http://www.eurekalert.org/pub_releases/2012-05/uoia-rtm051412.php

Research: Too much, too little noise turns off consumers, creativity

The sound of silence isn't so golden for consumers, and both marketers and advertisers should take note, says new research from a University of Illinois expert in new product development and marketing.

CHAMPAIGN, Ill. - According to published research from Ravi Mehta, a professor of business administration, ambient background noise turns out to be an important factor affecting creative cognition among consumers.

"We found that ambient noise is an important antecedent for creative cognition," Mehta said. "A moderate level of noise not only enhances creative problem-solving but also leads to a greater adoption of innovative products in certain settings."

In the article, Methta and co-authors Rui (Juliet) Zhu, of the University of British Columbia, and Amar Cheema, of the University of Virginia, explore how a moderate-level of ambient noise (about 70 decibels, equivalent to a passenger car traveling on a highway) enhances performance on creative tasks and increases the likelihood of consumers purchasing innovative products. Similarly, the researchers also studied how a high level of noise (85 decibels, equivalent to traffic noise on a major road) hurts creativity by reducing information processing.

"What we found is that there's an inverted-U relationship between noise level and creativity," Mehta said. "It turns out that around 70 decibels is the sweet spot. If you go beyond that, it's too loud, and the noise starts to negatively affect creativity. It's the Goldilocks principle – the middle is just right."

Using background noise commonly found in consumers' lives, the researchers show that, as noise increases, so does one's level of distraction.

"An increased level of distraction makes you think 'out-of-the-box' – what we call abstract thinking or abstract processing, which is a hallmark of increased creativity," Mehta said. "But when you start to go beyond that moderate level of noise what happens is that distraction becomes so huge that it really starts affecting the thought process. You really can't process information because the distraction is so pronounced. And that is what inhibits creativity.

"So a moderate level of noise produces just enough distraction to lead to higher creativity, but a very high level of noise induces too much distraction, which actually reduces the amount of processing, thus leading to lower creativity."

The research, which has important practical implications for inducing consumer behavior, should be useful for both advertisers and marketers, who typically strive to increase adoption rates of new and innovative products.

"We studied this in a consumer environment because previous research has only considered white noise or pink noise" – a variant of white noise, which sounds like the static buzz of an off-air TV station – "which you don't really find in consumer environments," Mehta said. "So in this case we used everyday multi-talker noise to find out how it affects consumer behavior in a consumption environment. In order to encourage adoption of new and innovative products, marketers might consider equipping their showrooms with a moderate level of ambient noise."

Mehta says the research is not only applicable to consumer research, but also to problem-solving in general.

"This is research that people can relate to almost immediately," he said. "I'm working in a coffee shop – how does the noise in the background volume of the music affect my performance?

It's also valuable for individuals looking for creative solutions to everyday problems, such as planning a dinner menu based on limited supplies or generating interesting research topics to study.

"Our findings imply that instead of burying oneself in a quiet room trying to figure out a solution, walking outside of one's comfort zone and getting into a relatively noisy environment like a cafe may actually trigger the brain to think abstractly, and thus generate creative ideas," Mehta said.

http://www.eurekalert.org/pub_releases/2012-05/uol-rrd051312.php

Researchers reveal different mechanisms of pain

Researchers at the University of Leeds have found a previously unknown mechanism through which pain is signalled by nerve cells

Researchers at the University of Leeds have found a previously unknown mechanism through which pain is signalled by nerve cells – a discovery that could explain the current failings in the drug development process for painkillers and which may offer opportunities for a new approach.

The team, led by Dr Nikita Gamper of the University's Faculty of Biological Sciences, is investigating the difference between persistent pain, such as toothache, and pain that results from the increased sensitivity of nerves in injured or diseased tissue (for example when we touch inflamed skin), known as hyperalgesia.

In research published online this week, (w/c 14 May) in Proceedings of the National Academy of Sciences (PNAS), Dr Gamper's team has discovered that these two types of pain are generated by the same nerves, but result from different underlying mechanisms.

The project, funded jointly by the Wellcome Trust and the Medical Research Council, investigated the painful effects of two substances that cause local inflammation: bradykinin and substance P. Both substances bind to specific receptors on nerve cells, generating signals to the central nervous system. Because the receptors are from the same family, it has always been presumed they stimulate the same signalling pathway. However, the team found that each receptor produces different signals; the one associated with bradykinin causing both hyperalgesia and persistent pain, whereas the one associated with substance P only caused hyperalgesia.

"Dr Gamper says: "Pain originates from a series of electrical signals sent by nerve cells in to the central nervous system and ultimately the brain. Despite much progress, we still don't know enough about the mechanisms by which these pain signals are generated. However, this research has shown that whilst the sensation of pain can be similar between various conditions, the underlying molecular mechanisms may in fact be very different."

Existing painkillers are 'non-specific', designed to generally dull the reception of these signals in the central nervous system, and some stronger pain killers can provoke unwanted side effects such as disorientation, drowsiness or nausea. So while the search for new better drugs is pressing, the lack of progress in developing targeted analgesics has led to several pharmaceutical companies dropping this area of research altogether.

"What's exciting about these findings is that substance P may actually suppress the activation of the pain sensing nerves themselves," says Dr Gamper.

"It's increasingly evident that current strategies for testing and validating new painkillers often do not take into account a possible difference in how pain signals are generated. For instance, drugs for persistent pain are often tested solely for their ability to reduce hyperalgesia, and as a result, some of the drugs that are effective in the lab, fail in subsequent clinical trials. These findings challenge current approaches in drug development research and may offer new strategies," he says.

http://www.eurekalert.org/pub_releases/2012-05/cndi-css051412.php

CNIO scientists successfully test the first gene therapy against aging-associated decline

Mouse lifespan extended up to 24 percent with a single treatment

A number of studies have shown that it is possible to lengthen the average life of individuals of many species, including mammals, by acting on specific genes. To date, however, this has meant altering the animals' genes permanently from the embryonic stage – an approach impracticable in humans. Researchers at the Spanish National Cancer Research Centre (CNIO), led by its director María Blasco, have proved that mouse lifespan can be extended by the application in adult life of a single treatment acting directly on the animal's genes. And they have done so using gene therapy, a strategy never before employed to combat ageing. The therapy has been found to be safe and effective in mice.

The results are published today in the journal EMBO Molecular Medicine. The CNIO team, in collaboration with Eduard Ayuso and Fátima Bosch of the Centre of Animal Biotechnology and Gene Therapy at the Universitat Autònoma de Barcelona (UAB), treated adult (one-year-old) and aged (two-year-old) mice, with the gene therapy delivering a "rejuvenating" effect in both cases, according to the authors.

Mice treated at the age of one lived longer by 24% on average, and those treated at the age of two, by 13%. The therapy, furthermore, produced an appreciable improvement in the animals' health, delaying the onset of age-related diseases – like osteoporosis and insulin resistance – and achieving improved readings on ageing indicators like neuromuscular coordination.

The gene therapy utilised consisted of treating the animals with a DNA-modified virus, the viral genes having been replaced by those of the telomerase enzyme, with a key role in ageing. Telomerase repairs the extremes of chromosomes, known as telomeres, and in doing so slows the cell's and therefore the body's biological clock. When the animal is infected, the virus acts as a vehicle depositing the telomerase gene in the cells.

This study "shows that it is possible to develop a telomerase-based anti-ageing gene therapy without increasing the incidence of cancer", the authors affirm. "Aged organisms accumulate damage in their DNA due to telomere shortening, [this study] finds that a gene therapy based on telomerase production can repair or delay this kind of damage", they add.

'Resetting' the biological clock

Telomeres are the caps that protect the end of chromosomes, but they cannot do so indefinitely: each time the cell divides the telomeres get shorter, until they are so short that they lose all functionality. The cell, as a result, stops dividing and ages or dies. Telomerase gets round this by preventing telomeres from shortening or even rebuilding them. What it does, in essence, is stop or reset the cell's biological clock.

But in most cells the telomerase gene is only active before birth; the cells of an adult organism, with few exceptions, have no telomerase. The exceptions in question are adult stem cells and cancer cells, which divide limitlessly and are therefore immortal – in fact several studies have shown that telomerase expression is the key to the immortality of tumour cells. It is precisely this risk of promoting tumour development that has set back the investigation of telomerase-based anti-ageing therapies.
In 2007, Blasco's group proved that it was feasible to prolong the lives of transgenic mice, whose genome had been permanently altered at the embryonic stage, by causing their cells to express telomerase and, also, extra copies of cancer-resistant genes. These animals live 40% longer than is normal and do not develop cancer. The mice subjected to the gene therapy now under test are likewise free of cancer. Researchers believe this is because the therapy begins when the animals are adult so do not have time to accumulate sufficient number of aberrant divisions for tumours to appear.
Also important is the kind of virus employed to carry the telomerase gene to the cells. The authors selected demonstrably safe viruses that have been successfully used in gene therapy treatment of haemophilia and eye disease. Specifically, they are non-replicating viruses derived from others that are non-pathogenic in humans.
This study is viewed primarily as "a proof-of-principle that telomerase gene therapy is a feasible and generally safe approach to improve healthspan and treat disorders associated with short telomeres", state Virginia Boccardi (Second University of Naples) and Utz Herbig (New Jersey Medical School-University Hospital Cancer Centre) in a commentary published in the same journal.
Although this therapy may not find application as an anti-ageing treatment in humans, in the short term at least, it could open up a new treatment option for ailments linked with the presence in tissue of abnormally short telomeres, as in some cases of human pulmonary fibrosis.

More healthy years

As Blasco says, "ageing is not currently regarded as a disease, but researchers tend increasingly to view it as the common origin of conditions like insulin resistance or cardiovascular disease, whose incidence rises with age. In treating cell ageing, we could prevent these diseases".
With regard to the therapy under testing, Bosch explains: "Because the vector we use expresses the target gene (telomerase) over a long period, we were able to apply a single treatment. This might be the only practical solution for an anti-ageing therapy, since other strategies would require the drug to be administered over the patient's lifetime, multiplying the risk of adverse effects".

http://www.eurekalert.org/pub_releases/2012-05/cmaj-scc050812.php

Smoked cannabis can help relieve muscle tightness and pain in people with multiple sclerosis

Benefits come with negative cognitive effects

People with multiple sclerosis may find that smoked cannabis provides relief from muscle tightness - spasticity - and pain, although the benefits come with adverse cognitive effects, according to a new study published in CMAJ (Canadian Medical Association Journal).
Many patients with multiple sclerosis suffer from spasticity, an uncomfortable and disabling condition in which the muscles become tight and difficult to control. While there are drugs to relieve spasticity, they can have adverse effects and do not always sufficiently improve the condition in some patients.
Researchers from the University of California, San Diego School of Medicine, conducted a randomized, double-blinded controlled trial with 30 participants to understand whether smoked cannabis can have an effect on muscle spasticity in people whose spasticity does not respond well to existing treatment. The average age of participants was 50 years, and 63% were female. More than half of the participants needed walking aids, and 20% used wheelchairs. Most trials have focused on the effect of oral cannabis rather than smoked cannabis.
Rather than rely on self-reporting by patients regarding their muscle spasticity - a subjective measure - health professionals rated the spasticity of each participant's joints on the modified Ashworth scale, a common objective tool to evaluate intensity of muscle tone. The researchers found that participants in the smoked cannabis group experienced an almost one-third decrease on the Ashworth scale - 2.74 points - from a baseline score of 9.3, meaning spasticity improved, compared with the placebo group. As well, pain scores decreased by about 50%.
"We saw a beneficial effect of smoked cannabis on treatment-resistant spasticity and pain associated with multiple sclerosis among our participants," writes Dr. Jody Corey-Bloom, Department of Neuroscience, University of California, San Diego, California, with coauthors. "Although generally well-tolerated by our participants, smoking cannabis was accompanied by acute cognitive effects."

Cognitive function was negatively affected in the smoked cannabis group but not with placebo, as measured by the ability to perform an addition test requiring focused attention. These effects were short term.
"Using an objective measure, we saw a beneficial effect of inhaled cannabis on spasticity among patients receiving insufficient relief from traditional treatments," conclude the authors. "Although generally well-tolerated, smoking cannabis had acute cognitive effects. Larger, long-term studies are needed to confirm our findings and determine whether lower doses can result in beneficial effects with less cognitive impact."

http://www.eurekalert.org/pub_releases/2012-05/ehs-tap051412.php

To avoid pain during an injection, look away

Common advice really does reduce discomfort, study in Pain reports

Philadelphia, PA – Health professionals commonly say, "Don't look and it won't hurt" before administering an injection, but is there any scientific basis for the advice? A group of German investigators has found that, in fact, your past experience with needle pricks, along with information you receive before an injection, shape your pain experience. Their research is published in the May issue of Pain®.
"Throughout our lives, we repeatedly experience that needles cause pain when pricking our skin, but situational expectations, like information given by the clinician prior to an injection, may also influence how viewing needle pricks affects pain," says lead author Marion Höfle, a doctoral student in the research Multisensory Integration group led by Dr. Daniel Senkowski, at the Charité - Universitätsmedizin Berlin and the University Medical Center Hamburg-Eppendorf.
While watching video clips showing a needle pricking a hand, a Q-tip touching the hand, or a hand alone, study participants concurrently received painful or non-painful electrical stimuli applied to their own hand. The clips were presented on a screen located above the participants' hand, giving the impression that the hand on the screen belonged to them.
Participants reported that their pain was more intense and more unpleasant when they viewed a needle pricking a hand than when they saw a hand alone. In addition, observing needle pricks increased the unpleasantness of pain compared to viewing Q-tip touches. These findings were paralleled by enhanced activity of the autonomic nervous system, as measured by pupil dilation responses. This demonstrates that previous painful experiences with needles enhance unpleasantness of pain when viewing needle pricks.
Situational expectations also influenced perceived pain intensity. Prior to the stimulation, participants were told that either the needle or the Q-tip clip was more likely to be associated with painful than with non-painful electrical stimulation. The researchers found that presentation of clips that were more likely to be associated with pain lead to higher pain intensity experiences than the presentation of clips that were less likely to be associated with pain. This shows that expectations regarding the painfulness of medical treatments influence the intensity of pain that the treatment ultimately produces.
Taken together, the study reveals several important findings. "Clinicians may be advised to provide information that reduces a patient's expectation about the strength of forthcoming pain prior to an injection," Höfle notes. She further states that, "because viewing a needle prick leads to enhanced pain perception as well as to enhanced autonomic nervous system activity, we've provided empirical evidence in favor of the common advice not to look at the needle prick when receiving an injection."

http://www.sciencedaily.com/releases/2012/05/120514104301.htm

Artificial Pancreas Gets First U. S. Outpatient Test

The University of Virginia School of Medicine has launched the first U.S. outpatient trial of a UVA-developed artificial pancreas that could make it easier for type 1 diabetes patients to manage their condition.

ScienceDaily - A research team led by Patrick Keith-Hynes, PhD, and Boris Kovatchev, PhD, reconfigured a smartphone into a hand-held device to monitor a patient's insulin pump and continuous glucose monitor (CGM). The device is intended to automate much of the work of monitoring and maintaining safe blood sugar levels now performed by patients such as 40-year-old Charlottesville resident Justin Wood, the first patient to participate in the UVA outpatient trial.

Living with type 1 diabetes

Diagnosed as having type 1 diabetes about 28 years ago, Wood uses an insulin pump to help regulate his blood sugar but must check his blood sugar by pricking his finger at least three to five times daily. He also needs to precisely estimate his food consumption -- especially the amount of carbohydrates -- to help properly adjust his insulin supply.
While managing his diabetes is largely second nature, Wood says, "It's something you think about -- either in the back of your mind or the forefront of your mind -- almost constantly."

Automating diabetes care

Wood tested a new approach when he checked into a Charlottesville hotel the night of April 19 for his two-day outpatient trial. He immediately liked the device. "The operating interface was very slick and very fast," he says. "The extra second or two you save pressing buttons adds up when you have to do it every day."

Beginning the following morning, Wood used the device to automatically read and balance his blood sugar level. At mealtimes -- as with his standard insulin pump -- he entered what he ate to help balance his blood sugar quicker. He came away impressed with the potential of the artificial pancreas.

"The device automates a lot of the tracking and monitoring I do now," he says. Wood estimated he could reduce the number of times he pricked his finger for blood sugar tests from at least three to five per day to no more than two a day. He sees the artificial pancreas as "a step forward in technology that could change my view and outlook on life." For Kovatchev, the outpatient trial was a significant change from previous inpatient trials at UVA where patients were monitored in a hospital room. "To see no visible medical items around the patient -- it was an amazing feeling to have."

Next steps in testing

The UVA team and other participants in the JDRF's Artificial Pancreas Project -- the University of California, Santa Barbara; Montpellier University Hospital in France; and the Universities of Padova and Pavia in Italy -- will continue outpatient testing through 2013 at UVA and three other locations. Researchers plan to enroll a total of 120 patients in the trial.

http://news.discovery.com/earth/seismic-lightning-record-120514.html

Lucky Strike: Lightning Brings Seismic Surprise

A stormy afternoon in Germany turned into a rare seismic experiment.

Content provided by Crystal Gammon, OurAmazingPlanet

As dark clouds rolled in from the west on a July afternoon last year, Klaus-G. Hinzen, a seismologist at the University of Cologne in Germany, knew a big storm was brewing. He was watching from the window of the university's earthquake observatory in Bensberg, a small town outside of Cologne, as lightning struck a nearby hotel. Less than a minute later, a flash took out a tree next to the earthquake lab itself, turning that stormy afternoon into a rare seismic experiment. "The main experience that we seismologists have with lightning strikes is a very bad one, because it often causes a lot of damage in the equipment. But the equipment didn't fail this time," Hinzen told OurAmazingPlanet. "It's a rare instance that you have a lightning strike so close to so many different seismometers and get a complete record of it."

Hinzen's seismic equipment recorded the lightning strike and its effects in shocking detail.

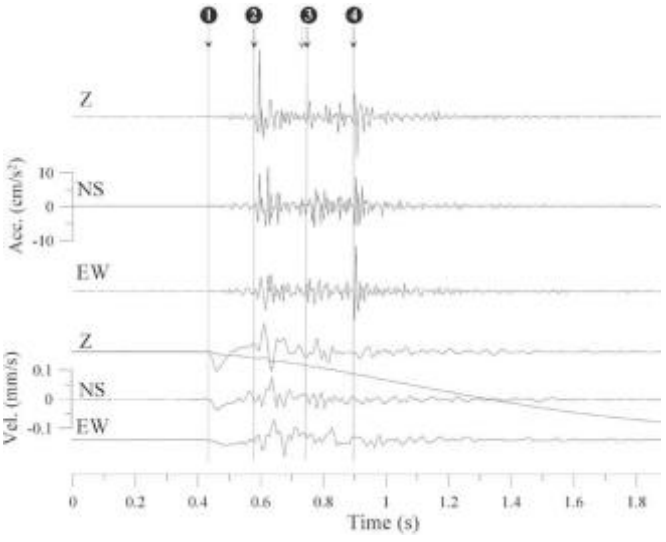
Anatomy of a lightning strike

When the bolt struck the big poplar tree that stood 174 feet (53 meters) from the lab, one of Hinzen's seismometers - a type of accelerometer called a strong-motion station, specifically tuned to pick up small ground movements - recorded a strong signal that lasted about one-tenth of a second.

The strong-motion station detected another spike a fraction of a second later, which Hinzen interprets as the thunderclap that accompanied the lightning. Then the 65-foot (20 meters) tree exploded, scattering debris in a 65-foot radius, and the station recorded a third set of ground shakes. "We think the current flowing through the tree heated the sap in the trunk so quickly that it turned into steam," Hinzen said. "This put enough pressure on the trunk that the tree basically exploded."

The fourth and final seismic signal came about two-tenths of a second later, when the high-pressure airwave from the exploding tree shook the ground near the strong-motion station. This airwave had moved slower than the ground wave from the explosion, Hinzen explained, because it was traveling through air instead of rock.

Altogether, from the lightning strike to the fallout from the tree explosion, the incident lasted less than half a second.



The seismometer record of the lightning strike and tree explosion. **CREDIT: Klaus-G. Hinzen**

A lucky strike

Hinzen was able to tease out these short-lived signals because the strong-motion station took very detailed measurements - 250 readings every second. "Lightning looks very different on a seismometer because the total

signal we see is very short compared to the ground motion you would see from a true earthquake," Hinzen said. "Before this, I would not have guessed we could resolve these very fast signals."
Another important factor was the earthquake observatory's advanced lightning protection system, which had been installed just a few years earlier. Without it, Hinzen said, the lightning would have fried the equipment that collected and stored the data.
All in all, it turned out to be a lucky strike for Hinzen. "It's just such a rare occurrence that it hit where we could record it," he said, "and it really shows how well these systems can perform." Hinzen's findings appear in this month's issue of the journal Seismological Research Letters.

http://nyti.ms/JqJfc5

Really? Red Wine Is Good for the Stomach

There are some who see wine as a sort of probiotic delivery system, capable of benefiting the stomach as well.

By ANAHAD O'CONNOR

THE FACTS When it comes to the health-promoting effects of red wine, its potential to protect against heart disease tends to get all the attention. But there are some who see it as a sort of probiotic delivery system, capable of benefiting the stomach as well.
Supplements and foods with probiotics - live micro-organisms that support digestive health - have become hugely popular. While probiotics are increasingly added to a variety of foods, some contain them naturally, especially fermented products like yogurt and wine.
Most doctors, of course, would never recommend drinking solely to aid digestive health. But researchers have wondered whether a boost in healthy bacteria may be a secondary benefit of red wine.
In studies on animals, for example, scientists have found that components of red wine seem to improve intestinal health, promoting the growth of beneficial bacteria. Research on human subjects is limited. But one recent study that examined the claim was published in The American Journal of Clinical Nutrition.
In it, a small number of healthy adults were instructed to avoid all alcohol for two weeks - a so-called washout period.
Then they went through three separate phases of 20 days each. In one, the subjects drank red wine, about a cup daily. In another, they drank the same amount of red wine daily, but this time with the alcohol removed. In the third, they drank up to 100 milliliters a day of gin each day.
In the end, the researchers found that both types of red wine produced improvements in the bacterial composition of the gut, lowered blood pressure and reduced levels of a protein associated with inflammation. Slight improvements in gut flora were seen among gin drinkers, but the effects in the wine drinkers were much more pronounced.
THE BOTTOM LINE According to research, red wine may improve digestive health.

http://www.scientificamerican.com/article.cfm?id=gene-linked-increased-risk-PTSD

Gene Linked to Increased Risk of PTSD

Variations in the PKCA gene and reports of emotionally affecting photos among 700 health young volunteers confirm hypotheses about the core role of memory in PTSD

By Mo Costandi of Nature magazine

European researchers have identified a gene that is linked to improved memory, but also to increased risk of post-traumatic stress disorder (PTSD).
Dominique de Quervain of the University of Basel in Switzerland and his colleagues recruited around 700 healthy young volunteers, obtaining DNA samples from them to analyze the sequence of their PRKCA gene. This gene is one of many known to be involved in the formation of emotional memories, and encodes an enzyme called protein kinase C-α. The researchers then showed the participants a series of emotionally affecting photographs and shortly afterwards asked them to write down short descriptions of the images. Participants carrying two copies of one variant within the PRKCA gene, dubbed the A allele, remembered the most details about the pictures. Those carrying two copies of the other variant -- the G allele -- remembered the least, with the performance of those carrying one copy of each variant lying somewhere in the middle.
The researchers then asked 394 additional participants to perform the same task while undergoing brain imaging. This confirmed that variations in PKRCA are linked to the capacity for emotional memory, and further revealed that they were also associated with differences in brain activity during memory encoding. The task activated a large network of brain regions, including the hippocampus and amygdala, two structures in the medial temporal lobe that are known to be involved in memory formation and emotion, respectively. The

brain scans also showed that the A allele was associated with increased activity in the lateral and medial prefrontal cortex, regions that belong to a network involved in the encoding of emotional memories.
Again, the increased activity in these areas was associated with the number of copies of the A allele carried by individuals -- people with two copies showed a larger increase in activity than those with just one.

Trauma survivors

The researchers finally examined the distribution of the A allele in a group of 347 survivors of the 1994 Rwandan genocide who had fled the civil war and were living in a Ugandan refugee camp. All had experienced multiple traumatic events during the civil war, but only 134 of them had been diagnosed with PTSD.
"The A allele was significantly over-represented in those with a diagnosis of PTSD," says de Quervain. "Carriers of this allele had a roughly 2-fold increase in risk for PTSD." The work is published today in Proceedings of the National Academy of Sciences.
Many researchers think that memory must have an important role in PTSD because traumatic memories are one of its core features, says de Quervain, "but it's very hard to tell that a predisposition for building stronger memory is also a risk for developing the condition".
For example, in 2007, de Quervain and his colleagues showed that a variant of the α2B adrenoceptor is also linked to enhanced formation of emotional and traumatic memories in both healthy Europeans and survivors of the Rwandan civil war, but it was not associated with an increased risk of PTSD.
"These findings are of considerable interest," says neurobiologist James McGaugh of the University of California, Irvine. "It's well established that emotional arousal enhances memory consolidation, and it's widely assumed that this may contribute to PTSD, but the finding is important as it provides genetic evidence consistent with that hypothesis."
The A allele is much more common in people of European than African descent, but exactly how this variation leads to differences in brain activity during the encoding of emotional memory is unclear. Large-scale genomic studies will probably uncover more gene variants associated with increased risk of developing PTSD, says de Quervain, and may provide a better understanding of the molecular mechanisms involved.

http://www.bbc.co.uk/news/magazine-17792624

Shark attacks: A magnetic solution?

An American chemist says he's found a substance - several, in fact - that can repel some of the most fearsome predators in the ocean. He wants to use his discovery to protect them, and us.

By Ari Daniel Shapiro PRI's The World

Eric Stroud stands on a pier on the island of North Bimini in the Bahamas. He looks down into the turquoise water. A couple of eagle rays and barracudas swim by.
"The current is ripping through here right now," he says. "The tide is going out. So any scent that's put here goes right to the outside of the channel, and that's where the big sharks are right now."
Stroud is setting up an experiment. He unwraps 20lbs (9kgs) of frozen sardines, drops them into a mesh bag tied to the pier, and tosses the bag into the water. He's hoping to attract a large bull shark.
"It's a fairly dangerous shark," he explains. "It can be aggressive, especially when provoked or cornered."
If a bull shark does turn up, he'll throw a large baited hook into the water. But it's not your typical fishhook. In fact, if all goes well, this hook won't catch any sharks.
For more than a decade, Stroud has been working to develop shark repellents. He used to work as a chemist in the pharmaceutical industry. Then, in the summer of 2001, he and his wife went on a cruise to Bermuda.
"We hit bad weather, and we were trapped in a cabin, and on the news was shark bite after shark bite," he says. "It seemed like everyone that stepped in the ocean in Florida was getting attacked by a shark that summer."
That's when his wife suggested he turn his talents to developing shark repellents. When they got home to New Jersey, he set up several small pools in his basement, and filled them with small sharks.
He watched how the sharks fed, swam, and behaved. Then, one day, he accidentally dropped a large magnet from his workbench. He noticed some small nurse sharks dart away. "That night, we put magnets into the water and couldn't believe the nurse sharks were extremely distressed and stayed away from them," he says.
Stroud thinks that was the moment he discovered that magnets repel sharks.
He demonstrates the effect at the Bimini Biological Field Station in the Bahamas. He stands waist-deep in water, just offshore, in a fenced-in pen in the sea. Several young Lemon sharks glide around the perimeter. One of Stroud's assistants captures one of them and slowly rotates it onto its back underwater. This puts the shark into a sleep-like state.
Then Stroud takes a magnet and spins it as he moves it towards the shark. The shark darts away suddenly.
"There you go," he says. "Look at that beautiful bend away from the magnet like he's repelled by it".

Sharks possess electrical sensors, called the ampullae of Lorenzini, that look like tiny freckles on their snouts. Biologists believe sharks use these sensors to detect the heartbeats of their prey and to navigate using the Earth's magnetic field.
Stroud suspects the spinning magnet overwhelms these electrical sensors. "It's probably something like a bright flashlight across your eyes," he says. "It's just temporarily blinding, and you're startled. And it's not pleasant."
Other shark experts believe magnets could have a potential use but it's too early to say.
Rob Lawrence, who has been working with great white sharks for more than 20 years and takes tourists in Cape Town cage diving, says: "It could work if a lot more research was done on this.
"Sharks have a lot of sensory organs in their snout so potentially the magnetic field could affect it.
"But people here in South Africa have looked into this and there hasn't been much success with it."
Geremy Cliff, head of research at KwaZulu-Natal Sharks Board, says an Australian study in 2009 suggested that magnets can repel five shark species, while they have little effect on one teleost (bony fish) species in a test tank environment.
"But the authors had raised concerns that the size and weight of the magnets was considerable and that many would be needed to keep sharks out of nets," he adds.
Stroud says other ocean species don't appear to be affected by magnets. "Bony fish, like tuna or swordfish, do not have this special organ. Therefore, they are not affected at all in the presence of magnets or metals."
He says the same is true for eels, invertebrates, and crabs. "We have not tested this on sea turtles - which, like sharks, use the Earth's magnetic field as a compass - but some early work by other researchers indicates they have no effect."
Stroud made his discovery in 2004. It helped him jumpstart a company he'd founded called SharkDefense, that aims to develop and commercialise shark repellents. He and his team tested other substances, and they found that some metals also interfere with a shark's electrical sensors. "Certain metals didn't work, others did", says Stroud. "You begin to hone down the periodic table". Particularly effective are rare-earth metals like samarium, neodymium, and praseodymium. His team are also in the process of testing various chemical shark repellents. Other deterrent products using electronic waves to deter sharks are already in use.
Stroud's original plan was to develop repellents to protect people, and he's working on ways to do that. For instance, he and his partners are researching a magnetic underwater fence that might keep sharks away from swimmers. But his main focus has switched to using repellents to protect sharks.
Many shark species are being overfished, and some are endangered. One reason is that fishermen trying to catch other fish often catch sharks by mistake. Stroud wondered - what if he could produce fish hooks that catch fish like tuna and halibut as usual, but that sharks avoid?
"We realised we could magnetise the fishing hook, and coat it with a rare earth metal," he says. "It looks just like a regular hook."
Several countries are now testing his so-called SMART hooks to see if they work. Some tests show a 60-70% reduction in the number of sharks caught.
Stroud received an award from the World Wildlife Fund for his invention, and he's hoping to sell the hooks commercially before long.
In the meantime, he continues to refine the design, trying new combinations of metals and magnets, and observing how they affect different types of sharks.

http://nyti.ms/KHUev7

A Mathematical Challenge to Obesity

Dr. Chow, a mathematician, has found that a food glut is behind America's weight problem.

By CLAUDIA DREIFUS

Carson C. Chow deploys mathematics to solve the everyday problems of real life. As an investigator at the National Institute of Diabetes and Digestive and Kidney Diseases, he tries to figure out why 1 in 3 Americans are obese.
We spoke at the recent annual meeting of the American Association for the Advancement of Science, where Dr. Chow, 49, gave a presentation on "Illuminating the Obesity Epidemic With Mathematics," and then later by telephone; a condensed and edited version of the interviews follows.

You are an M.I.T.-trained mathematician and physicist. How did you come to work on obesity?

In 2004, while on the faculty of the math department at the University of Pittsburgh, I married. My wife is a Johns Hopkins ophthalmologist, and she would not move. So I began looking for work in the Beltway area. Through the grapevine, I heard that the N.I.D.D.K., a branch of the National Institutes of Health, was building up its mathematics laboratory to study obesity. At the time, I knew almost nothing of obesity.

I didn't even know what a calorie was. I quickly read every scientific paper I could get my hands on.
I could see the facts on the epidemic were quite astounding. Between 1975 and 2005, the average weight of Americans had increased by about 20 pounds. Since the 1970s, the national obesity rate had jumped from around 20 percent to over 30 percent.
The interesting question posed to me when I was hired was, "Why is this happening?"

Why would mathematics have the answer?

Because to do this experimentally would take years. You could find out much more quickly if you did the math.
Now, prior to my coming on staff, the institute had hired a mathematical physiologist, Kevin Hall. Kevin developed a model that could predict how your body composition changed in response to what you ate. He created a math model of a human being and then plugged in all the variables - height, weight, food intake, exercise. The model could predict what a person will weigh, given their body size and what they take in.
However, the model was complicated: hundreds of equations. Kevin and I began working together to boil it down to one simple equation. That's what applied mathematicians do. We make things simple. Once we had it, the slimmed-down equation proved to be a useful platform for answering a host of questions.

What new information did your equation render?

That the conventional wisdom of 3,500 calories less is what it takes to lose a pound of weight is wrong. The body changes as you lose. Interestingly, we also found that the fatter you get, the easier it is to gain weight. An extra 10 calories a day puts more weight onto an obese person than on a thinner one.
Also, there's a time constant that's an important factor in weight loss. That's because if you reduce your caloric intake, after a while, your body reaches equilibrium. It actually takes about three years for a dieter to reach their new "steady state." Our model predicts that if you eat 100 calories fewer a day, in three years you will, on average, lose 10 pounds - if you don't cheat.
Another finding: Huge variations in your daily food intake will not cause variations in weight, as long as your average food intake over a year is about the same. This is because a person's body will respond slowly to the food intake.

Did you ever solve the question posed to you when you were first hired - what caused the obesity epidemic?

We think so. And it's something very simple, very obvious, something that few want to hear: The epidemic was caused by the overproduction of food in the United States.
Beginning in the 1970s, there was a change in national agricultural policy. Instead of the government paying farmers not to engage in full production, as was the practice, they were encouraged to grow as much food as they could. At the same time, technological changes and the "green revolution" made our farms much more productive. The price of food plummeted, while the number of calories available to the average American grew by about 1,000 a day.
Well, what do people do when there is extra food around? They eat it! This, of course, is a tremendously controversial idea. However, the model shows that increase in food more than explains the increase in weight.
In the 1950s, when I was growing up, people rarely ate out. Today, Americans dine out - with these large restaurant portions and oil-saturated foods - about five times a week.
Right. Society has changed a lot. With such a huge food supply, food marketing got better and restaurants got cheaper. The low cost of food fueled the growth of the fast-food industry. If food were expensive, you couldn't have fast food.
People think that the epidemic has to be caused by genetics or that physical activity has gone down. Yet levels of physical activity have not really changed in the past 30 years. As for the genetic argument, yes, there are people who are genetically disposed to obesity, but if they live in societies where there isn't a lot of food, they don't get obese. For them, and for us, it's supply that's the issue.
Interestingly, we saw that Americans are wasting food at a progressively increasing rate. If Americans were to eat all the food that's available, we'd be even more obese.

Any practical advice from your number crunching?

One of the things the numbers have shown us is that weight change, up or down, takes a very, very long time. All diets work. But the reaction time is really slow: on the order of a year.
People don't wait long enough to see what they are going to stabilize at. So if you drop weight and return to your old eating habits, the time it takes to crawl back to your old weight is something like three years. To help people understand this better, we've posted an interactive version of our model at bwsimulator.niddk.nih.gov. People can plug in their information and learn how much they'll need to reduce their intake and increase their

activity to lose. It will also give them a rough sense of how much time it will take to reach the goal. Applied mathematics in action!

What can Americans do to stem the obesity epidemic?

One thing I have concluded, and this is just a personal view, is that we should stop marketing food to children. I think childhood obesity is a major problem. And when you're obese, it's not like we can suddenly cut your food off and you'll go back to not being obese. You've been programmed to eat more. It's a hardship to eat less. Michelle Obama's initiative is helpful. And childhood obesity rates seem to be stabilizing in the developed world, at least. The obesity epidemic may have peaked because of the recession. It's made food more expensive.

You said earlier that nobody wants to hear your message. Why?

I think the food industry doesn't want to know it. And ordinary people don't particularly want to hear this, either. It's so easy for someone to go out and eat 6,000 calories a day. There's no magic bullet on this. You simply have to cut calories and be vigilant for the rest of your life.

This article has been revised to reflect the following correction:

Correction: May 16, 2012

The "Conversation With" article on Tuesday, about Carson Chow, a mathematician who studies obesity, misstated a statistic around which his work revolves. One in 3 Americans are obese - not merely overweight, a description that applies to 2 in 3 Americans.

http://www.eurekalert.org/pub_releases/2012-05/hfhs-rsn051512.php

Robot-assisted surgery now favored treatment for kidney cancer

Robot-assisted surgery has replaced another minimally invasive operation as the main procedure to treat kidney cancer while sparing part of the diseased organ

DETROIT – Robot-assisted surgery has replaced another minimally invasive operation as the main procedure to treat kidney cancer while sparing part of the diseased organ, and with comparable results, according to a new research study by Henry Ford Hospital urologists.

While the study shows that robot-assisted partial nephrectomy (RAPD), available only since 2004, may also offer fewer complications than laparoscopic partial nephrectomy (LPN), the researchers cautioned that available data did not allow them to consider such factors as surgical expertise and the complexity of each cancer.

"To the best of our knowledge, this study is the first to compare complication rates after RAPN and LPN," says Quoc-Dien Trinh, M.D., a Fellow at Henry Ford Hospital's Vattikuti Urology Institute and lead author of the study. The findings will be presented at the American Urological Association's Annual Meeting, May 19 to 23, in Atlanta.

Partial nephrectomy or PN, involves surgically removing only the diseased part of a cancerous kidney, compared to the once-standard treatment – radical nephrectomy or RN – in which the entire kidney, part of the ureter, the adrenal gland, and some surrounding tissue are removed. The less extreme PN became possible with improvements in 3D scanning technology, and not only offers obvious advantages over RN, but earlier studies found it results in an overall drop in related cardiovascular complications and death.

In LPN, the surgeon removes the kidney tumor through a small incision rather than a wide opening – less invasive but more technically challenging. The increasingly common use of surgical robots allows surgeons to operate with more precision in minimally invasive procedures.

Using the Nationwide Inpatient Sample (NIS), the Henry Ford Hospital researchers identified 1,174 patients who underwent minimally invasive PN from October 2008 to December 2009. Of those, 72.5 percent of the patients had robot-assisted surgery, while the remaining underwent LPN. The researchers found:

Overall complication rates both during and after surgery were essentially the same, as was the rate of blood transfusion and extended time in the hospital.

However, "statistically significant differences" were found for individual complications. Those undergoing RAPN had fewer neurologic, urinary, and bleeding problems.

A slightly higher percentage of LPN patients were white, but there was no difference according to gender, comorbidity (diseases or disorders in addition to kidney cancer), insurance status, or income level.

Significantly more RAPNs were performed at non-teaching hospitals, and most of those were in the Midwest. LPNs were more common in the Northeast.

"From a practical perspective, our results indicate that on average, similar intraoperative and postoperative outcomes, including transfusion rates, prolonged length of stay, and in-hospital mortality, are expected whether the patient undergoes RAPN or LPN," Trinh says.

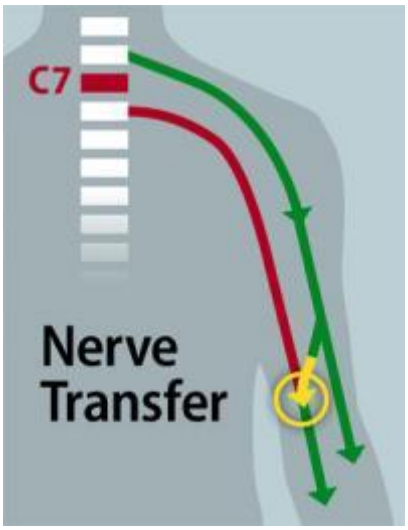
"But these results should be interpreted with care, because the NIS is unable to account for disease characteristics. Specifically, it's not known if more complex cases, or surgery for higher stage and grade cancers, are more often performed by robotic or laparoscopic procedures."
Kidney cancer rates in the U.S. have increased in recent years, in part because better technology and imaging techniques have allowed doctors to find more suspicious masses in the kidney. Much of the same technology has allowed surgeons to find and remove those tumors. At the same time, as studies showed that PN was as effective as RN in controlling cancer while resulting in better survival rates, it has become the standard treatment in both the U.S. and Europe. *Funding: Henry Ford Hospital*

http://www.eurekalert.org/pub_releases/2012-05/uom-ufm051512.php

Surgeons restore some hand function to quadriplegic patient

Technique could help those with C6, C7 spinal cord injuries

Surgeons at Washington University School of Medicine in St. Louis have restored some hand function in a quadriplegic patient with a spinal cord injury at the C7 vertebra, the lowest bone in the neck. Instead of operating on the spine itself, the surgeons rerouted working nerves in the upper arms. These nerves still "talk" to the brain because they attach to the spine above the injury.
Following the surgery, performed at Barnes-Jewish Hospital, and one year of intensive physical therapy, the patient regained some hand function, specifically the ability to bend the thumb and index finger. He can now feed himself bite-size pieces of food and write with assistance.
The case study, published online May 15 in the Journal of Neurosurgery, is, to the authors' knowledge, the first reported case of restoring the ability to flex the thumb and index finger after a spinal cord injury.
"This procedure is unusual for treating quadriplegia because we do not attempt to go back into the spinal cord where the injury is," says surgeon Ida K. Fox, MD, assistant professor of plastic and reconstructive surgery at Washington University, who treats patients at Barnes-Jewish Hospital. "Instead, we go out to where we know things work - in this case the elbow - so that we can borrow nerves there and reroute them to give hand function."
Although patients with spinal cord injuries at the C6 and C7 vertebra have no hand function, they do have shoulder, elbow and some wrist function because the associated nerves attach to the spinal cord above the injury and connect to the brain. Since the surgeon must tap into these working nerves, the technique will not benefit patients who have lost all arm function due to higher injuries - in vertebrae C1 through C5.
The surgery was developed and performed by the study's senior author Susan E. Mackinnon, MD, chief of the Division of Plastic and Reconstructive Surgery at Washington University School of Medicine. Specializing in injuries to peripheral nerves, she has pioneered similar surgeries to return function to injured arms and legs. Mackinnon originally developed this procedure for patients with arm injuries specifically damaging the nerves that provide the ability to flex the thumb and index finger. This is the first time she has applied this peripheral nerve technique to return limb function after a spinal cord injury.
"Many times these patients say they would like to be able to do very simple things," Fox says. "They say they would like to be able to feed themselves or write without assistance. If we can restore the ability to pinch, between thumb and index finger, it can return some very basic independence."
Mackinnon cautions that the hand function restored to the patient was not instantaneous and required intensive physical therapy. It takes time to retrain the brain to understand that nerves that used to bend the elbow now provide pinch, she says.
Though this study reports only one case, Mackinnon and her colleagues do not anticipate a limited window of time during which a patient with a similar spinal cord injury must be treated with this nerve transfer technique. This patient underwent the surgery almost two years after his injury. As long as the nerve remains connected to the support and nourishment of the spinal cord, even though it no longer "talks" to the brain, the nerve and its associated muscle remain healthy, even years after the injury.



To detour around the block in this patient's C7 spinal cord injury and return hand function, Mackinnon operated in the upper arms. There, the working nerves that connect above the injury (green) and the non-working nerves that connect below the injury (red) run parallel to each other, making it possible to tap into a functional nerve and direct those signals to a non-functional neighbor (yellow arrow). **Eric Young**

"The spinal cord is the control center for the nerves, which run like spaghetti all the way out to the tips of the fingers and the tips of the toes," says Mackinnon, the Sydney M. Shoenberg Jr. and Robert H. Shoenberg Professor and director of the School of Medicine's Center for Nerve Injury and Paralysis. "Even nerves below the injury remain healthy because they are still connected to the spinal cord. The problem is that these nerves no longer 'talk' to the brain because the spinal cord injury blocks the signals."

To detour around the block in this patient's C7 spinal cord injury and return hand function below the level of the injury, Mackinnon operated in the upper arms. There, the working nerves that connect above the injury and the non-working nerves that connect below the injury run parallel to each other, making it possible to tap into a functional nerve and direct those signals to a non-functional neighbor.

In this case, Mackinnon took a non-working nerve that controls the ability to pinch and plugged it into a working nerve that drives one of two muscles that flex the elbow. After the surgery, the bicep still flexes the elbow, but a second muscle, called the brachialis, that used to also provide elbow flexion, now bends the thumb and index finger.

"This is not a particularly expensive or overly complex surgery," Mackinnon says. "It's not a hand or a face transplant, for example. It's something we would like other surgeons around the country to do."

Detailed information for potential patients interested in nerve transfer surgery for C6 and C7 spinal cord injury will be available after 10 a.m. EDT Tuesday, May 15, 2012 at nerve.wustl.edu.

Mackinnon SE, Yee A, Ray WZ. Spinal cord injury bypass technique with nerve transfers for the restoration of hand function after spinal cord injury – case report and review of the literature. The Journal of Neurosurgery. Online May 15, 2012.

http://www.wired.com/wiredscience/2012/05/st_cuddy/

Power Postures Can Make You Feel More Powerful

Sit up straight and listen: Amy Cuddy has a plan to help you change your life. And it's easy.

By Danielle Venton

The Harvard psychologist recently completed a study demonstrating that positioning our bodies a certain way doesn't just tell people we're powerful, it actually makes us more powerful. And she has the data to prove it: Standing tall directly influences our biochemistry, increasing testosterone, decreasing cortisol, and generally making us feel dominant. So pull back those shoulders and stretch out. Stand like Superman and you'll become the Man of Steel.

What got you thinking about posture?

There is a gender grade gap in the MBA classroom; men slightly outperform women. It's competitive; you really have to get in there. I noticed in class that women tended to make themselves small, holding their wrist, wrapping their arms around themselves. Guys tended to make themselves bigger. They're leaning back, stretching out, draping their arms around chairs. We know from studies of facial feedback that if you smile, you fake yourself into feeling happier. We wondered whether just asking people to spread out would help them feel more powerful, and it did.

Aren't traits like this fixed?

Effective leaders have a classic hormone profile: high levels of testosterone, low levels of cortisol (a stress-associated hormone). But levels are flexible. When an individual takes over the alpha role, their testosterone rises and their cortisol drops. We found two minutes in a power pose - arms and legs stretched out - spikes a person's testosterone and drops their cortisol. It works for both genders. It's the ratio that's important.

What advice would you give a job-seeker?

One of our recent studies put people in either high- or low-power poses for a few minutes as they prepared to give a presentation in front of a panel of judges. The power posers came across as more enthusiastic and competent, even though they weren't posing during the speech. It seems the posing primed their brains to perform well. So if it's a phone interview, close the door and put your feet up on the desk. If you can't do that, find somewhere to stretch. A lot of students write and say, "I went to a bathroom stall, closed the door, stood on my toes, spread my feet, reached my arms out, put my shoulders back, and lifted my chin."

What about posture during the interview?

You don't want to go in and be totally dominant. But do make yourself as big as you can in a way that feels natural. The power posing beforehand is the way to optimize your brain. It's not that it makes you smarter or more likable. It affects your speaker presence - your confidence, enthusiasm, and ability to captivate.

What's next for your research?

One fun study: We're learning how big people perceive themselves. I work with a freakishly tall group of people, and I'm 5'5" But after teaching a good class, or when I'm feeling particularly powerful, I actually think I'm as tall as they are.

http://phys.org/news/2012-05-highly-women-families-increasingly-popular.html

For highly educated women, families are an increasingly popular option

An increasing number of highly educated women are opting for families, according to a national study co-authored by a University at Buffalo economist.

Qingyan Shang, an assistant professor at UB, says the study uncovers what may be the reversal of a trend by highly educated women. She says it is still too early to be certain, but the research clearly shows fertility rising for older, highly educated women since the 1990s. (Fertility is defined as the number of children a woman has had.) Childlessness also declined by roughly 5 percentage points between 1998 and 2008. "Women born in the late 1950s are the turning point," said Shang. Members of this group initially showed low fertility. But Shang said fertility increased for those members in their late 30s and early 40s.

The paper, co-authored by Bruce A. Weinberg, professor of economics at Ohio State University, appears online in the Journal of Population Economics and will be published in a forthcoming print edition.

Shang said two previous studies which examined fertility among highly educated women had limitations and came to conflicting conclusions.

One study focused only on women in their late 20s. Another study examined fertility for women in managerial positions. Using a sample of professional women makes the results difficult to interpret because women who have more children may switch to other occupations, according to Shang. "We did a more comprehensive study," said Shang. "We instead define the sample using education, which is less responsive to short-term fertility decisions."

The conclusions are derived from data gathered by the June Current Population Survey, compiled by the U.S. Bureau of Labor Statistics and U.S. Census Bureau. The researchers also used the Vital Statistics Birth Data from the National Center for Health Statistics as a second data set.

While the research did not directly address what factors might be contributing to the fertility increase, "We did list some possible explanations based on previous research," said Shang.

Shang mentioned the idea of "the learning story," where the decisions of previous generations inform later decisions by subsequent generations. There has also been an increased supply of personal services that have reduced childcare expenses. Other research shows men may be taking more responsibility for child care.

Shang and Weinberg also could not determine whether women are opting for families instead of their careers or in addition to their careers. "We know these women are opting for families," said Shang. "We don't know if they in turn are opting out of the labor market."

The researchers discovered an increase in multiple birth rates around 1990, suggesting fertility treatments may have played a role. "The data does not include information about whether women used fertility treatment," Shang said. "But we use the trends in plural birth rates to impute the share of the increase in fertility among highly educated women that is attributed to fertility treatment."

Shang said the study shows that fertility would have increased even in the absence of fertility treatments.

http://www.sciencedaily.com/releases/2012/05/120515181256.htm

New Look at Prolonged Radiation Exposure: At Low Dose-Rate, Radiation Poses Little Risk to DNA, Study

A new study from MIT scientists suggests that the guidelines governments use to determine when to evacuate people following a nuclear accident may be too conservative.

Anne Trafton, MIT News Office

ScienceDaily - The study, led by Bevin Engelward and Jacquelyn Yanch and published in the journal Environmental Health Perspectives, found that when mice were exposed to radiation doses about 400 times greater than background levels for five weeks, no DNA damage could be detected.

Current U.S. regulations require that residents of any area that reaches radiation levels eight times higher than background should be evacuated. However, the financial and emotional cost of such relocation may not be worthwhile, the researchers say.

"There are no data that say that's a dangerous level," says Yanch, a senior lecturer in MIT's Department of Nuclear Science and Engineering. "This paper shows that you could go 400 times higher than average background levels and you're still not detecting genetic damage. It could potentially have a big impact on tens if not hundreds of thousands of people in the vicinity of a nuclear powerplant accident or a nuclear bomb detonation, if we figure out just when we should evacuate and when it's OK to stay where we are."

Until now, very few studies have measured the effects of low doses of radiation delivered over a long period of time. This study is the first to measure the genetic damage seen at a level as low as 400 times background (0.0002 centigray per minute, or 105 cGy in a year).

"Almost all radiation studies are done with one quick hit of radiation. That would cause a totally different biological outcome compared to long-term conditions," says Engelward, an associate professor of biological engineering at MIT.

How much is too much?

Background radiation comes from cosmic radiation and natural radioactive isotopes in the environment. These sources add up to about 0.3 cGy per year per person, on average.

"Exposure to low-dose-rate radiation is natural, and some people may even say essential for life. The question is, how high does the rate need to get before we need to worry about ill effects on our health?" Yanch says.

Previous studies have shown that a radiation level of 10.5 cGy, the total dose used in this study, does produce DNA damage if given all at once. However, for this study, the researchers spread the dose out over five weeks, using radioactive iodine as a source. The radiation emitted by the radioactive iodine is similar to that emitted by the damaged Fukushima reactor in Japan.

At the end of five weeks, the researchers tested for several types of DNA damage, using the most sensitive techniques available. Those types of damage fall into two major classes: base lesions, in which the structure of the DNA base (nucleotide) is altered, and breaks in the DNA strand. They found no significant increases in either type.

DNA damage occurs spontaneously even at background radiation levels, conservatively at a rate of about 10,000 changes per cell per day. Most of that damage is fixed by DNA repair systems within each cell. The researchers estimate that the amount of radiation used in this study produces an additional dozen lesions per cell per day, all of which appear to have been repaired.

Though the study ended after five weeks, Engelward believes the results would be the same for longer exposures. "My take on this is that this amount of radiation is not creating very many lesions to begin with, and you already have good DNA repair systems. My guess is that you could probably leave the mice there indefinitely and the damage wouldn't be significant," she says.

Doug Boreham, a professor of medical physics and applied radiation sciences at McMaster University, says the study adds to growing evidence that low doses of radiation are not as harmful as people often fear.

"Now, it's believed that all radiation is bad for you, and any time you get a little bit of radiation, it adds up and your risk of cancer goes up," says Boreham, who was not involved in this study. "There's now evidence building that that is not the case."

Conservative estimates

Most of the radiation studies on which evacuation guidelines have been based were originally done to establish safe levels for radiation in the workplace, Yanch says -- meaning they are very conservative. In workplace cases, this makes sense because the employer can pay for shielding for all of their employees at once, which lowers the cost, she says.

However, "when you've got a contaminated environment, then the source is no longer controlled, and every citizen has to pay for their own dose avoidance," Yanch says. "They have to leave their home or their community, maybe even forever. They often lose their jobs, like you saw in Fukushima. And there you really want to call into question how conservative in your analysis of the radiation effect you want to be. Instead of being conservative, it makes more sense to look at a best estimate of how hazardous radiation really is."

Those conservative estimates are based on acute radiation exposures, and then extrapolating what might happen at lower doses and lower dose-rates, Engelward says. "Basically you're using a data set collected based on an acute high dose exposure to make predictions about what's happening at very low doses over a long period of time, and you don't really have any direct data. It's guesswork," she says. "People argue constantly about how to predict what is happening at lower doses and lower dose-rates."

However, the researchers say that more studies are needed before evacuation guidelines can be revised.

"Clearly these studies had to be done in animals rather than people, but many studies show that mice and humans share similar responses to radiation. This work therefore provides a framework for additional research and careful evaluation of our current guidelines," Engelward says.

"It is interesting that, despite the evacuation of roughly 100,000 residents, the Japanese government was criticized for not imposing evacuations for even more people. From our studies, we would predict that the population that was left behind would not show excess DNA damage -- this is something we can test using technologies recently developed in our laboratory," she adds.

The first author on these studies is former MIT postdoc Werner Olipitz, and the work was done in collaboration with Department of Biological Engineering faculty Leona Samson and Peter Dedon. These studies were supported by the DOE and by MIT's Center for Environmental Health Sciences.

Werner Olipitz, Dominika Wiktor-Brown, Joe Shuga, Bo Pang, Jose McFaline, Pallavi Lonkar, Aline Thomas, James T. Mutamba, Joel S. Greenberger, Leona D. Samson, Peter C. Dedon, Jacqueline C. Yanch, Bevin P. Engelward. Integrated Molecular Analysis Indicates Undetectable DNA Damage in Mice after Continuous Irradiation at ~400-fold Natural Background Radiation. Environmental Health Perspectives, 2012; DOI: 10.1289/ehp.1104294

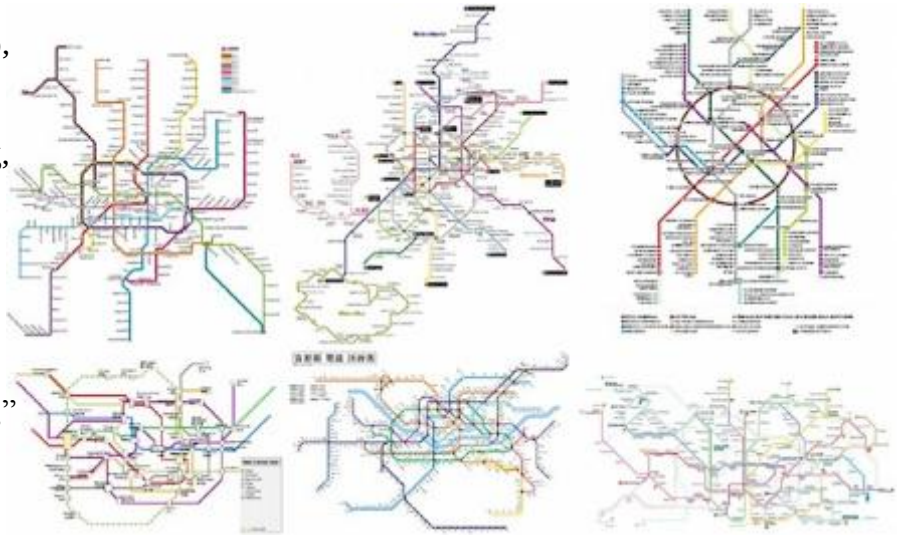
http://www.wired.com/wiredscience/2012/05/subway-convergence/

World's Subways Converging on Ideal Form

After decades of urban evolution, the world's major subway systems appear to be converging on an ideal form.

By Brandon Keim

On the surface, these core-and-branch systems - evident in New York City, Tokyo, London or most any large metropolitan subway - may seem intuitively optimal. But in the absence of top-down central planning, their movement over decades toward a common mathematical space may hint at universal principles of human self-organization. Understand those principles, and one might "make urbanism a quantitative science, and understand with data and numbers the construction of a city," said statistical physicist Marc Barthelemy of France's National Center for Scientific Research.



Sample of subway network structures from (clockwise, top left) Shanghai, Madrid, Moscow, Tokyo, Seoul and Barcelona. **Roth et al./JRSI**

In a May 15 Journal of the Royal Society Interface paper, Barthelemy and NCSR complex systems analyst Camille Roth focused a network analysis lens on the aforementioned cities' subways, along with Barcelona, Beijing, Berlin, Chicago, Madrid, Mexico, Moscow, Osaka, Paris, Seoul and Tokyo.

'One might understand with data and numbers the construction of a city.'

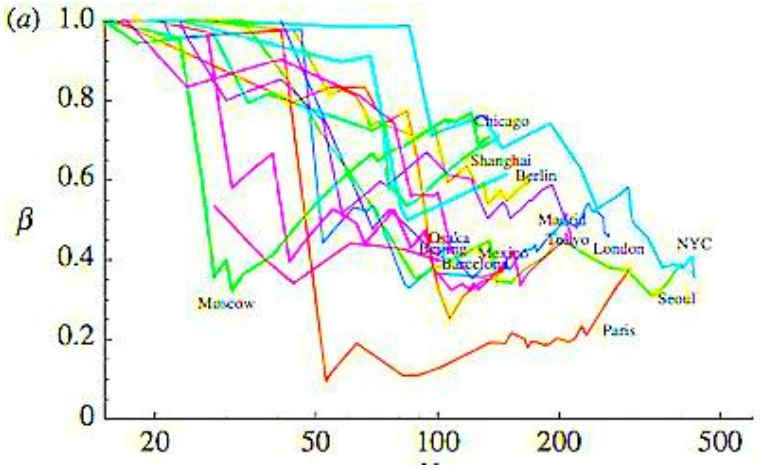
With equations used to study two-dimensional spatial networks, the class of network to which subways belong, the researchers turned stations and lines to a mathematics of nodes and branches. They repeated their analyses with data from each decade of a subway system's history, and looked for underlying trends.

Patterns emerged: The core-and-branch topology, of course, and patterns more fine-grained. Roughly half the stations in any subway will be found on its outer branches rather than the core. The distance from a city's center to its farthest terminus station is twice the diameter of the subway system's core. This happens again and again.

"Many other shapes could be expected, such as a regular lattice," said Barthelemy. "What we find surprising is that all these different cities, on different continents, with different histories and geographical constraints, lead finally to the same structure."

Subway systems seem to gravitate towards these ratios organically, through a combination of planning, expedience, circumstance and socioeconomic fluctuation, say the researchers.

This is a crucial point: If the subways followed a predetermined path, their evolution would only reflect a set plan. Instead, the convergence "is a sign that there are some basic, profound mechanisms that drive the development of urban systems," said Barthelemy.



City subway systems converge on a ratio for the number of stations on branch lines to the number in city cores. **Roth et al./JRSI**

According to Andrew Adamatzky, a University of West England computer scientist who uses creatures called slime molds to study optimal transportation networks, it's possible that engineers were influenced by early subway networks in London, Berlin and Paris.

But Adamatzky still called the results "very promising," saying that "when more data will be collected, then maybe they can suggest some useful theory of subway development."
Barthelemy's group says the trends they observed could next be cross-referenced with social shifts in cities. Their ultimate goal is a model of subway evolution based on real-world observations. With such a model, they could look for ways to tweak future transportation systems in optimal ways.
To be sure, this wouldn't be the first time that urbanists have tried to impose rationality and order on cities. The fruits of some such efforts - such as the vast, soulless housing projects of beloved of rectangle-obsessed modernists - proved bitter indeed.
But Barthelemy said his group's approach is different, seeking to improve on how people naturally organize themselves rather imposing abstract, arbitrary rules from above. "We don't have big ideas," Barthelemy said. "We're just in the process of trying to understand centuries of development."
Citation: "A long-time limit for world subway networks." By Camille Roth, Soong Moon Kang, Michael Batty and Marc Barthelemy. Proceedings of the Royal Society Interface, 15 May 2012.

http://www.wired.com/wiredscience/2012/05/the-benefits-of-being-bilingual/

The Benefits of Being Bilingual

A team of psychologists led by Boaz Keysar at the University of Chicago found that forcing people to rely on a second language systematically reduced human biases, allowing the subjects to escape from the usual blind spots of cognition

By Jonah Lehrer

Samuel Beckett, born in a suburb of Dublin in 1906, was a native English speaker. However, in 1946 Beckett decided that he would begin writing exclusively in French. After composing the first draft in his second language, he would then translate these words back into English. This difficult constraint – forcing himself to consciously unpack his own sentences – led to a burst of genius, as many of Beckett's most famous works (Malloy, Malone Dies, Waiting for Godot, etc.) were written during this period. When asked why he wrote first in French, Beckett said it made it easier for him to "write without style."
Beckett would later expand on these comments, noting that his use of French prevented him from slipping into his usual writerly habits, those crutches of style that snuck into his English prose. Instead of relying on the first word that leapt into consciousness – that most automatic of associations – he was forced by his second language to reflect on what he actually wanted to express. His diction became more intentional.
There's now some neat experimental proof of this Beckettian strategy. In a recent paper published in Psychological Science, a team of psychologists led by Boaz Keysar at the University of Chicago found that forcing people to rely on a second language systematically reduced human biases, allowing the subjects to escape from the usual blind spots of cognition. In a sense, they were better able to think without style.
The paper is a tour de force of cross-cultural comparison, as the scientists conducted six experiments on three continents ($n > 600$) in five different languages: English, Korean, French, Spanish and Japanese. Although all subjects were proficient in their second language, they were not "balanced bilingual."
The experiments themselves relied on classic paradigms borrowed from prospect theory, in which people are asked to make decisions under varying conditions of uncertainty and risk. For instance, native English speakers in Chicago who had learned Spanish in the classroom were given a $15 stake. Then, they were asked to make various bets based on a coin toss: If they correctly picked heads or tails, they would win $1.50, while an incorrect guess would cost them $1. From a rational perspective, these bets are a smart wager – a subject who chooses to bet on all 15 trials would most likely come out far ahead.
But people aren't rational creatures. When thinking in English, students only chose to bet 54 percent of their time; their fear of losses kept them from properly assessing the situation. However, when the same options were described in Spanish, subjects made significantly better decisions, choosing to place bets 71 percent of the time.
The scientists also found that thinking in a second language reduced our cognitive inconsistencies. Consider this scenario, pioneered by the great psychologists Amos Tversky and Daniel Kahneman:

The U.S. is preparing for the outbreak of an unusual Asian disease, which is expected to kill 600 people. Two alternative programs to combat the disease have been proposed. Assume that the exact scientific estimates of the consequences of the programs are as follows: If program A is adopted, 200 people will be saved. If program B is adopted, there is a one-third probability that 600 people will be saved and a two-thirds probability that no people will be saved. Which of the two programs would you favor?

When this question was put to a large sample of physicians, 72 percent chose option A, the safe-and-sure strategy, and only 28 percent chose program B, the risky strategy. In other words, physicians would rather save

a certain number of people for sure than risk the possibility that everyone might die. But what about this scenario:

The U.S. is preparing for the outbreak of an unusual Asian disease, which is expected to kill 600 people. Two alternative programs to combat the disease have been proposed. Assume that the exact scientific estimates of the consequences of the programs are as follows: If program C is adopted, 400 people will die. If program D is adopted, there is a one-third probability that nobody will die and a two-thirds probability that 600 people will die. Which of the two programs would you favor?

When the scenario was described in terms of deaths instead of survivors, physicians reversed their previous decision. Only 22 percent voted for option C, while 78 percent of them opted for option D, the risky strategy. Of course, this is a ridiculous shift in preference. The two different questions examine identical dilemmas; saving one-third of the population is the same as losing two-thirds. And yet, doctors reacted very differently depending on how the question was framed. When the possible outcomes were stated in terms of deaths – this is the "loss frame" – physicians were suddenly eager to take chances. They were so determined to avoid any alternative associated with a loss that they were willing to risk losing everything.

It turns out, however, that thinking bilingually can dramatically reduce this bias. When 121 American students were given a version of the scenario above, nearly 80 percent chose the safe option, just like those doctors. However, when the same situation was placed in a loss frame, that number plummeted to 47 percent. So far, so obvious: we are consistently inconsistent creatures.

But when native English speakers were presented with the same problem in Japanese, the inconsistency vanished. In both frames, the number of people choosing the safer option was just over 40 percent.

It's worth pointing out that these results are somewhat surprising. After all, one could also speculate that forcing people to think in a second language would consume scarce mental resources, thus making it harder to select the "rational" option. We'd be so distracted by our lack of fluency that we'd become even more reliant on our shortsighted instincts. Such a result would support reams of research showing that increasing the "cognitive load" of subjects can increase their bias.

But that's not what happened. Instead, the psychologists found that the reduced emotional valence of a second language – the words aren't so weighted with feeling – made it easier to resist the tug of loss aversion. (Similar results have been achieved with neurological patients who, after suffering a serious brain injury, are unable to experience any emotion at all.) The scientists argue that second-language thinking can systematically improve decision-making: "People who routinely make decisions in a foreign language might be less biased in their savings, investment and retirement decisions," they write. "Over a long time horizon, this might very well be beneficial." Given the known costs of loss aversion among financial traders – it's a huge issue – perhaps it's time that those on Wall Street begin thinking in a non-native tongue. If I were a risk manager at J.P. Morgan, I'd start recruiting bilingual employees.

This is only the latest study to capture the power of bilingualism. For instance, children raised in bilingual households show increased levels of self-control and appear better at learning abstract rules and ignoring irrelevant information. (These benefits seem to exist as early as 7 months of age.) Other studies have demonstrated that people who speak two languages are diagnosed with dementia, on average, about four years later than people who only speak one language. There are some confounding variables here, of course: It takes a certain kind of smarts to learn multiple forms of expression, and those smarts might act as a cognitive buffer. And yet, even when intelligence is controlled for, interesting differences persist.

What's behind these benefits? The answer appears to involve the extra processing triggered by holding multiple languages inside the head. Several studies using different methodologies have found that the brains of bilinguals typically activate both languages when communicating, even when only one language is relevant. This additional activity is not always helpful, which is why bilinguals are often slightly slower at retrieving their words from the depths of memory.

Nevertheless, learning how to cope with this constant interference – having to toggle back and forth between different forms of description – comes with lasting benefits. (A similar logic explains why people with Tourette's also exhibit enhanced cognitive control. Because they are constantly attempting to control their tics, they also learn how to restrain those impulses they'd like to do without. Practice makes perfect.)

Samuel Beckett argued that the constraints imposed by a second language were inseparable from its benefits. He was right. It's always easier to think with those words we know so well. But sometimes we need that pause of incomprehension, that blink of doubt that occurs when we encounter a verb tense we don't recognize or an adjective with an unclear set of connotations. Language isn't just the stuff of thought – it can also make our thoughts better.

And yet, let's not get too practical here. Lera Boroditsky, a psychologist at Stanford who has done some fascinating work on how language shapes thought, pointed out in an e-mail that the real benefits of bilingualism far exceed the marginal cognitive edge captured in these studies:

There is one very important advantage of learning other languages that I think beats any gains in cognitive control or delays in the onset of dementia. When you learn other languages you can then actually speak those languages, read those literatures, talk to new people in their native language, eaves-drop on their conversations on the bus, order off the menu, pick up that gorgeous stranger in the piazza. I think that's cooler than having a few extra points on the Wisconsin card-sorting task.

http://www.eurekalert.org/pub_releases/2012-05/mh-mhs051612.php

McLean Hospital study finds herbal extract may curb binge drinking

An extract of the Chinese herb kudzu dramatically reduces drinking and may be useful in the treatment of alcoholism and curbing binge drinking

Belmont, MA - An extract of the Chinese herb kudzu dramatically reduces drinking and may be useful in the treatment of alcoholism and curbing binge drinking, according to a new study by McLean Hospital and Harvard Medical School researchers.

"Our study is further evidence that components found in kudzu root can reduce alcohol consumption and do so without adverse side effects," said David Penetar, PhD, of the Behavioral Psychopharmacology Research Laboratory at McLean Hospital, and the lead author of the study. "Further research is needed, but this botanical medication may lead to additional methods to treat alcohol abuse and dependence."

In the study, published in the current issue of Drug and Alcohol Dependence, researchers in the Behavioral Psychopharmacology Research Laboratory at McLean Hospital looked at one of the major components of the kudzu root - the isoflavone puerarin - to determine whether it would reduce alcohol consumption in a laboratory simulation of an afternoon drinking session.

According to Penetar, puerarin was selected over other kudzu root components because its safety and efficacy have already been established in humans, particularly in China where it is approved for intravenous injection to treat coronary heart disease, myocardial infarction and angina. Puerarin is also less potent than other parts of the kudzu plant, so it has few side effects and has none of the estrogenic activity found in other components, making it safe for women.

In the study, Penetar and his colleagues looked at 10 men and women, all in their 20s and all reporting regularly consuming alcohol weekly. A laboratory at McLean Hospital was set up as an apartment, with TV, DVD player, reclining chair and other amenities. The unit was also stocked with a refrigerator full of each subject's favorite beer and other non-alcoholic beverages.

In an initial 90-minute session in the "apartment," each subject was allowed to consume as many beers as he or she wanted - up to a maximum of six. After the session, each was given either puerarin or a placebo and told to take it daily for a week. Then, each returned to do the experiment again. Two weeks later, the subjects returned for a third session to see if they had returned to their baseline drinking levels. After that, each subject was given the pill he or she didn't get the first time and told to take it for a week. Each then returned for a fourth and final drinking session.

The study showed that subjects taking puerarin drank significantly fewer beers - dropping from 3.5 beers on average to 2.4. "This was a simulation of a binge drinking opportunity and not only did we see the subjects drinking less, we noted that their rate of consumption decreased, meaning they drank slower and took more sips to finish a beer," explained Penetar. "While we do not suggest that puerarin will stop drinking all together, it is promising that it appears to slow the pace and the overall amount consumed."

The Behavioral Psychopharmacology Research Laboratory at McLean Hospital has been involved in a series of research projects for more than 10 years, looking at the ability of extracts of the kudzu root and its components to reduce excessive drinking with very encouraging results.

http://bit.ly/KwMYmn

Chikungunya virus loves warm New York winters

Warmer New York winters have a sting in the tail. The mosquito that carries chikungunya, a virus that causes joint pain, but isn't fatal, is flocking to the city in increasing numbers.

12:34 16 May 2012 by Amy Kraft

The virus, which originates in Africa, is carried by the Asian tiger mosquito (Aedes albopictus) and could become endemic in New York within a few years. Until now the bitter winters have kept mosquito numbers down, says Laura Harrington at Cornell University in Ithaca, New York.

Harrington estimates there is one Asian tiger mosquito for every five New Yorkers. Once that ratio flips to five insects per person, her model suggests that someone arriving in New York carrying the virus would have a 38 per cent chance of passing it on to another person through mosquito bites. The disease could become entrenched in the city at that level of infection, Harrington told the Inside Cornell event in New York City last week.

Isolated cases of chikungunya have already been reported in the US, but just like similar cases that showed up in Europe in 2007, seasonal changes in weather kept mosquito numbers down and the virus in check.

In Europe too, though, climate conditions are becoming more conducive for pathogen-carrying insects, including Asian tiger mosquitoes, suggesting chikungunya could become a problem there too (Journal of the Royal Society Interface, DOI: 10.1098/rsif.2012.0138).

"It isn't a question of if someone gets infected with the virus, but when – and how many [cases]," says Scott Weaver, an infectious disease specialist at the University of Texas Medical Branch in Galveston, who was not involved in the research.

Because there is no vaccine and no treatment for the virus, Harrington says US physicians should be looking for symptoms of chikungunya in their patients to prevent the disease from spreading.

http://nyti.ms/Jenxs5

New Drug Trial Seeks to Stop Alzheimer's Before It Starts

In a clinical trial that could lead to treatments that prevent Alzheimer's, people who are genetically guaranteed to develop the disease - but who do not yet have any symptoms - will for the first time be given a drug intended to stop it, federal officials announced Tuesday.

By PAM BELLUCK ***Dabrali Jimenez contributed reporting***

Experts say the study will be one of the few ever conducted to test prevention treatments for any genetically predestined disease. For Alzheimer's, the trial is unprecedented, "the first to focus on people who are cognitively normal but at very high risk for Alzheimer's disease," said Dr. Francis S. Collins, director of the National Institutes of Health.

Most participants will come from the world's largest family to experience Alzheimer's, an extended clan of 5,000 people who live in Medellín, Colombia, and remote mountain villages outside that city. Family members with a specific genetic mutation begin showing cognitive impairment around age 45, and full dementia around age 51, debilitated in their prime working years as their memories fade and the disease quickly assaults their ability to move, eat, speak and communicate.

Three hundred family members will participate in the initial trial. Those with the mutation will be years away from symptoms, some as young as 30.

"Because of this study, we do not feel as alone," said Gladys Betancur, 39, a family member. Her mother died of Alzheimer's, three of her siblings already have symptoms, and she had a hysterectomy because of her fears that she has the mutation and would pass it on to her children. "Sometimes we think that life is ending, but now we feel that people are trying to help us."

The $100 million study will last five years, but sophisticated tests may indicate in two years whether the drug helps delay memory decline or brain changes, said Dr. Eric M. Reiman, executive director of the Banner Alzheimer's Institute in Phoenix and a study leader.

Alzheimer's experts not involved in the study said that though only a small percentage of people with Alzheimer's have the genetic early-onset form that affects the Colombian family, the trial was expected to yield information that could apply to millions of people worldwide who will develop more conventional Alzheimer's.

"It offers a tremendous opportunity for us to answer a large number of questions, while at the same time offering these people some significant clinical help that otherwise they never would have had," said Dr. Steven T. DeKosky, an Alzheimer's researcher who is vice president and dean of the University of Virginia School of Medicine. Dr. DeKosky was part of a large group consulted early on, but is not involved in the study.

Some 5.4 million Americans have Alzheimer's, and the numbers are expected to swell as the baby boom generation ages. Dr. Reiman's team is planning a similar trial for people in the United States considered at increased risk for conventional late-onset Alzheimer's. The study announced Tuesday will include a small number of Americans with gene mutations guaranteed to cause early-onset Alzheimer's.

The drug trial is part of the federal government's first national plan to address Alzheimer's, which was unveiled Tuesday by Kathleen Sebelius, the secretary for health and human services. The government took the unusual step of assigning $50 million from the current year's N.I.H. budget to research considered too promising to wait, including the Colombia trial and a study on whether inhaled insulin can ease mild cognitive impairment, Dr.

Collins said. Another $100 million is proposed for 2013, mostly for research, but also for education, caregiver support and data collection.

Success for the Colombia trial is, of course, no sure thing. Many trials fail, and Alzheimer's research has so far found no treatment effective for more than several months. But experts say that trying drugs years before symptoms emerge could have greater potential because the brain would not yet be ravaged by the disease. The trial will be financed with $16 million from the National Institutes of Health, $15 million from private donors through the Banner Institute and about $65 million from Genentech, the drug's American manufacturer.

The drug, Crenezumab, attacks amyloid plaques in the brain. If it can forestall memory or cognitive problems, scientists will know that prevention or delay is possible and appears to lie in targeting amyloid years before dementia develops. Many, but not all, Alzheimer's researchers believe amyloid is an underlying cause of Alzheimer's.

In 2010, The New York Times reported on the pervasiveness of dementia in this large Colombian family and scientists' hopes of testing prevention drugs. But persuading pharmaceutical companies to invest took months. There are scientific and ethical issues involved with giving drugs to people who are healthy and people who live in a developing country, some of whom have little education, paltry incomes and longstanding superstitions about the disease they call La Bobera - the foolishness.

"The first thing I did was to ask myself the question, Are we taking advantage of these folks?" said Richard H. Scheller, Genentech's executive vice president of research and early development. "The answer was clearly no." The risks, he said, are balanced by the fact that if nothing is done, "they're going to get this terrible, terrible disease for sure."

The few trials of prevention therapies - involving ginkgo biloba, women's hormone replacement treatment and anti-inflammatory drugs - have involved people not guaranteed to get the disease. These therapies either failed or caused adverse side effects.

Testing drugs on that kind of population takes "too many healthy volunteers, too much money, and too many years," Dr. Reiman said.

The Colombian population is ideal because it is large enough to provide solid results, and it is easy to identify whom the disease will strike and when.

Crenezumab was chosen for the Colombia trial partly because it appears to have no negative side effects, unlike other drugs designed to clear amyloid from the brain, said Dr. Francisco Lopera, a Colombian neurologist who has worked with the family for decades and is a leader of the study. Other anti-amyloid treatments have caused edema in the blood vessels, an imbalance of fluid that can have serious consequences.

Crenezumab is currently being given in two clinical trials to people with mild to moderate symptoms of dementia in the United States, Canada and Western Europe to see if it can help reduce cognitive decline or amyloid accumulation, according to Genentech.

In the Colombia study, expected to start early next year, 100 family members with the mutation will receive the drug every two weeks in an injection at a hospital. Another 100 carriers will receive a placebo. And because many people do not want to know if they have the mutation, researchers will include 100 noncarriers in the study; they will receive a placebo.

Researchers have developed a sophisticated battery of five memory and cognitive tests that have been shown in other studies to detect subtle alterations in recall and thinking ability that usually go unnoticed. Dr. Pierre N. Tariot, director of the Banner Institute and a leader of the study, said the measurements would involve recalling words, naming objects, nonverbal reasoning, remembering time and place, and drawing tests involving copying complex figures.

Dr. Tariot said researchers would also assess changes in people's emotional state, "irritability, sadness, crying, anxiety, impulsivity - these are cardinal features of the disease as it emerges."

The scientists will take physiological measurements, including PET scans that measure amyloid and how glucose is metabolized in the brain, M.R.I. scans that measure whether the brain is shrinking, and cerebral spinal fluid tests that measure amyloid and tau, a protein in dying brain cells.

If any of these indicators are improved by the drug, Dr. Reiman said, scientists may then be able to treat one of these early physiological changes, just as high blood pressure and cholesterol are treated to prevent heart disease.

In Medellín, Marcela Agudelo, 17, has Alzheimer's on both sides of her family because her parents are distant cousins. Marcela watched her maternal grandmother die, and her father, 55, once a vibrant livestock trader, has deteriorated so much that he can no longer walk, talk or laugh.

With the research, "we have more hope for a cure," Marcela said, "or at least a better life."

http://bit.ly/KPFU3T

Biological clock began ticking 2.5 billion years ago

Exactly how and when life began keeping time is unclear, but a candidate for the original biological clock may solve the mystery.

16 May 2012 by Debora MacKenzie

OUR core physiology relies on subtle organic timers: disrupt them, and effects range from jet lag to schizophrenia. Exactly how and when life began keeping time is unclear, but a candidate for the original biological clock may solve the mystery.

Biological clocks are ubiquitous in nature, so the first clock should pre-date the evolutionary parting of the ways that led to modern groups of organisms. All the clocks found so far are unique to different groups of organisms, though. Not so the clock discovered by Akhilesh Reddy at the University of Cambridge and colleagues. In an enzyme called peroxiredoxin (PRX), they seem to have found a grandfather clock - one that is common to nearly all life.

PRX gets rid of poisonous, highly reactive oxygen (ROS), which is produced by oxygen-based metabolism. And the enzyme oscillates: it flits between an active and inactive state, depending on whether oxygen is bound to the active site. Using antibodies that bind only to the oxidised enzyme, the team found that PRX oxidation keeps cycling independently on a 24-hour cycle, even when organisms were kept in constant light or constant dark.

Moreover, they found this PRX cycle in mice, fruit flies, a plant, a fungus, an alga, bacteria and even in archaea - the most primitive of all cellular life (Nature, DOI: 10.1038/nature11088). That suggests PRX evolved early in life's history. A gene sequence analysis suggests it did so 2.5 billion years ago, during the Great Oxygenation Event (GOE) - a critical interval when the oxygen released by photosynthesis began to accumulate in the atmosphere.

Reddy thinks PRX protected primitive cells from ROS damage by surging when peaks in photosynthesis related to daylight temporarily bumped up levels of oxygen. "Initially this was externally driven," he says. Then PRX began oscillating spontaneously in anticipation of this load - thus becoming an independent daily clock. "Organisms with this anticipatory ability would be better adapted than organisms that merely 'reacted' to things as they happened," Reddy says. Because all forms of life appear to dance to the metabolic rhythm of PRX oxidation, Reddy believes it pre-dates the other gene-related clocks that organisms carry.

It may even have driven their evolution. A gene-related clock, unique to cyanobacteria, appears to have evolved alongside PRX. What is more, another archaean that lives without oxygen and never had to deal with ROS has no PRX clock - and no circadian rhythms at all.

When PRX emerged 2.5 billion years ago, the Earth spun faster and a day lasted only 11 hours. "It will have adapted to the lengthening of the day-night cycle over time," says Reddy.

It may have done more than adapt - day lengths best suited to biological clocks may have coincided with times during which life made important evolutionary leaps. Ioannis Karafyllidis of the Democritus University of Thrace in Xanthi, Greece, has found that the cycling of the cyanobacterial clock resonates, or works most efficiently, at periods of 11 and 21 hours. These are the day lengths of the GOE and the Cambrian explosion of life, around 530 million years ago (Biosystems, DOI: 10.1016/j.biosystems.2012.02.008).

It would be interesting, Karafyllidis says, to know if PRX - despite adapting to our longer days - has the same intrinsic resonance.

http://www.sciencedaily.com/releases/2012/05/120516140016.htm

Alzheimer's Gene Causes Brain's Blood Vessels to Leak Toxins and Die

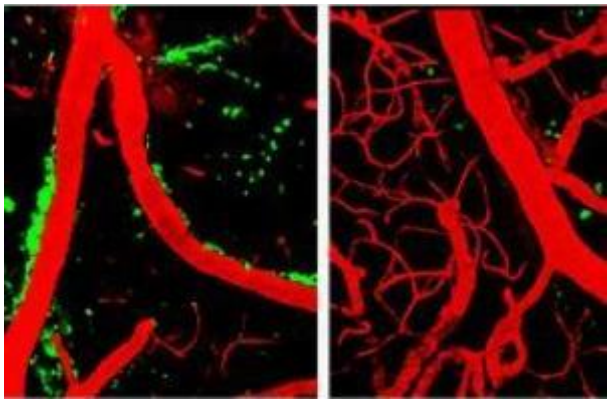
A well-known genetic risk factor for Alzheimer's disease triggers a cascade of signaling that ultimately results in leaky blood vessels in the brain

ScienceDaily - A well-known genetic risk factor for Alzheimer's disease triggers a cascade of signaling that ultimately results in leaky blood vessels in the brain, allowing toxic substances to pour into brain tissue in large amounts, scientists report May 16 in the journal Nature.

The results come from a team of scientists investigating why a gene called ApoE4 makes people more prone to developing Alzheimer's. People who carry two copies of the gene have roughly eight to 10 times the risk of getting Alzheimer's disease than people who do not.

A team of scientists from the University of Rochester, the University of Southern California, and other institutions found that ApoE4 works through cyclophilin A, a well-known bad actor in the cardiovascular system, causing inflammation in atherosclerosis and other conditions. The team found that cyclophilin A opens the gates to the brain assault seen in Alzheimer's.

"We are beginning to understand much more about how ApoE4 may be contributing to Alzheimer's disease," said Robert Bell, Ph.D., the post-doctoral associate at Rochester who is first author of the paper. "In the presence of ApoE4, increased cyclophilin A causes a breakdown of the cells lining the blood vessels in Alzheimer's disease in the same way it does in cardiovascular disease or abdominal aneurysm. This establishes a new vascular target to fight Alzheimer's disease."



The team found that ApoE4 makes it more likely that cyclophilin A will accumulate in large amounts in cells that help maintain the blood-brain barrier, a network of tightly bound cells that line the insides of blood vessels in the brain and carefully regulates what substances are allowed to enter and exit brain tissue.

The left photo shows destructive proteins (green) lining blood vessels in living brain tissue of mice with the human ApoE4 gene; after the drug cyclosporine A is added, the harmful proteins are nearly gone (right). **University of Rochester Medical Center**

ApoE4 creates a cascade of molecular signaling that weakens the barrier, causing blood vessels to become leaky. This makes it more likely that toxic substances will leak from the vessels into the brain, damaging cells like neurons and reducing blood flow dramatically by choking off blood vessels.

Doctors have long known that the changes in the brain seen in Alzheimer's patients -- the death of crucial brain cells called neurons -- begins happening years or even decades before symptoms appear. The steps described in Nature discuss events much earlier in the disease process.

The idea that vascular problems are at the heart of Alzheimer's disease is one championed for more than two decades by Berislav Zlokovic, M.D., Ph.D., the leader of the team and a neuroscientist formerly with the University of Rochester Medical Center and now at USC. For 20 years, Zlokovic has investigated how blood flow in the brain is affected in people with the disease, and how the blood-brain barrier allows nutrients to pass into the brain, and harmful substances to exit the brain.

At Rochester, Zlokovic struck up a collaboration with Bradford Berk, M.D., Ph.D.,a cardiologist and CEO of the Medical Center. For more than two decades Berk has studied cyclophilin A, showing how it promotes destructive forces in blood vessels and how it's central to the forces that contribute to cardiovascular diseases like atherosclerosis and heart attack.

"As a cardiologist, I've been interested in understanding the role of cyclophilin A in patients who suffer from cardiovascular illness," said Berk, a professor at the Aab Cardiovascular Research Institute. "Now our collaboration in Rochester has resulted in the discovery that it also has an important role in Alzheimer's disease. The finding reinforces the basic research enterprise -- you never know when knowledge gained in one area will turn out to be crucial in another."

In studies of mice, the team found that mice carrying the ApoE4 gene had five times as much cyclophilin A compared to other mice in cells known as pericytes, which are crucial to maintaining the integrity of the blood-brain barrier. Blood vessels died, blood did not flow as completely through the brain as it did in other mice, and harmful substances like thrombin, fibrin, and hemosiderin, entered the brain tissue.

When the team blocked the action of cyclophilin A, either by knocking out its gene or by using the drug cyclosporine A to inhibit it, the damage in the mice was reversed. Blood flow resumed to normal, and unhealthy leakage of toxic substances from the blood vessels into the brain was slashed by 80 percent.

The team outlined the chain of events involved. Briefly:

When ApoE4 is present, cyclophilin A is much more plentiful;

Cyclophilin A causes an increase in a the inflammatory molecule NF Kappa B;

NF Kappa B boosts levels of certain types of molecules known as MMPs or matrix metalloproteinases that are known to damage blood vessels, reducing blood flow.

Altogether, the activity results in a dramatic boost in the amount of toxic substances in brain tissue. And when the cascade is interrupted at any of several points -- when ApoE4 is not present, when cyclophilin A is blocked or shut off, or when NF Kappa B or the MMPs are inhibited -- the blood-brain barrier is restored, blood flow returns to normal, and toxic substances do not leak into brain tissue.

For many years, researchers studying Alzheimer's disease have been focused largely on amyloid beta, a protein structure that accumulates in the brains of patients with Alzheimer's disease. The latest works points up the importance of other approaches, said Zlokovic, an adjunct professor at Rochester. At USC, Zlokovic is also

deputy director of the Zilkha Neurogenetic Institute, director of the Center for Neurodegeneration and Regeneration, and professor and chair of the Department of Physiology and Biophysics.
"Our study has shown major neuronal injury resulting from vascular defects that are not related to amyloid beta," said Zlokovic. "This damage results from a breakdown of the blood-brain barrier and a reduction in blood flow.
"Amyloid beta definitely has an important role in Alzheimer's disease," added Zlokovic. "But it's very important to investigate other leads, perhaps where amyloid beta isn't as centrally involved."
In addition to Bell, Berk and Zlokovic, authors include, from Rochester, Ethan Winkler, Itender Singh, Abhay Sagare, Rashid Deane, Zhenhua Wu, and Jan Sallstrom. Additional authors include David Holtzman from Washington University School of Medicine, and Christopher Betsholtz and Annika Armulik of the Karolinska Institutet in Sweden.
At Rochester, Zlokovic's team was anchored in the Center for Neurodegenerative and Brain Vascular Disorders, which was directed by Zlokovic, and in the Department of Neurosurgery. Bell was a graduate student with Zlokovic and now does research in the laboratory of Joseph Miano, Ph.D., at the Aab Cardiovascular Research Institute.
The work was funded by the National Institute of Neurological Disorders and Stroke and the National Institute on Aging. Robert D. Bell, Ethan A. Winkler, Itender Singh, Abhay P. Sagare, Rashid Deane, Zhenhua Wu, David M. Holtzman, Christer Betsholtz, Annika Armulik, Jan Sallstrom, Bradford C. Berk, Berislav V. Zlokovic. Apolipoprotein E controls cerebrovascular integrity via cyclophilin A. Nature, 2012; DOI: 10.1038/nature11087

http://boingboing.net/2012/05/17/coffee-associated-with-the-opp.html

Coffee associated with the opposite of death, according to new scientific study

A large prospective study published today in the New England Journal of Medicine showed that "coffee consumption was inversely associated with total and cause-specific mortality."

By Xeni Jardin at 5:19 pm Thursday, May 17

In other words, data showed that there is a connection between drinking coffee and not necessarily dying. Sort of. "Whether this was a causal or associational finding cannot be determined from our data," the summary concludes.
Boing Boing science editor Maggie Koerth-Baker is on the road today, so I can't enlist her science-fu in interpreting the details of this study. But I think what they're trying to tell us is that while drinking coffee does not necessarily cause you to live longer, it is associated with the opposite of dying sooner. I'm going to have a cup while you all argue it out in the comments.

http://www.sciencenews.org/view/generic/id/340733/title/Coffee_gives_jolt_to_life_span

Coffee gives jolt to life span

Java consumption linked to slightly increased longevity

By Nathan Seppa

It's the news that coffee addicts have been waiting for: Drinking several cups of coffee every day may help you live longer. A study of more than 400,000 people finds that drinking coffee may reduce the risk of death from heart disease, stroke and even infections, researchers report in the May 17 New England Journal of Medicine.
Scientists have long puzzled over the notion that a stimulant could provide a health benefit. "There's been a concern for a long time" that coffee could even be detrimental, says study coauthor Neal Freedman, an epidemiologist at the National Cancer Institute in Bethesda, Md. "Our results might provide some reassurance for long-term coffee drinkers."
Since the study volunteers weren't randomly assigned to drink coffee or not, the research has the limitations of being observational in nature. But with data from 402,260 participants, the results are "very powerful" and unlikely to be superseded by another coffee study anytime soon, says Roy Ziegelstein, a cardiologist at the Johns Hopkins Bayview Medical Center. "This might be as good as it gets," he says.
Freedman and his colleagues analyzed data provided by men and women who completed a detailed questionnaire that included information about coffee intake as part of a medical study in the mid-1990s. The researchers excluded people who had previously had cancer, heart disease or some other serious illness and recorded the remaining volunteers' mortality status through 2008 by checking death records.
During a median follow-up of 13.6 years, people who drank two or more cups of coffee per day were 10 to 16 percent less likely to have died than nondrinkers. A single cup a day provided less apparent benefit. Women seemed to get more out of drinking ample java than men; women who drank six cups of coffee per day had a 15 percent reduced risk of death compared with nondrinkers, while men consuming that much had only a 10 percent reduced risk.

More than two cups a day seemed to offer some protection against death due to heart disease, respiratory ailments and diabetes, while four or more cups a day imparted apparent benefits against stroke and infections. The researchers accounted for differences between coffee drinkers and nondrinkers such as body mass, smoking status and the consumption of alcohol, red meat, white meat, vitamins, fruits and vegetables.
Caffeine may not play a big role in coffee's apparent benefit. Decaffeinated coffee consumption was associated with about the same longevity edge as regular. "There are a huge number of chemically active components aside from caffeine in coffee," says Rachel Huxley, an epidemiologist at the University of Minnesota School of Public Health in Minneapolis. "Given that the relationship between coffee intake and reduced mortality is not confined to one particular disease suggests that there are a lot of possible mechanisms involved."

http://www.bbc.co.uk/news/health-18091708

NHS 'should consider giving statins to healthy people'

Thousands of heart attacks and strokes could be prevented if the cholesterol-lowering drugs, statins, were more widely prescribed, research suggests.

By James Gallagher Health and science reporter, BBC News

The study of 175,000 patients, in the Lancet, said even very low-risk patients benefited from the medication.
The Oxford researchers says the NHS should consider giving statins to healthy people. The NHS drugs watchdog, NICE, is reviewing the evidence. However, statins have been linked to side-effects such as kidney failure.

'Unparalleled' detail

They are among the most widely prescribed drugs in the UK and have long been known to help people at high risk of heart attack and stroke. However, there has been considerable debate over medicating healthy people - both whether it works at all and if it would be socially acceptable. Researchers at the University of Oxford say they have investigated the issue in "unparalleled" detail. Their review of 27 trials concluded that statins significantly reduced the risk of heart attack and stroke for everyone.
Current rules from NICE - the National Institute for Health and Clinical Excellence - recommend statins for people who have a 20% or greater chance of developing cardiovascular disease within 10 years.
Doctors look at a patient's age, blood pressure, cholesterol levels and lifestyle to work out the risk.
One of the researchers, Prof Colin Baigent, told the BBC: "We've been taught over the years that high cholesterol is the thing that matters; you mustn't have high cholesterol.
"But what we've actually learned is that, whatever your level of cholesterol, reducing it further is beneficial.
"Whatever your level of risk, the benefits greatly exceed any known hazard."
He calculates that lowering the threshold for prescribing statins to a 10% risk of cardiovascular disease within a decade would lead to five million more people taking the drugs.
This in turn would save 2,000 lives and prevent 10,000 heart attacks or strokes every year, he said.
Prof Baigent said: "Half of [these] deaths come out of the blue in people who were previously healthy.
"If we are going to prevent that half of cardiac or stroke deaths, then we've got to consider treating healthy people. "It can't be done any other way."

Caution urged

He, alongside fellow researchers, is now calling on NICE to review the evidence for giving statins to more people. NICE, which sets drugs policy for England and Wales, said it was updating its guidelines.
The organisation said: "New evidence on statin treatment thresholds that has become available since publication of the original NICE guideline, including the study reported in the Lancet, will be considered as part of our review." Their conclusions will be published towards the end of 2013.
One of the questions will be over side-effects. Statins have been linked to liver problems, kidney failure, muscle weakness and an increased risk of diabetes.
Prof Shah Ebrahim, from the London School of Hygiene and Tropical Medicine, conducted a large review of the evidence last year. His results urged caution, and Prof Shah said doctors should stop prescribing to healthy patients. He now says: "This research provides further evidence that statins are an effective and safe way of reducing the risk of heart attacks and strokes even among people at quite low risk of these conditions."
He suggests that universal prescribing to the over-50s might be appropriate, as 83% of 50-year old men have a 10% risk of cardiovascular disease in the next 10 years.
"The benefits of giving statins to everyone over the age of 50 would probably save the NHS money in the long run, owing to the savings in health care costs from the heart attacks and strokes prevented."
However, he questioned whether it would be good for people or society to resort to mass medication for lifestyle issues.

http://www.eurekalert.org/pub_releases/2012-05/uobc-pah051612.php

Parents are happier than non-parents, new research suggests

New research by psychologists at three North American universities, including the University of British Columbia, finds that parents experience greater levels of happiness and meaning from life than non-parents.

The findings, which contrast sharply with recent scholarship and popular beliefs, suggest that parents are happier caring for children than they are during other daily activities. The research also suggests that the benefits of parenthood appear more consistently in men and older and married parents.

To be published in the journal Psychological Science, the findings are among a new wave of research that suggests that parenthood comes with relatively more positives than negatives, despite the added responsibilities. The research also dovetails with emerging evolutionary perspectives that suggest parenting may be a fundamental human need.

"This series of studies suggest that parents are not nearly the 'miserable creatures' we might expect from recent studies and popular representations," says UBC Psychology Prof. Elizabeth Dunn, who co-authored the study with colleagues at the University of California, Riverside and Stanford University. "If you went to a large dinner party, our findings suggest that the parents in the room would be as happy or happier than those guests without children."

Over three studies, the researchers tested whether parents are happier overall than their childless peers, if parents feel better moment-to-moment than non-parents, and whether parents experience more positive feelings when taking care of children than during their other daily activities. The consistency of their findings, based on data and participants in both the U.S. and Canada, provides strong evidence challenging the notion that children are associated with reduced well-being, the researchers say.

The study identifies age and marital status as factors in parental happiness. "We find that if you are older (and presumably more mature) and if you are married (and presumably have more social and financial support), then you're likely to be happier if you have children than your childless peers," says co-author Sonja Lyubomirsky, a professor of psychology at UC Riverside. "This is not true, however, for single parents or very young parents."

Fathers in particular expressed greater levels of happiness, positive emotion and meaning in life than their childless peers. "Interestingly, the greater levels of parental happiness emerged more consistently in fathers than mothers," says Dunn. "While more research is needed on this topic, it suggests that the pleasures of parenthood may be offset by the surge in responsibility and housework that arrives with motherhood," she says.

The researchers also found that the stresses associated with single parenthood did not wipe out the greater feelings of meaning and reward associated with having children.

"We are not saying that parenting makes people happy, but that parenthood is associated with happiness and meaning," Lyubomirsky says. "Contrary to repeated scholarly and media pronouncements, people may find solace that parenthood and child care may actually be linked to feelings of happiness and meaning in life."

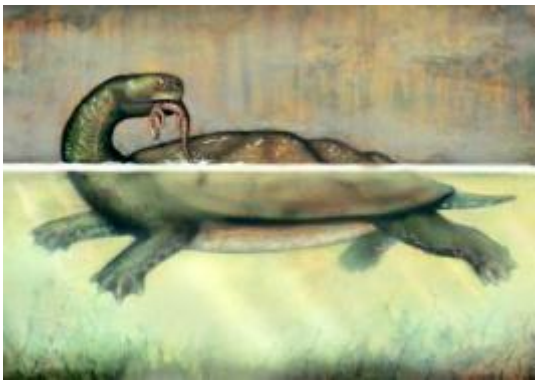
In addition to Dunn, Lyubomirsky and Nelson, paper co-authors include lead author S. Katherine Nelson, a doctoral candidate at UC Riverside, UBC doctoral candidate Kostadin Kushlev and Stanford University postdoctoral scholar Tammy English.

To read the study, In Defense of Parenthood: Children Are Associated With More Joy Than Misery, visit www.ubc.ca/news.

http://www.eurekalert.org/pub_releases/2012-05/ncsu-agt051712.php

Ancient giant turtle fossil revealed

Picture a turtle the size of a Smart car, with a shell large enough to double as a kiddie pool.



Paleontologists from North Carolina State University have found just such a specimen – the fossilized remains of a 60-million-year-old South American giant that lived in what is now Colombia.

The turtle in question is Carbonemys cofrinii, which means "coal turtle," and is part of a group of side-necked turtles known as pelomedusoides. The fossil was named Carbonemys because it was discovered in 2005 in a coal mine that was part of northern Colombia's Cerrejon formation. The specimen's skull measures 24 centimeters, roughly the size of a regulation NFL football. The shell which was recovered nearby - and is believed to belong to the same species - measures 172 centimeters, or about 5 feet 7 inches, long.

That's the same height as Edwin Cadena, the NC State doctoral student who discovered the fossil.

IMAGE: This is a reconstruction of Carbonemys preying upon a small crocodylomorph.

"We had recovered smaller turtle specimens from the site. But after spending about four days working on uncovering the shell, I realized that this particular turtle was the biggest anyone had found in this area for this time period – and it gave us the first evidence of giantism in freshwater turtles," Cadena says.
Smaller relatives of Carbonemys existed alongside dinosaurs. But the giant version appeared five million years after the dinosaurs vanished, during a period when giant varieties of many different reptiles – including Titanoboa cerrejonensis, the largest snake ever discovered – lived in this part of South America. Researchers believe that a combination of changes in the ecosystem, including fewer predators, a larger habitat area, plentiful food supply and climate changes, worked together to allow these giant species to survive.
Carbonemys' habitat would have resembled a much warmer modern-day Orinoco or Amazon River delta.
In addition to the turtle's huge size, the fossil also shows that this particular turtle had massive, powerful jaws that would have enabled the omnivore to eat anything nearby – from mollusks to smaller turtles or even crocodiles.
Thus far, only one specimen of this size has been recovered. Dr. Dan Ksepka, NC State paleontologist and research associate at the North Carolina Museum of Natural Sciences, believes that this is because a turtle of this size would need a large territory in order to obtain enough food to survive. "It's like having one big snapping turtle living in the middle of a lake," says Ksepka, co-author of the paper describing the find. "That turtle survives because it has eaten all of the major competitors for resources. We found many bite-marked shells at this site that show crocodilians preyed on side-necked turtles. None would have bothered an adult Carbonemys, though – in fact smaller crocs would have been easy prey for this behemoth."
The paleontologists' findings appear in the Journal of Systematic Palaeontology. Dr. Carlos Jaramillo from the Smithsonian Tropical Research Institute in Panama and Dr. Jonathan Bloch from the Florida Museum of Natural History contributed to the work. The research was funded by grants from the Smithsonian Institute and the National Science Foundation.

"New pelomedusoid turtles from the late Palaeocene Cerrejon Formation of Colombia and their implications for phylogeny and body size evolution"

Authors: Edwin Cadena, Dan Ksepka, North Carolina State University; Carlos Jaramillo, Smithsonian Tropical Research Institute, Panama; Jonathan Bloch, Florida Museum of Natural History
Published: In the Journal of Systematic Palaeontology
Abstract: *Pelomedusoides comprises five moderate-sized extant genera with an entirely southern hemisphere distribution, but the fossil record of these turtles reveals a great diversity of extinct taxa, documents several instances of gigantism, and indicates a complex palaeobiogeographical history for the clade. Here, we report new pelomedusoid turtle fossils from the late Palaeocene Cerrejon Formation of Colombia. The most complete of these is represented by a large skull (condylobasal length ´ = 16 cm) and is described as Carbonemys cofrinii gen. et sp. nov. (Podocnemididae). Carbonemys is incorporated into a parsimony analysis utilizing a modified morphological character matrix designed to test relationships within Panpelomedusoides, with the addition of molecular data from seven genes (12S RNA, cytochrome b, ND4, NT3, R35, RAG-1 and RAG-2) drawn from previous studies of extant Podocnemididae. C. cofrinii is recovered within Podocnemididae in the results of both morphology-only and combined morphological and molecular (total evidence) analyses. However, molecular data strongly impact the inferred relationships of C. cofrinii and several other fossil taxa by altering the relative positions of the extant taxa Peltocephalus and Erymnochelys. This resulted in C. cofrinii being recovered within the crown clade Podocnemididae in the morphology-only analysis, but outside of Podocnemididae in the combined analysis. Two panpodocnemidid turtle taxa of uncertain affinities are represented by new diagnostic shell material from the Cerrejon Formation, though we refrain from naming them pending discovery of associated cranial material. One of these shells potentially belongs to C. cofrinii and represents the second largest pleurodiran turtle yet discovered. Analysis of pelomedusoid body size evolution suggests that climatic variation is not the primary driver of major body size changes. Cerrejon turtles also demonstrate that at least two major subclades of Podocnemididae were already in place in the neotropics by the Early Cenozoic.*

http://phys.org/news/2012-05-copper-potential-benefit-cancer-treatment.html

'Copper pump's' potential benefit in cancer treatment

New understanding of 'copper pump' in cells could prime discovery of anti-cancer drugs

Phys.org - A team of University of California, San Diego researchers has made new discoveries about a copper-transporting protein in the membranes of human cells that drug-discovery scientists can co-opt for the development of new anti-cancer drugs.
The findings, published May 9 as an online-first paper in Cell Biochemistry and Biophysics, describe how the copper transporter works as a biochemical pump to seize copper atoms outside of a cell and whisks the atoms through the otherwise impervious cell membrane into the cell cytoplasm. The same pump transports the platinum-containing drug cisplatin into cancer cells to help kill them. Igor Tsigelny, a research scientist at the university's San Diego Supercomputer Center and Department of Neurosciences, is lead author of the paper.

The body needs only a tiny amount of copper, but the little that is needed acts as a key component of vital cellular enzymes, including superoxide dismutase, cytochrome c oxidase, lysyl oxidase and dopamine β-hydrolase.

Researchers have shown before that that human copper transporter 1 (hCTR1) protein also participates in transport of the platinum-containing cisplatin, one of the most widely used anti-cancer drugs. Once platinum-containing cisplatin molecules enter a tumor cell, the molecules interact with the cell's DNA and kill it in a process that has been extensively studied by Stephen B. Howell, a professor of medicine at the UC San Diego Moores Cancer Center.

The way that hCTR1 works is a focus of research by Howell and other cancer researchers because cisplatin and similar drugs somehow lose their punch: they are effective anti-cancer drugs when first administered, but lose much of their effectiveness during cancer relapses. Some researchers theorize that the diminished effect of cisplatin could be due to a change in hCTR1 in cancer cells.

New insights derived by the UC San Diego team is leading to a better understanding of what happens to the protein transporter and that knowledge could possibly be used to design a better version of cisplatin or an entirely new drug to take advantage of the new information.

In addition to cancer researchers, the hCTR1 has been a mystery to cell biologists. Until recently, they didn't know whether the transporter protein formed dimers, or trimers. In a 2006 breakthrough that was refined in 2009, scientists confirmed that the trimer is the predominant structure, which was confirmed by the pioneering work of Northwestern University Professor Vincenz Unger.

Unger's team identified the structure of the part of the hCTR1 transporter protein that spans the cell membrane. But they were not able to determine the structure of the part of the protein that extends to the outside of the membrane. Because of that gap in knowledge, they were not able to obtain a high-resolution 3-D map of the protein's structure.

SDSC's Tsigelny and his colleagues set out to create a complete, detailed 3-D model of the transporter. "There is no magic bullet in protein modeling, especially when we do not have a direct homologous template of another protein crystal structure," Tsigelny said. "We predicted the structure of the protein on the level of information available at the current time, but this model needed to be checked with actual experimental results."

Any model that Tsigelny's team came up with would have to answer questions that had evaded scientists for years. For example, why is the extracellular end of the transporter so flexible? While the flexibility frustrated Unger's ability to determine its 3-D structure, was the flexible tip of the protein stable enough to support its copper-transporting function?

Would the positively charged metal ions be transported electrostatically? And how does the transporter initially corral metal ions at pick-up points on the cell exterior and drop them off inside?

Tsigelny's team used a computationally rigorous approach to find the answers.

So-called molecular dynamics modeling studies showed that the path the metal ions take through the intra-membrane transporter channel is stable despite the innate flexibility of the protein. In addition, while electrostatic forces worked well to hold positively charged metal ions like magnets at the extracellular and intracellular ends of the transporter protein, the passage of the metal atoms through an interior channel in the protein must be caused by another means.

Searching the protein data bank

To help to understand the metals' interaction with protein, Tsigelny's team invented a new programming tool called METBIND, which works like a chemistry search engine. The program tried to find the possible binding sites of copper and platinum (along with other metal ions) as they interact with the hCTR1 protein and then move along it.

They checked the validity of their METBIND program with all possible copper-protein binding arrangements reported in the 74,000 proteins in the Protein Data Bank. To the Tsigelny team's surprise, the METBIND program correctly predicted 80 percent of all known copper binding sites in all 636 copper-binding proteins in the Protein Data Bank. They then focused the METBIND search engine on hCTR1.

They looked for individual atoms in the protein that could be placed within 3.5 Angstrom units of a hypothetical copper ion. One Angstrom unit is equal to one hundred-millionth (10 -8) of a centimeter. They identified six histidine residues in the protein that bind copper (and probably platinum) as the first step in the metal transport process.

They identified nine negatively charged amino acids in the part of the hCTR1 protein that stick out into the extracellular medium waiting for oppositely charged copper or platinum ions to pass by. When the ions arrive, the hCTR1 protein grabs them firmly.

They also found that the hCTR1 trimer creates a neutral channel with a set of triads of methionine amino acids. The triads shepherd copper or platinum ions through the cell membrane into the interior cytoplasm. Each of the methionines is important: if one is lost, copper transport is inhibited. The same effect of methionines has been reported for yeast copper transporter (yCTR).
"Drug developers are interested in the selective transport of platinum and other metal ions into cells to invoke a desired effect, and this study provides a blue print for how they could search for drugs to enhance those effects," Tsigelny said. *Provided by University of California - San Diego*

http://www.wired.com/wiredscience/2012/05/methods-for-studying-coincidences/

Methods for Studying Coincidences

One of my favorite mathematics papers of all time is called "Methods for Studying Coincidences." By Persi Diaconis and Frederick Mosteller, it aims to provide a rigorous mathematical framework for the study of coincidences.

By Samuel Arbesman

Using probabilistic analysis, the paper explores everything from why we see newly learned words almost immediately after first learning them, to why double lottery winners exist, to even the frequency of meeting people with the same birthday. They even explore whether or not we can statistically state that Shakespeare used alliteration, or if the frequency of words with similar-sounding beginnings could simply be explained by chance alone.
For example, when it comes to newly learned words, we are often astonished that as soon as we learn a new word, we begin to see it quite frequently, or at least soon after we learn it. Now it could just be due to our heightened perception. But Diaconis and Mosteller argue that statistics can also explain why this happens. A newly learned word is generally quite rare, as otherwise we would have known it already. And for some of these rare words, they will appear far later in our experience (i.e., later in life) than the average expected time, assuming they adhere to what is known as a Poisson process. Furthermore, some of these late-appearing words might also reappear much more rapidly than we expect. Since we know that there are many rare words in each language, we therefore shouldn't be surprised if some fraction of these rare words appear in our daily lives in close proximity, yielding the appearance of coincidence.
Their analyses hinge on something that we often forget: while something might seem astonishing and a remarkable coincidence, if enough people are involved, chances are very good that one of them will have something "coincidental" happen to them. Think double lottery winners. This leads us to the Law of Truly Large Numbers:

> With a large enough sample, any outrageous thing is likely to happen. The point is that truly rare events, say events that occur only once in a million [as the mathematician Littlewood (1953) required for an event to be surprising] are bound to be plentiful in a population of 250 million people. If a coincidence occurs to one person in a million each day, then we expect 250 occurrences a day and close to 100,000 such occurrences a year.

> Going from a year to a lifetime and from the population of the United States to that of the world (5 billion at this writing), we can be absolutely sure that we will see incredibly remarkable events. When such events occur, they are often noted and recorded. If they happen to us or someone we know, it is hard to escape that spooky feeling.

Ultimately, they conclude that coincidences are often in the mind of the observer and not in the probabilities. The whole paper is well worth a read.

http://www.sciencedaily.com/releases/2012/05/120517131703.htm

Extended Daily Fasting Overrides Harmful Effects of a High-Fat Diet

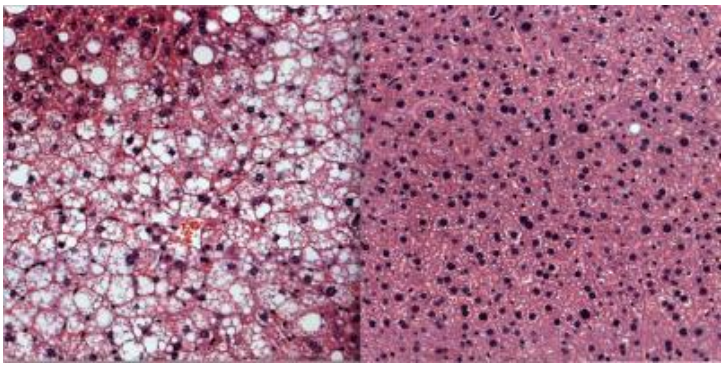
Study May Offer Drug-Free Intervention to Prevent Obesity and Diabetes

ScienceDaily - It turns out that when we eat may be as important as what we eat. Scientists at the Salk Institute for Biological Studies have found that regular eating times and extending the daily fasting period may override the adverse health effects of a high-fat diet and prevent obesity, diabetes and liver disease in mice.
In a paper published May 17 in Cell Metabolism, scientists from Salk's Regulatory Biology Laboratory reported that mice limited to eating during an 8-hour period are healthier than mice that eat freely throughout the day, regardless of the quality and content of their diet. The study sought to determine whether obesity and metabolic diseases result from a high-fat diet or from disruption of metabolic cycles.
"It's a dogma that a high-fat diet leads to obesity and that we should eat frequently when we are awake," says Satchidananda Panda, an associate professor in the Regulatory Biology Laboratory and senior author of the

paper. "Our findings, however, suggest that regular eating times and fasting for a significant number of hours a day might be beneficial to our health."

Panda's team fed two sets of mice, which shared the same genes, gender and age, a diet comprising 60 percent of its calories from fat (like eating potato chips and ice-cream for all your meals). One group of mice could eat whenever they wanted, consuming half their food at night (mice are primarily nocturnal) and nibbling throughout the rest of the day. The other group was restricted to eating for only eight hours every night; in essence, fasting for about 16 hours a day. Two control groups ate a standard diet comprising about 13 percent of calories from fat under similar conditions.

After 100 days, the mice who ate fatty food frequently throughout the day gained weight and developed high cholesterol, high blood glucose, liver damage and diminished motor control, while the mice in the time-restricted feeding group weighed 28 percent less and showed no adverse health effects despite consuming the same amount of calories from the same fatty food. Further, the time-restricted mice outperformed the ad lib eaters and those on a normal diet when given an exercise test.



These images of liver tissue show the difference in fat accumulation between two groups of mice fed a high-fat diet. A mouse allowed to eat 24 hours a day (left) had much higher levels of liver fat (white) than one restricted to an 8-hour daily feeding window (right). **Salk Institute for Biological Studies**

"This was a surprising result," says Megumi Hatori, a postdoctoral researcher in Panda's laboratory and a first author of the study. "For the last 50 years, we have been told to reduce our calories from fat and to eat smaller meals and snacks throughout the day. We found, however, that fasting time is important. By eating in a time-restricted fashion, you can still resist the damaging effects of a high-fat diet, and we did not find any adverse effects of time-restricted eating when eating healthy food."

Hatori cautioned that people should not jump to the conclusion that eating lots of unhealthy food is alright as long as we fast. "What we showed is under daily fasting the body can fight unhealthy food to a significant extent," she says. "But there are bound to be limits."

Obesity is a major health challenge in many developed countries, reaching global pandemic proportions. According to the Centers for Disease Control and Prevention, more than one-third of American adults and 17 percent of youth are obese. Obesity increases the risk of a number of health conditions including: high blood pressure, high cholesterol and type 2 diabetes. Lifestyle modifications, including eating a healthy diet and daily exercise, are first-line interventions in the fight against obesity. The Salk study suggests another option for preventing obesity by preserving natural feeding rhythms without altering dietary intake.

Scientists have long assumed that the cause of diet-induced obesity in mice is nutritional; however, the Salk findings suggest that the spreading of caloric intake through the day may contribute, as well, by perturbing metabolic pathways governed by the circadian clock and nutrient sensors.

The Salk study found the body stores fat while eating and starts to burn fat and breakdown cholesterol into beneficial bile acids only after a few hours of fasting. When eating frequently, the body continues to make and store fat, ballooning fat cells and liver cells, which can result in liver damage. Under such conditions the liver also continues to make glucose, which raises blood sugar levels. Time-restricted feeding, on the other hand, reduces production of free fat, glucose and cholesterol and makes better use of them. It cuts down fat storage and turns on fat burning mechanisms when the animals undergo daily fasting, thereby keeping the liver cells healthy and reducing overall body fat.

The daily feeding-fasting cycle activates liver enzymes that breakdown cholesterol into bile acids, spurring the metabolism of brown fat -- a type of "good fat" in our body that converts extra calories to heat. Thus the body literally burns fat during fasting. The liver also shuts down glucose production for several hours, which helps lower blood glucose. The extra glucose that would have ended up in the blood -- high blood sugar is a hallmark of diabetes -- is instead used to build molecules that repair damaged cells and make new DNA. This helps prevent chronic inflammation, which has been implicated in the development of a number of diseases, including heart disease, cancer, stroke and Alzheimer's. Under the time-restricted feeding schedule studied by Panda's lab, such low-grade inflammation was also reduced.

"Implicit in our findings," says Panda, "is that the control of energy metabolism is a finely-tuned process that involves an intricate network of signaling and genetic pathways, including nutrient sensing mechanisms and the

circadian system. Time-restricted feeding acts on these interwoven networks and moves their state toward that of a normal feeding rhythm."
Amir Zarrinpar, a co-first author on the paper from the University of California San Diego, said it was encouraging that a simple increase in daily fasting time prevented weight gain and the onset of disease. "Otherwise, this could have been only partly achieved with a number of different pills and with adverse side effects," he says.
The multimillion-dollar question is what these findings mean for humans. Public health surveys on nutrition have focused on both the quality and quantity of diet, but they have inherent flaws such as sampling bias, response bias and recall errors that make the results questionable. Thus, says Panda, with the current data it is difficult to connect when we eat, what we eat with how much weight we gain.
"The take-home message," says Panda, "is that eating at regular times during the day and overnight fasting may prove to be beneficial, but, we will have to wait for human studies to prove this."
The good news, he adds, is that most successful human lifestyle interventions were first tested in mice, so he and his team are hopeful their findings will follow suit. If following a time-restricted eating schedule can prevent weight gain by 10 to 20 percent, it will be a simple and effective lifestyle intervention to contain the obesity epidemic.

Other researchers on the study were Christopher Vollmers, Amir Zarrinpar, Luciano DiTacchio, Shubhroz Gill, Mathias Leblanc, Amandine Chaix, Matthew Joens and James A.J. Fitzpatrick, from the Salk Institute; and Eric A. Bushong and Mark H. Ellisman, of the University of California, San Diego.
This work was partially supported by the Pew Scholars Program in Biomedical Sciences, NIH grant R01DK091618 to M.M., Sanofi Discovery Innovation Grant, and Anderson Foundation support to S.P.; JSPS fellowship to M.H.; Blasker Science and Technology Grant Award to C.V.; NIH grant T32DK007202 to A.Z.; and NIGMS grant 8P41GM103412 to M.H.E.
Megumi Hatori, Christopher Vollmers, Amir Zarrinpar, Luciano DiTacchio, Eric A. Bushong, Shubhroz Gill, Mathias Leblanc, Amandine Chaix, Matthew Joens, James A.J. Fitzpatrick, Mark H. Ellisman, Satchidananda Panda. Time-Restricted Feeding without Reducing Caloric Intake Prevents Metabolic Diseases in Mice Fed a High-Fat Diet. Cell Metabolism, 2012; DOI: 10.1016/j.cmet.2012.04.019

http://bit.ly/Jz6uyQ

Buried microbes exist at limit between life and death

Look and learn, sloths: the microbes deep beneath the Pacific ocean take inactivity to new heights.

19:01 17 May 2012 by Colin Barras

Look and learn, sloths: the microbes deep beneath the Pacific ocean take inactivity to new heights. They are so slow on the uptake of nutrients from their environment that they barely classify as alive. Their very existence could help define the limit between life and death.
Paradoxically, though, they may also be among the oldest living organisms on Earth.
Everything happens slowly in the North Pacific gyre, one of the five largest ocean gyres in the world. Sand and mud washing off the continents rarely finds its way there, so the seafloor accumulates sediment at a sluggish rate. The clay just 30 metres below the seafloor was deposited 86 million years ago, almost 20 million years before Tyrannosaurus rex graced the Earth.
That clay contains so little energy in the form of nutrients that it should be incapable of supporting a living community. Microbes have been found in other, only slightly more energy-rich communities below the seafloor, though.
In a bid to hone in on the lower energy limits for life, Hans Røy at Aarhus University in Denmark probed the clays below the North Pacific gyre. Under the microscope, he found a community made up of bacteria and single-celled organisms called archaea in vanishingly small numbers.
"There are only 1000 tiny cells in 1 cubic centimetre of sediment, so finding just one is literally like hunting for a needle in a haystack."

Lower limit for life

The microbes rely on oxygen, carbon and other nutrients in their deep environment to live, but Røy's team found that carbon is so limited that the cells respire oxygen 10,000 times slower than bacteria in lab-grown cultures.
Røy thinks the microbial community is so sparse, and the metabolic rates so low, that the nutrient levels probably represent the bare minimum required to keep cellular enzymes and DNA working. "It looks like we have reached the absolute lower limit for the metabolism of cells," he says.

Yuki Morono at the Japan Agency for Marine-Earth Science and Technology in Nankoku, Japan, recently studied similar low-energy microbial communities below the Pacific seafloor near Japan. Under a microscope, he says, the microbes show few signs of life. "They appear to be dead by our time scale."
But when Morono's team treated the cells to what he calls a "luxury meal" of glucose and other nutrients, most of them incorporated some food – suggesting that they are, in fact, alive. "Their lives are just very slow compared with ours," he says.

Extreme life spans

Because of their remarkably slow metabolic rates, individual cells may have extremely long life spans, says Røy. The cells Morono's team examined looked intact, yet it would take each of them hundreds or thousands of years to generate enough energy to go through cell division and produce daughter cells. That means some of Morono's cells could be thousands of years old.
Røy says his cells could be older still. Elsewhere on Earth, life is primarily concerned with building up enough energy to fuel reproduction. In extremely energy-poor communities, though, reproduction makes less sense because it creates new rivals that also need to feed. "If you can just barely meet your energy requirement, then it is suicide to divide into two," he says. He thinks it makes more sense for the cells to use the energy they gather to repair cellular molecules that have been damaged over centuries of use instead of fuelling cell division.
With communities like this, getting enough cells to learn more about them is a challenge. "You can make pure-culture studies with organisms with a doubling time up to a couple of weeks, maybe a month. Beyond that, you simply do not get dense enough cultures [to study] within a reasonable time," says Røy. "It is safe to say that we do not know anything about the adaptations to low energy life that these organisms might have – only the thermodynamic limits which constrains them."

Røy et al: Science, DOI: 10.1126/science.1219424; Morono et al: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.1107763108

http://www.bbc.co.uk/news/health-18107151

Father calls for organ donation lessons in schools

A father who lost his son to leukaemia is calling for secondary schools and colleges to include one lesson on how to donate stem cells, blood and organs.

Keith Sudbury wants to raise awareness by making donation part of the curriculum for students aged 16 and over. His son Adrian received a stem cell transplant which gave him an extra year of life, but died aged 27. Blood cancer charity Anthony Nolan is supporting the idea of 'Adrian's Law'.
Adrian spent the last two years of his life campaigning for better education about stem cell donation.
He took a petition to Downing Street and met the then Prime Minister Gordon Brown to talk about the campaign to get more young people to register as donors.
With Adrian's Law, his parents Kay and Keith want the message to reach more young people and they hope that there will be a Private Member's Bill in the Commons to highlight its importance.
"We urgently need more people willing to donate blood and stem cells," Keith Sudbury said.
"By taking this message to students 16 years and over we can grow the first generation of potential lifesavers who really understand what it means to donate blood, organs and stem cells."

Match up

Targeting this age group is important because young people are much more likely to be selected as a match for a stem cell donation, and yet 18-30 year olds only make up 12% of the register.
The Anthony Nolan register is used to match donors willing to donate their blood stem cells to people who need life-saving bone marrow transplants - like leukaemia patients. Only one in 1,000 people who join the stem cell register will get called to donate their stem cells, and it is a simple process.
There are two methods of extracting stem cells. The first is through a vein in the arm and the second is from the bone marrow in the pelvis. "It's a no brainer really. The more you educate people, the more people will join the register, the more matches you have and the more lives are saved," Keith says.

'Phenomenal'

There are currently almost 1,600 people in the UK waiting for a stem cell transplant and 37,000 worldwide.
But charity Anthony Nolan says they can only find a matching donor for half the people who come to them in desperate need of a transplant.
Henny Braund, chief executive of Anthony Nolan, said the response from presenting Adrian's story in schools has been "phenomenal". "Thousands of teenagers have signed up.
"Taking this to 700,000 young people a year would help change the culture around donation and save thousands of lives. "Adrian's Law will help young people grow into potential lifesavers."

http://www.wired.com/wiredscience/2012/05/microbes-at-the-edge-of-space/

Microbes at the Edge of Space

Researchers have learned that the Earth's biosphere extends to much higher altitudes than previously suspected - up to 100,000 feet or more

By Jeffrey Marlow

In the mid-1800s, Irish potato farmers began to notice something unusual: soon after harvest, potatoes decayed into slimy black mush, utterly inedible masses of goo. In a country where 30% of the population depended on the potato as a primary source of nutrition, this was a problem, and "expert" panels convened, ultimately concluding that underground volcanic gases or locomotive emissions were to blame. Scientists have since revealed the culprit to be the pathogenic protist P. infestans, but the damage was already done: a million people had died, and a million more had hopped on boats off of the seemingly cursed island.

Some historians believe that P. infestans was transported through potato seed exports that ultimately reached Ireland, but is it possible that the pathogen took a more unexpected route? Could it have been swept up by the wind, lofted into the atmosphere, and moved halfway around the planet?

To Edward Wright, the atmospheric transport of epidemic-inducing pathogens like P. infestans is, if not a proven fact of historical record, at least a very real and worrying possibility. Wright is a project manager for Citizens in Space, a group devoted to the idea of science and space exploration for and by the masses. Driven in part by the epidemiological implications of airborne microbes, Citizens in Space is sponsoring the High Altitude Astrobiology Challenge, a $10,000 competition to detect organisms at the edge of space.

"Researchers have learned that the Earth's biosphere extends to much higher altitudes than previously suspected," says Wright, "up to 100,000 feet or more." Indeed, thousands of microbial species have been found in the upper atmosphere, traveling up to thousands of kilometers. The best-studied "atmospheric bridge" is between North Africa and the Caribbean. Each year, up to one billion tons of dust are swept up by Sahara winds, and with a million bacteria per gram of sand, enormous quantities of biomass come along for the ride. The upper atmosphere is not a particularly hospitable environment, and researchers have traditionally assumed that the dry, UV-zapped, nutrient-poor environment would kill off any stowaways. And although the jury is still out on whether these organisms can actively metabolize and grow in the atmosphere, they can find refuge in protective mineral grains or form spores.

This unexpected biosphere could be more than just a microbiological curiosity: "The upper atmosphere could serve as a global transport system for disease organisms," notes Wright. Christina Kellogg and Dale Griffin published a review of desert dust transport and its potentially unsavory implications. They note that although human pathogens were found in Sahara-sourced dust, "there are no reports as yet of human infectious diseases related to long distance dispersal of desert dust." But the threat isn't only to people: a fungus in African dust is likely behind widespread coral disease in the Caribbean, and agricultural systems may be next. "The limited genetic diversity of many modern crops," writes Kellogg, "increases the risk that a disease outbreak could quickly achieve worldwide distribution given that many of the plants are clones with identical susceptibility."

In order to better characterize these risks – and address more fundamental questions of if and how microbes might make a living on the edge of space – Citizens in Space is hoping to incentivize high atmosphere scientific innovation. Wright describes the ground rules: "we're looking for something that actually collects microbes. We also want the hardware to be reproducible by other citizen scientists, on a citizen-science budget. No unobtanium or one-of-a-kind parts." Shortlisted projects will be subjected to high-altitude balloon flights and wind-tunnel tests, which will monitor the scientific value of the entries.

And just in case the $10,000 weren't enough to get you tinkering, there's another added bonus: a chance to test our your experiment aboard an XCOR suborbital space flight. "We will be training ten citizen astronauts to fly as payload operators," says Wright, "and we want them to have interesting, useful scientific experiments that produce new knowledge."

http://www.bbc.co.uk/news/world-us-canada-18127654

US baby boomers urged to take hepatitis C blood test

Testing tubes for Hep C, among other diseases The CDC is recommending a one-time blood test to check for the virus

US baby boomers have been advised by health officials for the first time to get tested for the liver-destroying virus hepatitis C.

Those born between 1945-1965 are most likely to be infected but it is thought only a quarter of this generation has been tested for the virus.

The US Centers for Disease Control (CDC) believes its campaign could save more than 120,000 lives.

The CDC estimates some 17,000 hepatitis C infections currently occur each year.
Health officials believe hundreds of thousands of infections occurred each year in the 1970s and '80s, when baby boomers would have been young adults.
The disease, which was first identified in 1989, can take decades to cause liver damage. Many of those infected may not even be aware of their condition.
One reason for the CDC advice is that from 1999-2007 the number of Americans dying from hepatitis C-related diseases nearly doubled.
Two million of the 3.2 million Americans known to be infected with the blood-borne virus are baby boomers.
CDC officials believe new testing could lead to 800,000 more baby boomers seeking treatment.
Many infections of hepatitis C come from sharing needles to inject drugs. Before widespread screening began in 1992, it was also transmitted through blood transfusions.
"The CDC views hepatitis C as an unrecognised health crisis for the country, and we believe the time is now for a bold response," said Dr John Ward, the CDC's hepatitis chief.

http://www.eurekalert.org/pub_releases/2012-05/uoc--dff051712.php

Drug found for parasite that is major cause of death worldwide

Research by a collaborative group of scientists has led to identification of an existing drug that is effective against Entamoeba histolytica.

Research by a collaborative group of scientists from UC San Diego School of Medicine, UC San Francisco and Wake Forest School of Medicine has led to identification of an existing drug that is effective against Entamoeba histolytica. This parasite causes amebic dysentery and liver abscesses and results in the death of more than 70,000 people worldwide each year.
Using a high-throughput screen for drugs developed by the research team, they discovered that auranofin – a drug approved by the US Food and Drug Administration 25 years ago for rheumatoid arthritis – is very effective in targeting an enzyme that protects amebae from oxygen attack (thus enhancing sensitivity of the amebae to reactive oxygen-mediated killing).
The results of the work, led by Sharon L. Reed, MD, professor in the UCSD Departments of Pathology and Medicine and James McKerrow, MD, PhD, professor of Pathology in the UCSF Sandler Center for Drug Discovery, will be published in the May 20, 2012 issue of Nature Medicine.
Entamoeba histolytica is a protozoan intestinal parasite that causes human amebiasis, the world's fourth leading cause of death from protozoan parasites. It is listed by the National Institutes of Health as a category B priority biodefense pathogen. Current treatment relies on metronidazole, which has adverse effects, and potential resistance to the drug is an increasing concern.
"Because auranofin has already been approved by the FDA for use in humans, we can save years of expensive development," said Reed. "In our studies in animal models, auranofin was ten times more potent against this parasite than metronidazole."
In a mouse model of amebic colitis and a hamster model of amebic liver abscess, the drug markedly decreased the number of parasites, damage from inflammation, and size of liver abscesses.
"This new use of an old drug represents a promising therapy for a major health threat, and highlights how research funded by the National Institutes of Health can benefit people around the world," said Reed. The drug has been granted "orphan-drug" status (which identifies a significant, newly developed or recognized treatment for a disease which affects fewer than 200,000 persons in the United States) and UC San Diego hopes to conduct clinical trials in the near future.
Additional contributors to the study include first author Anjan Debnath, Shamila S. Gunatilleke and James H. McKerrow, UCSF Sandler Center for Drug Discovery; Derek Parsonage and Leslie B. Poole, Wake Forest School of Medicine; Rosa M. Andrade, Chen He, Eduardo R. Cobo and Ken Hirata, UC San Diego School of Medicine; Steven Chen and Michelle R. Arkin, UCSF; Guillermina García-Rivera, Esther Orozco and Máximo B. Martínez, Instituto Politécnico Nacional, Mexico City; and Amy M. Barrios, University of Utah, Salt Lake City.
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