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Commonly Used Drug Can Limit Radiation Damage to Lungs and Heart for Cancer Patients

Damage caused to the heart and lungs by radiotherapy treatment of tumours in the chest region can be limited by the administration of an ACE inhibitor

Unavoidable damage caused to the heart and lungs by radiotherapy treatment of tumours in the chest region can be limited by the administration of an ACE inhibitor, a drug commonly used in the treatment of cardiovascular disease, a group of Dutch researchers have found. [1]

Common cancers such as breast, esophagus, lung, and Hodgkin's lymphoma are frequently treated with radiotherapy, but the radiation dose that can be given safely is limited by the sensitivity of the health lung tissue which is also irradiated.

The lung is a particularly complex and sensitive organ and strategies for protecting it from radiotherapy damage, apart from limiting the dose given and, therefore, the efficacy of the treatment, are few. Presenting the research to the 2nd Forum of the European Society for Radiotherapy and Oncology (ESTRO) today (Sunday), Dr Sonja Van der Veen, MSc, from the University Medical Centre, Groningen, The Netherlands, said that she had set out with colleagues to see whether the use of an ACE inhibitor could protect against early radiation-induced lung toxicity (RILT). Previous studies had shown that damage to blood vessels can play an important role in the development of RILT [2], so the researchers irradiated the lungs, heart, or heart and lungs of rats and administered the ACE inhibiter captopril immediately after treatment. The rats' lung functions were then measured at two-weekly intervals.

"After eight weeks, when early lung toxicity is usually at its height, we found that captopril improved the rats' heart and lung functions, but we were surprised to find that this only occurred when the heart was included in the irradiation field," said Dr Van der Veen. "This was not due to protection of the lung blood vessels, which were equally damaged with or without captopril. So we investigated further and found that the captopril treatment improved the heart's function and decreased the level of fibrosis in the heart soon after irradiation. So these new findings show that ACE inhibition decreases RILT by reducing direct acute heart damage."

Irradiating the heart leads to the development of fibrosis, which stiffens it, and this in turn leads to problems in the relaxation of the left ventricle. Due to this, blood flow from the lungs into the heart is hindered, and this can cause pulmonary damage. However, after treatment with captopril, the researchers observed an improvement in ventricular relaxation in the irradiated hearts.

Dr Van der Veen and her colleagues are now collaborating with a research group from the Mayo Clinic, Rochester, Minnesota (USA), in order to design a randomised clinical trial where patients who are treated with radiation to the thoracic area including the heart will be treated with either an ACE inhibitor or a placebo after irradiation.

Much progress has been made in radiation treatment over recent years, but in breast cancer, for example, most women still receive high doses to the heart, and this is known to increase the risk of heart disease. A recent study [3] has shown that for each Gray (Gy) [4] of radiation, there is a 7.4% increase in the occurrence of a subsequent major coronary event.

"Given that most women will receive a dose of between 1 and 5 Gray, and that the dangers are even greater for women with existing cardiac risk factors or coronary disease, this is still a big problem," said Dr Van der Veen.

Rats were chosen for the study because, unlike mice, they are big enough for researchers to be able to irradiate different part of the lungs and heart. The researchers believe that the way in which ACE inhibition works in both animals and humans is similar.

"We are confident that our clinical trial will see the same protective effect in humans as that which we have seen in rats," said Dr Van der Veen. "We will also now begin to study the late effects of ACE inhibition on RILT to see whether it affords similar protection. We believe that our results suggest a promising strategy for shielding patients from radiation damage and improving their quality of life, while at the same time allowing them to receive a high enough dose to ensure the effective treatment of their cancer."

President of ESTRO, Professor Vincenzo Valentini, a radiation oncologist at the Policlinico Universitario A. Gemelli, Rome, Italy, said: "This study underlines the importance of translational research. The understanding of anti-cancer mechanisms, as well as of protective opportunities discovered in the experimental environment, is of upmost importance in the era of personalised medicine. This research provides further evidence of the importance of testing experimental theories in the clinical environment to the ultimate benefit of patients."

[1] ACE (angiotensin-converting enzyme) Inhibitors are a class of drugs usually used for treating high blood pressure and heart failure.

[2] Ghobadi G, Bartelds B, van der Veen SJ, Dickinson MG, Brandenburg S, Berger RM, et al. Lung irradiation induces pulmonary vascular remodelling resembling pulmonary arterial hypertension. Thorax 2012 Apr;67(4):334-341
[3] Darby SC, Ewertz M, McGale P, Bennet AM, Blom-Goldman U, Bronnum D, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med 2013 Mar 14;368(11):987-998.
[4] One Gray is the absorption of one joule of energy, in the form of ionising radiation, per kilogram of matter.

http://www.sciencedaily.com/releases/2013/04/130421152401.htm

First 2,000-Year-Long Temperature Reconstructions for Individual Continents

Past Global Changes (PAGES) project, which reconstructed temperature over the past 1,000 to 2,000 years

Past climate change varied remarkably between regions. This is demonstrated in a new study coordinated by the international Past Global Changes (PAGES) project, which reconstructed temperature over the past 1,000 to 2,000 years.

It is the first comprehensive temperature reconstruction on a continental scale. One of its main findings is that a general cooling trend, caused by different factors (e.g. orbital-driven insolation and changes in solar and volcanic activity), was ubiquitous across all continental-scale regions and was reversed by a distinct warm trend beginning at the end of the 19th century.

The scale of this project is impressive. Some 80 researchers from all over the world collaborated on the study, which has just been published in the scientific journal Nature Geoscience. In one of the widest-ranging efforts yet undertaken to reconstruct climate across the globe, the international author team evaluated data from all continents to track the evolution of temperatures over the past one to two millennia.

This major project was initiated and coordinated by the Past Global Changes (PAGES) organization. PAGES was established in 1991 to facilitate international research into understanding climatic and environmental dynamics by studying the past.

The program receives funding mainly from the Swiss and US national science foundations. In 2006, ambitious scientists in the PAGES network decided to organize an initiative to reconstruct the climate of the last 2000 years in unprecedented quality.

The first results of the collective effort have now been published. "A key aspect of the consortium effort was to engage regional experts who are intimately familiar with the evidence for past climate changes within their regions," says Heinz Wanner, emeritus professor at the University of Bern and one of the original architects of the PAGES 2k Network.

"Several mathematical procedures were applied to reconstruct the continental temperature time series and they were compared to assess the extent to which the main conclusions of the study stood up to the different analytical approaches." Previous attempts to reconstruct temperature changes focused on hemispheric or global-scale averages, which are important, but overlook the pronounced regional-scale differences that occur along with global changes, he points out.

Natural climate archives and documentary sources

For the present study, "Continental-scale temperature variability during the last two millennia," the researchers drew up temperature curves for large regions at seven continents, using 511 local temperature records. These were based on the analysis of tree rings, pollen, corals, lake and marine sediments, ice cores and stalagmites as well as historical documents.

In most cases the data used were highly resolved, attesting to short-term variations over decades or less, rather than smoothing over centuries. In Africa, there were too few records to accurately determine long-term temperature changes for that continent. Nevertheless, the expansive new dataset will undoubtedly be used in future studies, including for comparisons with the output of climate models used to help project future climate change.

The evolution of temperature across all the continents was noticeably more similar within the hemispheres than between the Northern and Southern Hemisphere. "Distinctive periods, such as the Medieval Warm Period or the Little Ice Age stand out, but do not show a globally uniform pattern," says professor Heinz Wanner.

By around 1500 AD temperatures did indeed fall below the long-term mean everywhere. However, in the Arctic, Europe and Asia this temperature drop occurred several decades earlier than in North America and the Southern Hemisphere. These new findings will certainly stimulate vibrant discussions within the research community, Wanner believes.

Long-term cooling trend reversed

The most consistent feature across the regions over the last 2,000 years was a long-term cooling trend, which was likely caused by a combination of factors such as an overall increase in volcanic activity, a decrease in solar irradiance, changes in land cover, and slow changes in earth's orbit. This cooling only came to an end toward the end of the 19th century.

The warming during the last century has reversed this long-term cooling, the study found. It remained cold only in Antarctica. An analysis of the average temperatures over 30-year periods indicates that interval from 1971-2000 was probably warmer than any other 30-year period in the last 1,400 years.
Cooler 30-year periods between the years 830 and 1910 AD were particularly pronounced during weak solar activity and strong tropical volcanic eruptions. Both phenomena often occurred simultaneously and led to a drop in the average temperature during five distinct 30- to 90-year intervals between 1251 and 1820.
Warming in the 20th century was on average twice as large in the northern continents as it was in the Southern Hemisphere. During the past 2,000 years, some regions experienced warmer 30-year intervals than during the late 20th century. For example, in Europe the years between 21 and 80 AD were possibly warmer than the period 1971-2000.

http://www.eurekalert.org/pub_releases/2013-04/wkh-uno041913.php

Using nitrous oxide for anesthesia doesn't increase -- and may decrease -- complications and death

2 studies add new data to debate over safety of N2O as surgical anesthetic

San Francisco, CA. - Giving nitrous oxide as part of general anesthesia for noncardiac surgery doesn't increase the rate of complications and death—and might even decrease the risk of such events, according to a pair of studies in the May issue of *Anesthesia & Analgesia*, official journal of the International Anesthesia Research Society (IARS).
But an accompanying series of editorials points out some important limitations of the two studies—which can't completely overcome previous concerns about the safety of using nitrous oxide (N2O) as a surgical anesthetic.

Is Nitrous Oxide Safe for Surgical Anesthesia?

Nitrous oxide is the world's oldest general anesthetic, but there's a long history of debate regarding its appropriate role in modern surgical anesthesia. Although nitrous oxide provides effective sedation and pain control, it has known disadvantages and side effects. A previous study, called "ENIGMA-I," reported a small but significant increase in myocardial infarction (heart attack) among patients receiving nitrous oxide as part of anesthesia for noncardiac surgery (procedures other than heart surgery).
The two new studies, based on large patient databases, question the harmful effects of nitrous oxide. Dr Kate Leslie of Royal Melbourne Hospital, Australia, and colleagues analyzed data from a previous study of more than 8,300 patients undergoing surgery. That study was designed to assess the effects of giving one type of blood pressure drug (beta-blockers) during surgery, not the effects of nitrous oxide.
Dr Leslie and colleagues compared the risk of death or serious complications after surgery for patients who versus did not receive nitrous oxide as part of anesthesia. Twenty-nine percent of patients in the study received nitrous oxide.
The results showed comparable rates of adverse outcomes between groups. With or without nitrous oxide, the overall rate of death or serious complications was approximately seven percent, including about a six percent rate of myocardial infarction. Risk of death after surgery was about three percent in both groups.
Outcomes remained similar on "propensity score" analysis—a technique accounting for characteristics making patients more or less likely to receive nitrous oxide. Use of nitrous oxide varied widely between the different countries and hospitals participating in the study.

No Increase in Risks with N2O—But 'More Definitive' Studies Needed

Dr Alparslan Turan of the Cleveland Clinic and colleagues outcomes reviewed more than 49,000 patients undergoing noncardiac surgery between 2005 and 2009. In this study, 45 percent of patients received nitrous oxide.
The results suggested a significant reduction in the risk of death after surgery for patients receiving nitrous oxide: about one-third lower than in patients who did not receive nitrous oxide. There was also a significant 17 percent reduction in the combined rate of major complications and death.
Surprisingly, nitrous oxide was specifically associated with a 40 percent reduction in the risk of major lung- and breathing-related complications. However, the authors acknowledge the risk of "selection bias"—anesthesiologists may have avoided using nitrous oxide in patients at risk of lung problems. Again, the findings remained significant on propensity score analysis.
In one of three accompanying editorials, Thomas R. Vetter, MD, MPH, and Gerald McGwin, Jr, MS, PhD, of University of Alabama at Birmingham highlight some important limitations of the study data. They note that, although both studies were large, they were not randomized trials—the strongest type of scientific evidence.
Drs Vetter and McGwin emphasize that even sophisticated techniques like propensity score analysis can't account for all of the differences between groups that may have affected responses to nitrous oxide. They note

that a randomized "ENIGMA-II" study is underway, and may provide "additional, perhaps more definitive insight" on the risks and potential benefits of using nitrous oxide as part of general anesthesia.
Read the article: "This Wonder-Working Gas"
Read the article: Comparing Apples to Oranges: Just Say No to N2O?
Read the article: Nitrous Oxide and Cardiovascular Outcome: Perspective from the POISE Trial
Read the article: Association Between Nitrous Oxide and Postoperative Mortality and Morbidity After Noncardiac Surgery
Read the article: Nitrous Oxide and Serious Morbidity and Mortality in the POISE Trial

http://bit.ly/15OZppM

The psychology of J.C. Penney

Why shoppers like it when retailers play games with prices

By Rachel Ehrenberg

Last year, J.C. Penney CEO Ron Johnson put an end to "fake prices," the ones that customers see but rarely pay because of coupons and sales. Instead, the clothing retailer decided to sell items at cheaper everyday prices in an effort to "stop playing games" with consumers. By June, Johnson had conceded that this strategy wasn't working. Penney brought back coupons in September; the return of clearance racks soon followed. But it may have been too late for Johnson; he got the boot on April 8 after a mere 17 months on the job.

Johnson may have thought he was doing customers a favor by making the shopping experience a more rational exchange of goods for their hard-earned currency. But by not showing marked-down prices, Penney's removed an element that helps shoppers feel rational. Seeing that marked-down price next to a higher original price provides an important yardstick for gauging whether we should buy something.

The original price of a sale item provides what sociologists and marketers refer to as anchoring. It brings a sense of certainty to the uncertain, giving the shopper a wisp of information for evaluating purchases. Since most of us are pretty disconnected from where our products come from and how they are made, we often use price as a major data point when it comes to evaluating whether that sweater, headset or jar of jam is worth buying. We see a $14 shirt, and conclude based on its price that it must be a low-quality garment made in a sweatshop somewhere by overworked, underpaid workers. On the other hand, seeing a red line through the $50 price tag on a shirt that's marked down to $14 indicates to us that the shirt is of high quality and that for $14, it is a steal.

The influence of this anchor price is comforting; it lends an air of rationality to our decision making. But in reality, there's little that's rational about it. (Or about much of how we decide to part with our money — just ask any casino owner, used car salesman or faux Nigerian prince.) A classic experiment demonstrating anchoring was conducted more than 30 years ago. Psychologists Amos Tversky and Daniel Kahneman of Hebrew University in Jerusalem asked study participants to watch a roulette wheel spin and then to estimate a particular quantity having nothing to do with roulette. In one instance, the wheel was rigged to stop on 10 for some participants, on 65 for others. Then the researchers asked the participants to estimate the percentage of African countries belonging to the United Nations.

Just seeing the roulette wheel number influenced how participants estimated the second number, the researchers reported in a paper in Science in 1974. On average, those who saw the wheel stop at 10 estimated that 25 percent of African countries were members of the United Nations at the time. Those who saw the wheel stop at 65 estimated 45 percent. (The true figure was upwards of 90 percent, depending on how you count countries. Kahneman was awarded the economics Nobel in 2002; Tversky died in 1996).

Anchoring has since been studied in numerous contexts. Its effects show up whether you are making a bid on a house, negotiating a salary or debating whether to buy a shirt. More recently, researchers have investigated where some of this decision making goes on in your brain. In one experiment, scientists gave volunteers $20 and had them look at products on a video screen while an fMRI machine scanned their brains. After seeing a product, such as a box of Godiva chocolates, they saw how much it cost and had to decide whether or not they would buy it.

When the volunteers saw something they liked, there was a burst of activity in their nucleus accumbens, a little area deep in the brain that's associated with anticipating something good (and also linked to addiction). Their brains also betrayed the thrill of spotting a deal: There was activity in the medial prefrontal cortex, a favorite hangout of the reward chemical dopamine. During those moments, the insula, a region whose duties include the dismal task of anticipating loss and pain, was shut down.

Of course, Johnson made many other changes at J.C. Penney. No single thing can be blamed for his downfall. But the no-sales strategy removed an opportunity for shoppers to get a little dopamine kick and feel rational at the same time. Johnson should have known this — he came to J.C. Penney from Apple, a company that's used price anchoring masterfully. When Steve Jobs introduced the iPad, he told his audience that if you listened to

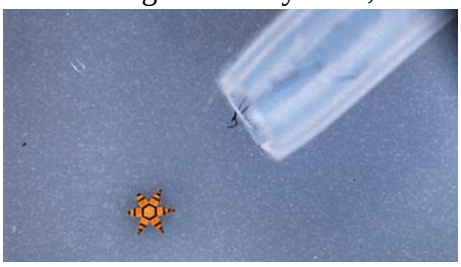
the pundits, an iPad would cost $999. A big $999 loomed on the screen behind him for nearly a full minute while Jobs went on about price goals. Then the reveal: The iPad would cost $499. The audience went wild.
*A. Tversky and D. Kahneman. **Judgment under Uncertainty: Heuristics and Biases**. Science. Vol. 185, September 27, 1974, p. 1124. doi: 10.1126/science.185.4157.1124*

http://www.eurekalert.org/pub_releases/2013-04/jhu-tdh042313.php

Team deploys hundreds of tiny untethered surgical tools in first animal biopsies

New way to perform biopsies that could provide a more effective way to access narrow conduits in the body as well as find early signs of cancer or other diseases

By using swarms of untethered grippers, each as small as a speck of dust, Johns Hopkins engineers and physicians say they have devised a new way to perform biopsies that could provide a more effective way to access narrow conduits in the body as well as find early signs of cancer or other diseases.
In two recent peer-reviewed journal articles, the team reported successful animal testing of the tiny tools, which require no batteries, wires or tethers as they seize internal tissue samples.
The devices are called "mu-grippers," incorporating the Greek letter that represents the term for "micro." Instead of relying on electric or pneumatic power, these star-shaped tools are autonomously activated by the body's heat, which causes their tiny "fingers" to close on clusters of cells. Because the tools also contain a magnetic material, they can be retrieved through an existing body opening via a magnetic catheter.



This image depicts an mu-gripper near the opening of an endoscopic catheter. **Evin Gultepe, Gracias Lab, Johns Hopkins University.**

In the April print edition of Gastroenterology, the researchers described their use of the mu-grippers to collect cells from the colon and esophagus of a pig, which was selected because its intestinal tract is similar to that of humans. Earlier this year, the team members reported in the journal Advanced Materials that they had successfully inserted the mu-grippers through the mouth and stomach of a live animal and released them in a hard-to-access place, the bile duct, from which they obtained tissue samples.
"This is the first time that anyone has used a sub-millimeter-sized device -- the size of a dust particle -- to conduct a biopsy in a live animal," said David Gracias, an associate professor of chemical and biomolecular engineering whose lab team developed the microgrippers. "That's a significant accomplishment. And because we can send the grippers in through natural orifices, it is an important advance in minimally invasive treatment and a step toward the ultimate goal of making surgical procedures noninvasive."
Another member of the research team, physician Florin M. Selaru of the Johns Hopkins School of Medicine, said the mu-grippers could lead to an entirely new approach to conducting biopsies, which are considered the "gold standard" test for diagnosing cancer and other diseases.
The advantage of the mu-grippers, he said, is that they could collect far more samples from many more locations. He pointed out that the much larger forceps used during a typical colonoscopy may remove 30 to 40 pieces of tissue to be studied for signs of cancer. But despite a doctor's best intentions, the small number of specimens makes it easy to miss diseased lesions.
"What's the likelihood of finding the needle in the haystack?" said Selaru, an assistant professor in the Division of Gastroenterology and Hepatology. "Based on a small sample, you can't always draw accurate inferences. We need to be able to do a larger statistical sampling of the tissue. That's what would give us enough statistical power to draw a conclusion, which, in essence, is what we're trying to do with the microgrippers. We could deploy hundreds or even thousands of these grippers to get more samples and a better idea of what kind of or whether a disease is present."
Although each mu-gripper can grab a much smaller tissue sample than larger biopsy tools, the researchers said each gripper can retrieve enough cells for effective microscopic inspection and genetic analysis. Armed with this information, they said, the patient's physician could be better prepared to diagnose and treat the patient.
This approach would be possible through the latest application of the Gracias lab's self-assembling tiny surgical tools, which can be activated by heat or chemicals, without relying on electrical wires, tubes, batteries or tethers. The low-cost devices are fabricated through photolithography, the same process used to make computer chips. Their fingerlike projections are made of materials that would normally curl inward, but the team adds a polymer resin to give the joints rigidity and to keep the digits from closing.
Prior to a biopsy, the grippers are kept on ice, so that the fingers remain in this extended position. An endoscopy tool then is used to insert hundreds of grippers into the area targeted for a biopsy. Within about five minutes, the warmth of the body causes the polymer coating to soften, and the fingers curl inward to grasp some tissue. A magnetic tool is then inserted to retrieve them.

Although the animal testing results are promising, the researchers said the process will require further refinement before human testing can begin. "The next step is improving how we deploy the grippers," Selaru said. "The concept is sound, but we still need to address some of the details. The other thing we need to do is thorough safety studies."
Further development can be costly, however. The team has applied for grants to fund advances in the project, which is protected by provisional patents obtained through the Johns Hopkins Technology Transfer Office. Biotechnology investors might also help move the project forward.
"It is more a question of money than time as to how long it will take before we could use this in human patients," Selaru said
Along with Gracias and Selaru, the Johns Hopkins researchers who contributed significantly to the two journal articles were Evin Gultepe, Sumitaka Yamanaka, Eun Shin and Anthony Kalloo. Additional contributors were Kate E. Laflin, Sachin Kadam, Yoosun Shim, Alexandru V. Olaru, Berkeley Limketkai, Mouen A. Khashab and Jatinder S. Randhawa. The researchers are affiliated with School of Medicine, the Whiting School of Engineering and the Johns Hopkins Institute for NanoBioTechnology. Funding for this research has come from the National Institutes of Health, the National Science Foundation, the Flight Attendants Medical Research Institute and the Broad Medical Research Institute.

http://www.eurekalert.org/pub_releases/2013-04/wuso-ats042313.php

ALS trial shows novel therapy is safe

An investigational treatment for an inherited form of Lou Gehrig's disease has passed an early phase clinical trial for safety, researchers at Washington University School of Medicine in St. Louis and Massachusetts General Hospital report.

The researchers have shown that the therapy produced no serious side effects in patients with the disease, also known as amyotrophic lateral sclerosis (ALS). The phase 1 trial's results, available online in Lancet Neurology, also demonstrate that the drug was successfully introduced into the central nervous system.
The treatment uses a technique that shuts off the mutated gene that causes the disease. This approach had never been tested against a condition that damages nerve cells in the brain and spinal cord.
"These results let us move forward in the development of this treatment and also suggest that it's time to think about applying this same approach to other mutated genes that cause central nervous system disorders," says lead author Timothy Miller, MD, PhD, assistant professor of neurology at Washington University. "These could include some forms of Alzheimer's disease, Parkinson's disease, Huntington's disease and other conditions."
ALS destroys nerves that control muscles, gradually leading to paralysis and death. For treatment of the disease, the sole FDA-approved medication, Riluzole, has only a marginal effect.
Most cases of ALS are sporadic, but about 10 percent are linked to inherited mutations. Scientists have identified changes in 10 genes that can cause ALS and are still looking for others.
The study focused on a form of ALS caused by mutations in a gene called SOD1, which account for 2 percent of all ALS cases. Researchers have found more than 100 mutations in the SOD1 gene that cause ALS.
"At the molecular level, these mutations affect the properties of the SOD1 protein in a variety of ways, but they all lead to ALS," says Miller, who is director of the Christopher Wells Hobler Lab for ALS Research at the Hope Center for Neurological Disorders at Washington University.
Rather than try to understand how each mutation causes ALS, Miller and his colleagues focused on blocking production of the SOD1 protein using a technique called antisense therapy.
To make a protein, cells have to copy the protein-building instructions from the gene. Antisense therapy blocks the cell from using these copies, allowing researchers to selectively silence individual genes.
"Antisense therapy has been considered and tested for a variety of disorders over the past several decades," Miller says. "For example, the FDA recently approved an antisense therapy called Kynamro for familial hypercholesterolemia, an inherited condition that increases cholesterol levels in the blood."
Miller and colleagues at the University of California-San Diego devised an antisense drug for SOD1 and successfully tested it in an animal model of the disease.
Merit Cudkowicz, MD, chief of neurology at Massachusetts General Hospital, was co-PI of the phase I clinical safety trial described in the new paper. Clinicians at Barnes-Jewish Hospital, Massachusetts General Hospital, Johns Hopkins Hospital and the Methodist Neurological Institute in Houston gave antisense therapy or a placebo to 21 patients with SOD1-related ALS. Treatment consisted of spinal infusions that lasted 11 hours.
The scientists found no significant difference between side effects in the control and treatment groups. Headache and back pain, both of which are often associated with spinal infusion, were among the most common side effects.
Immediately after the injections, the researchers took spinal fluid samples. This let them confirm the antisense drug was circulating in the spinal fluid of patients who received the treatment.

To treat SOD1-related ALS in the upcoming phase II trial, researchers will need to increase the dosage of the antisense drug. As the dose rises, they will watch to ensure that the therapy does not cause harmful inflammation or other side effects as it lowers SOD1 protein levels.
"All the information that we have so far suggests lowering SOD1 will be safe," Miller says. "In fact, completely disabling SOD1 in mice seems to have little to no effect. We think it will be OK in patients, but we won't know for sure until we've conducted further trials."
The therapy may one day be helpful in the more common, noninherited forms of ALS, some of which may be linked to problems with the SOD1 protein. "Before we can consider using this same therapy for sporadic ALS, we need more evidence that SOD1 is a major contributor to these forms of the disorder," Miller says.
The trial was conducted with support from ISIS Pharmaceuticals, which co-owns a patent on the SOD1 antisense drug.
Miller TM, Pestronk A, David W, Rothstein J, Simpson E, Appel SH, Andres PL, Mahoney K, Allred P, Alexander K, Ostrow LW, Schoenfeld D, Macklin EA, Norris DA, Manousakis G, Crisp M, Smith R, Bennett CF, Bishop KM, Cudkowicz ME. An antisense oligonucleotide against SOD1 delivered intrathecally for patients with SOD1 familial amyotrophic lateral sclerosis: a phase 1, randomised first-in-man study. Lancet Neurology, online May 29, 2013.
The clinical trial was funded by the Muscular Dystrophy Association, the ALS Association and Isis Pharmaceuticals.

http://www.eurekalert.org/pub_releases/2013-04/plos-crf041913.php

Clenching right fist may give better grip on memory

Study suggests clenching right hand may help form memories, left may help recall words

Clenching your right hand may help form a stronger memory of an event or action, and clenching your left may help you recollect the memory later, according to research published April 24 in the open access journal PLOS ONE by Ruth Propper and colleagues from Montclair State University.
Participants in the research study were split into groups and asked to first memorize, and later recall words from a list of 72 words. There were 4 groups who clenched their hands; One group clenched their right fist for about 90 seconds immediately prior to memorizing the list and then did the same immediately prior to recollecting the words. Another group clenched their left hand prior to both memorizing and recollecting. Two other groups clenched one hand prior to memorizing (either the left or right hand) and the opposite hand prior to recollecting. A control group did not clench their fists at any point.
The group that clenched their right fist when memorizing the list and then clenched the left when recollecting the words performed better than all the other hand clenching groups. This group also did better than the group that did not clench their fists at all, though this difference was not statistically 'significant'.
"The findings suggest that some simple body movements - by temporarily changing the way the brain functions- can improve memory. Future research will examine whether hand clenching can also improve other forms of cognition, for example verbal or spatial abilities," says Ruth Propper, lead scientist on the study.
The authors clarify that further work is needed to test whether their results with word lists also extend to memories of visual stimuli like remembering a face, or spatial tasks, such as remembering where keys were placed. Based on previous work, the authors suggest that this effect of hand-clenching on memory may be because clenching a fist activates specific brain regions that are also associated with memory formation.
Citation: Propper RE, McGraw SE, Brunye TT, Weiss M (2013) Getting a Grip on Memory: Unilateral Hand Clenching Alters Episodic Recall. PLoS ONE 8(4): e62474.doi:10.1371/journal.pone.0062474
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http://www.bbc.co.uk/news/health-22261475

Walk-to-burn-calorie menu 'diet aid'

Menus displaying the exercise needed to burn calories in meals can help people consume less, a US study suggests.

By Michelle Roberts Health editor, BBC News online

Diners given this extra information ordered and ate less calorific food than other customers, a team at Texas Christian University found. Knowing it takes two hours of brisk walking to burn off a cheeseburger may be more of a warning than being told how many calories it contains, the researchers say. They now plan larger trials.
Researchers Dr Meena Shah and Ashlei James divided 300 volunteers aged 18 to 30 randomly into three groups. One received a menu without any calorie information, another menus with the calories displayed, and the third menus that showed both calories and the amount of exercise needed to burn them off. All of the menus offered the same choice of food and drink, which included burgers, sandwiches, salad, chips, soft drinks and water.

None of the volunteers was aware of the reason for the study and the researchers took into account hunger levels when interpreting their findings.
The group given the menus with the extra information about how much brisk walking would be needed to burn off the food ordered and ate much less than the group who had menus with no calorie information. They consumed 100 fewer calories, on average, as a result.
Dr Shah said: "This is the first study to look at the effects of displaying minutes of brisk walking needed to burn food calories on the calories ordered and consumed. "This study suggests there are benefits."
The researchers say brisk walking is something nearly everyone can relate to.

Calorie counting

"We can't generalise to a population over age 30, so we will further investigate this in an older and more diverse group," Dr Shah added. They will present their findings at the Experimental Biology 2013 meeting in Boston.
Victoria Taylor, senior dietician at the British Heart Foundation, said clearly signposting healthy options and nutritional content helped people make informed choices when ordering food. But she added: "While displaying the amount of exercise needed to burn calories is an interesting idea, there's more to a heart-healthy diet than calorie counting. "Restaurants can also take steps to make meals healthier by serving appropriate portion sizes and reducing the amount of salt, saturated fat and sugar in their dishes. "Whether eating at home or dining out, a balanced diet with plenty of fruit and veg is the best way to protect your heart."

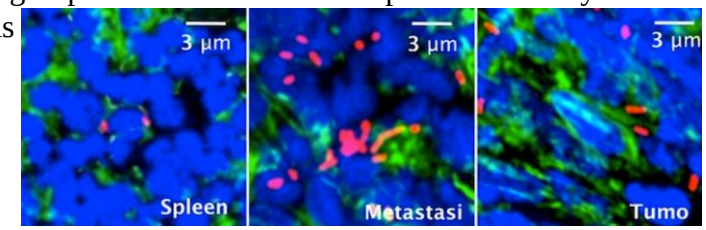
http://www.wired.com/wiredscience/2013/04/radioactive-microbes/

Radioactive Microbes Nuke Tumor Cells

Delivering radiation directly to the cancer cells using genetically modified bacteria halts cancer's spread

By Elizabeth Norton, ScienceNOW

Despite the advances made against many types of cancer, pancreatic cancer remains grimly resistant to treatment. Only about 4% of patients survive for 5 years, mainly because of the disease's vicious ability to metastasize, or spread to other parts of the body. Now, a group of researchers has hit upon a novel way to halt its spread: delivering radiation directly to the cancer cells using genetically modified bacteria. In a study of mice carrying human tumors, the therapy shrank the rodent's primary tumors while sparing healthy tissue; it also blasted cancer cells that had spread throughout the animals, reducing their number by up to 90%.



Radioactive bacteria (red) destroy cancer cells from the inside. **Claudia Gravekamp/Albert Einstein College of Medicine, New York**

The cancer-targeting microorganism, Listeria monocytogenes, is a rod-shaped bacterium that penetrates the cells of the people and animals that it infects. Although the pathogen can cause severe illness, such as meningitis, a healthy person's immune system can usually destroy it before any damage is done. Because of the bacterium's ability to burrow inside key immune cells called macrophages, some researchers use weakened Listeria with bits of tumor DNA attached to teach the body's immune system to recognize and destroy cancerous cells that might otherwise slip by unnoticed.
As part of this effort, immunobiologist Claudia Gravekamp, then at the California Pacific Medical Center Research Institute in San Francisco, was studying such an attenuated Listeria-based vaccine in mice carrying a highly aggressive, metastatic form of breast cancer. In 2009, Gravekamp and her colleagues found that the bacteria did more than spur the immune system to attack the cancer cells. The microbes infected and killed the cancer cells directly, while having no effect on healthy tissue. Encouraged by these results, the scientists wondered if Listeria could be used to deliver cancer-fighting therapies straight to tumor cells, including metastatic ones.
Moving to the Albert Einstein College of Medicine in New York City, Gravekamp teamed up with radiobiologist Ekaterina Dadachova and colleagues to combine modified Listeria with the radioactive compound rhenium-188, which they attached to an engineered protein called a monoclonal antibody that sticks to the bacterium. Over the course of 16 days (including a weeklong break), they injected mice already infected with a highly metastatic form of pancreatic cancer with the "labeled" bacteria. The radioactive bacteria treatment reduced the number of metastatic cells by 90% compared with mice given a saline solution, the team reports online today in the Proceedings of the National Academy of Sciences. The attenuated Listeria alone decreased metastatic cells by 50%. The treatment's effect on the original tumor was less dramatic, but still impressive: The combination of Listeria and radiation shrank the tumor by 64%, and Listeria alone by about 20% compared with saline-treated mice.

There was also very little damage to healthy tissue. The treatment's extreme precision results from its ability to turn the cancer cells' own defenses against them, Gravekamp explains. In healthy tissue, the immune system swiftly clears out the modified bacteria. Cancer cells, however, have ways of shutting down immune activity in their vicinity. For example, they produce proteins called cytokines that tell infection-fighting immune cells to back off and recruit "suppressor" cells directly from the bone marrow that help cancel the immune attack. "By turning off the immune cells that would have protected them, the cancer cells make themselves uniquely vulnerable to the treatment," Gravekamp says. "We envision this approach as a second-line therapy, which would follow either surgery or radiation to remove the primary tumor," she says.

Co-author Dadachova adds that although a 90% reduction in metastatic cells is impressive, the remaining 10% are still potentially fatal. She believes that it's possible to get the success rate to 100%, by using longer-lasting forms of radiation.

"This is an innovative and promising approach for a bad, bad disease," says Fred Gorelick, a clinician and researcher at Yale University who specializes in diseases of the pancreas. He cautions, though, that some issues should be addressed in further research to make the treatment a realistic approach for humans. For example, although early clinical trials of Listeria-based vaccines have shown that the neutralized bacterium produces only mild flulike symptoms in human patients with cervical cancer, the various methods of genetically disarming the bacteria should be explored to find the safest approach for people gravely ill with pancreatic cancer, because these patients are likely to already have weak immune systems. Gorelick would also like to make sure that no dangerous levels of radiation are released as the bacteria die, noting that some buildup was seen in the kidney tissue of the mice treated in the new study.

But, he says, "the number of new cases of pancreatic cancer every year is 40,000, and the number of deaths every year is 40,000." The prospects for that condition are bleak enough to allow for a degree of risk that might not be acceptable in less serious types of cancer, Gorelick concludes.

http://www.eurekalert.org/pub_releases/2013-04/d-ssd042313.php

Study shows drinking one 12oz sugar-sweetened soft drink a day can increase the risk of type 2 diabetes by 22 percent

Drinking one (or one extra)[1] 12oz serving size of sugar-sweetened soft drink a day can be enough to increase the risk of developing type 2 diabetes by 22%, a new study suggests.

The research is published in Diabetologia (the journal of the European Association for the Study of Diabetes) and comes from data in the InterAct consortium[2]. The research is by Dr Dora Romaguera, Dr Petra Wark and Dr Teresa Norat, Imperial College London, UK, and colleagues.

Since most research in this area has been conducted in North American populations, the authors wanted to establish if a link between sweet beverage consumption and type 2 diabetes existed in Europe. They used data on consumption of juices and nectars, sugar-sweetened soft drinks and artificially sweetened soft drinks collected across eight European cohorts participating in the European Prospective Investigation into Cancer and Nutrition (EPIC study; UK, Germany, Denmark, Italy, Spain, Sweden, France, Italy, Netherlands)[3], covering some 350,000 participants.

As part of the InterAct project, the researchers did a study which included 12,403 type 2 diabetes cases and a random sub-cohort of 16,154 identified within EPIC. The researchers found that, after adjusting for confounding factors, consumption of one 12oz (336ml) serving size of sugar-sweetened soft drink per day increased the risk of type 2 diabetes by 22%. This increased risk fell slightly to 18% when total energy intake and body-mass index (BMI) were accounted for[4] (both factors that are thought to mediate the association between sugar-sweetened soft drink consumption and diabetes incidence). This could indicate that the effect of sugar-sweetened soft drink on diabetes goes beyond its effect on body weight.

The authors also observed a statistically significant increase in type 2 diabetes incidence related to artificially sweetened soft drink consumption, however this significant association disappeared after taking into account the BMI of participants; this probably indicates that the association was not causal but driven by the weight of participants (i.e. participants with a higher body weight tend to report higher consumption of artificially sweetened drinks, and are also more likely to develop diabetes). Pure fruit juice and nectar[5] consumption was not significantly associated with diabetes incidence, however it was not possible using the data available to study separately the effect of 100% pure juices from those with added sugars.

The authors say the increased risk of diabetes among sugar-sweetened soft drink consumers in Europe is similar to that found in a meta-analysis of previous studies conducted mostly in North America (that found a 25% increased risk of type 2 diabetes associated with one 12 oz daily increment of sugar-sweetened beverage consumption).

Dr Romaguera concludes: "Given the increase in sweet beverage consumption in Europe, clear messages on the unhealthy effect of these drinks should be given to the population."

Notes to editors:

[1] The increased risk of 22% is for each extra 12oz sugar sweetened drink, so would apply to someone who had 1 drink versus someone who had 0, or someone who had 2 drinks versus someone who had 1, etc.

[2] The InterACT consortium is investigating, among other things, nutritional factors and physical activity to study the association of nutritional, dietary and physical activity behaviours with incident diabetes in the nested case-cohort study and to contribute to the analysis of gene-lifestyle interaction. It is a sub-division of the EPIC study, which was designed to investigate the relationships between diet, nutritional status, lifestyle and environmental factors and the incidence of cancer and other chronic diseases.

[3] The centres involved were France, Italy, Spain, Denmark, UK (Oxford, Cambridge), Netherlands (Bilthoven, Utrecht), Germany (Heidelberg, Potsdam), Sweden (Umea, Malmo)

[4] Extra info from Dr Romaguera: The 22% figure is used as the top line because it is widely accepted by the scientific community that these models should not be adjusted for BMI. In the meta-analysis comparison with other studies from the USA, the risk is those studies is NOT adjusted by BMI. That makes it possible to compare the two sets of results (25% increased risk in North American studies versus 22% in Europe).

[5] nectars (UK and USA definition) are fruit juices that have been diluted to some extent and may contain additives (sugar or sweeteners)

http://www.eurekalert.org/pub_releases/2013-04/uoc-pan042313.php

Psychopaths are not neurally equipped to have concern for others

Psychopaths lack the basic neurophysiological "hardwiring" that enables them to care for others

Prisoners who are psychopaths lack the basic neurophysiological "hardwiring" that enables them to care for others, according to a new study by neuroscientists at the University of Chicago and the University of New Mexico.

"A marked lack of empathy is a hallmark characteristic of individuals with psychopathy," said the lead author of the study, Jean Decety, the Irving B. Harris Professor in Psychology and Psychiatry at UChicago.

Psychopathy affects approximately 1 percent of the United States general population and 20 percent to 30 percent of the male and female U.S. prison population. Relative to non-psychopathic criminals, psychopaths are responsible for a disproportionate amount of repetitive crime and violence in society. "This is the first time that neural processes associated with empathic processing have been directly examined in individuals with psychopathy, especially in response to the perception of other people in pain or distress," he added.

The results of the study, which could help clinical psychologists design better treatment programs for psychopaths, are published in the article, "Brain Responses to Empathy-Eliciting Scenarios Involving Pain in Incarcerated Individuals with Psychopathy," which appears online April 24 in the journal JAMA Psychiatry.

Joining Decety in the study were Laurie Skelly, a graduate student at UChicago; and Kent Kiehl, professor of psychology at the University of New Mexico.

For the study, the research team tested 80 prisoners between ages 18 and 50 at a correctional facility. The men volunteered for the test and were tested for levels of psychopathy using standard measures. They were then studied with functional MRI technology, to determine their responses to a series of scenarios depicting people being intentionally hurt. They were also tested on their responses to seeing short videos of facial expressions showing pain.

The participants in the high psychopathy group exhibited significantly less activation in the ventromedial prefrontal cortex, lateral orbitofrontal cortex, amygdala and periaqueductal gray parts of the brain, but more activity in the striatum and the insula when compared to control participants, the study found.

The high response in the insula in psychopaths was an unexpected finding, as this region is critically involved in emotion and somatic resonance. Conversely, the diminished response in the ventromedial prefrontal cortex and amygdala is consistent with the affective neuroscience literature on psychopathy. This latter region is important for monitoring ongoing behavior, estimating consequences and incorporating emotional learning into moral decision-making, and plays a fundamental role in empathic concern and valuing the well-being of others.

"The neural response to distress of others such as pain is thought to reflect an aversive response in the observer that may act as a trigger to inhibit aggression or prompt motivation to help," the authors write in the paper. "Hence, examining the neural response of individuals with psychopathy as they view others being harmed or expressing pain is an effective probe into the neural processes underlying affective and empathy deficits in psychopathy," the authors wrote.

Decety is one of the world's leading experts on the biological underpinnings of empathy. His work also focuses on the development of empathy and morality in children. The study with prisoners was supported with a $1.6 million grant from the National Institute of Mental Health.

http://www.eurekalert.org/pub_releases/2013-04/meae-run042313.php

Researchers use nasal lining to breach blood/brain barrier

Discovery widens treatment options for neurodegenerative and central nervous system disease

BOSTON - Neurodegenerative and central nervous system (CNS) diseases represent a major public health issue affecting at least 20 million children and adults in the United States alone. Multiple drugs exist to treat and potentially cure these debilitating diseases, but 98 percent of all potential pharmaceutical agents are prevented from reaching the CNS directly due to the blood-brain barrier.

Using mucosa, or the lining of the nose, researchers in the department of Otology and Laryngology at the Massachusetts Eye and Ear/Harvard Medical School and the Biomedical Engineering Department of Boston University have demonstrated what may be the first known method to permanently bypass the blood-brain barrier, thus opening the door to new treatment options for those with neurodegenerative and CNS disease. Their study is published on PLOS ONE.

Many attempts have been made to deliver drugs across the blood-brain barrier using methods such as osmotic disruption and implantation of catheters into the brain, however these methods are temporary and prone to infection and dislodgement.

"As an endoscopic skull base surgeon, I and many other researchers have helped to develop methods to reconstruct large defects between the nose and brain using the patient's own mucosa or nasal lining," said Benjamin S. Bleier, M.D., Otolaryngologist at Mass. Eye and Ear and HMS Assistant Professor.

Study co-author Xue Han, Ph.D., an assistant professor of Biomedical Engineering at Boston University, said, "The development of this model enables us to perform critical preclinical testing of novel therapies for neurological and psychiatric diseases."

Inspired by recent advances in human endoscopic transnasal skull based surgical techniques, the investigators went to work to develop an animal model of this technique and use it to evaluate transmucosal permeability for the purpose of direct drug delivery to the brain.

In this study using a mouse model, researchers describe a novel method of creating a semi-permeable window in the blood-brain barrier using purely autologous tissues to allow for higher molecular weight drug delivery to the CNS. They demonstrated for the first time that these membranes are capable of delivering molecules to the brain which are up to 1,000-times larger than those excluded by the blood-brain barrier.

"Since this is a proven surgical technique which is known to be safe and well tolerated, this data suggests that these membranes may represent the first known method to permanently bypass the blood-brain barrier using the patient's own tissue," Dr. Bleier said. "This method may open the door for the development of a variety of new therapies for neurodegenerative and CNS disease.

Future studies will be directed towards developing clinical trials to test this method in patients who have already undergone these endoscopic surgeries."

The study was supported by a grant from the Michael J. Fox Foundation for Parkinson's Research and represents a collaborative effort between Mass. Eye and Ear and Dr. Xue Han of the Biomedical Engineering Department at Boston University. Other authors include Richie E. Kohman, Rachel E. Feldman and Shrestha Ramanlal.

http://www.eurekalert.org/pub_releases/2013-04/uom-vrc042413.php

Video reveals cancer cells' Achilles' heel

Scientists from the Manchester Collaborative Centre for Inflammation Research (MCCIR) have discovered why a particular cancer drug is so effective at killing cells.

Their findings could be used to aid the design of future cancer treatments. Professor Daniel Davis and his team used high quality video imaging to investigate why the drug rituximab is so effective at killing cancerous B cells. It is widely used in the treatment of B cell malignancies, such as lymphoma and leukaemia - as well as in autoimmune diseases like rheumatoid arthritis.

Using high-powered laser-based microscopes, researchers made videos of the process by which rituximab binds to a diseased cell and then attracts white blood cells known as natural killer (NK) cells to attack. They discovered that rituximab tended to stick to one side of the cancer cell, forming a cap and drawing a number of proteins over to that side. It effectively created a front and back to the cell - with a cluster of protein molecules massed on one side.

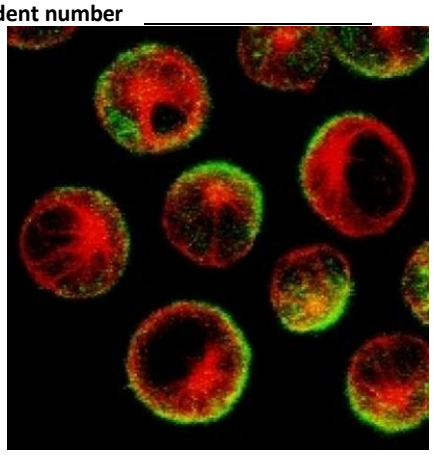
But what surprised the scientists most was how this changed the effectiveness of natural killer cells in destroying these diseased cells. When the NK cell latched onto the rituximab cap on the B cell, it had an 80% success rate at killing the cell. In contrast, when the B cell lacked this cluster of proteins on one side, it was killed only 40% of the time.

Professor Davis says: "These results were really unexpected. It was only possible for us to unravel the mystery of why this drug was so effective, through the use of video microscopy. By watching what happened within the

cells we could clearly identify just why rituximab is such an effective drug – because it tended to reorganise the cancerous cell and make it especially prone to being killed."

He continues: "What our findings demonstrate is that this ability to polarise a cell by moving proteins within it should be taken into consideration when new antibodies are being tested as potential treatments for cancer cells. It appears that they can be up to twice as effective if they bind to a cell and reorganise it."

The findings from this study have been published online today on the website of the journal Blood. The research was carried out in collaboration with MedImmune, the global biologics research and development arm of AstraZeneca.



***This image shows cancerous B cells that have been treated with rituximab. The protein CD20 (shown in green) has been drawn to the side of the cells. When the Natural Killer white blood cells approach they will stand an 80 percent chance of killing the cell if they latch on to the side where the protein has collected* Video MCCIR**

Commenting on the research Dr Matt Sleeman, Senior Director of Biology at MedImmune said: "Not only is this a great observation that can influence how we as a biotech company identify and design future therapies, it also shows the innovative 'out of the box' thinking that can be achieved by working in close partnership with academics at the top of their field. This unique partnership, bringing together industry and academia, demonstrates a real catalyst of scientific change within the UK, and I am excited by the potential of the MCCIR to bring further innovation that could ultimately bring benefit to patients."

Much of the research for this study was carried out during Professor Davis' time at Imperial College London. He will be continuing to use high quality video imaging at a microscopic level to investigate immunology at the MCCIR.

Professor Davis and MedImmune would like to acknowledge the funding they received from the Medical Research Council which helped make this study possible. The aim of the grant was to bring industry and academia closer together.

http://www.eurekalert.org/pub_releases/2013-04/vt-hpd042413.php

Humans passing drug resistance to animals in protected Africa, Virginia Tech study says

Research identifies the coupled nature of humans, animals and environment

A team of Virginia Tech researchers has discovered that humans are passing antibiotic resistance to wildlife, especially in protected areas where numbers of humans are limited. In the case of banded mongoose in a Botswana study, multidrug resistance among study social groups, or troops, was higher in the protected area than in troops living in village areas. The study also reveals that humans and mongoose appear to be readily exchanging fecal microorganisms, increasing the potential for disease transmission.

"The research identifies the coupled nature of humans, animals, and the natural environment across landscapes, even those designated as protected," said Kathleen Alexander, an associate professor of wildlife in Virginia Tech's College of Natural Resources and Environment. "With few new antibiotics on the horizon, wide-scale antibiotic resistance in wildlife across the environment presents a critical threat to human and animal health. As humans and animals exchange microorganisms, the threat of emerging disease also increases."

The National Science Foundation-funded research project investigating how pathogens might move between humans and animals was published today (April 24, 2013) by EcoHealth. "Tracking Pathogen Transmission at the Human-Wildlife Interface: Banded Mongoose and Escherichia coli" is co-authored by Risa Pesapane of Portsmouth, Va., then a wildlife sciences master's student at Virginia Tech; microbiologist Monica Ponder, an assistant professor of food science and technology in Virginia Tech's College of Agriculture and Life Sciences; and Alexander, who is the corresponding author.

Alexander and Ponder are both affiliated with Virginia Tech's Fralin Life Science Institute. Alexander, a veterinarian and researcher with the nonprofit Center for African Resources: Animals, Communities, and Land Use (CARACAL), has been conducting a long-term ecological study of banded mongoose in the region.

The researchers collected fecal samples from three troops of banded mongoose living in Botswana's Chobe National Park and three troops living in villages outside the park.

"Banded mongoose forage in garbage resources and search for insects in fecal waste, including human sources found in the environment," said Alexander. "Mongoose contact with other wildlife and humans, and broad occurrence across the landscape, makes this species an ideal candidate for evaluating microbial exchange and the potential for pathogens to be transmitted and emerge at the human-wildlife interface."

With the exception of one mongoose troop, all study animals had some level of their range overlap with human populations. Two of the study troops had home ranges that included ecotourism facilities in the protected area,

with some contact with humans and development "but at a much lower level than in the village troops," the article reported.
Fecal samples were collected from these mongoose troops living in a protected area and in surrounding villages. Human feces were collected from sewage treatment facilities, environmental spills, and bush latrines or sites of open-air defecation within mongoose home ranges. The team used Escherichia coli (E. coli), which is commonly found in the gut of humans and animals, as a model microorganism to investigate the potential for microorganisms to move between humans and wildlife. They evaluated the degree of antibiotic resistance considered an important signature of bacteria that arise from human sources. The researchers also extracted data from the local hospital to assess antibiotic resistance among patients and identify resistance patterns in the region. Like many places in Africa, antibiotics are widely available and there are few controls on the dispensing of such drugs.
The project screened for nine locally available antimicrobials, including ampicillin, tetracycline, doxycycline, and streptomycin, as well as ceftiofur, a veterinary drug not available in the study area. The researchers discovered 57 percent of banded mongoose had E. coli that was antibiotic resistant. "Resistance was identified among individuals in all sampled troops," the article reports. The animals were most commonly resistant to ampicillin, followed by doxycyline, tetracycline, and streptomycin. But it was the prevalence of multidrug resistance that was most alarming. "There was a significant difference between troops in protected area and those outside the park, although not what you might expect," said Alexander.
One troop in the town of Kazungula, outside the protected area, had the lowest level of multidrug resistance among sampled mongoose, while a troop from the protected area living near an ecotourism facility had the highest levels. At least one sampled mongoose in this particular troop in the protected area was resistant to each of the 10 antibiotics screened in the study.
As is common of mongoose that live near humans, the troop near the ecotourism facility utilized the opportunities presented by its human neighbors, setting up residence in the drain fields of the open septic tanks servicing the employee accommodations and foraging around employee living quarters, including eating food remains from dishes left outside. One interaction between the employees resulted in an unexpected finding - the kitchen staff fed raw meat waste from commercially produced chickens to mongoose. "This may be how the mongoose developed resistance to ceftiofur," said Alexander. The one troop living in an undisturbed region of the park was resistant to only ampicillin. "These findings reinforce the significance of human impacts to natural environments, even when human numbers are low," said Alexander.
The article reports that mongoose were resistant to the same antibiotics as humans in the region, but at a lower level. Of human fecal samples collected in the mongoose home ranges, 80.3 percent were resistant to at least one antibiotic. Of the human clinical samples screened at the local hospital, 89.9 percent of various isolated bacteria species were resistant to at least one antibiotic.
"This work identifies direct support for the possibility that direct human fecal contamination of the environment is an important potential source of microbial exposure and transmission to wildlife living in these areas," said Ponder, who was with the U.S. Centers for Disease Control and Prevention before coming to Virginia Tech. "Ecotourism developments are important for conservation and economic growth, but the associated human waste, which includes garbage as well as feces and waste water, may expose wildlife to human-associated pathogens and antibiotic resistance, ultimately increasing future threats to human health," said Alexander.
The project was funded by a National Science Foundation (NSF) Dynamics of Coupled Natural and Human Systems award, the Morris Animal Foundation, and the WildiZe Foundation. The NSF Scholarships in Science, Technology, Engineering, and Mathematics program also provided partial financial support for Pesapane.
"The impact of microbial exchange and antibiotic resistance accumulation in mongoose may extend through food webs," the researchers conclude. "Mongoose are eaten by a large number of avian, reptile, and mammalian predators including domestic dogs. Thus, the cascading effects of exposure of wildlife species to human waste-associated microbes can impact an array of susceptible species across an ecosystem and in turn increase human exposure, coupling humans and natural systems in complicated ways."
They recommend closed sewage systems, wildlife-proofed trash receptacles, and prohibiting feeding poultry and livestock products from kitchen waste to either wildlife or domestic animals. "As we change our natural environments, these modifications can in turn impact our own health," said Alexander. "We are working with the Botswana Ministry of Health and Ministry of Environment, Wildlife, and Tourism to minimize these impacts and develop sustainable approaches to the protection of human, wildlife, and ecosystem health."
Pesapane said the research experience reinforced that "the issue of global sustainability and health is multifaceted, and an interdisciplinary approach is vital to achieving progress in managing health threats at this complex interface."

Pointing out the interconnectedness of human health and wellbeing and conservation of natural resources, she said, "We cannot begin to address issues of conservation without also improving quality of life in neighboring communities.
"The Virginia Tech/CARACAL program under the NSF-funded program embodied this concept with expanded program focus beyond research in the Chobe region to include educational outreach and partnered efforts with the Government of Botswana to improve the quality of life for the citizens of Botswana," she added.
Pesapane, who completed her master's in wildlife science at Virginia Tech in December 2011, is now project director of Rural System Inc. "My experience with the Alexander lab, its nonprofit affiliate CARACAL, and my education in the fish and wildlife conservation department at Virginia Tech provided a solid foundation for an inspiring career in global conservation," she said.
"Our next step," Alexander said, "is to begin to unravel the interdependent natural and human drivers of microorganism exchange, emergence of disease, and spread of antibiotic resistance among wildlife and across environments. This will be essential to our ability to effectively manage this interface and protect the health of humans, wildlife, and environments on which we depend."

http://www.eurekalert.org/pub_releases/2013-04/uoc--rea042413.php

Rethinking early atmospheric oxygen

Model results from a UC Riverside research team open the possibility of a more dynamic biological oxygen cycle on the early Earth than previously supposed

RIVERSIDE, Calif. — A research team of biogeochemists at the University of California, Riverside has provided a new view on the relationship between the earliest accumulation of oxygen in the atmosphere, arguably the most important biological event in Earth history, and its relationship to the sulfur cycle.
A general consensus exists that appreciable oxygen first accumulated in Earth's atmosphere around 2.4 to 2.3 billion years ago. Though this paradigm is built upon a wide range of geological and geochemical observations, the famous "smoking gun" for what has come to be known as the "Great Oxidation Event" (GOE) comes from the disappearance of anomalous fractionations in rare sulfur isotopes.
"These isotope fractionations, often referred to as 'mass-independent fractionations,' or 'MIF' signals, require both the destruction of sulfur dioxide by ultraviolet energy from the sun in an atmosphere without ozone and very low atmospheric oxygen levels in order to be transported and deposited in marine sediments," said Christopher T. Reinhard, the lead author of the research paper and a former UC Riverside graduate student. "As a result, their presence in ancient rocks is interpreted to reflect vanishingly low atmospheric oxygen levels continuously for the first ~2 billion years of Earth's history."
However, diverse types of data are emerging that point to the presence of atmospheric oxygen, and, by inference, the early emergence of oxygenic photosynthesis hundreds of millions of years before these MIF signals disappear from the rock record. These observations motivated Reinhard and colleagues to explore the possible conditions under which inherited MIF signatures may have persisted in the rock record long after oxygen accumulated in the atmosphere.
Using a simple quantitative model describing how sulfur and its isotopes cycle through the Earth's crust, the researchers discovered that under certain conditions these MIF signatures can persist within the ocean and marine sediments long after O2 increases in the atmosphere. Simply put, the weathering of rocks on the continents can transfer the MIF signal to the oceans and their sediments long after production of this fingerprint has ceased in an oxygenated atmosphere.
"This lag would blur our ability to date the timing of the GOE and would allow for dynamic rising and falling oxygen levels during a protracted transition from an atmosphere without oxygen to one rich in this life-giving gas," Reinhard said. Study results appear in Nature's advanced online publication on April 24.
Reinhard explained that once MIF signals formed in an oxygen-poor atmosphere are captured in pyrite and other minerals in sedimentary rocks, they are recycled when those rocks are later uplifted as mountain ranges and the pyrite is oxidized.
"Under certain conditions, this will create a sort of 'memory effect' of these MIF signatures, providing a decoupling in time between the burial of MIF in sediments and oxygen accumulation at Earth's surface," he said.
According to the researchers, the key here is burying a distinct MIF signal in deep sea sediments, which are then subducted and removed from Earth's surface.
"This would create a complementary signal in minerals that are weathered and delivered to the oceans, something that we actually see evidence of in the rock record," said Noah Planavsky, the second author of the research paper and a former UC Riverside graduate student now at Caltech. "This signal can then be perpetuated through time without the need to generate it within the atmosphere contemporaneously."

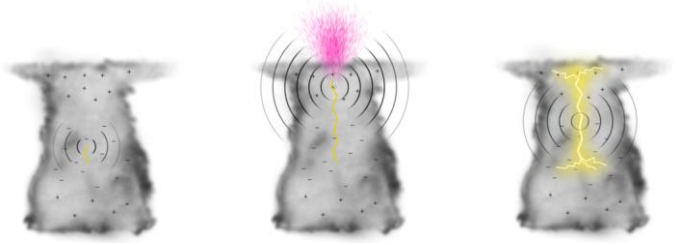
Reinhard, now a postdoctoral fellow at Caltech and soon to be an assistant professor at Georgia Institute of Technology, explained that although the researchers' new model provides a plausible mechanism for reconciling recent conflicting data, this can only occur when certain key conditions are met — and these conditions are likely to have changed through time during Earth's long early history.
"There is obviously much further work to do, but we hope that our model is one step toward a more integrated view of how Earth's crust, mantle and atmosphere interact in the global sulfur cycle," he said.
Timothy W. Lyons, a professor of biogeochemistry at UCR and the principal investigator of the research project noted that this is a fundamentally new and potentially very important way of looking at the sulfur isotope record and its relationship to biospheric oxygenation.
"The message is that sulfur isotope records, when viewed through the filter of sedimentary recycling, may challenge efforts to precisely date the GOE and its relationship to early life, while opening the door to the wonderful unknowns we should expect and embrace," he said.
The research was supported by an O.K. Earl Postdoctoral Fellowship in the Division of Geological and Planetary Sciences at Caltech to Reinhard, a National Science Foundation postdoctoral fellowship to Planavsky, and a NASA Exobiology grant to Lyons.

http://phys.org/news/2013-04-scientists-dark-lightning-linked-visible.html

Scientists detect dark lightning linked to visible lightning

Researchers have identified a burst of high-energy radiation known as 'dark lightning" immediately preceding a flash of ordinary lightning.

Phys.org - The new finding provides observational evidence that the two phenomena are connected, although the exact nature of the relationship between ordinary bright lightning and the dark variety is still unclear, the scientists said.
"Our results indicate that both these phenomena, dark and bright lightning, are intrinsic processes in the discharge of lightning," said Nikolai Østgaard, who is a space scientist at the University of Bergen in Norway and led the research team. He and his collaborators describe their findings in an article recently accepted in Geophysical Research Letters—a journal of the American Geophysical Union.



Three images, left to right, of the same thundercloud depict a less-than-10-milliseconds-long sequence of events: (left) formation within the cloud of a small channel, or 'leader,' of electrical conductivity (yellow line) with weak emission of radio signals (ripples), to (middle) a burst of both dark lightning (pink) and radio waves (larger ripples), to (right) a discharge of bright lightning and more radio waves. Credit: Studio Gohde

Dark lightning is a burst of gamma rays produced during thunderstorms by extremely fast moving electrons colliding with air molecules. Researchers refer to such a burst as a terrestrial gamma ray flash.
Dark lightning is the most energetic radiation produced naturally on Earth, but was unknown before 1991. While scientists now know that dark lightning naturally occurs in thunderstorms, they do not know how frequently these flashes take place or whether visible lightning always accompanies them.
In 2006, two independent satellites—one equipped with an optical detector and the other carrying a gamma ray detector—coincidentally flew within 300 kilometers (186 miles) of a Venezuelan storm as a powerful lightning bolt exploded within a thundercloud. Scientists were unaware then that a weak flash of dark lightning had preceded the bright lightning.
But last year, Østgaard and his colleagues discovered the previously unknown gamma ray burst while reprocessing the satellite data. "We developed a new, improved search algorithm…and identified more than twice as many terrestrial gamma flashes than originally reported," said Østgaard. He and his team detected the gamma ray flash and a discharge of radio waves immediately preceding the visible lightning.
"This observation was really lucky," Østgaard said. "It was fortuitous that two independent satellites - which are traveling at 7 kilometers per second (4.3 miles per second) - passed right above the same thunderstorm right as the pulse occurred." A radio receiver located 3,000 kilometers (1864 miles) away at Duke University in Durham, North Carolina detected the radio discharge. The satellites' observations combined with radio-wave data provided the information that Østgaard and his team used to reconstruct this ethereal electrical event, which lasted 300 milliseconds.
Østgaard and his team suspect that the flash of dark lightning was triggered by the strong electric field that developed immediately before the visible lightning. This strong field created a cascade of electrons moving at close to the speed of light. When those relativistic electrons collided with air molecules, they generated gamma

rays and lower energy electrons that were the main electric current carrier that produced the strong radio pulse before the visible lightning.
Dark and bright lightning may be intrinsic processes in the discharge of lightning, Østgaard said, but he stressed that more research needs to be done to elucidate the link.
The European Space Agency is planning on launching the Atmospheric Space Interactions Monitor (ASIM) within the next three years, which will be able to better detect both dark and visible lightning from space, said Østgaard, who is part of the team that is building the ASIM gamma-ray detector.
Dark lightning has remained a perplexing phenomenon due to scientific limitations and a dearth of measurements, Østgaard explained.
"Dark lightning might be a natural process of lightning that we were completely unaware of before 1991," he noted. "But it is right above our heads, which makes it very fascinating."
More information: "Simultaneous observations of optical lightning and terrestrial gamma ray flash from space" onlinelibrary.wiley.com/doi/10.1002/grl.50466/abstract

http://phys.org/news/2013-04-asymmetry-human-brain-cognition-primates.html

Asymmetry of human brain enhances cognition compared to other primates

New research shows that the human brain has higher levels of asymmetry than chimpanzees.

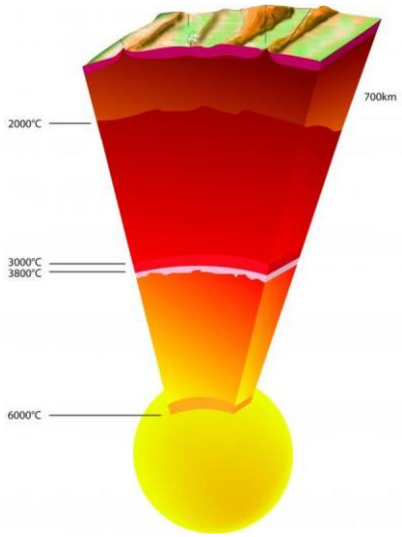
Phys.org - This may be what elevates our cognition above that of other primates, according to the paper published in Proceedings of the Royal Society B today.
The human brain is asymmetric in structure and function, but until now it has been poorly understood how this compares with other primates. Researchers from The George Washington University analysed in vivo MRI scans of 72 chimpanzees (aged 6 to 50 years old) and 73 humans (aged 18 to 60) . They found that the brain form of humans displays elevated levels of asymmetry compared to chimpanzees.
The flexible asymmetry of the human scans is caused by environmental factors during development. This signals enhanced plasticity in the evolving human brain which was fundamental in the development of human cognitive abilities.
This is the first time that scientists have used in vivo MRI scans for this purpose. Comparing brain asymmetry in vivo rather than using fossilised skulls allowed Dr Aida Gómez-Robles and her team to observe the higher levels of fluctuating asymmetry in human brains. The researchers thus conclude that the more asymmetric human brain may help explain our enhanced cognitive ability over chimpanzees and other primates.
More information: Gomez-Robles, A., Hopkins, W. and Sherwood, C. Increased morphological asymmetry, evolvability and plasticity in human brain evolution, Proceedings of the Royal Society B. dx.doi.org/10.1098/rspb.2013.0575

http://www.eurekalert.org/pub_releases/2013-04/esrf-tec042213.php

The Earth's center is 1,000 degrees hotter than previously thought

New results solve a 20-year conflict between theory and experiment

Grenoble - Scientists have determined the temperature near the Earth's centre to be 6000 degrees Celsius, 1000 degrees hotter than in a previous experiment run 20 years ago. These measurements confirm geophysical models that the temperature difference between the solid core and the mantle above, must be at least 1500 degrees to explain why the Earth has a magnetic field. The scientists were even able to establish why the earlier experiment had produced a lower temperature figure. The results are published on 26 April 2013 in Science.
The research team was led by Agnès Dewaele from the French national technological research organization CEA, alongside members of the French National Center for Scientific Research CNRS and the European Synchrotron Radiation Facility ESRF in Grenoble (France).
The Earth's core consists mainly of a sphere of liquid iron at temperatures above 4000 degrees and pressures of more than 1.3 million atmospheres. Under these conditions, iron is as liquid as the water in the oceans. It is only at the very centre of the Earth, where pressure and temperature rise even higher, that the liquid iron solidifies.



This artist's view depicts the different layers of the Earth and their representative temperatures: crust, upper and lower mantle (brown to red), liquid outer core (orange) and solid inner core (yellow). The pressure at the border between the liquid and the solid core (highlighted) is 3.3 million atmospheres, with a temperature now confirmed as 6000 degrees Celsius. **Credit: ESRF**

Analysis of earthquake-triggered seismic waves passing through the Earth, tells us the thickness of the solid and liquid cores, and even how the pressure in the Earth increases with depth. However these waves do not provide

information on temperature, which has an important influence on the movement of material within the liquid core and the solid mantle above. Indeed the temperature difference between the mantle and the core is the main driver of large-scale thermal movements, which together with the Earth's rotation, act like a dynamo generating the Earth's magnetic field. The temperature profile through the Earth's interior also underpins geophysical models that explain the creation and intense activity of hot-spot volcanoes like the Hawaiian Islands or La Réunion.

To generate an accurate picture of the temperature profile within the Earth's centre, scientists can look at the melting point of iron at different pressures in the laboratory, using a diamond anvil cell to compress speck-sized samples to pressures of several million atmospheres, and powerful laser beams to heat them to 4000 or even 5000 degrees Celsius."In practice, many experimental challenges have to be met", explains Agnès Dewaele from CEA, "as the iron sample has to be insulated thermally and also must not be allowed to chemically react with its environment. Even if a sample reaches the extreme temperatures and pressures at the centre of the Earth, it will only do so for a matter of seconds. In this short timeframe it is extremely difficult to determine whether it has started to melt or is still solid".

This is where X-rays come into play. "We have developed a new technique where an intense beam of X-rays from the synchrotron can probe a sample and deduce whether it is solid, liquid or partially molten within as little as a second, using a process known diffraction", says Mohamed Mezouar from the ESRF, "and this is short enough to keep temperature and pressure constant, and at the same time avoid any chemical reactions".

The scientists determined experimentally the melting point of iron up to 4800 degrees Celsius and 2.2 million atmospheres pressure, and then used an extrapolation method to determine that at 3.3 million atmospheres, the pressure at the border between liquid and solid core, the temperature would be 6000 +/- 500 degrees. This extrapolated value could slightly change if iron undergoes an unknown phase transition between the measured and the extrapolated values.

When the scientists scanned across the area of pressures and temperatures, they observed why Reinhard Boehler, then at the MPI for Chemistry in Mainz (Germany), had in 1993 published values about 1000 degrees lower. Starting at 2400 degrees, recrystallization effects appear on the surface of the iron samples, leading to dynamic changes of the solid iron's crystalline structure. The experiment twenty years ago used an optical technique to determine whether the samples were solid or molten, and it is highly probable that the observation of recrystallization at the surface was interpreted as melting.

"We are of course very satisfied that our experiment validated today's best theories on heat transfer from the Earth's core and the generation of the Earth's magnetic field. I am hopeful that in the not-so-distant future, we can reproduce in our laboratories, and investigate with synchrotron X-rays, every state of matter inside the Earth," concludes Agnès Dewaele.

S. Anzellini et al.: Melting of Iron at earth's Inner Core Boundary based on Fast X-ray Diffraction, Science 26 April 2013
R. Boehler, Temperatures in the Earth's core from melting-point measurements of iron at high static pressures, Nature 363, 534 - 536 (10 June 1993); doi:10.1038/363534a0

http://phys.org/news/2013-04-iron-primeval-seas-rusted-bacteria.html

Iron in primeval seas rusted by bacteria

Researchers from the University of Tübingen have been able to show for the first time how microorganisms contributed to the formation of the world's biggest iron ore deposits.

Phys.org - The biggest known deposits – in South Africa and Australia – are geological formations billions of years old. They are mainly composed of iron oxides – minerals we know from the rusting process. These iron ores not only make up most of the world demand for iron – the formations also help us to better understand the evolution of the atmosphere and climate, and provide important information on the activity of microorganisms in the early history of life on Earth.

The extent to which microbes in the Earth's ancient oceans contributed to the formation of iron deposits was previously unknown. Now an international team of researchers from the US, Canada and Germany has published new findings in the journal Nature Communications. Led by University of Tübingen geomicrobiologist Professor Andreas Kappler of the Center for Applied Geoscience, they found evidence of which microbes contributed to the formation of the iron ores, and were able to show how different metabolic processes can be distinguished in the rock formations today.

The iron in the Earth's ancient oceans was spat out of hot springs on the seafloor as dissolved, reduced ferrous [Fe(II)] iron. But most of today's iron ore is oxidized, ferric [Fe(III)] iron in the form of "rust minerals" – indicating that the Fe(II) was oxidized as it was deposited. The classic model for the formation of iron deposits suggested that the Fe(II) from the Earth's core was oxidized by the oxygen produced by cyanobacteria (blue-

green algae). This process can happen either chemically (as in the formation of rust) or by the action of microaerophilic iron-oxidizing bacteria.
But scientists are still debating at what point the Earth's atmosphere contained enough oxygen (produced by cyanobacteria) to allow the formation of big iron deposits. The oldest known iron ores were deposited in the Precambrian period and are up to four billion years old (the Earth itself is estimated to be about 4.6 billion years old). At this very early stage in geological history, there was little or no oxygen in the atmosphere. So the very oldest banded iron formations cannot be the result of O2-dependent oxidation.
In 1993, bacteria were discovered which do not need oxygen but can oxidize Fe(II) by using energy from light (anoxygenic phototrophic iron-oxidizing bacteria). Studies by Professor Kappler's team in 2005 and 2010 showed that these bacteria transform dissolved ferric iron into iron oxide (rust) – like the material in the early iron ores. Now, the geomicrobiologists from Tübingen have been able to demonstrate that, by examining the identity and structural properties of the iron minerals, it is possible to tell that the minerals were deposited by iron-oxidizing microbes and not by oxygen made available by the action of cyanobacteria. To do this, the researchers placed different amounts of organic material together with iron minerals into gold capsules and increased the pressure and temperature to simulate the transformation of the minerals over geological time. They ended up with structures of iron carbonate minerals (siderite, FeCO3), just as they occur in geological iron formations. In particular, they were able to distinguish iron carbonate structures which had been formed in the presence of a rather small amount of organic compounds (microbial biomass) from those formed in the presence of a larger amount.
This research not only provides the first clear evidence that microorganisms were directly involved in the deposition of Earth's oldest iron formations; it also indicates that large populations of oxygen-producing cyanobacteria were at work in the shallow areas of the ancient oceans, while deeper water still reached by the light (the photic zone) tended to be populated by anoxyenic or micro-aerophilic iron-oxidizing bacteria which formed the iron deposits.
More information: Koehler, I. et al. (2013) Biological carbon precursor to dianetic siderite spherulites in banded iron formations. Nature Communications. dx.doi.org/10.1038/ncomms2770

http://www.eurekalert.org/pub_releases/2013-04/yu-ars042213.php

Autism risk spotted at birth in abnormal placentas

Measuring an infant's risk of developing autism by looking for abnormalities in his/her placenta at birth

Researchers at the Yale School of Medicine have figured out how to measure an infant's risk of developing autism by looking for abnormalities in his/her placenta at birth, allowing for earlier diagnosis and treatment for the developmental disorder. The findings are reported in the April 25 online issue of Biological Psychiatry.
One out of 50 children are diagnosed with an autism spectrum disorder in the United States each year, according to the Centers for Disease Control and Prevention (CDC), but the diagnosis is usually made when these children are 3 to 4 years of age or older. By then the best opportunities for intervention have been lost because the brain is most responsive to treatment in the first year of life.
Senior author Harvey Kliman, M.D., research scientist in the Department of Obstetrics, Gynecology & Reproductive Sciences at the Yale School of Medicine, and research collaborators at the MIND Institute at the University of California, Davis, have found that abnormal placental folds and abnormal cell growths called trophoblast inclusions are key markers to identify newborns who are at risk for autism.
Kliman and his team examined 117 placentas from infants of at-risk families, those with one or more previous children with autism. These families were participating in a study called Markers of Autism Risk in Babies – Learning Early Signs. Kliman compared these at-risk placentas to 100 control placentas collected by the UC Davis researchers from the same geographic area.
The at-risk placentas had as many as 15 trophoblast inclusions, while none of the control placentas had more than two trophoblast inclusions. Kliman said a placenta with four or more trophoblast inclusions conservatively predicts an infant with a 96.7% probability of being at risk for autism.
Currently, the best early marker of autism risk is family history. Couples with a child with autism are nine times more likely to have another child with autism. Kliman said that when these at-risk families have subsequent children they could employ early intervention strategies to improve outcomes. "Regrettably couples without known genetic susceptibility must rely on identification of early signs or indicators that may not overtly manifest until the child's second or third year of life," said Kliman.
"I hope that diagnosing the risk of developing autism by examining the placenta at birth will become routine, and that the children who are shown to have increased numbers of trophoblast inclusions will have early interventions and an improved quality of life as a result of this test," Kliman added.

Other authors on the study include Kaitlin Anderson, Kristin Milano, and Saier Ye of Yale University; and Cheryl Walker, Daniel Tancredi, Isaac Pessah, and Irva Hertz-Picciotto of UC Davis.
This work was supported by the National Institutes of Health (1 P01 ES11269 and R01 ES 015359), the U.S. Environmental Protection Agency through the Science to Achieve Results (STAR) program (R829388 and R833292), the MIND Institute at the University of California, Davis, and the Yale University Reproductive and Placental Research Unit.
Citation: Biological Psychiatry, Published online (April 25, 2013)

http://www.eurekalert.org/pub_releases/2013-04/eaft-nsp042413.php

New studies prove lethal link between alcohol, weight

Research announced today at the International Liver CongressTM 2013 has revealed the deadly impact that alcohol and body weight have on liver disease.

Amsterdam, The Netherlands - Women should forgo the wine and doughnuts after a new study found the harmful combination of high alcohol intake and high body mass index (BMI) causes an increased risk of chronic liver disease.

The study analysed a cohort of over 107,000 women to investigate how a female's weight and alcohol consumption affected their chances of suffering and dying from chronic liver disease.

EASL's Scientific Committee Member Dr. Daniele Prati said this research involved a large study to investigate the combined influence of a person's alcoholic intake and BMI on the liver. Dr. Prati said:

"It's well known that alcohol and a person's weight are major causes of chronic liver disease however there has been a need for a large population study to compare these factors' influences on each other. Interestingly, the research found the combination of a woman's drinking habits and weight has an important effect on liver health and life expectancy."

More than 107,000 women across the United Kingdom who took part in the study were classed with a low or high BMI (<25 or ≥ 25) and a low or high alcohol intake (between 0-15 or over 15 units per week). BMI is a measure for human body shape based on an individual's weight and height, with people scoring ≥ 25 classified as overweight. The study found risk was significantly increased in the group of women with a high BMI and high alcohol intake, with these participants more likely to suffer from chronic liver disease.

Dr. Prati explained: "These findings will have a significant impact on how we can help millions of people across the world at risk of developing liver disease. Women are at particular risk as they are twice as sensitive as men to alcohol related liver damage and developing a more severe form of the disease at lower doses with shorter durations of alcohol consumption.

Based on this research we know that a person with low BMI and high alcoholic intake have a greater risk of developing chronic liver disease compared to a woman with a high BMI who doesn't drink very much. More research is required to determine the exact thresholds for each risk factor that independently and in combination increase the risk of chronic liver disease but this is an important first step in the right direction."

Other new research released at the congress showcased a strong link between the development of hepatocellular carcinoma (HCC) in alcoholic cirrhosis patients and metabolic fatty liver disease. The study found that patients with alcoholic cirrhosis who also have fatty liver disease and are overweight, obese or type 2 diabetic are more likely to develop HCC.

The research examined 100 patients who received transplants for alcoholic end stage liver disease to analyse the impact of both fatty liver and metabolic risk factors such as obesity and type 2 diabetes on the development of HCC in patients.

The results showed more patients with HCC had been frequently overweight (54% compared to 14% of non-HCC patients) or diabetic (43% compared to 22% of non-HCC patients). Half (50%) of patients who had fatty liver disease and were overweight, obese or had type 2 diabetes were found to have HCC compared to just 6% of patients with HCC without these other conditions.

Dr. Prati commented: "Fatty liver and alcohol have long been known as risk factors for HCC but this study tested their combined effect in patients with alcoholic cirrhosis.

These findings show patients suffering from alcoholic cirrhosis who also have a history of fatty liver disease, obesity or type 2 diabetes have a higher risk of developing liver cancer. The results will be useful to improve the management of patients with cirrhosis, and to identify cancer at early stages."

Worldwide, HCC accounts for approximately 5.4% of all cancers and causes 695,000 deaths per year, including 47,000 deaths in Europe per annum. Europe has the highest rate of alcohol consumption in the world with one in seven adults consuming more than the recommended average daily amount.

Disclaimer: the data referenced in this release is based on the submitted abstract. More recent data may be presented at the International Liver Congress™ 2013.

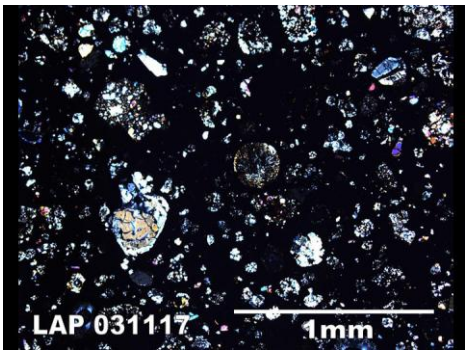
http://bit.ly/10MDhv9

Supernova Dust Fell to Earth in Antarctic Meteorites

Two primitive meteorites collected in Antarctica appear to contain grains of silica—the stuff of quartz and sand—forged in an ancient supernova that predates the birth of the solar system.

By John Matson | April 24, 2013

In fact, some researchers believe that it was just such a stellar explosion that triggered the formation of the solar system from a cloud of dust and gas billions of years ago. Whether or not the Antarctic meteorites contain a record of that fateful cataclysm, they do contain a supernova by-product that has never before been found on Earth.



Antarctic meteorite A section of the LaPaz Icefield 031117 meteorite, **courtesy of NASA.**

Researchers have identified so-called presolar grains in several primitive meteorites, which more or less preserve the chemistry of the raw materials from which they formed at the dawn of the solar system. Some presolar grains spilled into the molecular cloud that would become the solar system from nearby supernovae, and some seem to have arrived on the winds expelled from aging stars.

Presolar grains stand out from the rest because of their unusual mix of chemical isotopes, "which cannot be explained by any known process acting in the solar system," according to a study in the May 1 issue of the Astrophysical Journal Letters. "Their isotopic compositions can only be explained by nuclear reactions occurring in stellar environments."

In the new study (pdf), Pierre Haenecour of Washington University in St. Louis and his colleagues analyzed two meteorites collected in Antarctica in 2003, each named for a geographic feature near the spot where the meteorite fell. (Antarctica makes an ideal hunting ground for dark-colored meteorites, which stand out clearly against the ice fields.) Grove Mountains 021710, found by a Chinese expedition, and LaPaz Icefield 031117, collected by U.S. searchers, each harbor presolar grains of silica (SiO_2), the researchers found, as evidenced by the grains' enrichment in a heavy isotope of oxygen known as oxygen 18. That signature points to the grains' formation in a type II supernova—the explosion initiated by the collapse of a massive star's core. Other researchers had spotted presolar silica in meteorites before, but those grains had different isotopic signatures that indicated that they came from an aging star called an asymptotic giant branch (AGB) star rather than from a supernova.

The conclusion by Haenecour and his colleagues that a supernova seeded our corner of space with silica grains, among other types of dust, lends laboratory support to a 2008 study, using the Spitzer Space Telescope, that spotted the possible spectral signature of silica in the remnant of a supernova that exploded in the Milky Way so recently that its light reached Earth just 300 or so years ago.

Amassing and analyzing these presolar grains is more than just an exercise in interstellar history—a shock wave from a nearby supernova or the gentler expulsions of an AGB star could have stirred a cloud of dust and gas to collapse into the system of sun and planets that we inhabit today. Collecting presolar detritus allows astrophysicists a glimpse into the violent inner workings of dying stars and may ultimately help pinpoint just how the solar system came to be.

http://www.eurekalert.org/pub_releases/2013-04/uadb-doa042513.php

Discovery of a gene that controls 3 different diseases

The gene could also be involved in breast and ovarian cancer

An international research consortium led by the Universitat Autònoma de Barcelona (UAB), the CIBERER and the University of Wurzburg (Germany) has discovered a gene that can cause three totally different diseases, depending on how it is altered.

The researchers, using next-generation massive ultrasequencing techniques, have sequenced the over 20,000 genes of a Fanconi anaemia patient's genome. By adopting this strategy they have succeeded in identifying pathogenic mutations responsible for this disease in the ERCC4 gene, which had already been linked to two other rare diseases: xeroderma pigmentosum and a type of progeria. The latter are characterised by heightened sensitivity to sunlight, susceptibility to skin cancer and, in the case of progeria, premature aging. Fanconi anaemia, on the other hand, is characterised by progressive anaemia, congenital malformations and a high risk of developing leukaemia and mouth tumours. The ERCC4 gene can therefore be responsible for three different diseases.

The researchers have shown that this gene is involved in two DNA repair mechanisms by which cells maintain the stability of the genome, in such a way that the balance between these two repair systems will determine

which of the three diseases the patient will contract. "This is a rather exceptional case, since there are few precedents of a single gene being involved in two independent physiological mechanisms and causing three clinically different diseases", points out UAB professor Dr Jordi Surrallés.
These findings, published today in the "American Journal of Human Genetics", as well as improving the diagnosis and genetic characterisation of rare diseases, will allow new therapeutic strategies to be applied, like gene therapy or the selection of healthy, compatible embryos to cure siblings through umbilical cord transplants.
The findings add to our knowledge of the two DNA repair mechanisms, which are so important for maintaining the stability of our genes and preventing cancer in the general population. In fact, the researchers point to the importance of going on to study this gene's possible role in breast cancer and ovarian cancer.
The study was co-directed by Dr. Jordi Surrallés, a UAB professor and researcher with the Biomedical Research Network on Rare Diseases (CIBERER) and Dr. Detlev Schindler, a professor at the University of Wurzburg. Participating in it were researchers from the VU University Medical Center (Netherlands), the Erasmus University of Rotterdam (Netherlands), Stony Brook University (New York, USA), the CNIO and the CIEMAT in Madrid, and the company Sistemas Genómicos, based in Valencia. The lead author, Massimo Bogliolo, is a researcher at the CIBERER and a lecturer at the UAB, attached to Dr. Surrallés group.

http://www.bbc.co.uk/news/uk-scotland-edinburgh-east-fife-22281918

Rib and implant used to create Bonebridge ear for Edinburgh deaf man

A piece of rib and a bone conduction implant have been used in a pioneering operation to treat an Edinburgh man's hereditary deafness.

Brian Hogg, 29, was fitted with an implant called a Bonebridge and given the new ear by NHS Lothian surgeons. Mr Hogg is the first person in the UK to have the procedure. NHS Lothian said the specialist implant operation was carried out in December 2012 at the Lauriston Building in Edinburgh.

Ear drum

The Bonebridge device is fitted in the ear and is used when a patient is unable to have a conventional external hearing aid fitted.
Alex Bennett, an NHS Lothian ear, nose and throat consultant performed the procedure. Mr Bennett said: "This is a truly innovative procedure and I'm sure the device will make a significant difference to Brian and many other patients like him. "The Bonebridge implant is intended to improve hearing by replicating the actions of the ear drum. "A discreet audio processor, which is attached to the patient's head, picks up sound waves which are then amplified by the implant and passed to the inner ear through the skull bone. "These sound waves are then interpreted by the brain as sound."
Mr Hogg was born with Treacher Collins Syndrome, meaning he could not wear conventional hearing aids as they are styled to fit in and around the top and middle of the ear. Mr Hogg said: "After the new implant was been fitted I've noticed a huge difference in the range of sounds I can hear. "The sound quality is much better and I can hear noises at a distance now, which my previous device didn't pick up. "The Bonebridge implant is so light, it's practically weightless. It's tailored to most closely match my normal hearing range.
"When you think about how far mobile phone technology has come in the last 10 years, there have been similar advances in hearing aids. "The new implant is a really big step forward in technology and I'm very grateful to the team of consultants for fitting the implant for me."
Dr Ingeborg Hochmair, managing director of MED-EL, which designed the implant, said: "Our innovative development of the Bonebridge will considerably improve the lives of patients. "We consider this new development a great success. The Bonebridge is the culmination of decades of experience gathered in the development of hearing implant solutions."

http://www.sciencedaily.com/releases/2013/04/130428144925.htm

Conversion from 'Bad' Fat to Good Fat

Scientists from ETH Zurich have shown for the first time that brown and white fat cells in a living organism can be converted from one cell type to the other.

Their work, using mice as a model organism, provides important new insights into the origin of brown fat cells, which is a prerequisite for the development of successful anti-obesity therapies.
Two types of fat cells can be found in mammals and hence in humans: White fat cells function mainly as highly flexible energy stores which are filled in times of calorie abundance. The fat is stored in the form of lipid droplets, which are mobilized when energy is needed. Diametrically opposed in function are the so-called brown adipocytes: These cells specialize in burning energy in the form of fat and sugar to produce heat. New-born babies possess substantial amounts of brown fat and utilize it to maintain body temperature. Since it was recently shown that brown adipocytes also exist in adult humans, research has focused on understanding how

brown adipocytes are formed. The ultimate goal of these efforts is to increase brown adipocyte number and activity in obese humans, allowing them to burn excess calories and thus reduce weight.

Against the current belief

It is known that both humans and mice can adapt to cold temperatures by forming brown fat cells within their white fat depots. These cells are called "brite" fat cells (brown-in-white) and are less common at warmer versus colder temperatures. However, the origin of these special brown adipocytes has remained a matter of debate. The prevalent hypothesis was that brite cells are formed from special precursor cells and are removed when no longer needed. The alternate idea of a direct interconversion between white and brown fat cells gained less attention. By demonstrating that this interconversion does occur and is one of the main contributors to brite fat cell formation, the current belief has been challenged.

Genetically labelled fat cells

To demonstrate how brite fat cells are formed the researchers in the laboratory of Christian Wolfrum, a professor at the Institute of Food, Nutrition and Health, generated mice that allowed them to genetically label specific fat cells. These animals were kept in a changing environment: starting at 8°C for a week and for several weeks afterwards at normal room temperature. During the cold exposure, the mice formed brown adipocytes in their white fat depots -- a process called "britening." After warm adaptation the fat tissue turned white again. Using the genetic markers the scientists concluded from these experiments that white fat cells can convert into brown fat cells and vice versa. As humans have the same type of cells as mice it is likely that the same process occurs in humans upon cold stimulation.

Treatments against obesity

"To develop new treatment strategies we need to find ways to convert white into brown adipocytes," says Wolfrum. Most of the research has focused on identifying the precursor cells for brown fat cells, an approach that may be insufficient. Future work will address the question of how to manipulate this interconversion process either by pharmacological or by nutritional means.

This approach would represent a novel strategy. "Current anti-obesity therapies target the energy intake side of the equation by controlling appetite and the uptake of nutrients," says Wolfrum. The pharmacological treatments that are available are not very efficient and usually are associated with side effects. In contrast, this novel approach to treat obesity would target the energy expenditure side of the equation by promoting brown fat formation.

Matthias Rosenwald, Aliki Perdikari, Thomas Rülicke, Christian Wolfrum. Bi-directional interconversion of brite and white adipocytes. Nature Cell Biology, 2013; DOI: 10.1038/ncb2740

http://www.bbc.co.uk/news/health-22315715

Parasite 'resistant to malaria drug artemisinin'

New drug-resistant strains of the parasite that causes malaria have been identified by scientists.

By Rebecca Morelle Science reporter, BBC World Service

Researchers found parasites in western Cambodia that are genetically different from other strains around the world. These organisms are able to withstand treatment by artemisinin - a frontline drug in the fight against malaria. Reports of drug resistance in the area first emerged in 2008. The problem has since spread to other parts of South East Asia. The study is published in the journal Nature Genetics.

The lead author, Dr Olivo Miotto, of the University of Oxford and Mahidol University in Thailand, said: "All the most effective drugs that we have had in the last few decades have been one by one rendered useless by the remarkable ability of this parasite to mutate and develop resistance. "Artemisinin right now works very well. It is the best weapon we have against the disease, and we need to keep it."

Genetic fingerprint

Western Cambodia has been described by scientists as a hotspot for malaria resistance. They do not understand why, but since the 1950s parasites there have developed a resistance to a succession of malaria drugs. The problem has spread to other parts of Asia and Africa. Now scientists are worried the same thing will happen with artemisinin. This drug is used widely around the world against the mosquito-borne disease and can treat an infection in a few days when it is used in combination with other drugs.

To investigate, scientists sequenced the genomes of 800 malaria-causing parasites (Plasmodium falciparum) collected from around the world. "When we compared the DNA of the parasites in Cambodia, they seem to have formed some new populations that we have not really seen elsewhere," Dr Miotto said.

The international team found three distinct groups of drug-resistant parasites present in the area.

The researchers said they did not yet understand what genetic mutations had occurred that enabled the parasites to withstand artemisinin treatment. But they said that understanding their genetic fingerprint would help them to quickly spot and track these strains if they spread further.

Dr Miotto said: "It could be a tool for detecting in real time the emergence of drug resistance."
The World Health Organization has stated that a major objective is to stop the spread of malaria parasites resistant to drugs. According to its latest estimates, there were about 219 million cases of malaria in 2010 and 660,000 deaths. Africa is the most affected continent: about 90% of all malaria deaths occur there.

http://www.sciencedaily.com/releases/2013/04/130428230347.htm

Subclinical Thyroid Condition Associated With Increased Cardiovascular Mortality

Having high thyroid activity, and even "high-normal" levels, is a significant risk factor for cardiovascular and all-cause mortality, according to work which has received an award at the European Congress of Endocrinology in Copenhagen.

Subclinical hyperthyroidism is diagnosed when the levels of Thyroid Stimulating Hormone (TSH) are low, but the free hormones thyroxine (T4) and triiodothyronine (T3) are within normal range. You may have no symptoms at all, or symptoms such as the classical symptoms of an overactive thyroid -- weight loss, higher blood pressure, nervousness, etc. These symptoms may be mild. TSH is produced as a signal from the pituitary gland to produce more thyroid hormones, so low TSH implies that the body sees that your thyroid is tending to overactivity.
Now a group of Danish researchers led by Dr Christian Selmer studied the thyroid test results of more than half a million individuals who underwent thyroid testing in Copenhagen between 2000 and 2009. They found that those with subclinical hyperthyroidism were significantly more likely to die from cardiovascular disease. They also found that even patients having only slightly elevated thyroid activity, but still within the range which would be considered normal, showed a tendency to higher cardiovascular and other mortality.
The group looked at the results of 574,595 patients who had undergone testing. 95.9% of these patients showed normal thyroid function. However 6,264 patients exhibited subclinical hyperthyroidism, 706 of whom subsequently died of various causes. According to Christian Selmer:
"According to our work, 15% of deaths in the subclinical hyperthyroidism group could be attributed to the condition."
Even those at the high end of the normal range showed an increase in mortality. There were 13,434 patients in this range. 1,013 of these patients died of various causes, with 17% of the deaths associated with the thyroid condition. The authors emphasised that it is difficult to put exact numbers on the actual excess deaths caused by the condition for a variety of reasons. They state that they do not know if treatment of these conditions will in fact eliminate these excess deaths. This will be the goal of further studies.
Dr Christian Selmer, Research Fellow at Gentofte University Hospital, Denmark, and a winner of a Young Investigator Award at the European Congress of Endocrinology, said: "Let's keep this in context. Of the more than half million people who were tested, 50,612 subsequently died from all causes. According to our figures, this includes around 278 deaths which can be attributed to the subclinical thyroid or "high-normal" conditions we looked at, but it is important to remember that this is a calculated figure; we can't point to an individual and say he or she died because of the condition, and subclinical hyperthyroidism is one of many risk factors. Nevertheless, this needs to be taken seriously. I think that the take-home message is that if a person has a family history with any thyroid problem, or has any signs of thyroid problems, then they should go for a check-up. More than that, their family doctors need to be aware that any sign of thyroid abnormality can affect cardiovascular health, and they should act accordingly."

http://phys.org/news/2013-04-scientists-rare-dinosaur-skin-fossil.html

Scientists study rare dinosaur skin fossil to determine skin colour for first time

One of the only well preserved dinosaur skin samples ever found is being tested at the Canadian Light Source (CLS) synchrotron to determine skin colour and to explain why the fossilized specimen remained intact after 70-million years.

University of Regina physicist Mauricio Barbi said the hadrosaur, a duck-billed dinosaur from the Late Cretaceous period (100-65 million years ago), was found close to a river bed near Grand Prairie, Alberta.
The area has a robust "bone bed" but Barbi is not yet sure why the fossil preserved so well.
"As we excavated the fossil, I thought that we were looking at a skin impression. Then I noticed a piece came off and I realized this is not ordinary – this is real skin. Everyone involved with the excavation was incredibly excited and we started discussing research projects right away."

University of Regina physicist Mauricio Barbi and a rare hadrosaur skin sample.

Barbi said this is only the third three-dimensional dinosaur skin specimen ever found worldwide.
"This fossil is fascinating because it can tell us so much about the life and the appearance of the dinosaurs in the area."
But there are almost more questions than answers, he said.
One question is whether the hadrosaur skin was green or grey, like most dinosaurs are portrayed, or was it a completely different colour. Barbi said he can use the CLS to look at unique structures called melanosomes, cellular organelles the contain pigments that control the color of an animal's skin.
"If we are able to observe the melanosomes and their shape, it will be the first time pigments have been identified in the skin of a dinosaur," said Barbi. "We have no real idea what the skin looks like. Is it green, blue, orange…There has been research that proved the colour of some dinosaur feathers, but never skin."
Using light at the CLS mid-infrared (Mid-IR) beamline, Barbi and CLS scientists are also looking for traces of organic and inorganic elements that could help determine the hadrosaur's diet and why the skin sample was preserved almost intact.
For the experiment, the sample is placed in the path of the infrared beam and light reflects off of it. During the experiment, chemical bonds of certain compounds will create different vibrations. For example, proteins, sugars and fats still found in the skin will create unique vibrational frequencies that scientists can measure.

Hadrosaur skin sample.

"It is astonishing that we can get information like this from such an old sample," said Tim May, CLS Mid-IR staff scientist. "Skin has fat and lots of dead cells along with many inorganic compounds. We can reflect the infrared beam off the sample and we can analyze the samples to give us very clear characteristics."
May said that infrared techniques are so accurate at determining chemical characteristics that it is known as the "fingerprint region" of the light spectrum.
But perhaps the greatest question Barbi is trying to answer at the CLS is how the fossil remained intact for around 70-million years.
"What's not clear is what happened to this dinosaur and how it died," he said. "There is something special about this fossil and the area where it was found, and I am going to find out what it is."