ability to fight off infection, we could potentially develop a treatment for atherosclerosis," added Dr Monaco.

The researchers studied sections of the carotid artery with atherosclerosis, taken from 58 patients after a stroke. They broke down the artery tissue using enzymes, until the researchers had a suspension of single cells in liquid. They analysed the liquid after four days and found that the cells had produced an unusually large amount of inflammatory molecules and enzymes that damage arteries.

The researchers then grew the cells with several different antibodies designed to block different receptors and molecules involved in the inflammation process. The researchers showed that blocking TLR-2 using an antibody reduced the production of inflammation molecules and enzymes dramatically.

The team now hopes to pinpoint specific parts of molecules that switch on TLR-2 and trigger inflammation.

Seeing family for the holidays? Scientists discover how the stress might kill you

New research in the Journal of Leukocyte Biology shows the link between the nervous and immune systems and how breaking that link might lead to new treatments for a wide range of autoimmune disorders

If you ever thought the stress of seeing your extended family over the holidays was slowly killing you - bad news: a new research report in the December 2009 print issue of the Journal of Leukocyte Biology (http://www.jleukbio.org) shows that you might be right. Here's the good news: results from the same study might lead to entirely new treatments that help keep autoimmune diseases like lupus, arthritis, and eczema under control. That's because researchers from the University of Connecticut Health Center have found that the same part of our nervous system that is responsible for the fight-or-flight response (called the sympathetic

nervous system) also controls regulatory T cells, which are used by the body to end an immune response once a foreign invader has been removed or destroyed.

"We show for the first time that the nervous system controls the central immune police cells, called regulatory T cells," said Robert E. Cone, Ph.D., a senior researcher in whose laboratory the work was done at the University of Connecticut Health Center. "This further shows that it is imperative to concentrate on the neuro-immune interactions and to understand how these two different systems, the immune and nervous systems, interact."

To make this discovery, Cone, Sourojit Bhowmick and colleagues injected some mice with a drug called 6-hyroxydopamine (6-OHDA) that selectively removes sympathetic nerves located in different organs, or a saline solution. Mice injected with 6-OHDA, which effectively severed the link between the nervous system and the immune system had twice as many regulatory T cells as the control group in their spleens and lymph nodes. Further analysis showed that the increase in regulatory T cells resulted from an increase in a protein called "TGF-beta," which directs the development and survival of regulatory T cells. With this information in hand, Cone and colleagues then sought to see if 6-OHDA would prevent autoimmune disorders from developing. To do this, they injected 6-OHDA or a saline solution into mice before subjecting them and a control group to conditions known to cause an autoimmune disease similar to multiple sclerosis in humans. Unlike the control group, the mice treated with 6-OHDA did not develop the autoimmune disease, showing that not only can the sympathetic nervous system negatively affect the immune system, but it also shows how it might be possible to prevent or stop autoimmune disorders.

"Ever since Hans Seyle's groundbreaking work on stress, scientists have been trying to understand why stressful situations often exacerbate autoimmune diseases and cause re-emergence of latent infections," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology. "In true fight or flight situations, stress can be a lifesaver, but understanding how the neurological response to the stress of everyday events such as seeing your family around the holidays impacts immune responses should provide opportunities for new therapies."

Big freeze plunged Europe into ice age in months

In the film, ‘The Day After Tomorrow’ the world enters the icy grip of a new glacial period within the space of just a few weeks. Now new research shows that this scenario may not be so far from the truth after all.

William Patterson, from the University of Saskatchewan in Canada, and his colleagues have shown that switching off the North Atlantic circulation can force the Northern hemisphere into a mini ‘ice age’ in a matter of months. Previous work has indicated that this process would take tens of years.

Around 12,800 years ago the northern hemisphere was hit by a mini ice-age, known by scientists as the Younger Dryas, and nicknamed the ‘Big Freeze’, which lasted around 1300 years. Geological evidence shows that the Big Freeze was brought about by a sudden influx of freshwater, when the glacial Lake Agassiz in North America burst its banks and poured into the North Atlantic and Arctic Oceans. This vast pulse, a greater volume than all of North America’s Great Lakes combined, diluted the North Atlantic conveyor belt and brought it to a halt.

Without the warming influence of this ocean circulation temperatures across the Northern hemisphere plummeted, ice sheets grew and human civilisation fell apart.

Previous evidence from Greenland ice cores has indicated that this sudden change in climate occurred over the space of a decade or so. Now new data shows that the change was amazingly abrupt, taking place over the course of a few months, or a year or two at most.

Patterson and his colleagues have created the highest resolution record of the ‘Big Freeze’ event to date, from a mud core taken from an ancient lake, Lough Monreach, in Ireland. Using a scalpel layers were sliced from the core, just 0.5mm thick, representing a time period of one to three months.

Carbon isotopes in each slice reveal how productive the lake was, while oxygen isotopes give a picture of temperature and rainfall. At the start of the ‘Big Freeze’ their new record shows that temperatures plummeted and lake productivity stopped over the course of just a few years. “It would be like taking Ireland today and moving it up to Svalbard, creating icy conditions in a very short period of time,” says Patterson, who presented the findings at the European Science Foundation BOREAS conference on humans in the Arctic, in Rovaniemi, Finland.

Meanwhile, their isotope record from the end of the Big Freeze shows that it took around two centuries for the lake and climate to recover, rather than the abrupt decade or so that ice cores indicate. “This makes sense because it would take time for the ocean and atmospheric circulation to turn on again,” says Patterson.

Looking ahead to the future Patterson says there is no reason why a ‘Big Freeze’ shouldn’t happen again. “If the Greenland ice sheet melted suddenly it would be catastrophic,” he says.

This study was part of a broad network of 38 individual research teams from Europe, Russia, Canada and the USA forming the European Science Foundation EUROCORES programme 'Histories from the North – environments, movements, narratives' (BOREAS). This highly interdisciplinary initiative brought together scientists from a wide range of disciplines including humanities, social, medical, environmental and climate sciences.

UAB physician urges changes in diagnosis for sore throat in young adults

BIRMINGHAM, Ala. – New analysis from the University of Alabama at Birmingham (UAB) suggests that physicians need to re-think their diagnosis and treatment of sore throat, or pharyngitis, in adolescents and young adults to consider a more newly identified and potentially dangerous culprit as the source of that infection.

Currently, physicians are taught to suspect group A streptococcal bacteria as the primary cause of pharyngitis. But according to findings published Dec. 1 in the Annals of Internal Medicine, physicians also should look for the presence of bacteria called Fusobacterium necrophorum when treating sore throat in young adults and adolescents that worsens or is strep-negative.

"F. necrophorum, which only has been recognized as a potential cause of pharyngitis in adolescents and young adults in the past five years, may cause up to 10 percent of sore throat in those 15-24 years of age," said Robert Centor, M.D., professor of internal medicine, associate dean of medicine at UAB and the paper's lead author. "More important, F. necrophorum is associated with a rare but life-threatening complication called Lemierre syndrome."

Lemierre syndrome mostly affects adolescents and young adults and rarely is seen in pre-adolescents. It begins with a sore throat, followed by an infected jugular vein after four to five days. Abscesses in other parts of the body may occur. Approximately 5 percent of people who get Lemierre syndrome die.

Group A strep also is associated with a serious complication - rheumatic fever - but the incidence rate of Lemierre syndrome following exposure to F. necrophorum is much higher and associated with greater morbidity and mortality. "The risk of Lemierre syndrome exceeds the risk of acute rheumatic fever, which is the classic reason that physicians worry about sore throats," said Centor.

Centor said clinicians should expand their diagnostic process for adolescents and young adults with sore throat to consider F. necrophorum, especially if the sore throat does not improve within three to five days. Centor said physicians need to be aware of the red flags that might indicate Lemierre syndrome, including unilateral neck swelling, rigors, night sweats or high fevers. There is not a routine test for F. necrophorum pharyngitis and a CT scan is required to detect Lemierre syndrome

Aggressive treatment with antibiotics such as a combination of penicillin and metronidazole or with clindamycin alone is appropriate. Centor said he hopes this analysis will lead to better diagnostic tests for the presence of F. necrophorum.

Coverage of inexpensive drugs may increase length and quality of life after heart attack

Many who must pay out-of-pocket for life-saving drug regimen are not filling their prescriptions, researchers say

Toronto, Ont, - Providing free medications to people after heart attack could add years to patients' lives at a relatively low cost for provincial governments, according to a new study by researchers at St. Michael's Hospital in Toronto.

"Many patients are not benefiting from effective prescribed medications because they simply don't fill their prescriptions," says Dr. Irfan Dhalla, the study's lead author and a physician at St. Michael's Hospital. "There is growing evidence that having to pay for medications out of pocket is a major reason."

Public coverage of pharmaceuticals in Canada is neither universal nor uniform because the Canada Health Act covers only physician and hospital services. According to data published in 2005, 11 per cent of Canadians had only catastrophic public coverage, and 4 per cent had no coverage at all.

The goal of the study was to demonstrate to policymakers what would happen if governments fully covered the costs of five heart attack medications - a beta blocker, low-dose aspirin, an ACE inhibitor, a statin, and a relatively new drug called clopidogrel - which are routinely prescribed for patients who have survived a heart attack.

The use of these effective and relatively inexpensive drugs has led to a dramatic decline in deaths from cardiovascular disease in recent years. Between 1980 and 2000, mortality from cardiovascular disease in Canada decreased by approximately 50%.

The researchers compared the benefits and the costs of two options:

* The "status quo" option reflects the current situation across Canada where people who don't have private drug insurance or who aren't eligible for government-funded drug programs are expected to pay the full cost of their prescriptions after a heart attack.

* The "full coverage" option would see governments pay the full cost of five recommended medications.

Implementing the full-coverage strategy for the five medications would result in average survival of 7.02 quality-adjusted life-years (QALYs) after heart attack at an average cost of $20,423 per patient, the study found. The status quo strategy resulted in an average survival of 6.13 QALYs at an average cost of $17,173 per patient.

(In health care research, the term "QALY" is used to describe survival time based not just on quantity of years but also on quality of life. A year in perfect health is considered equal to 1.0 QALY. The value of a year in ill health would be lower - for example, a year spent in hospital might have a value equal to 0.5 QALY.)

"Full coverage would save lives at very low cost and would be cost-effective compared to the status quo," says Dr. Dhalla. "Our model suggests that providing free medications to people after heart attack would result in one more year of life for each additional $3,663 spent by government. We used very conservative assumptions, and it is quite possible that a full coverage strategy would even be cost-saving for governments over the long-term."

The researchers say any added cost would be significantly below current thresholds used to decide whether new drugs and medical devices should be eligible for public funding.

Although the study looked at heart attack because that is where the evidence is strongest, there are many diseases where cheap, effective medications are available.

"Policy makers may wish to consider providing medications free of charge to all patients with chronic illnesses where specific drug treatments are known to be both highly cost-effective and associated with poor adherence - for example, preventing kidney and cardiovascular disease in patients with diabetes," Dr. Dhalla says. "Providing medications free of charge where they are likely to have the most value is one way policy makers can allocate limited public resources more efficiently."

Silver lining effect study, 'I have some good news and some bad news,' in INFORMS journal

Communicating "I have some good news and some bad news" is better than combining messages into a single, bleak result when small gains and large losses occur together, according to a study in the current issue of Management Science, the flagship journal of the Institute for Operations Research and the Management Sciences (INFORMS®).

"The Silver Lining Effect: Formal Analysis and Experiments" is by Peter Jarnebrant of the European School of Management and Technology and Olivier Toubia and Eric Johnson of Columbia University.

The authors ask how people's choices change when they are presented with information in either of two ways: as an integrated whole or as two segregated pieces. For example, they ask, does an investor prefer a statement showing only an aggregate loss of $95 – or one showing a loss of $100 and a gain of $5?

The authors follow upon work first done by RH Thaler in 1985.

"Thaler's intuition was that decision makers would prefer to mentally separate a small gain from a big loss, thus providing a silver lining to the loss," explains Prof. Olivier Toubia, one of the authors. This study provides new tests to the original assumptions.

The authors also tested to determine the threshold balance – for example, if subjects also prefer the information divided when there is a more even, 50/50 split in gain and loss.

The authors determined that the smaller the positive amount ($5 in the above example) and the larger the negative one ($95), the more people prefer that the information be presented in separate sections rather than summed together.

"When the loss gets larger, you're more likely to want to separate a small gain from that loss," explains Toubia.

This perception plays better with customers who are less loss averse, they determined.

The observation, the authors write, is important for decision makers in finance, retailing, and other organizations.

In finance, for example, a mutual fund posting a quarterly loss would be better perceived by investors if the accompanying information pointed out the portions of the portfolio that posted a gain.

In a retailing example, automobile manufacturers and dealers will be better appreciated by potential customers if they price a car at $20,000 with a $500 rebate than if they price the same car at $19,500.

They reached their conclusion through two experiments with online respondents. In the first, involving an online panel, respondents were asked to imagine losing their jobs and having to choose between two new job possibilities offering different mixes of lost winter and summer vacation time. In the second experiment, with a group who signed on via the Amazon.com company Mechanical Turk, respondents rated four sets of gambles involving a one in three chance of winning. In one set of gambles, the gain and loss were presented separately; in another, the total amount was combined.

Heavy metal paradox could point toward new therapy for Lou Gehrig's disease

CORVALLIS, Ore. – New discoveries have been made about how an elevated level of lead, which is a neurotoxic heavy metal, can slow the progression of amyotrophic lateral sclerosis, or Lou Gehrig's disease – findings that could point the way to a new type of therapy.

The results surprised researchers, since lead is also a known risk factor for ALS. This paradox is still not fully understood, and at this point would not form the basis for a therapy, as lead is toxic for the nervous system. But scientists say the phenomenon may lead to promising alternative approaches to the gene therapies that are now a focus of study.

The research was just published in Neurobiology of Disease, a professional journal, by researchers from the Instituto Clemente Estable and the University of the Republic in Montevideo, Uruguay, and at Oregon State University. The research has been supported by the National Institutes of Health.

"We know that environmental exposure to lead is a risk factor for ALS," said Joseph Beckman, holder of the Ava Helen Pauling Chair in the Linus Pauling Institute and director of the Environmental Health Sciences Center at OSU. "That's why it's so surprising that, according to studies done with laboratory animals, higher levels of lead appear to significantly reduce motor neuron loss and progression of ALS."

Research will continue to explore the underlying mechanisms that may be causing this, Beckman said. But the findings also raise immediate questions about the wisdom of chelation therapy in efforts to treat ALS, which many people have tried despite no evidence that it works. Chelation therapy tries to remove heavy metals from the body, including lead.

"Many people have spent thousands of dollars on chelation therapy to treat ALS, despite a lack of scientific evidence that heavy metals are causing the disease," Beckman said. "These findings about the potential protective mechanism of lead now raise concerns about the rationale for chelation therapy in treating ALS."

ALS is a progressive, fatal neurodegenerative disease that causes muscle weakness and atrophy throughout the body. There is no known cure, and it affects about 2-3 out of every 100,000 people each year.

According to Beckman, some of the findings about the role of lead in this disease evolved out of collaborative research OSU is doing with universities in Uruguay, where significant numbers of children from impoverished families are suffering from lead poisoning caused by setting up camps over abandoned lead factories near Montevideo. "In this area there are huge problems with lead poisoning, mostly in children," Beckman said. "People are being exposed through their water, food, other environmental sources, and we've worked there for a number of years to learn more about the neurotoxicity of lead exposure."

Lead appears to have some interaction with astrocytes, Beckman said, a special type of cell that is believed to influence the spread of ALS. Astrocytes are a major component of brain cells and, in healthy systems, help to support neurons, defend them against infection and injury and remove neurons when they become damaged.

This delicate process, however, may get disrupted in ALS, at which point astrocytes are believed to play a role in causing inappropriate motor neuron death. "These systems are very carefully balanced and many factors have to work together," Beckman said. "The proper functioning of astrocytes is essential to life, but their dysfunction may lead to disease. We think that lead somehow is modulating the neuroinflammatory actions of astrocytes and, in the case of ALS, helping to shift their balance back to one of protection, rather than damage."

When that happens, researchers say, it appears that astrocytes can stimulate the production of "vascular endothelial growth factor," which in turn protects motor neurons. Researchers around the world see increases in this growth factor as a possible way to help treat ALS, and most work is now focused on gene therapies to accomplish that. More research is necessary to determine the mechanisms by which lead has this protective effect, which may help to identify pharmacological targets for the disease.

The levels of lead that were therapeutic in the mice have toxic risk in adult humans, the researchers pointed out. However, as more is learned about how lead is affecting ALS, alternatives to lead might be found to accomplish the same goal.

"Available evidence supports the view that astrocytes are key targets of lead and respond to it by inducing neuroprotective pathways," the researchers wrote in their report. "Our results suggest that lead activates a novel pathway able to reduce neuroinflammation and slow neurodegeneration in ALS."

Well

In Month of Giving, a Healthy Reward

By TARA PARKER-POPE

When Cami Walker of Los Angeles learned three years ago that she had multiple sclerosis, her health and her spirits plummeted - until she got an unusual prescription from a holistic health educator.

Stuart Bradford

Ms. Walker, now 36, scribbled the idea in her journal. And though she dismissed it at first, after weeks of fatigue, insomnia, pain and preoccupation with her symptoms, she decided to give it a try. The treatment and her experience with it are summed up in the title of her new book, "29 Gifts: How a Month of Giving Can Change Your Life" (Da Capo Press).

Ms. Walker gave a gift a day for 29 days - things like making supportive phone calls or saving a piece of chocolate cake for her husband. The giving didn't cure her multiple sclerosis, of course. But it seems to have had a startling effect on her ability to cope with it. She is more mobile and less dependent on pain medication. The flare-ups that routinely sent her to the emergency room have stopped, and scans show that her disease has stopped progressing.

"My first reaction was that I thought it was an insane idea," Ms. Walker said. "But it has given me a more positive outlook on life. It's about stepping outside of your own story long enough to make a connection with someone else."

And science appears to back her up. "There's no question that it gives life a greater meaning when we make this kind of shift in the direction of others and get away from our own self-preoccupation and problems," said Stephen G. Post, director of the Center for Medical Humanities, Compassionate Care and Bioethics at Stony Brook University on Long Island and a co-author of "Why Good Things Happen to Good People" (Broadway, 2007). "But it also seems to be the case that there is an underlying biology involved in all this."

An array of studies have documented this effect. In one, a 2002 Boston College study, researchers found that patients with chronic pain fared better when they counseled other pain patients, experiencing less depression, intense pain and disability.

Another study, at the Buck Institute for Age Research in Novato, Calif., also found a strong benefit to volunteerism, and after controlling for a number of variables, showed that elderly people who volunteered for more than four hours a week were 44 percent less likely to die during the study period.

How giving can lead to mental and physical changes in health isn't entirely clear, although studies suggest that altruism may be an antidote to stress. A Miami study of patients with H.I.V. found that those with strong altruistic characteristics had lower levels of stress hormones.

By contrast, being self-centered may be damaging to health. In one study of 150 heart patients, researchers found that people in the study who had more "self-references" (those who talked about themselves at length or used more first-person pronouns) had more severe heart disease and did worse on treadmill tests.

And like Ms. Walker, numerous people have reported feeling better after helping others. A 1988 Psychology Today article dubbed the effect the "helper's high." Analyzing two separate surveys of a total of 3,200 women who regularly volunteered, the article described a physical response from volunteering, similar to the results of vigorous exercise or meditation. The strongest effect was seen when the act of altruism involved direct contact with other people.

For Ms. Walker, a former creative director for an advertising agency, most of the gifts involved time, emotional support or small acts of kindness. After the first 29 days, she began a new cycle, a pattern she continues. Neither she nor Mbali Creazzo, the spiritual adviser who taught her about the month of giving, knows why it is 29 days rather than 30 or 31 - it may have something to do with the lunar cycle, which is 29.5 days.

Ms. Walker says she now approaches daily giving as a crucial part of her treatment, just like regular medication. She has also found new purpose in her experience and started a Web site, 29gifts.org, that encourages giving to improve health.

"Giving for 29 days is not suggested as a cure for anything," Ms. Walker said. "It's simply a coping mechanism and a simple tool you can use that can help you change your thinking about whatever is going on. If you change your thinking, you change your experience."

Dr. Post, of Stony Brook, agreed. "To rid yourself of negative emotional states," he said, "you need to push them aside with positive emotional states.

"And the simplest way to do that is to just go out and lend a helping hand to somebody."

Loneliness can be contagious

People who feel lonely spread that feeling to others

Loneliness, like a bad cold, can spread among groups of people, research at the University of Chicago, the University of California-San Diego and Harvard shows.

Using longitudinal data from a large-scale study that has been following health conditions for more than 60 years, a team of scholars found that lonely people tend to share their loneliness with others. Gradually over time, a group of lonely, disconnected people moves to the fringes of social networks.

"We detected an extraordinary pattern of contagion that leads people to be moved to the edge of the social network when they become lonely," said University of Chicago psychologist John Cacioppo, one member of

the study team and one of the nation's leading scholars of loneliness. "On the periphery people have fewer friends, yet their loneliness leads them to losing the few ties they have left."

Other members of the study team were James Fowler, Associate Professor of Political Science at the University of California-San Diego, and Nicholas Christakis, Professor of Medicine and Professor of Medical Sociology in the Harvard Medical School.

Before relationships are severed, people on the periphery transmit feelings of loneliness to their remaining friends, who also become lonely. "These reinforcing effects mean that our social fabric can fray at the edges, like a yarn that comes loose at the end of a crocheted sweater," said Cacioppo, the Tiffany & Margaret Blake Distinguished Service Professor in Psychology.

Because loneliness is associated with a variety of mental and physical diseases that can shorten life, Cacioppo said it is important for people to recognize loneliness and help those people connect with their social group before the lonely individuals move to the edges. The scholars' findings were published in the article, "Alone in the Crowd: The Structure and Spread of Loneliness in a Large Social Network," published in the December issue of the Journal of Personality and Social Psychology.

For the study, the team examined records of the Framingham Heart Study, which has studied people in Framingham, Mass. since 1948. The original group, including more than 5,209 people, was originally studied for the risks of cardiovascular disease.

The study has since been expanded to include about 12,000 people, as the children and the grandchildren of the original group and others have been included to diversify the population sample. The Framingham study now includes more tests, including measures of loneliness and depression. The second generation in the study, which includes 5,124 people, was the focus of the loneliness research. Because the study is longitudinal, researchers kept in touch with the subjects every two to four years and accordingly collected names of friends who knew the subjects. Those records became an excellent source of information about the people's social networks.

By constructing graphs that charted the subjects' friendship histories and information about their reports of loneliness, researchers were able to establish a pattern of loneliness that spread as people reported fewer close friends. The data showed that lonely people "infected" the people around them with loneliness, and those people moved to the edges of social circles.

The team found that the next-door neighbors in the survey who experienced an increase of one day of loneliness a week prompted an increase in loneliness among their neighbors who were their close friends. The loneliness spread as the neighbors spent less time together.

Previous work suggested that women rely on emotional support more than men do, and in this study women were more likely than men to report "catching" loneliness from others. People's chances of becoming lonely were more likely to be caused by changes in friendship networks than changes in family networks.

Research also shows that as people become lonely, they become less trustful of others, and a cycle develops that makes it harder for them to form friendships. Societies seem to develop a natural tendency to shed these lonely people, something that is mirrored in tests of monkeys, who tend to drive off members of their groups who have been removed from a colony and then reintroduced, Cacioppo said.

That pattern makes it all the more important to recognize loneliness and deal with it before it spreads, he said. "Society may benefit by aggressively targeting the people in the periphery to help repair their social networks and to create a protective barrier against loneliness that can keep the whole network from unraveling," he said.

The research was supported by a grant from the National Institute on Aging.

"Previous research has shown that loneliness and lack of social connection can have a significant negative effect on the overall health and well-being of older people," said Richard Suzman, Ph.D., director of the NIA's Division of Behavioral and Social Research, which funded the research. "This pioneering research into the connections of individuals within their social networks has important implications for the larger issue of social interactions and health."

Doulas may indicate failings in patient care, warns doctor

Personal view: Encounters with a doula: is the system failing new mothers?

The presence of doulas (paid birth assistants) during labour may alter the doctor-patient dynamic and can compromise communication and therefore patient care, warns a doctor on bmj.com today.

Furthermore, the need for doulas implies a failing of medical and midwifery services and also the support provided by family and friends, says Dr Abhijoy Chakladar who was working at Worthing Hospital in West Sussex when he first encountered a doula.

He describes how his first encounter with a doula on the labour ward compromised his communication during an anaesthetic consultation and therefore compromised the care he delivered. "I found myself

disconcerted by the doula's presence as I was unfamiliar with her role," he says. "In retrospect, I should have confirmed everyone's roles and established ground rules acceptable to all involved on entering the situation."

Hired birthing partners are unregulated, not part of clinical obstetric teams, and therefore should not be involved in the making of clinical decisions. There is no nationally recognised certification for doulas and it is possible to work without training. The Nursing and Midwifery Council recognises doulas solely as emotional support for mothers and as unqualified persons they cannot substitute for registered midwives.

There are approximately 1000 doulas working in the UK offering packages including antenatal visits, labour, postnatal visits, and on-call periods, charging between £400 and £900. In 2005, there were an estimated 100,000 doula-supported births in the USA.

As the trend grows here, the author wonders whether the doula business is actually necessary or whether it is exploiting for profit unspoken fears over NHS perinatal care and the seemingly limitless market for birth-related products and services,

Dr Chakladar says he is disappointed by the real or perceived need for doulas. He believes that availability of this commercial service implies that current social structures do not support pregnant couples adequately and that healthcare professionals may not be able to support their patients as they would like to.

We May Be Born With an Urge to Help

By NICHOLAS WADE

What is the essence of human nature? Flawed, say many theologians. Vicious and addicted to warfare, wrote Hobbes. Selfish and in need of considerable improvement, think many parents.

But biologists are beginning to form a generally sunnier view of humankind. Their conclusions are derived in part from testing very young children, and partly from comparing human children with those of chimpanzees, hoping that the differences will point to what is distinctively human.

The somewhat surprising answer at which some biologists have arrived is that babies are innately sociable and helpful to others. Of course every animal must to some extent be selfish to survive. But the biologists also see in humans a natural willingness to help.

When infants 18 months old see an unrelated adult whose hands are full and who needs assistance opening a door or picking up a dropped clothespin, they will immediately help, Michael Tomasello writes in "Why We Cooperate," a book published in October. Dr. Tomasello, a developmental psychologist, is co-director of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany.

The helping behavior seems to be innate because it appears so early and before many parents start teaching children the rules of polite behavior.

"It's probably safe to assume that they haven't been explicitly and directly taught to do this," said Elizabeth Spelke, a developmental psychologist at Harvard. "On the other hand, they've had lots of opportunities to experience acts of helping by others. I think the jury is out on the innateness question."

But Dr. Tomasello finds the helping is not enhanced by rewards, suggesting that it is not influenced by training. It seems to occur across cultures that have different timetables for teaching social rules. And helping behavior can even be seen in infant chimpanzees under the right experimental conditions. For all these reasons, Dr. Tomasello concludes that helping is a natural inclination, not something imposed by parents or culture.

Infants will help with information, as well as in practical ways. From the age of 12 months they will point at objects that an adult pretends to have lost. Chimpanzees, by contrast, never point at things for each other, and when they point for people, it seems to be as a command to go fetch something rather than to share information.

For parents who may think their children somehow skipped the cooperative phase, Dr. Tomasello offers the reassuring advice that children are often more cooperative outside the home, which is why parents may be surprised to hear from a teacher or coach how nice their child is. "In families, the competitive element is in ascendancy," he said.

As children grow older, they become more selective in their helpfulness. Starting around age 3, they will share more generously with a child who was previously nice to them. Another behavior that emerges at the same age is a sense of social norms. "Most social norms are about being nice to other people," Dr. Tomasello said in an interview, "so children learn social norms because they want to be part of the group."

Children not only feel they should obey these rules themselves, but also that they should make others in the group do the same. Even 3-year-olds are willing to enforce social norms. If they are shown how to play a game, and a puppet then joins in with its own idea of the rules, the children will object, some of them vociferously.

Where do they get this idea of group rules, the sense of "we who do it this way"? Dr. Tomasello believes children develop what he calls "shared intentionality," a notion of what others expect to happen and hence a sense of a group "we." It is from this shared intentionality that children derive their sense of norms and of expecting others to obey them.

Shared intentionality, in Dr. Tomasello's view, is close to the essence of what distinguishes people from chimpanzees. A group of human children will use all kinds of words and gestures to form goals and coordinate activities, but young chimps seem to have little interest in what may be their companions' minds.

If children are naturally helpful and sociable, what system of child-rearing best takes advantage of this surprising propensity? Dr. Tomasello says that the approach known as inductive parenting works best because it reinforces the child's natural propensity to cooperate with others. Inductive parenting is simply communicating with children about the effect of their actions on others and emphasizing the logic of social cooperation.

"Children are altruistic by nature," he writes, and though they are also naturally selfish, all parents need do is try to tip the balance toward social behavior.

The shared intentionality lies at the basis of human society, Dr. Tomasello argues. From it flow ideas of norms, of punishing those who violate the norms and of shame and guilt for punishing oneself. Shared intentionality evolved very early in the human lineage, he believes, and its probable purpose was for cooperation in gathering food. Anthropologists report that when men cooperate in hunting, they can take down large game, which single hunters generally cannot do. Chimpanzees gather to hunt colobus monkeys, but Dr. Tomasello argues this is far less of a cooperative endeavor because the participants act on an ad hoc basis and do not really share their catch.

An interesting bodily reflection of humans' shared intentionality is the sclera, or whites, of the eyes. All 200 or so species of primates have dark eyes and a barely visible sclera. All, that is, except humans, whose sclera is three times as large, a feature that makes it much easier to follow the direction of someone else's gaze. Chimps will follow a person's gaze, but by looking at his head, even if his eyes are closed. Babies follow a person's eyes, even if the experimenter keeps his head still.

Advertising what one is looking at could be a risk. Dr. Tomasello argues that the behavior evolved "in cooperative social groups in which monitoring one another's focus was to everyone's benefit in completing joint tasks."

This could have happened at some point early in human evolution, when in order to survive, people were forced to cooperate in hunting game or gathering fruit. The path to obligatory cooperation - one that other primates did not take - led to social rules and their enforcement, to human altruism and to language.

"Humans putting their heads together in shared cooperative activities are thus the originators of human culture," Dr. Tomasello writes.

A similar conclusion has been reached independently by Hillard S. Kaplan, an anthropologist at the University of New Mexico. Modern humans have lived for most of their existence as hunter gatherers, so much of human nature has presumably been shaped for survival in such conditions. From study of existing hunter gatherer peoples, Dr. Kaplan has found evidence of cooperation woven into many levels of human activity.

The division of labor between men and women - men gather 68 percent of the calories in foraging societies - requires cooperation between the sexes. Young people in these societies consume more than they produce until age 20, which in turn requires cooperation between the generations. This long period of dependency was needed to develop the special skills required for the hunter gatherer way of life.

The structure of early human societies, including their "high levels of cooperation between kin and nonkin," was thus an adaptation to the "specialized foraging niche" of food resources that were too difficult for other primates to capture, Dr. Kaplan and colleagues wrote recently in The Philosophical Transactions of the Royal Society. We evolved to be nice to each other, in other words, because there was no alternative.

Much the same conclusion is reached by Frans de Waal in another book published in October, "The Age of Empathy." Dr. de Waal, a primatologist, has long studied the cooperative side of primate behavior and believes that aggression, which he has also studied, is often overrated as a human motivation.

"We're preprogrammed to reach out," Dr. de Waal writes. "Empathy is an automated response over which we have limited control." The only people emotionally immune to another's situation, he notes, are psychopaths.

Indeed, it is in our biological nature, not our political institutions, that we should put our trust, in his view. Our empathy is innate and cannot be changed or long suppressed. "In fact," Dr. de Waal writes, "I'd argue that biology constitutes our greatest hope. One can only shudder at the thought that the humaneness of our societies would depend on the whims of politics, culture or religion."

The basic sociability of human nature does not mean, of course, that people are nice to each other all the time. Social structure requires that things be done to maintain it, some of which involve negative attitudes toward others. The instinct for enforcing norms is powerful, as is the instinct for fairness. Experiments have shown that people will reject unfair distributions of money even it means they receive nothing.

"Humans clearly evolved the ability to detect inequities, control immediate desires, foresee the virtues of norm following and gain the personal, emotional rewards that come from seeing another punished," write three

Harvard biologists, Marc Hauser, Katherine McAuliffe and Peter R. Blake, in reviewing their experiments with tamarin monkeys and young children.

If people do bad things to others in their group, they can behave even worse to those outside it. Indeed the human capacity for cooperation "seems to have evolved mainly for interactions within the local group," Dr. Tomasello writes.

Sociality, the binding together of members of a group, is the first requirement of defense, since without it people will not put the group's interests ahead of their own or be willing to sacrifice their lives in battle. Lawrence H. Keeley, an anthropologist who has traced aggression among early peoples, writes in his book "War Before Civilization" that, "Warfare is ultimately not a denial of the human capacity for cooperation, but merely the most destructive expression of it."

The roots of human cooperation may lie in human aggression. We are selfish by nature, yet also follow rules requiring us to be nice to others.

"That's why we have moral dilemmas," Dr. Tomasello said, "because we are both selfish and altruistic at the same time."

Tumor-attacking virus strikes with 'one-two punch'

COLUMBUS, Ohio – Ohio State University cancer researchers have developed a tumor-attacking virus that both kills brain-tumor cells and blocks the growth of new tumor blood vessels.

Their research shows that viruses designed to kill cancer cells – oncolytic viruses – might be more effective against aggressive brain tumors if they also carry a gene for a protein that inhibits blood-vessel growth.

The protein, called vasculostatin, is normally produced in the brain. In this study, an oncolytic virus containing the gene for this protein in some cases eliminated human glioblastoma tumors growing in animals and significantly slowed tumor recurrence in others. Glioblastomas, which characteristically have a high number of blood vessels, are the most common and devastating form of human brain cancer. People diagnosed with these tumors survive less than 15 months on average after diagnosis.

"This is the first study to report the effects of vasculostatin delivery into established tumors, and it supports further development of this novel virus as a possible cancer treatment," says study leader Balveen Kaur, associate professor of neurological surgery and a researcher with the Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute. "Our findings suggest that this oncolytic virus is a safe and promising strategy to pursue for the treatment of human brain tumors.

"This study shows the potential of combining an oncolytic virus with a natural blood-vessel growth inhibitor such as vasculostatin. Future studies will reveal the potential for safety and efficacy when used in combination with chemotherapy and radiation therapy," she says. The findings were recently published online in the journal Molecular Therapy.

Jayson Hardcastle, a graduate student in Dr. Kaur's laboratory, injected the cancer-killing virus, called RAMBO (for Rapid Antiangiogenesis Mediated By Oncolytic virus), directly into human glioblastoma tumors growing either under the skin or in the brains of mice.

Of six animals with tumors under the skin, those treated with RAMBO survived an average of 54 days. In addition, three of the RAMBO mice were tumor-free at the end of the experiment. Control animals treated with a similar virus that lacked the vasculostatin gene, on the other hand, survived an average of 26 days and none were tumor-free.

Of the animals with a human glioblastoma in the brain, five were treated with RAMBO and lived an average of 54 days. One animal remained tumor-free for more than 120 days. Control animals, by comparison, lived an average of 26 days with no long-term survivors.

In another experiment, the investigators followed the course of tumor changes in animals with tumors in the brain. After an initial period of tumor shrinkage, the remaining cancer cells began regrowing around day 13 in animals given the virus that lacked the blood-vessel inhibitor. In animals treated with RAMBO, tumor regrowth didn't begin until about day 39.

"With additional research, this virus could lead to a new therapeutic strategy for combating cancer," Kaur says.

Homicide Rates Linked To Trust In Government, Sense Of Belonging, Study Suggests

COLUMBUS, Ohio – When Americans begin routinely complaining about how they hate their government and don't trust their leaders, it may be time to look warily at the homicide rate.

In researching the new book American Homicide (Harvard University Press, 2009), an Ohio State University historian tried to make sense of changing homicide rates by sifting through records of tens of thousands of homicides in the United States and western Europe over the past four centuries.

He concluded that people's views about the legitimacy of government and how much they identify with their fellow citizens play a major role in how often they kill each other – much more so than the usual theories revolving around guns, poverty, drugs, race, or a permissive justice system.

"The predisposition to murder is rooted in feelings and beliefs people have toward government and their fellow citizens," said Randolph Roth, author of the book and professor of history at Ohio State.

"It is these factors, which may seem impossibly remote from murder, that hold the key to understanding why the United States is so homicidal today."

While Roth said his theory may seem strange at first, it fits the evidence much better than all the other theories about what drives people to murder.

"You look at all the other theories, and they die a horrible death in the face of the evidence," he said.

That includes theories held dear by both conservatives and liberals. If you look at the evidence over time, poverty and unemployment don't lead to higher murder rates, as many liberals argue, he said. But locking up criminals, using the death penalty, and adding more police don't hold the murder rate down either, as conservatives claim.

At any one point in time, researchers may find an association between one of these causes and homicide rates in a particular area. But once you try to apply those theories more broadly, at different places and in different eras, the links disappear.

For example, during the Great Depression the homicide rate in the United States went down, even while poverty was increasing. In the 1960s, the United States had more police and more people in prison than nearly any other nation on earth, along with strong economic growth – and yet the murder rate skyrocketed.

"Criminologists make a case for one theory or another by going through records for a short period of time. But if they try the same theory in colonial America or the early 20th century, it won't fit. That's where it helps to have a historical perspective," Roth said.

In his analysis, Roth found four factors that relate to the homicide rate in parts of the United States and western Europe throughout the past four centuries: the belief that one's government is stable and its justice and legal systems are unbiased and effective; a feeling of trust in government officials and a belief in their legitimacy; a sense of patriotism and solidarity with fellow citizens; and a belief that one's position is society is satisfactory and that one can command respect without resorting to violence.

When those feelings and beliefs are strong, homicide rates are generally low, regardless of the time or place, Roth said. But when people are unsure about their government leaders, don't feel connected to the rest of society, and feel they don't have opportunity to command respect in the community, homicide rates go up.

This theory helps explain why the United States generally has had one of the highest murder rates since the mid-nineteenth century of any advanced Western democracy, Roth said.

"As Americans, so many of us hate or distrust our government. You can see it today in the anti-government rallies in Washington, D.C. and elsewhere. It's been part of our culture since the very beginning, but especially since the Civil War, and it is one reason why we have such a high homicide rate," he said.

Roth said the results of his analysis provide some warnings for the future. Data from early this year suggests the homicide rate in the United States fell during the first half of this year, which makes sense as the nation rallied around a new president who promised to help unite the country.

But events of recent months suggest the tide may be turning, and that we may soon return to the divisive, polarized politics that the candidates of both major parties tried to transcend in the recent presidential election, he said. Roth said his analysis applies to murder among unrelated adults. Domestic violence follows a different trajectory.

Many people wonder how seemingly remote and abstract feelings about the government can lead to murder, he said. "It has to do with trust. If I feel empowered, if I feel included in the community, if I feel like I matter to the people around me, if I feel the government will protect me and my family, I can go about my daily life with confidence. Small slights and disagreements don't bother me as much," he said.

"But if I feel powerless in society, if I feel like I can't get a fair shake from my government, and feel cut off from my neighbors, it affects how I live my life. Small disagreements and indignities that you may otherwise brush off as insignificant can enrage you, and can in some cases lead to violence and murder."

But how can researchers measure things like trust and belief in government a hundred or more years ago, when there weren't public opinion polls tracking how people felt?

As a historian, Roth said he has found many different indirect indictors that show how people felt about their political leaders and their fellow citizens. For example, Roth has found that one of the best predictors of increases and declines in America's homicide rate in the past was the percentage of new counties named for national heroes – an indirect measure of how Americans felt about their nation and one another.

The homicide rate was lowest in the 1820s and 1830s when the proportion of new counties named for American heroes reached its peaked. When the proportion of new counties named for national heroes plummeted, as it did during the sectional crisis that tore apart the North and South, homicide rates increased dramatically. "When Americans stopped identifying with each other through national heroes, they killed each other more often," Roth said.

While measuring trust in government and fellow citizens provides one challenge for historians, the other is figuring out homicide rates before the advent of national crime statistics.

To do this, Roth created the Historical Violence Database, housed at Ohio State, which allows researchers to examine data from many studies of homicides from a variety of time periods and places. This database now includes information on tens of thousands of homicides in different areas of the United States and western Europe from medieval times to the present.

The database includes detailed studies of homicides in places as different as New York City, Holmes County, Ohio, and regions in the far West and Deep South.

"We have been able to test theories in a lot of places at a lot of different time periods," he said.

The lesson he takes away from the research, Roth said, is that the best way to reduce homicide rates has nothing to do with guns, or police, or courts or even economics.

"Political leadership has the greatest opportunity to have a real impact on homicide rates," he said. "It is difficult, I know, but we need a leader who can unite the country around some values and beliefs that we can all accept. That said, leadership can be effective only if the conflicts within a society are manageable. When they become unmanageable, as they did during the Civil War, even a great leader like Abraham Lincoln can't pull the nation together and keep homicide in check."

News Release : In CO2-rich Environment, Some Ocean Dwellers Increase Shell Production

In a striking finding that raises new questions about carbon dioxide's (CO2) impact on marine life, Woods Hole Oceanographic Institution (WHOI) scientists report that some shell-building creatures - such as crabs, shrimp and lobsters - unexpectedly build more shell when exposed to ocean acidification caused by elevated levels of atmospheric carbon dioxide (CO2).

Because excess CO2 dissolves in the ocean - causing it to "acidify" - researchers have been concerned about the ability of certain organisms to maintain the strength of their shells. Carbon dioxide is known to trigger a process that reduces the abundance of carbonate ions in seawater - one of the primary materials that marine organisms use to build their calcium carbonate shells and skeletons.

The concern is that this process will trigger a weakening and decline in the shells of some species and, in the long term, upset the balance of the ocean ecosystem.

But in a study published in the Dec. 1 issue of Geology, a team led by former WHOI postdoctoral researcher Justin B. Ries found that seven of the 18 shelled species they observed actually built more shell when exposed to varying levels of increased acidification. This may be because the total amount of dissolved inorganic carbon available to them is actually increased when the ocean becomes more acidic, even though the concentration of carbonate ions is decreased.

"Most likely the organisms that responded positively were somehow able to manipulate…dissolved inorganic carbon in the fluid from which they precipitated their skeleton in a way that was beneficial to them," said Ries, now an assistant professor in marine sciences at the University of North Carolina. "They were somehow able to manipulate CO2…to build their skeletons."

Organisms displaying such improvement also included calcifying red and green algae, limpets and temperate urchins. Mussels showed no effect.

The conch shell at left was exposed to current CO2 levels; the shell at right was exposed to the highest levels in the study. **(Tom Kleindinst, Woods Hole Oceanographic Institution)**

"We were surprised that some organisms didn't behave in the way we expected under elevated CO2," said Anne L. Cohen, a research specialist at WHOI and one of the study's co-authors. "What was really interesting was that some of the creatures, the coral, the hard clam and the lobster, for example, didn't seem to care about CO2 until it was higher than about 1,000 parts per million [ppm]." Current atmospheric CO2 levels are about 380 ppm, she said. Above this level, calcification was reduced in the coral and the hard clam, but elevated in the lobster

The “take-home message, “ says Cohen, is that “we can’t assume that elevated CO2 causes a proportionate decline in calcification of all calcifying organisms.” WHOI and the National Science Foundation funded the work.

Conversely, some organisms - such as the soft clam and the oyster - showed a clear reduction in calcification in proportion to increases in CO2. In the most extreme finding, Ries, Cohen and WHOI Associate Scientist Daniel C. McCorkle exposed creatures to CO2 levels more than seven times the current level.

This led to the dissolving of aragonite - the form of calcium carbonate produced by corals and some other marine calcifiers. Under such exposure, hard and soft clams, conchs, periwinkles, whelks and tropical urchins began to lose their shells. “If this dissolution process continued for sufficient time, then these organisms could lose their shell completely,” Ries said, “rendering them defenseless to predators.”

“Some organisms were very sensitive,” Cohen said, “some that have commercial value. But there were a couple that didn’t respond to CO2 or didn’t respond till it was sky-high - about 2,800 parts per million. We’re not expecting to see that [CO2 level] anytime soon.”

The researchers caution, however, that the findings - and acidification’s overall impact - may be more complex than it appears. For example, Cohen says that available food and nutrients such as nitrates, phosphates and iron may help dictate how some organisms respond to carbon dioxide.

“We know that nutrients can be very important,” she says. “We have found that corals for example, that have plenty of food and nutrients can be less sensitive” to CO2. “In this study, the organisms were well fed and we didn’t constrain the nutrient levels. I wouldn’t make any predictions based on these results. What these results indicate to us is that the organism response to elevated CO2 levels is complex and we now need to go back and study each organism in detail.”

Ries concurs that any possible ramifications are complex. For example, the crab exhibited improved shell-building capacity, and its prey, the clams, showed reduced calcification. “This may initially suggest that crabs could benefit from this shift in predator-pray dynamics. But without shells, clams may not be able to sustain their populations, and this could ultimately impact crabs in a negative way, as well,” Ries said.

The larger of these two pencil urchins was exposed to currrent CO2 levels; the smaller was exposed to the highest CO2 levels in the study. **(Tom Kleindinst, Woods Hole Oceanographic Institution)**

In addition, Cohen adds, even though some organisms such as crabs and lobsters appear to benefit under elevated CO2 conditions, the energy they expend in shell building under these conditions “might divert from other important processes such as reproduction or tissue building.”

Since the industrial revolution, Ries noted, atmospheric carbon dioxide levels have increased from 280 to nearly 400 ppm. Climate models predict levels of 600 ppm in 100 years, and 900 ppm in 200 years.

“The oceans absorb much of the CO2 that we release to the atmosphere,” Ries says. However, he warns that this natural buffer may ultimately come at a great cost.

“It’s hard to predict the overall net effect on benthic marine ecosystems," he says. “In the short term, I would guess that the net effect will be negative. In the long term, ecosystems could re-stabilize at a new steady state. “The bottom line is that we really need to bring down CO2 levels in the atmosphere.”

Antarctica served as climatic refuge in Earth's greatest extinction event

The largest known mass extinction in Earth's history, about 252 million years ago at the end of the Permian Period, may have been caused by global warming. A new fossil species suggests that some land animals may have survived the end-Permian extinction by living in cooler climates in Antarctica. Jörg Fröbisch and Kenneth D. Angielczyk of The Field Museum together with Christian A. Sidor from the University of Washington have identified a distant relative of mammals, Kombuisia antarctica, that apparently survived the mass extinction by living in Antarctica.

The new species belongs to a larger group of extinct mammal relatives, called anomodonts, which were widespread and represented the dominant plant eaters of their time. "Members of the group burrowed in the ground, walked the surface and lived in trees," said Fröbisch, the lead author of the study. "However, Kombuisia antarctica, about the size of a small house cat, was considerably different from today's mammals - it likely laid eggs, didn't nurse its young and didn't have fur, and it is uncertain whether it was warm blooded," said Angielczyk, Assistant Curator of Paleomammology at The Field Museum. Kombuisia antarctica was not a direct ancestor of living mammals, but it was among the few lineages of animals that survived at a time when a majority of life forms perished.

Scientists are still debating what caused the end-Permian extinction, but it was likely associated with massive volcanic activity in Siberia that could have triggered global warming. When it served as refuge,

Antarctica was located some distance north of its present location, was warmer and wasn't covered with permanent glaciers, said the researchers. The refuge of Kombuisia in Antarctica probably wasn't the result of a seasonal migration but rather a longer-term change that saw the animal's habitat shift southward. Fossil evidence suggests that small and medium sized animals were more successful at surviving the mass extinction than larger animals. They may have engaged in "sleep-or-hide" behaviors like hibernation, torpor and burrowing to survive in a difficult environment.

Earlier work by Fröbisch predicted that animals like Kombuisia antarctica should have existed at this time, based on fossils found in South Africa later in the Triassic Period that were relatives of the animals that lived in Antarctica. "The new discovery fills a gap in the fossil record and contributes to a better understanding of vertebrate survival during the end-Permian mass extinction from a geographic as well as an ecological point of view," Fröbisch said.

The team found the fossils of the new species among specimens collected more than three decades ago from Antarctica that are part of a collection at the American Museum of Natural History. "At the time those fossils were collected, paleontologists working in Antarctica focused on seeking evidence for the existence of a supercontinent, Pangaea, that later split apart to become separate land masses," said Angielczyk. The fossils collected in Antarctica provided some of the first evidence of Pangaea's existence, and further analysis of the fossils can refine our understanding of events that unfolded 250 million years ago.

"Finding fossils in the current harsh conditions of Antarctica is difficult, but worthwhile," said Angielczyk. "The recent establishment of the Robert A. Pritzker Center for Meteoritics and Polar Studies at The Field Museum recognizes the growing importance of the region," he said.

This research is part of a collaborative study of Dr. Jörg Fröbisch (Department of Geology, Field Museum, Chicago), Dr. Kenneth D. Angielczyk (Department of Geology, Field Museum, Chicago), and Dr. Christian A. Sidor (Burke Museum and Department of Biology, University of Washington), which will be published online December 3, 2009 in Naturwissenschaften. Funding for this research was provided through a Postdoctoral Research Fellowship of the German Research Foundation (Deutsche Forschungsgemeinschaft) to J. Fröbisch and grants of the National Science Foundation to C. A. Sidor.

Balancing protein intake, not cutting calories, may be key to long life

Getting the correct balance of proteins in our diet may be more important for healthy ageing than reducing calories, new research funded by the Wellcome Trust and Research into Ageing suggests.

The research may help explain why 'dietary restriction' (also known as calorie restriction) – reducing food intake whilst maintaining sufficient quantities of vitamins, minerals and other important nutrients – appears to have health benefits. In many organisms, such as the fruit fly (Drosophila), mice, rats and the Rhesus monkey, these benefits include living longer. Evidence suggests that dietary restriction can have health benefits for humans, too, though it is unclear whether it can increase longevity.

Dietary restriction can have a potentially negative side effect, however: diminished fertility. For example, the female fruit fly reproduces less frequently on a low calorie diet and its litter size is reduced, though its reproductive span lasts longer. This is believed to be an evolutionary trait: in times of famine, essential nutrients are diverted away from reproduction and towards survival.

To understand whether the health benefits of dietary restriction stem from a reduction in specific nutrients or in calorie intake in general, researchers at the Institute of Healthy Ageing, UCL (University College London), measured the effects of manipulating the diet of female fruit flies. The results of the study are published today in the journal Nature.

The fruit flies were fed a diet of yeast, sugar and water, but with differing amounts of key nutrients, such as vitamins, lipids and amino acids. The researchers found that varying the amount of amino acids in the mixture affected lifespan and fertility; varying the amount of the other nutrients had little or no effect.

In fact, when the researchers studied the effect further, they found that levels of a particular amino acid known as methionine were crucial to maximising lifespan without decreasing fertility. Adding methionine to a low calorie diet boosted fertility without reducing lifespan; likewise, reducing methionine content in a high calorie diet prolonged lifespan. Previous studies have also shown that reducing the intake of methionine in rodents can help extend lifespan.

"By carefully manipulating the balance of amino acids in the diet, we have been able to maximise both lifespan and fertility," explains Dr Matthew Piper, one of the study authors. "This indicates that it is possible to extend lifespan without wholesale dietary restriction and without the unfortunate consequence of lowering reproductive capacity."

Amino acids are the building blocks of life as they form the basis of proteins. Methionine is one of the most important amino acids at it is essential to the formation of all proteins. Whilst proteins are formed naturally in the body, we also consume proteins from many different food types, including meat and dairy products, soy-

derived food such as tofu, and pulses. The relative abundance of methionine differs depending on the food type in question; it occurs in naturally high levels in foods such as sesame seeds, Brazil nuts, wheat germ, fish and meats.

"In the past, we have tended to think that the amount of protein is what is important to our diet," says Dr Piper. "We've shown here that in flies – and this is likely to be the case for other organisms – the balance of amino acids in the diet can affect health later in life. If this is the case for humans, then the type of protein will be more important.

"It's not as simple as saying 'eat less nuts' or 'eat more nuts' to live longer – it's about getting the protein balance right, a factor that might be particularly important for high protein diets, such as the Atkins diet or body builders' protein supplements."

Because the effects of dietary restriction on lifespan appears to be evolutionarily conserved – occurring in organisms from yeast to monkeys – scientists believe that the mechanisms may also be conserved. This opens up the possibility of using these organisms as models to study how dietary restriction works.

Although the human genome has around four times the number of genes as the fruit fly genome, there is a close relationship between many of these genes. Since it is easy to create mutants and carry out experiments on fruit flies, the functions of many fly genes have been established and newly discovered human genes can often be matched against their fly counterparts. Therefore, even though the fruit fly does not on the surface resemble humans, many findings about its basic biology can be interpreted for human biology.

Treatments for asthma and pre-term labor may increase risk of autism in developing fetus

New York, NY - Commonly prescribed beta 2 adrenergic agonist drugs for the treatment of asthma in pregnant women as well as pre-term labor may increase the incidence of autism-spectrum disorders, psychiatric pathology, cognitive problems and poor school performance in their children, according to a new study published in the December 2009 issue of the American Journal of Obstetrics & Gynecology.

Beta 2 adrenergic agonist drugs as a class are widely used in obstetrics as tocolytics to inhibit or slow down labor and bronchodilators, but may act as functional and behavioral teratogens when given continuously in the mid to late second or early third trimesters. By correlating the basic science and clinical data, investigators observed that when given prenatally, these drugs can cause functional and behavioral disorders by permanently altering the balance of sympathetic and parasympathetic tone in the individual. Animal studies support the concept that in humans prenatal exposure to continuous high doses of beta 2 adrenergic agonists can permanently dysregulate signaling from the beta 2 adrenergic receptor.

Researchers show how sympathetic overactivity and disease are correlated, citing studies that show the association between in utero exposure to beta 2 adrenergic agonists in humans and later development of these conditions. The authors also offer recommendations for safe practice in obstetrics in light of the teratogenic risk posed by beta 2 adrenergic agonists.

Writing in the article, Frank R. Witter, MD, , Johns Hopkins University School of Medicine and Johns Hopkins University Bloomberg School of Public Health, and co-authors state, "Given the risk of long-term neurophysiologic and behavioral impairment, the use of beta 2 adrenergic agonists should be limited to proven indications when alternate drugs are ineffective or unavailable and the risks of the untreated disease to the mother and fetus are greater than the risk of the beta 2 adrenergic agonist. Treatment duration should be as short as clinically feasible. Further ongoing surveillance of the use of these agents in pregnancy is needed to refine the parameters for their safe use in pregnancy. Future pharmacogenetics research is also needed to better characterize the highest risk group for teratogenesis from these agents."

Echoing the concerns, Roberto Romero, MD, Chief, Perinatology Research Branch, Program Director for Obstetrics and Perinatology, Intramural Division, NICHD, NIH, DHHS and Associate Editor of the American Journal of Obstetrics & Gynecology, states that "The observations reviewed by the authors call for a re-examination of the commonly accepted safety of these agents during pregnancy."

The article is "In Utero Beta 2 Adrenergic Agonist Exposure and Adverse Neurophysiologic and Behavioral Outcomes" by Frank R. Witter, MD, Andrew W. Zimmerman, MD, James P. Reichmann, MBA, and Susan L. Connors, MD. It appears in American Journal of Obstetrics & Gynecology, Volume 201, Issue 6 (December 2009) published by Elsevier.

Autism and schizophrenia could be genetic opposites

* 11:33 02 December 2009 **by Bob Holmes**

Autism and schizophrenia may be two sides of the same coin, suggests a review of genetic data associated with the conditions. The finding could help design complementary treatments for the two disorders.

Though autism was originally described as a form of schizophrenia a century ago, evidence for a link has remained equivocal. One theory puts the conditions at opposite ends of a developmental spectrum.

To investigate, Bernard Crespi, an evolutionary biologist at Simon Fraser University in Vancouver, Canada, and colleagues gathered data on all known genetic variants associated with each condition, then looked for patterns of co-occurrence.

The researchers found four regions in the genome which dramatically affect the risk of autism or schizophrenia. Called "copy-number variants", these are stretches of DNA with seemingly accidental duplications or deletions. Crespi's team found that the presence of a particular variant – a duplication, say – was often associated with autism while the opposite variation – a deletion of the genetic material – was linked to schizophrenia.

The results fit with other evidence that autism may be caused by overdevelopment of specific brain regions and schizophrenia by underdevelopment, says Crespi.

If they are indeed opposites, work on one disorder may inform work on its counterpart, he says.

Journal reference: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.0906080106

Chances of surviving cardiac arrest at home or work unchanged in 30 years

Analysis shows getting a pulse back at the scene is the best predictor of survival

ANN ARBOR, Mich. – The chance of surviving an out-of-hospital cardiac arrest has not improved since the 1950s, according to a report by the University of Michigan Health System.

The analysis shows only 7.6 percent of victims survive an out-of-hospital cardiac arrest, a number that has not changed significantly in almost 30 years. It's a dismal trend considering enormous spending on heart research, new emergency care protocols, and the advent of new drugs and devices such as defibrillators.

Each year, 166,000 people experience cardiac arrest – an event during which the heart stops beating – away from a hospital.

Physicians report in the current issue of Circulation: Cardiovascular Quality and Outcomes that there are some key factors that can make a difference in saving lives when cardiac arrest happens at home, a hotel, restaurant or workplace.

"Our study shows that patients with a heart rhythm that can be shocked, or who have bystander CPR or a pulse restored at the scene have a much greater chance of survival," says lead author Comilla Sasson, M.D., a Robert Wood Johnson Scholar and emergency medicine physician at the U-M Health System.

Although half of cardiac arrests are witnessed by a bystander, according to the study, only 32 percent, or about 1 in every 3 people, is receiving bystander CPR.

This is the first study that looks at the associations between five clinical variables and overall survival from an out-of-hospital cardiac arrest. The variables studied include: witnessed by emergency medical services provider, bystander CPR, types of heart rhythm - asystole (motionless) vs. ventricular fibrillation (rapid or twitching) and return of spontaneous circulation.

Researchers evaluated data on 142,740 patients from 79 studies published internationally between January 1950 and August 2008. Here's what researchers found:

* Of the more than 140,000 patients, only 23.8 percent survived to hospital admission, and 7.6 percent, or about 1 in 10 people, lived to be discharged from the hospital.

* Cardiac arrest victims who received CPR from a bystander or an emergency medical services provider, and those who had a shockable heart rhythm, referred to as ventricular fibrillation, were more likely to survive.

* The strongest predictor of survival was a return of spontaneous circulation, meaning a pulse was restored at the scene. Among them, 15.5 percent (in low-performing EMS systems) to 33.6 percent (in high performing EMS systems) survived.

"Increasing bystander CPR rates, increasing the awareness and use of devices to shock the heart, and keeping paramedics on scene until they restore a person's pulse needs to occur if we are ever going to change our dismal survival rate," Sasson says.

Places like Seattle, which has the highest rates of cardiac arrest survival in the country, are doing these three basic things exceptionally well, says the U-M physician. "We can learn a lot from that emergency response system," she says.

The lack of progress in survival across the U.S. and abroad may be linked to an aging population, a lower number of people who are found in a shockable rhythm, which is associated with the highest chance of survival, and longer EMS drives due to the increasing size of cities and traffic congestion, authors write.

While the overall rate of out-of-hospital cardiac arrest survival has not improved, the field of cardiac and cerebral resuscitation is rapidly evolving.

Most of the studies in the analysis were conducted before the advent of therapeutic hypothermia, a body cooling treatment that has shown to benefit resuscitated patients. U-M C.S. Mott Children's Hospital is leading a clinical trial to evaluate therapeutic hypothermia to prevent brain damage in children who have cardiac arrest.

Studies did not distinguish between patients treated with traditional CPR and those cared for under new American Heart Association guidelines for CPR which emphasizes chest compressions over mouth-to-mouth resuscitation.

Additional authors: *Mary A.M. Rogers, Ph.D., University of Michigan Department of Internal Medicine; Jason Dahl, M.D., University of Rochester, Rochester, N.Y. and Arthur L. Kellerman, M.D., MPH, Emory University, Atlanta, Ga.*
Funding:*Robert Wood Johnson Foundation* ***Reference:****Circulation: Cardiovascular Quality and Outcomes, Vol. CQ-3, Issue 1.*

Suzaku spies treasure trove of intergalactic metal

Every cook knows the ingredients for making bread: flour, water, yeast, and time. But what chemical elements are in the recipe of our universe? Most of the ingredients are hydrogen and helium. These cosmic lightweights fill the first two spots on the famous periodic table of the elements.

Less abundant but more familiar to us are the heavier elements, meaning everything listed on the periodic table after hydrogen and helium. These building blocks, such as iron and other metals, can be found in many of the objects in our daily lives, from teddy bears to teapots.

Recently astronomers used the Suzaku orbiting X-ray observatory, operated jointly by NASA and the Japanese space agency, to discover the largest known reservoir of rare metals in the universe.

Suzaku detected the elements chromium and manganese while observing the central region of the Perseus galaxy cluster. The metallic atoms are part of the hot gas, or "intergalactic medium," that lies between galaxies.

"This is the first detection of chromium and manganese from a cluster," says Takayuki Tamura, an astrophysicist at the Japan Aerospace Exploration Agency who led the Perseus study. "Previously, these metals were detected only from stars in the Milky Way or from other galaxies. This is the first detection in intergalactic space."

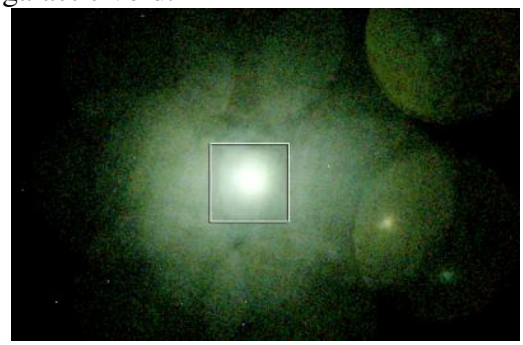
The cluster gas is extremely hot, so it emits X-ray energy. Suzaku's instruments split the X-ray energy into its component wavelengths, or spectrum. The spectrum is a chemical fingerprint of the types and amounts of different elements in the gas. The portion of the cluster within Suzaku's field of view is some 1.4 million light-years across, or roughly one-fifth of the cluster's total width. It contains a staggering amount of metal atoms. The chromium is 30 million times the sun's mass, or 10 trillion times Earth's mass. The manganese reservoir weighs in at about 8 million solar masses.

Exploding stars, or supernovas, forge the heavy elements. The supernovas also create vast outflows, called superwinds. These galactic gusts transport heavy elements into the intergalactic void.

Harvesting the riches of the Perseus Cluster is not possible. But researchers will mine the Suzaku X-ray data for scientific insights.

"By measuring metal abundances, we can understand the chemical history of stars in galaxies, such as the numbers and types of stars that formed and exploded in the past," Tamura says.

The Suzaku study data show it took some 3 billion supernovas to produce the measured amounts of chromium and manganese. And over periods up to billions of years, superwinds carried the metals out of the cluster galaxies and deposited them in intergalactic space.



This image from the Japanese Advanced Satellite for Cosmology and Astrophysics shows the X-ray glow of the 100-million-degree Fahrenheit gas that fills the Perseus cluster. The white box indicates the area explored by the Suzaku X-ray telescope to detect chromium and manganese. The image is about two degrees wide, or four times the apparent width of a full moon. **JAXA**

A complete history of the universe should include an understanding of how, when, and where the heavy elements formed -- the chemical elements essential to life itself. The Suzaku study contributes to a larger ongoing effort to take a chemical census of the cosmos. "It's a part of learning the entire history of chemical element formation in the universe," notes Koji Mukai, who heads the Suzaku Guest Observer program at NASA's Goddard Space Flight Center in Greenbelt, Md.

With more than 10,000 galaxy clusters known, astronomers have just barely begun their work. "The current Suzaku result cannot answer these big questions immediately," Tamura says, "but it is one of the first steps to understand the chemical history of the universe."

The study appeared in the November 1 issue of The Astrophysical Journal Letters

Music and speech based on human biology

DURHAM, N.C. – A pair of studies by Duke University neuroscientists shows powerful new evidence of a deep biological link between human music and speech.

The two new studies found that the musical scales most commonly used over the centuries are those that come closest to mimicking the physics of the human voice, and that we understand emotions expressed through

music because the music mimics the way emotions are expressed in speech. Composers have long exploited the perception of minor chord music as sad and major chord music as happy, now the Duke team thinks they know why.

In a paper appearing in the Journal of the Acoustical Society of America (JASA), the Duke team, led by Dale Purves, a professor of neurobiology, found that sad or happy speech can be categorized in major and minor intervals, just as music can. So your mother was right: It's not only the words you say, but how you say them.

In a second paper appearing Dec. 3 in the online journal PLOS One, Kamraan Gill, another member of the team, found the most commonly used musical scales are also based on the physics of the vocal tones humans produce.

"There is a strong biological basis to the aesthetics of sound," Purves said. "Humans prefer tone combinations that are similar to those found in speech."

This evidence suggests the main biological reason we appreciate music is because it mimics speech, which has been critical to our evolutionary success, said Purves, who is also director of Duke's Neuroscience and Behavioral Disorders Program and executive director of the A*STaR Neuroscience Research Partnership at the Duke-NUS Graduate Medical School in Singapore.

To study the emotional content of music, the Duke team collected a database of major and minor melodies from about 1,000 classical music compositions and more that 6,000 folk songs and then analyzed their tonal qualities.

They also had 10 people speak a series of single words with 10 different vowel sounds in either excited or subdued voices, as well as short monologues.

The team then compared the tones that distinguished the major and minor melodies with the tones of speech uttered in the different emotional states. They found the sound spectra of the speech tones could be sorted the same way as the music, with excited speech exhibiting more major musical intervals and subdued speech more minor ones. The tones in speech are a series of harmonic frequencies, whose relative power distinguishes the different vowels. Vowels are produced by the physics of air moving through the vocal cords; consonants are produced by other parts of the vocal tract.

In the PLOS One paper, the researchers argue the harmonic structure of vowel tones forms the basis of the musical scales we find most appealing. They show the popularity of musical scales can be predicted based on how well they match up with the series of harmonics characteristic of vowels in speech.

Although there are literally millions of scales that could be used to divide the octave, most human music is based on scales comprised of only five to seven tones. The researchers argue the preference for these particular tone collections is based on how closely they approximate the harmonic series of tones produced by humans. Though they only worked with western music and spoken English, there is reason to believe these findings are more widely applicable. Most of the frequency ratios of the chromatic musical scale can be found in the speech of a variety of languages. Their analysis included speakers of Mandarin Chinese, said Duke neuroscience graduate student Daniel Bowling, who is the first author on the JASA paper, and this showed similar results.

"Our appreciation of music is a happy byproduct of the biological advantages of speech and our need to understand its emotional content," Purves said.

It would be hard to say whether singing or speech came first, but graduate student Dan Bowling supposes "emotional communication in both speech and music is rooted in earlier non-lingual vocalizations that expressed emotion."

"In Search of Music's Biological Roots" Duke Magazine - http://www.dukemagazine.duke.edu/issues/050608/music1.html

Hawaiian hot spot has deep roots

Washington, D.C.—Hawaii may be paradise for vacationers, but for geologists it has long been a puzzle. Plate tectonic theory readily explains the existence of volcanoes at boundaries where plates split apart or collide, but mid-plate volcanoes such as those that built the Hawaiian island chain have been harder to fit into the theory. A classic explanation, proposed nearly 40 years ago, has been that magma is supplied to the volcanoes from upwellings of hot rock, called mantle "plumes," that originate deep in the Earth's mantle. Evidence for these deep structures has been sketchy, however. Now, a sophisticated array of seismometers deployed on the sea floor around Hawaii has provided the first high-resolution seismic images of a mantle plume extending to depths of at least 1,500 kilometers (932 miles).

This unprecedented glimpse of the roots of the Hawaiian "hot spot" is the product of an ambitious project known as PLUME, for Plume-Lithosphere Undersea Melt Experiment, which collected and analyzed two years of data from sea floor and land-based seismometers.

"One of the reasons it has taken so long to create these kinds of images is because many of the major hot spots are located in the middle of the oceans, where it has been difficult to put seismic instruments," says study co-author Sean Solomon, director of the Carnegie Institution's Department of Terrestrial Magnetism. "The Hawaiian region is also distant from most of the earthquake zones that are the sources of the seismic waves that

are used to create the images. Hawaii has been the archetype of a volcanic hotspot, and yet the deep structure of Hawaii has remained poorly resolved. For this study we were able to take advantage of a new generation of long-lived broad band seismic instruments that could be set out on the seafloor for periods of a year at a time."

The PLUME seismic images show a seismic anomaly beneath the island of Hawaii, the chain's largest and most volcanically active island. Critics of the plume model have argued that the magma in hot spot volcanoes comes from relatively shallow depths in the upper mantle (less than 660 kilometers), not deep plumes, but the anomaly observed by the PLUME researchers extends to at least 1,500 kilometers. Rock within the anomaly is also calculated to be significantly hotter than its surroundings, as predicted by the plume model.

"This has really been an eye-opener," says Solomon. "It shows us that the anomalies do extend well into the lower mantle of the Earth."

Erik Hauri, also of Carnegie's Department of Terrestrial Magnetism, led the geochemical component of the research. "We had suspected from geochemistry that the center of the plume would be beneath the main island, and that turns out to be about where the hot spot is centered," he says. "We also predicted that its width would be comparable to the size of island of Hawaii and that also turned out to be true. But those predictions were merely theoretical. Now, for the first time, we can really see the plume conduit."

Has the question of hot spots and mantle plumes been settled at last? "We believe that we have very strong evidence that Hawaii is underlain by a plume that extends at least to 1,500 kilometers depth," says Solomon. "It may well extend deeper, we can't say on the basis of our data, but that is addressable with global datasets, now that our data have been analyzed. So it's a very strong vote in favor of the plume model."

The lead author of the study, published in the December 4, 2009 issue of Science, is Cecily Wolfe, a former Carnegie Fellow at the Carnegie Institution's Department of Terrestrial Magnetism now at the University of Hawaii at Manoa. Other authors are S.C. Solomon and E.H. Hauri, Carnegie Institution for Science; G. Laske and J.A. Orcutt, Scripps Institution of Oceanography; J. A. Collins and R.S. Detrick, Woods Hole Oceanographic Institution; and D. Bercovici, Yale University. The PLUME project is supported by the National Science Foundation.

December 3, 2009 10:36 AM

Reform movement for English libel law gathers momentum

Roger Highfield, editor, New Scientist magazine

Calls for reform of the draconian libel laws in force in England and Wales have finally caught the ears of those in high places.

The formation of British justice secretary Jack Straw's working group on libel reform has been announced in the House of Lords, in the wake of his earlier statements about the "unbalanced" laws on defamation and slander. There is also an imminent report on privacy, press standards and libel from the House of Commons select committee on culture, media and sport.

Science journalists and academics are among those who have complained vociferously about the current libel laws in England and Wales, with the case of bestselling science writer and broadcaster Simon Singh becoming a cause célèbre for the libel reform movement.

A 2008 article written by Singh for British newspaper The Guardian included critical observations of the effectiveness of chiropractic and the evidence for the effectiveness of its treatments. A writ from the British Chiropractic Association soon followed, with the BCA alleging that Singh had impugned its reputation.

Singh decided to defend the action but lost the preliminary hearing when David Eady, the country's leading libel judge, ruled in favour of the BCA. Singh has had to find £100,000 to fund his defence - but has recently been granted leave to appeal by John Laws, a lord justice of appeal.

If Straw makes good on his promises, future defendants may face much smaller bills and a more robust public-interest defence. So what does Singh make of Straw's announcement? "It's significant that there are now positive noises being made at the highest level," he told me. "But now is not the time to back off and assume that it is merely a matter of time before change occurs.

"The campaign for libel reform will be moving up a gear in December in order to further galvanise public support and to make the issue of libel a priority for politicians. It is critical that scientists and everybody else who cares about the robust and fair discussion of ideas continues to back the campaign for libel reform."

Against this backdrop, Index on Censorship, the anti-censorship organisation, and English Pen, a group that backs persecuted writers, have jointly issued a report that makes a number of proposals on reform.

These include capping costs and damages, shifting the burden of proof to the complainant, expanding the notion of the public-interest defence and ensuring that no case should be heard in the UK unless at least 10 per cent of copies of the relevant publication have been circulated here. You can read more at libelreform.org.

Government whip Denis Tunnicliffe said the House of Lords libel reform working group would consider these recommendations, explaining that "the government are indeed concerned about 'libel tourism'" - the

phenomenon whereby actions relating to a publication that originated outside England and Wales are brought in London, where the legal environment is perceived as friendlier to plaintiffs than in US or Europe.

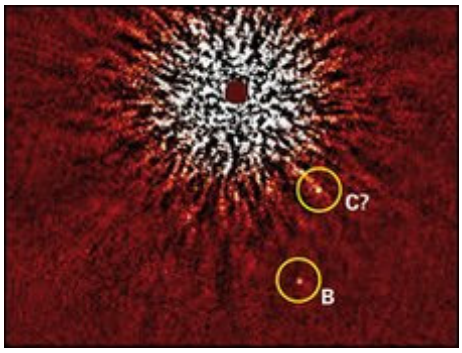
But speaking at a legal conference, Eady said that judges "in the front line" only knew of libel tourists from what they "read in the papers". "It is not a phenomenon that we actually come across in our daily lives," he said.

His comments represent a challenge to Straw and underline how a change to the law will only come if campaigners maintain the momentum for reform during the forthcoming British general election and beyond.

Cool find in hunt for exoplanets

By Jason Palmer Science and technology reporter, BBC News

Astronomers have published an image of the coolest planet outside our solar system that has been pictured directly. The new find is more similar to our own Solar System than prior pictured exoplanets, in terms of the parent star's type and the planet's size. However, the surface temperature is a scorching 280-370C, and could still prove to be a brown dwarf star. The results, published in Astrophysical Journal, were obtained by a new camera on the Subaru telescope in Hawaii.



The planet, called GJ758B, may well have a sister, GJ758C

Among more than 400 known exoplanets, only 10 have been imaged directly, rather than detecting them via measurements of their parent stars' light or movement. The task is notoriously difficult, akin to discerning a match next to a floodlight at a distance of kilometres.

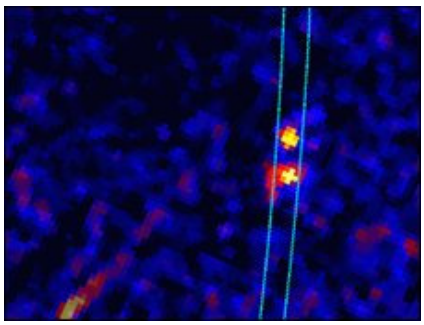
One good turn

The new HiCIAO camera makes it possible to spot exoplanets next to their parent stars through a process called angular differential imaging. In this approach, successive pictures are taken when a target star is directly overhead in the sky and possible exoplanets appear to rotate around it; any specks of light due to the measurement stay put and can be subtracted.

In two observations in May and August, an international team of researchers led by the Max Planck Institute for Astronomy focused the telescope on GJ758, a star about 50 light-years away.

They found a so-called gas giant planet of a mass somewhere between 10 and 40 times that of Jupiter, in an oval-shaped orbit around the star. It is presently at a distance about the same as between our Sun and Neptune.

Because of the elliptical orbit, its average distance from its host star is about one-and-a-half times that between our Sun and Pluto. Because it remains so hot despite the considerable distance from its star, the researchers believe it is still in the process of contracting. As is the case with many potential exoplanets of that estimated mass, GJ758B may be a brown dwarf star.



Exoplanets are tough to picture directly, but methods are being refined

"We can see how warm this thing is but we don't know for how long it has cooled, because we don't know the age of the system - that's the tricky part," said Markus Janson, one of the authors on the paper now at the University of Toronto.

Knowing the age as well as the temperature of GJ758B will help determine exactly how massive it is, and thereby if it is in fact a planet or a brown dwarf. "One thing we want to do is to examine the star, because determining the properties of the star is the easiest way to determine the age of the star," he told BBC News.

However, the August observation turned up another interesting possibility. "We also want to follow up on another candidate in the system that can be seen in the images, but we have to see if it's actually bound to the star, or whether it's something that's just there by chance." The team will continue its measurements on the parent star and investigate the second candidate - GJ758C - in the spring of 2010.

Mice holding back muscular dystrophy research

Humans and mice have previously unknown and potentially critical differences in one of the genes responsible for Duchenne muscular dystrophy (DMD). Researchers writing in the open access journal BMC Biology have found that two major features of a key DMD gene are present in most mammals, including humans, but are specifically absent in mice and rats, calling into question the use of the mouse as the principal model animal for studying DMD.

Roland Roberts led a team of researchers from King's College London, UK, and was funded by the Muscular Dystrophy Campaign. The team made the discovery while studying α-dystrobrevin, a component of the dystrophin protein complex that is disordered in DMD. Roberts said, "Two previously unrecognized features (a gene switch or promoter and a novel binding site for the adaptor protein syntrophin) are encoded by the α-

dystrobrevin gene of almost all four-legged animals except mice. We assume that this tardy recognition of key features of a gene that has been intensively studied since its discovery 13 years ago is due to the predominance of the mouse as the model organism for studying DMD and the specific destruction of these parts of the gene in the mouse".

A major consequence of these findings is that mice (and their rat and hamster relatives) are likely to be particularly poor models in which to study the effects of DMD on the brain. Roberts added, "The brain is the major site of α-dystrobrevin expression and we now know that the mouse is missing more than 50% of the brain α-dystrobrevins. The fact that there are fundamental differences between the brains of mice and humans potentially limits our understanding of the role of dystrobrevins and DMD-related complexes in this organ. In fact, almost all of our knowledge of the function of α-dystrobrevin has been gleaned from the mouse".

DMD is a fatal skeletal myopathy, causing loss of muscle tissue throughout the body. It is also associated with substantial neurological effects including learning difficulties, night blindness, defective color vision and a suggestion of personality disorders, so studying the mechanisms in the brain underlying these effects is crucial.

Notes to Editors: *1. Profound human/mouse differences in alpha-dystrobrevin isoforms: a novel syntrophin-binding site and promoter missing in mouse and rat Sabrina V Boehm, Panayiotis Constantinou, Sipin Tan, Hong Jin and Roland G Roberts BMC Biology (in press)*

Study confirms that cannabis is beneficial for multiple sclerosis

Cannabis can reduce spasticity in multiple sclerosis (MS) patients. A systematic review, published in the open access journal BMC Neurology, found that five out six randomized controlled trials reported a reduction in spasticity and an improvement in mobility.

Shaheen Lakhan and Marie Rowland from the Global Neuroscience Initiative Foundation, Los Angeles, USA, searched for trials evaluating the cannabis extracts delta9-tetrahydrocannabinol (THC) and cannabidiol (CBD). According to Lakhan, "We found evidence that combined THC and CBD extracts may provide therapeutic benefit for MS spasticity symptoms".

Spasticity, involuntary muscle tension or contraction, is a common symptom of MS. Many existing therapies for this symptom are ineffective, difficult to obtain, or associated with intolerable side effects. In this study, reported incidence of side effects from cannabis, such as intoxication, varied greatly depending on the amount of cannabis needed to effectively limit spasticity, but the researchers note that side effects were also seen in the placebo groups. They add, "Considering the distress and limitations spasticity brings to individuals with MS, it is important to carefully weigh the potential for side effects with the potential for symptom relief ".

Lakhan concludes, "The therapeutic potential of cannabinoids in MS is comprehensive and should be given considerable attention".

Notes to Editors: *1. Whole plant cannabis extracts in the treatment of spasticity in multiple sclerosis: a systematic review Shaheen E Lakhan and Marie Rowland BMC Neurology (in press)*

Poisonous Poisson

In contrast to the exhaustive research into venom produced by snakes and spiders, venomous fish have been neglected and remain something of a mystery. Now, a study of 158 catfish species, published in the open access journal BMC Evolutionary Biology, has catalogued the presence of venom glands and investigated their biological effects.

Jeremy Wright, from the University of Michigan, USA, carried out the investigation. He said, "I used histological and toxicological techniques to elucidate the diversity and distribution of venomous catfish. I found that at least 1250, and possibly over 1600 species of catfish may be venomous, a number far greater than any previous estimate of venomous catfish diversity"

Catfish venom glands are found in association with sharp, bony spines along the leading edge of the dorsal and pectoral fins, which can be locked into place when the catfish is threatened. When a spine enters a potential predator, the membrane surrounding the venom gland cells is torn, releasing venom into the wound. Wright describes how catfish venoms are neurotoxic and hemolytic, and are capable of producing a variety of effects such as severe pain, ischemia, muscle spasm and respiratory distress. However, as any one species examined produces no more than three distinct toxins in its venom, each species may not display all of these properties.

Wright's analyses indicate that there are at least two independent evolutionary origins of catfish venom glands. In addition, the toxic peptides show strong similarities with, and might be derived from, previously characterized toxins found in catfish epidermal secretions. "Further examination of the chemical composition of the venoms will provide valuable insight into the mechanisms and potential selective factors driving venom evolution in fishes", comments Wright.

1. Diversity, phylogenetic distribution, and origins of venomous catfishesJeremy J Wright BMC Evolutionary Biology (in press)

Green tea chemical combined with another may hold promise for treatment of brain disorders

Watertown, MA—Scientists at Boston Biomedical Research Institute (BBRI) and the University of Pennsylvania have found that combining two chemicals, one of which is the green tea component EGCG, can prevent and destroy a variety of protein structures known as amyloids. Amyloids are the primary culprits in fatal brain disorders such as Alzheimer's, Huntington's, and Parkinson's diseases. Their study, published in the current issue of Nature Chemical Biology (December 2009), may ultimately contribute to future therapies for these diseases.

"These findings are significant because it is the first time a combination of specific chemicals has successfully destroyed diverse forms of amyloids at the same time," says Dr. Martin Duennwald of BBRI, who co-led the study with Dr. James Shorter of University of Pennsylvania School of Medicine.

For decades a major goal of neurological research has been finding a way to prevent the formation of and to break up and destroy amyloid plaques in the brains and nervous systems of people with Alzheimer's and other degenerative diseases before they wreak havoc.

Amyloid plaques are tightly packed sheets of proteins that infiltrate the brain. These plaques, which are stable and seemingly impenetrable, fill nerve cells or wrap around brain tissues and eventually (as in the case of Alzheimer's) suffocate vital neurons or brain cells, causing loss of memory, language, motor function and eventually premature death.

To date, researchers have had no success in destroying plaques in the human brain and only minimal success in the laboratory. One reason for these difficulties in finding compounds that can dissolve amyloids is their immense stability and their complex composition. Yet, Duennwald experienced success in previous studies when he exposed amyloids in living yeast cells to EGCG. Furthermore, he and his collaborators also found before that DAPH-12, too, inhibits amyloid production in yeast.

In their new study, the team decided to look in more detail at the impact of these two chemicals on the production of different amyloids produced by the yeast amyloid protein known as PSI+. They chose this yeast amyloid protein because it has been studied extensively in the past, and because it produces varieties of amyloid structures that are prototypes of those found in the damaged human brain. Thus, PSI+ amyloids are excellent experimental paradigms to study basic properties of all amyloid proteins.

The team's first step was to expose two different amyloid structures produced by yeast (e.g., a weak version and a strong version) to EGCG. They found that the EGCG effectively dissolved the amyloids in the weaker version. To their surprise, they found that the stronger amyloids were not dissolved and that some transformed to even stronger versions after exposure to EGCG. The team then exposed the yeast amyloid structures to a combination of the EGCG and the DAPH-12 and found that all of the amyloid structures broke apart and dissolved. The next steps for the research team will be to explore the mechanism and potency of such a combinatorial therapy for the treatment of diverse neurodegenerative diseases.

"Our findings are certainly preliminary and we need further work to fully comprehend the effects of EGCG in combination with other chemicals on amyloids. Yet, we see our study as a very exciting initial step towards combinatorial therapies for the treatment of amyloid-based diseases," says Duennwald.

Authors of the study include: Martin L Duennwald and Chan Chung from Boston Biomedical Research Institute and Nicholas P Lopreiato, Elizabeth A Sweeny, M Noelle Knight, James Shorter, Huan Wang, and Blake E Roberts from the Department of Biochemistry and Biophysics, University of Pennsylvania School of Medicine.

Risk of blood clot after surgery higher and lasts longer than previously thought

Research: Duration and magnitude of the postoperative risk of venous thromboembolism in middle aged women: Prospective cohort study

The risk of having a potentially fatal blood clot after surgery is higher and lasts for longer than had previously been thought, concludes new research published on bmj.com today. This has important implications as most patients receive preventive (anti-clotting) therapy only whilst in hospital, or for up to five weeks after certain high-risk operations. And those undergoing day surgery are unlikely to be considered for preventive therapy at all.

The risk of venous thromboembolism (a collective term for deep vein thrombosis and pulmonary embolism) is known to increase after surgery, particularly after major orthopaedic (joint) surgery. The risk is thought to be highest during the first few weeks after an operation but little is known about the exact pattern and scale of this increased risk.

So an international team of researchers set out to examine the pattern of increased risk of venous thromboembolism over time and after different types of surgery Their findings are based on NHS hospital

admission and death records for 947,454 middle aged UK women recruited in 1996-2001 as part of the Million Women Study. Each woman was tracked for an average of 6.2 years.

Compared to the risk without surgery, women were almost 70 times more likely to be admitted with venous thromboembolism during the first six weeks after an inpatient operation and almost 10 times more likely after a day case operation.

The risks were lower but still elevated 7-12 weeks after surgery, and in most cases the risk remained for at least one year. Risk also varied considerably by type of surgery, being highest after inpatient surgery for hip or knee replacement, cancer and fracture.

In real terms, this means that 1 in 140 middle aged women in the UK will be admitted to hospital with venous thromboembolism during the 12 weeks after any inpatient surgery, 1 in 45 after hip or knee replacement surgery, and 1 in 85 after surgery for cancer. This compares with 1 in 815 after day case procedure and only 1 in 6,200 women during a 12 week period without surgery.

These findings suggest that there is a substantially increased risk of venous thromboembolism after many different types of surgery that lasts for up to 12 weeks postoperatively, conclude the authors.

This study broadens our previous understanding of short term risk of venous thromboembolism in certain types of surgery, particularly for day case surgery, says Alexander (Ander) Cohen, a vascular physician at King's College Hospital, in an accompanying editorial.

He also suggests that the event rates derived from this study "are probably much lower than the true values, mainly because many deep vein thromboses and pulmonary embolisms are undiagnosed, untreated, and managed out of hospital."

These findings indicate that we should be investigating the rates of venous thromboembolism, the use of preventive anti-clotting therapy, and the length of therapy in a wider range of patients. They should also make us consider whether treatment should be extended for more than five weeks in any group of patients, he concludes.

Popular diabetes drugs linked to increased risk of heart failure and death

Research: Risk of cardiovascular disease and all cause mortality among patients with type 2 diabetes prescribed oral antidiabetes drugs: Retrospective cohort study using UK general practice research database

Sulphonylureas, a type of drug widely used to treat type 2 diabetes, carries a greater risk of heart failure and death compared with metformin, another popular antidiabetes drug. The findings, published on bmj.com today, suggest clinically important differences in the cardiovascular safety profiles of different antidiabetes drugs, and support recommendations that favour metformin as first-line therapy for type 2 diabetes.

Type 2 diabetes affects more than 180 million people worldwide and is associated with at least a two-fold increased risk of death, mainly from cardiovascular disease. Oral antidiabetes drugs are widely used to help control blood sugar levels, but there are concerns that some may increase cardiovascular risk.

So a team of researchers led by Professor Paul Elliott from Imperial College London set out to investigate the risk of heart attack (myocardial infarction), congestive heart failure and death from any cause associated with prescription of different types of oral antidiabetes drugs. They used data from 91,521 men and women (average age 65 years) with diabetes included in the UK General Practice Research Database between 1990 and 2005. Factors that could potentially affect the results were taken into account.

Metformin was the most commonly prescribed drug (74.5% of patients), followed by second generation sulphonylureas (63.5%).

Compared with metformin, both first and second generation sulphonylureas were associated with significant (up to 61%) excess risk of all cause mortality, and second generation sulphonylureas with up to 30% excess risk of congestive heart failure.

Another class of antidiabetes drugs called thiazolidinediones were not associated with risk of heart attack, and there was significantly (up to 39%) lower risk of all cause mortality associated with pioglitazone use compared with metformin.

"The sulphonylureas, along with metformin, have long been considered the mainstay of drug treatment for type 2 diabetes. Our findings suggest a relatively unfavourable risk profile of sulphonylureas compared with metformin," say the authors. As such, they support the recommendations of the American Diabetes Association and International Diabetes Federation that favour metformin as the initial treatment for type 2 diabetes.

UCSB, UCL scientists rescue visual function in rats using induced pluripotent stem cells

Santa Barbara, Calif. - An international team of scientists has rescued visual function in laboratory rats with eye disease by using cells similar to stem cells. The research shows the potential for stem cell-based therapies to treat age-related macular degeneration in humans.

A team led by Dennis Clegg, of UC Santa Barbara, and Pete Coffey, of University College London (UCL), published their work in two papers, including one published this week in the journal PloS One. The first paper was published in the October 27 issue of the journal Stem Cells.

The scientists worked with rats that have a mutation which causes a defect in retinal pigmented epithelial (RPE) cells and leads to photoreceptor death and subsequent blindness. Human RPE cells were derived from induced pluripotent stem cells - embryonic stem cell-like cells that can be made from virtually any cell in the body, thus avoiding the controversy involved in using stem cells derived from embryos. Pluripotent means that the cells can become almost any cell in the body.

In experiments spearheaded by UCL's Amanda Carr, the team found that by surgically inserting stem cell-derived RPE into the retinas of the rats before photoreceptor degeneration, vision was retained. They found that the rats receiving the transplant tracked their visual focus in the direction of moving patterns more efficiently than control groups that did not receive a transplant.

"Although much work remains to be done, we believe our results underscore the potential for stem-cell based therapies in the treatment of age-related macular degeneration," said Sherry Hikita, an author on both papers and director of UCSB's Laboratory for Stem Cell Biology.

Dave Buchholz, first author of the article in Stem Cells, explained that by using induced stem cells that can be derived from patients, the scientists avoid immune rejection that might occur when using embryonic stem cells.

According to Buchholz, "RPE cells are essential for visual function. Without RPE, the rod and cone photoreceptors die, resulting in blindness. This is the basic progression in age-related macular degeneration. The hope is that by transplanting fresh RPE, derived from induced pluripotent stem cells, the photoreceptors will stay healthy, preventing vision loss."

The research is the result of a collaboration between research groups led by Clegg, professor in the Department of Molecular, Cellular & Developmental Biology and co-director of UCSB's Center for Stem Cell Biology and Engineering, and Pete Coffey, professor of Cellular Therapy and Visual Sciences at University College London and director of the London Project to Cure Blindness. Other authors include Amanda Carr, Anthony Vugler, Jean Lawrence, Carlos Gias, Li Li Chen, Ahmad Ahmado, Ma'ayan Semo, Matthew Smart, Shazeen Hasan, and Lyndon da Cruz at UCL, and Buchholz, Hikita, Teisha Rowland, Amy Friedrich, Cassidy Hinman, and Lincoln Johnson at UCSB.

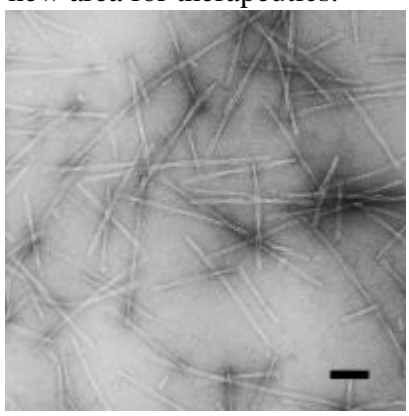
New therapy targets for amyloid disease

A major discovery is challenging accepted thinking about amyloids – the fibrous protein deposits associated with diseases such as Alzheimer's and Parkinson's – and may open up a potential new area for therapeutics.

It was believed that amyloid fibrils - rope-like structures made up of proteins sometimes known as fibres - are inert, but that there may be toxic phases during their formation which can damage cells and cause disease.

But in a paper published today [04 December 2009] in the Journal of Biological Chemistry, scientists at the University of Leeds have shown that amyloid fibres are in fact toxic - and that the shorter the fibre, the more toxic it becomes.

"This is a major step forward in our understanding of amyloid fibrils which play a role in such a large number of diseases," said Professor Sheena Radford of the Astbury Centre for Structural Molecular Biology and the Faculty of Biological Sciences.



These are amyloid fibrils **University of Leeds**

"We've revisited an old suspect with very surprising results. Whilst we've only looked in detail at three of the 30 or so proteins that form amyloid in human disease, our results show that the fibres they produce are indeed toxic to cells especially when they are fragmented into shorter fibres. "

Amyloid deposits can accumulate at many different sites in the body or can remain localised to one particular organ or tissue, causing a range of different diseases. Amyloid deposits can be seen in the brain, in diseases such as Parkinson's and Alzheimer's, whereas in other amyloid diseases deposits can be found elsewhere in the body, in the joints, liver and many other organs. Amyloid deposits are also closely linked to the development of Type II diabetes.

Professor Radford said: "Problems in the self-assembly process that results in the formation of amyloid are a natural consequence of longer life. In fact 85 per cent of all cases of disease caused by amyloid deposits are seen in those over the age of sixty or so."

The study was funded by the Wellcome Trust and the Biotechnology and Biological Sciences Research Council (BBSRC), supporting a team that included both cell biologists and biophysicists.

The next stage of this work is to look at a greater number of proteins that form amyloid fibres in order to consolidate these findings, says co-author and cell biologist Dr Eric Hewitt. "What we've discovered is fundamental and offers a whole new area for those working on therapeutics in this area. We anticipate that when we look at amyloid fibres formed from other proteins, they may well follow the same rules."

The team also hopes to discover why the shorter amyloid fibres are more toxic that their longer counterparts.

"It may be that because they're smaller it's easier for them to infiltrate cells," says Dr Hewitt. "We've observed them killing cells, but we're not sure yet exactly how they do it. Nor do we know whether these short fibres form naturally when amyloid fibres assemble or whether some molecular process makes them disassemble or fragment into shorter fibres. These are our next big challenges."

Where are the female scientists in research articles?

A recent research article published in the journal Scientometrics by a team from the University of Extremadura (UEX) has proved something that was already obvious to its scientific community – the extreme imbalance between the visibility of its male and female scientists. Only 20% of the university's articles studied had female lead authors, while the percentage of male lead authors stood at 50%. The remaining articles were led by authors from other universities.

"The percentage of documents with female involvement is very low when compared to the overall authorship of scientific production at the UEX", Vicente Guerrero, lead researcher of the study and a professor in the Faculty of Biblioteconomics and Documentation at UEX, tells SINC. The results of this work have been published in the latest issue of the journal Scientometrics.

The differences between men and women are clear, both in the overall number of articles published and in the count of the most important research positions according to gender. **SINC**

The differences between men and women are clear, both in the overall number of articles published and in the count of the most important research positions according to gender. Women account for between 10% and 15% of overall authorship of the articles studied, between 12% and 20% of lead authors and between 6% and 17% of last-position signatories, while their male counterparts account for between 35% and 50% in terms of the total number of articles produced, between 44% and 62% of lead authors and between 43% and 58% of last-position signatories.

The researchers cross referenced their study with the ISI Web of Science database in the United States to look at all the scientific articles published by UEX in collaboration with different Spanish and international universities between 1990 and 2005. The data were broken down by categories, areas and the gender of the researchers. They then carried out an analysis on the basis of scientific areas and authorship in order to identify the lead authors and the researchers signing the articles in last position, indicating the greatest levels of responsibility.

"Women have experienced a certain lag in getting involved in research in comparison with men, and have produced or are working on their doctoral theses, but still do not have much presence in terms of leading research work, whether because of this delay or other obligations that prevent them from dedicating so much to research", the researcher points out.

When broken down by scientific areas, Health Sciences account for the highest number of women leading the signing of articles, with a percentage of 20%, followed by Basic Sciences, at 18%. However, women account for only 7% of the lead authors of research work in Engineering and Architecture. In terms of the final signatory position, the highest figures for women are once again in Health Sciences, at more than 13%, followed by Basic Sciences (10%) and Engineering and Architecture (9%).

References: *'Visibility and responsibility of women in research papers through the order of signatures: the case of the University of Extremadura, 1990-2005'. Scientometrics. 81 (1): 225-238, octubre de 2009.*

Murderous plants: Victorian Gothic, Darwin and modern insights into vegetable carnivory

Mark W. Chase, Maarten J. M. Christenhusz, Dawn Sanders and Michael F. Fay

Darwin's interest in carnivorous plants was in keeping with the Victorian fascination with Gothic horrors, and his experiments on them were many and varied, ranging from what appears to be idle curiosity (e.g. what will happen if I place a human hair on a Drosera leaf?) to detailed investigations of mechanisms. Mechanisms for capture and digestion of prey vary greatly among the six (or more) lineages of flowering plants that have well-developed carnivory, and some are much more active than others. Passive carnivory is common in some groups, and one, Roridula (Roridulaceae) from southern Africa, is so passively carnivorous that it requires the presence of an insect intermediate to derive any benefit from prey trapped on its leaves. Other groups not generally considered to be carnivores, such as Stylidium (Stylidiaceae), some species of Potentilla (Rosaceae),

Proboscidea (Martyniaceae) and Geranium (Geraniaceae), that have been demonstrated to both produce digestive enzymes on their epidermal surfaces and be capable of absorbing the products, are putatively just as 'carnivorous' as Roridula. There is no clear way to discriminate between cases of passive and active carnivory and between non-carnivorous and carnivorous plants – all intermediates exist. Here, we document the various angiosperm clades in which carnivory has evolved and the degree to which these plants have become 'complete carnivores'. We also discuss the problems with definition of the terms used to describe carnivorous plants. © 2009 The Linnean Society of London, Botanical Journal of the Linnean Society, 2009, 161, 329–356.
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Contested signs of mass cannibalism

A research team argues that hundreds of people were butchered and eaten at a 7,000-year-old German site

By Bruce Bower

***CANNIBALISM CLUES A new analysis of human bones unearthed in one deposit at a Neolithic site in Germany (left) led researchers to conclude that people had been cut apart and eaten there, perhaps as part of a ritual sacrifice. Another deposit (right) contained human skullcaps typical of those found throughout the site.*F. Haak, GDKE Rheinland-Pfalz, Direktion Archaologie, Speyer**

At a settlement in what is now southern Germany, the menu turned gruesome 7,000 years ago. Over a period of perhaps a few decades, hundreds of people were butchered and eaten before parts of their bodies were thrown into oval pits, a new study suggests.

Cannibalism at the village, now called Herxheim, may have occurred during ceremonies in which people from near and far brought slaves, war prisoners or other dependents for ritual sacrifice, propose anthropologist Bruno Boulestin of the University of Bordeaux 1 in France and his colleagues. A social and political crisis in central Europe at that time triggered various forms of violence, the researchers suspect.

"Human sacrifice at Herxheim is a hypothesis that's difficult to prove right now, but we have evidence that several hundred people were eaten over a brief period," Boulestin says. Skeletal markings indicate that human bodies were butchered in the same way as animals.

Herxheim offers rare evidence of cannibalism during Europe's early Neolithic period, when farming first spread, the researchers report in the December Antiquity. Artifacts found at Herxheim come from the Linear Pottery Culture, which flourished in western and central Europe from about 7,500 to 7,000 years ago.

Two archaeologists who have studied human bones unearthed a decade ago at Herxheim reject the new cannibalism hypothesis. In a joint statement to Science News, Jörg Orschiedt of the University of Leipzig in Germany and Miriam Haidle of Senckenberg Research Institute and Natural History Museum in Frankfurt say that Boulestin's evidence better fits a scenario in which the dead were reburied at Herxheim following dismemberment and removal of flesh from bones. Evidence of ceremonial reburial practices has been reported for many ancient societies.

If further work confirms large-scale cannibalism at Herxheim, "this would be very surprising indeed, simply in terms of the scale involved," remarks archaeologist Rick Schulting of the University of Oxford in England.

Until now, the only convincing evidence of Neolithic cannibalism came from 6,000-year-old bones in a French cave, Boulestin holds. A 1986 report concluded that the remains of various animals and at least six people were butchered and discarded there. Again, Orschiedt and Haidle say, reburial rather than cannibalism may explain those findings.

Herxheim was first excavated from 1996 to 1999, yielding remains of a large structure, pottery and what appeared to be two parallel ditches encircling the settlement. Closer inspection revealed that the ditches had been formed by overlapping pits that had been dug over several centuries, apparently not exclusively to hold the dead.

Initial excavations of these pits yielded deposits of large numbers of human and dog bones.

Work from 2005 to 2008 - led by Andrea Zeeb-Lanz and Fabian Haack of the archaeology division of Germany's Directorate General for Cultural Heritage - unearthed additional human bones, mainly skulls and limb bones bearing incisions. Remains of an estimated 500 people have been found so far.

Pottery resting among the bones accumulated over no more than a few decades, the researchers say. Some pieces came from Neolithic sites located 400 kilometers from Herxheim.

The pits that surrounded Herxheim provided no protection from invaders but may have marked a symbolic boundary for a ceremonial settlement, Boulestin proposes. At first, Boulestin's team, like Orschiedt and Haidle, thought that the dead were brought to Herxheim for ceremonial reburial.

But Boulestin and his colleagues' opinion changed after they analyzed 217 reassembled human bones from one deposit, representing at least 10 individuals.

Damage typical of animal butchery appears on the bones, including that produced by a technique to separate the ribs from the spine, the scientists say. Heads were skinned and muscles removed from the brain case in order to remove the skullcap. Incisions and scrapes on jaws indicate that tongues were cut out.

Scrape marks inside the broken ends of limb bones indicate that marrow was removed.

People most likely made the chewing marks found near intentionally broken ends of hand and arm bones, Boulestin says.

Ongoing work at Herxheim has found signs of cannibalism on the bones of hundreds of other individuals, with only a few exceptions, he adds.

JAR FROM AFARA vase found among human bones at Herxheim was imported, as it displays a decorative style typical of a Neolithic society based about 100 kilometers to the north. **Pascal Disdier, CNRS, Universite Marc Block Strasbourg 2**

But proving that ancient Europeans consumed human body parts "is nearly impossible," Orschiedt and Haidle assert. The absence of lower jaws and skull bases from the new Herxheim material favors a reburial scenario, the researchers say, in which these components were ritually removed before skulls were placed in pits.

Boulestin's notion of a Neolithic social and political crisis rests on generally accepted evidence of massacres of dozens of people at three central European sites approximately 7,000 years ago. Other regional settlements, including Herxheim, were abandoned around that time.

Planned chemical analyses of bones from Herxheim will indicate whether some individuals grew up eating foods from distant regions, a sign that they were transported to the site. Such evidence would support either a cannibalism or reburial hypothesis.

It's not yet clear that a widespread crisis actually affected early Neolithic peoples, comments archaeologist Nick Thorpe of the University of Winchester in England.

Whatever actually happened at Herxheim, facial bones were smashed beyond recognition, "giving an impression of the destruction of individual identity, a kind of psychic violence against the person," Thorpe says.

'Rational drug design' identifies fragments of FDA-approved drugs relevant to emerging viruses

If H5N1 (avian flu) or H1N1/09 (swine flu) develop resistance to current therapies

A massive, data-crunching computer search program that matches fragments of potential drug molecules to the known shapes of viral surface proteins has identified several FDA-approved drugs that could be the basis for new medicines -- if emerging viruses such as the H5N1(avian flu) or H1N1/09 (swine flu) develop resistance to current antiviral therapies -- according to a presentation at the American Society for Cell Biology (ASCB) 49th Annual Meeting, Dec. 5-9, 2009 in San Diego.

The compounds were identified through a "rational drug design" project in the laboratory of Andrew McCammon, Ph.D., HHMI investigator at the University of California at San Diego.

The McCammon lab honed the search algorithms that helped identify the second generation of anti-HIV drugs.

Like fitting a key to a lock, computer search algorithms take the known shapes of drugs and match them, one after another, to the known shapes of disease-related proteins.

In the study presented at the ASCB conference, Daniel B. Dadon, a member of the McCammon lab, will explain how the search targeted the neuraminidase proteins, one of the two major sets of glycoproteins on the outer surface of influenza viruses.

Because biomolecules don't sit still - they're moving targets - scientists must consider how the protein can slightly shift position or shape. Dadon said, "A single picture of a sleeping cheetah, for example, might suggest that the animal is always lethargic. In reality, a cheetah is dynamic, spending much of its time sitting, running, climbing, attacking, and walking."

The successful capture of cheetahs or influenza viruses requires an understanding of their motions over time.

A search algorithm that accounts for the flexibility of the molecular docking sites is at the core of the McCammon group's relaxed complex scheme (RCS).

After studying neuraminidase flexibility, the researchers created a virtual library of drug-like molecules by mixing and matching parts of various FDA-approved drugs. The information gained from the RCS simulations was used to identify molecules in this new library that would best inhibit neuraminidase function.

Six compounds were predicted to inhibit neuraminidase better than FDA-approved drugs such as oseltamivir, peramivir and zanamivir.

The computer data also suggests that some of these compounds may target other parts of the neuraminidase protein. The ability to target these additional parts of the neuraminidase protein could prove useful if the new viruses develop resistance to current therapies.