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Caffeine against Alzheimer's disease

A team of researchers working with Prof. Dr. Christa E. Muller from the University of Bonn demonstrates a positive effect on tau deposits

As part of a German-French research project, a team led by Dr. Christa E. Müller from the University of Bonn and Dr. David Blum from the University of Lille was able to demonstrate for the first time that caffeine has a positive effect on tau deposits in Alzheimer's disease. The two-years project was supported with 30,000 Euro from the non-profit Alzheimer Forschung Initiative e.V. (AFI) and with 50,000 Euro from the French Partner organization LECMA. The initial results were published in the online edition of the journal "Neurobiology of Aging."

Tau deposits, along with beta-amyloid plaques, are among the characteristic features of Alzheimer's disease. These protein deposits disrupt the communication of the nerve cells in the brain and contribute to their degeneration. Despite intensive research there is no drug available to date which can prevent this detrimental process. Based on the results of Prof. Dr. Christa Müller from the University of Bonn, Dr. David Blum and their team, a new class of drugs may now be developed for the treatment of Alzheimer's disease.

Caffeine, an adenosine receptor antagonist, blocks various receptors in the brain which are activated by adenosine. Initial results of the team of researchers had already indicated that the blockade of the adenosine receptor subtype A2A in particular could play an important role. Initially, Prof. Müller and her colleagues developed an A2A antagonist in ultrapure and water-soluble form (designated MSX-3). This compound had fewer adverse effects than caffeine since it only blocks only the A2A adenosine receptor subtype, and at the same time it is significantly more effective. Over several weeks, the researchers then treated genetically altered mice with the A2A antagonist. The mice had an altered tau protein which, without therapy, leads to the early development of Alzheimer's symptoms.

In comparison to a control group which only received a placebo, the treated animals achieved significantly better results on memory tests. The A2A antagonist displayed positive effects in particular on spatial memory. Also, an amelioration of the pathogenic processes was demonstrated in the hippocampus, which is the site of memory in rodents.

"We have taken a good step forward," says Prof. Müller. "The results of the study are truly promising, since we were able to show for the first time that A2A adenosine receptor antagonists actually have very positive effects in an animal model simulating hallmark characteristics and progression of the disease. And the adverse effects are minor."

The researchers now want to test the A2A antagonist in additional animal models. If the results are positive, a clinical study may follow. "Patience is required until A2A adenosine receptor antagonists are approved as new therapeutic agents for Alzheimer's disease. But I am optimistic that clinical studies will be performed," says Prof. Müller.

Publication: Laurent, C., Eddarkaoui, S., Derisbourg, M., Leboucher, A., Demeyer, D., Carrier, S., Schneider, M., Hamdane, M., Müller, C.E., Buee, L. & Blum, D. (2014). Beneficial effects of caffeine in a transgenic model of Alzheimer's disease-like Tau pathology. Neurobiology of Aging. http://www.neurobiologyofaging.org/article/S0197-4580%2814%2900284-X/abstract

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Ancient shrimp-like animals had 'modern' hearts and blood vessels

In 520 million-year-old fossil deposits resembling an 'invertebrate version of Pompeii,' researchers have found an ancestor of modern crustaceans revealing the first-known cardiovascular system in exquisitely preserved detail

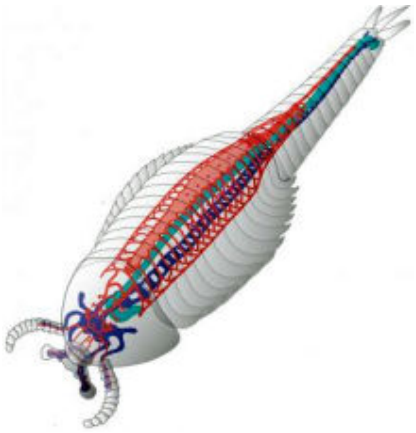
An international team of researchers from the University of Arizona, China and the United Kingdom has discovered the earliest known cardiovascular system, and the first to clearly show a sophisticated system complete with heart and blood vessels, in fossilized remains of an extinct marine creature that lived over half a billion years ago. The finding sheds new light on the evolution of body organization in the animal kingdom and shows that even the earliest creatures had internal organizational systems that strongly resemble those found in their modern descendants.

"This is the first preserved vascular system that we know of," said Nicholas Strausfeld, a Regents' Professor of Neuroscience at the University of Arizona's Department of Neuroscience, who helped analyze the find.

Being one of the world's foremost experts in arthropod morphology and neuroanatomy, Strausfeld is no stranger to finding meaningful and unexpected answers to long-standing mysteries in the remains of creatures that went extinct so long ago scientists still argue over where to place them in the evolutionary tree.

The 3-inch-long fossil was entombed in fine dustlike particles – now preserved as fine-grain mudstone - during the Cambrian Period 520 million years ago in what today is the Yunnan province in China. Found by co-author

Peiyun Cong near Kunming, it belongs to the species Fuxianhuia protensa, an extinct lineage of arthropods combining advanced internal anatomy with a primitive body plan.



"Fuxianhuia is relatively abundant, but only extremely few specimens provide evidence of even a small part of an organ system, not even to speak of an entire organ system," said Strausfeld, who directs the UA Center for Insect Science. "The animal looks simple, but its internal organization is quite elaborate. For example, the brain received many arteries, a pattern that appears very much like a modern crustacean."

In fact, Strausfeld pointed out, Fuxianhuia's vascular system is more complex than what is found in many modern crustaceans.

"It appears to be the ground pattern from which others have evolved," he said. "Different groups of crustaceans have vascular systems that have evolved into a variety of arrangements but they all refer back to what we see in Fuxianhuia."

This image shows a schematic reconstruction of the animal, outlining the cardiovascular system in red, the brain and central nervous system in blue and the gut in green. **Nicholas Strausfeld**

"Over the course of evolution, certain segments of the animals' body became specialized for certain things, while others became less important and, correspondingly, certain parts of the vascular system became less elaborate," Strausfeld said.

Strausfeld helped identify the oldest known fossilized brain in a different specimen of the same fossil species, as well as the first evidence of a completely preserved nervous system similar to that of a modern chelicerates, such as a horseshoe crab or a scorpion.

"This is another remarkable example of the preservation of an organ system that nobody would have thought could become fossilized," he said.

In addition to the exquisitely preserved heart and blood vessels, outlined as traces of carbon embedded in the surrounding mineralized remains of the fossil, it also features the eyes, antennae and external morphology of the animal.

Using a clever imaging technique that selectively reveals different structures in the fossil based on their chemical composition, collaborator Xiaoya Ma at London's Natural History Museum was able to identify the heart, which extended along the main part of the body, and its many lateral arteries corresponding to each segment. Its arteries were composed of carbon-rich deposits and gave rise to long channels, which presumably took blood to limbs and other organs.

"With that, we can now start speculating about behavior," Strausfeld explained. "Because of well-supplied blood vessels to its brain, we can assume this was a very active animal capable of making many different behavioral choices."

Researchers can only speculate as to why the chemical reactions that occurred during the process of fossilization allowed for this unusual and rare kind of preservation, and as to why only select tissues were preserved between a few rare and different specimen.

"Presumably the conditions had to be just right," Strausfeld said. "We believe that these animals were preserved because they were entombed quickly under very fine-grained deposits during some kind of catastrophic event, and were then permeated by certain chemicals in the water while they were squashed flat. It is an invertebrate version of Pompeii."

Possibly, only one in thousands of fossils might have such a well-preserved organ system, Strausfeld said.

At the time Fuxianhuia crawled on the seafloor or swam through water, life had not yet conquered land.

"Terrible sand storms must have occurred because there were probably no plants that could hold the soils," Strausfeld said. "The habitats of these creatures must have been inundated with massive fallouts from huge storms."

Tsunamis may also be the cause for the exceptional preservation.

"As the water withdraws, animals on the seafloor dry," Strausfeld said. "When the water rushed back in, they might become inundated with mud. Under normal circumstances, when animals die and are left to rot on the seafloor, they become unrecognizable. What happened to provide the kinds of fossils we are seeing must have been very different."

The article, "An exceptionally preserved arthropod cardiovascular system from the early Cambrian," will be published in Nature Communications on Monday, April 7, 2014. Strausfeld's co-authors are Xiaoya Ma, Peiyun Cong and Xianguang Hou of the Yunnan Key Laboratory for Palaeobiology at Yunnan University in Kunming, China, and Gregory D. Edgecombe of the Department of Earth Sciences at the The Natural History Museum in London.

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Genetic predisposition to liking amphetamine reduces risk of schizophrenia and ADHD

Supports a long-standing hypothesis that dopamine is related to schizophrenia and ADHD

Genetic variants associated with enjoying the effects of d-amphetamine—the active ingredient in Adderall—are also associated with a reduced risk for developing schizophrenia and attention deficit hyperactivity disorder (ADHD), report scientists from the University of Chicago in the Proceedings of the National Academy of Sciences on April 7. The results support a long-standing hypothesis that dopamine, the neurotransmitter connected with the euphoric effects of amphetamine, is related to schizophrenia and ADHD.

"Some of the variants that make you like amphetamine also appear to make you less likely to develop schizophrenia and ADHD," said study leader Abraham Palmer, PhD, associate professor of human genetics at the University of Chicago. "Our study provides new insights into the biology of amphetamine and how it relates to the biology of risk for these psychiatric diseases."

Palmer and his team previously conducted a genome-wide association study (GWAS) to identify genetic variants associated with experiencing the euphoric effects of amphetamine, which is thought to affect risk for drug abuse. Almost 400 volunteers were given d-amphetamine in a double-blind, placebo-controlled experiment. They were then asked to report how the drug made them feel using carefully designed questionnaires. The researchers measured genetic differences between these subjects at approximately a million sites throughout the genome to identify variations in the DNA code known as single nucleotide polymorphisms, or SNPs. They assessed the relationships between each of these SNPs and sensitivity to amphetamine.

Using data from other large-scale GWAS studies, the team examined these same SNPs for possible overlapping associations with psychiatric disorders. Through rigorous statistical testing they found that an unexpectedly large number of SNPs were associated with both sensitivity to amphetamine and risk of developing schizophrenia or ADHD. This suggested that these traits are influenced by a common set of genetic variants. Moreover, a significant proportion of this observed overlap appeared to be caused by variants that increased enjoyment of the effects of amphetamine but decreased the risk for both psychiatric diseases.

The researchers performed similar analyses for traits that were not expected to be related to amphetamine sensitivity, such as height, irritable bowel disease and Parkinson's disease. In all of these cases they observed no more overlapping SNPs than would have been expected by chance alone.

"While this approach would not be a useful diagnostic test, we expect that people who like the effects of amphetamine would be slightly less likely to develop schizophrenia and ADHD," Palmer said. "And people who did not like amphetamine, we would predict, are slightly more likely to develop these diseases."

"What is particularly striking is that by examining people's responses for just a few hours after taking a drug, we can identify an underlying genetic propensity that can manifest as a psychiatric disease over the course of a lifetime," he adds.

These results provide unique genetic evidence for the role of dopamine in schizophrenia and ADHD. Schizophrenia is commonly treated using drugs that block dopamine signaling, while ADHD is treated using drugs, including d-amphetamine itself, that enhance dopamine signaling. Despite opposite treatments, amphetamine-liking SNPs reduced the risk for developing both diseases, suggesting that dopamine's role is more complex than hypothesized.

The study also offers a new direction for the analysis of a wide range of similar genetic studies, particularly ones with smaller sample sizes. By analyzing the results of those studies for overlap with data from much larger genetic studies, promising genetic variants that would otherwise never stand out among the noise of hundreds of thousands of other random variants can be identified. "Our approach offers a promising new direction for studying complex psychiatric behaviors using the whole-genome approach," said co-author Harriet de Wit, PhD, professor of psychiatry and behavioral neuroscience at the University of Chicago.

The team plans to further study the SNPs identified in this study for their functional roles in amphetamine liking, schizophrenia and ADHD. In addition, Palmer hopes to explore genetic predispositions toward liking or disliking other therapeutic drugs and whether sensitivity to those drugs might also overlap with the diseases for which these drugs are used.

"When we use a drug treatment, we know exactly what systems have been perturbed," Palmer said. "So when we see overlap for alleles that affect how you respond to drugs and a disease, we can hone in on what those alleles are doing biologically. This is instrumental for translating those results into new treatments and cures, which is the ultimate reason for performing genetic studies of disease."

The study, "Genetic variation associated with euphorigenic effects of d-amphetamine is associated with diminished risk for schizophrenia and attention deficit hyperactivity disorder," was supported by the National Institutes of Health. Additional authors include Amy B. Hart, Eric R. Gamazon, Barbara E. Engelhardt, Pamela Sklar, Anna K. Kähler, Christina M. Hultman,

Patrick F. Sullivan, Benjamin M. Neale, Stephen V. Faraone, Psychiatric Genomics Consortium: ADHD Subgroup and Nancy J. Cox.

http://www.eurekalert.org/pub_releases/2014-04/uob-gtb040714.php#rssowlmlink

Green tea boosts your brain

First evidence that green tea extract enhances the cognitive functions

Green tea is said to have many putative positive effects on health. Now, researchers at the University of Basel are reporting first evidence that green tea extract enhances the cognitive functions, in particular the working memory. The Swiss findings suggest promising clinical implications for the treatment of cognitive impairments in psychiatric disorders such as dementia. The academic journal Psychopharmacology has published their results.

In the past the main ingredients of green tea have been thoroughly studied in cancer research. Recently, scientists have also been inquiring into the beverage's positive impact on the human brain. Different studies were able to link green tea to beneficial effects on the cognitive performance. However, the neural mechanisms underlying this cognitive enhancing effect of green tea remained unknown.

Better memory

In a new study, the researcher teams of Prof. Christoph Beglinger from the University Hospital of Basel and Prof. Stefan Borgwardt from the Psychiatric University Clinics found that green tea extract increases the brain's effective connectivity, meaning the causal influence that one brain area exerts over another. This effect on connectivity also led to improvement in actual cognitive performance: Subjects tested significantly better for working memory tasks after the admission of green tea extract.

For the study healthy male volunteers received a soft drink containing several grams of green tea extract before they solved working memory tasks. The scientists then analyzed how this affected the brain activity of the men using magnetic resonance imaging (MRI). The MRI showed increased connectivity between the parietal and the frontal cortex of the brain. These neuronal findings correlated positively with improvement in task performance of the participants. «Our findings suggest that green tea might increase the short-term synaptic plasticity of the brain», says Borgwardt.

Clinical implications

The research results suggest promising clinical implications: Modeling effective connectivity among frontal and parietal brain regions during working memory processing might help to assess the efficacy of green tea for the treatment of cognitive impairments in neuropsychiatric disorders such as dementia.

http://bit.ly/1hy5o8u

Almost half of new electricity is now clean and green

That's a lot of clean power. Almost half of new electricity generation is now renewable, and the costs of wind and solar power are falling sharply.

14:43 07 April 2014 by Fred Pearce

It "should give governments confidence to forge a robust climate agreement" next year, says Achim Steiner, director of the United Nations Environment Programme (UNEP).

This comes a week before the Intergovernmental Panel on Climate Change's assessment of how to prevent dangerous climate change. The IPCC will stress the importance of quickly converting to renewables.

The latest annual Global Trends in Renewable Energy Investment, published today by UNEP, reveals that 44 per cent of all generating capacity installed last year around the world was renewable. That is despite a 14 per cent decline in renewables investment, and in new electricity generally.

But the politics of green energy are changing fast. China is now the world's leader, having overtaken Europe. Last year, China invested $56 billion in green power.

Going clean

The green bubble seems to have burst in cash-strapped Europe, which was the vanguard of renewable energy for more than a decade. The continent cut investment by 44 per cent.

The only big exception was the UK, which increased investment by 12 per cent despite rumblings of discontent in the governing Conservative party. For the first time, the UK outspent Germany, with projects like the giant Westermost Rough wind farm leading the way.

Japanese investment also soared, increasing by 80 per cent. This was thanks to a rush to install solar panels, after nuclear power stations were closed following the 2011 Fukushima disaster.

Renewables kept 1.2 billion tonnes of carbon dioxide from being emitted in 2013, says report author Ulf Moslener of the Frankfurt School of Finance & Management in Germany. Aside from hydroelectric dams, photovoltaic solar panels and onshore wind turbines are the biggest contributors.

The cost of generating solar power has fallen by 25 per cent since 2009, and the cost of wind power has fallen 53 per cent over the same period. As a result, the report says a growing number of such projects are being built without any subsidy. What's more, share prices in clean-energy companies, which have been in free fall since the start of the global recession, rose 54 per cent last year.

http://bit.ly/1hpnZTl

Volcanic blasts hint that Mercury is a migrant planet

Like its traveller god namesake, the planet Mercury is hard to pin down. It now seems that volcanic blasts have rocked it for aeons, and this doesn't mesh with theories of its birth.

17:48 07 April 2014 by Jacob Aron

It even raises the prospect that Mercury may have formed further out in the solar system and migrated in.
Such volcanic explosions happen on Earth when lava boils water and volatile compounds underground, and they smash through the surface. Mercury, though, is closer to the sun, so any volatiles within should have boiled off as the planet formed 4.5 billion years ago.
That view changed during fly-bys in 2008, when NASA's Messenger probe spotted volcanic ash deposits and telltale vents in the ground. Still, the blasts could have happened just after Mercury's birth.
Now, Timothy Goudge of Brown University in Providence, Rhode Island, and his colleagues have analysed higher resolution images taken when the probe began orbiting Mercury in 2011.
They looked at 51 deposits and their source vents and found that some were more eroded – by material flung up by impacts, say – than others, so they can't all have formed at the same time. What's more, most of the vents were inside impact craters, which can be dated, suggesting that the explosions occurred intermittently between 3.5 and 1 billion years ago, not just after Mercury formed.

Wandering planet?

The results should challenge planetary scientists to come up with new ideas about Mercury's birth, says Goudge. "The formation mechanism for Mercury now has to be able to explain this observation of volatiles in the planet's interior."
David Rothery of the Open University in Milton Keynes, UK, who has also spotted relatively young vents in Messenger data but was not involved in this work, agrees: "We have a mystery about how Mercury formed."
Rothery suggests the possibility that Mercury formed further out and migrated in. Astronomers think gas giants like Jupiter and Saturn may have migrated from their orbits in the early days of the solar system, so perhaps something similar happened to Mercury as well. "We're at a bit of a loss," he adds.
The idea that volcanic explosions rocked Mercury for most of its existence also clashes with another theory about its formation: that a large object might have hit the youthful Mercury and destroyed most of its crust. This is used to explain the mystery of why the modern Mercury has a large core and thin crust – but such an impact would also have removed any volatiles, apparently ruling out volcanic explosions.
Rothery is part of the team working on BepiColombo, a joint mission between Europe and Japan due to launch in 2016 and reach Mercury in 2024. It is equipped with more advanced sensors that could clear things up. "When we know Mercury's composition and its geological evolution more clearly, we will be able to pose better questions about how it formed," he says.

Journal reference: Journal of Geophysical Research: Planets, DOI: 10.1002/2013JE004480

http://bit.ly/1ghskXF

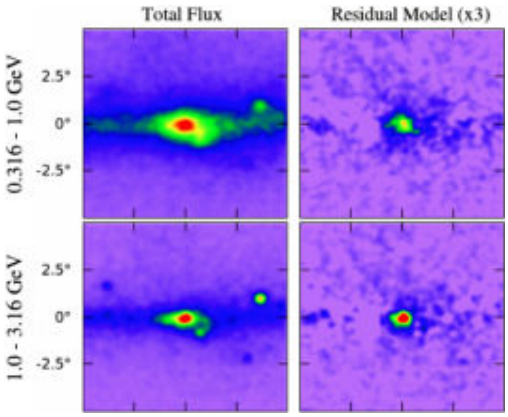
Fermi telescope detects signal that could be annihilating dark matter

Distribution and energy is what we'd expect when WIMPs collide.

by John Timmer - Apr 8 2014, 2:15am TST

Researchers using data obtained by the orbiting Fermi Telescope may have found the first clear, direct evidence of dark matter in our own galaxy. The signal comes in the form of an excess of gamma rays coming from an area surrounding the galactic core, and it appears to be exactly what we'd expect from a weakly interacting massive particle, or WIMP. Perhaps as significantly, however, there are no known astronomical features that can produce a signal like this.
The Universe provides plenty of evidence that dark matter exists. Everything from the behavior of galaxies to the structure of galaxy clusters indicates that there's more matter present than we can detect. We have spotted instances of gravitational lensing by matter in what appears to be largely empty space. Even the cosmic microwave background, which reveals the details of the Big Bang, indicates that most of the matter in the Universe is in the dark category.
But when it comes to identifying the particles that actually comprise dark matter, we've tended to look closer to home. Searches in the Large Hadron Collider, which could produce dark matter in its atom-smashing debris,

came up empty. Direct detections of dark matter collisions with normal atoms sometimes produced promising results, only to have a different experiment shoot them down.
But another category of experiments has looked where the evidence already exists: in the skies. When the densities of dark matter are high enough, two of its particles could collide with each other, producing energetic debris. By looking at the places where we expect the highest concentrations of dark matter and seeing if there's an excess of certain types of radiation, we might be able to detect signs of these dark matter collisions.
A group of astronomers have now reanalyzed data obtained by the Fermi Gamma-ray Space Telescope to look for signs of these annihilations. A few years back, Fermi made the news for finding an excess of gamma rays that could be an indication of dark matter collisions at the Milky Way's core, but the community as a whole wasn't convinced by the analysis. In the intervening time, the Fermi team gathered more data and, perhaps more significantly, tagged each detection with an indication of how confident they are in the instrument's ability to assign a direction to its source.
The new analysis took advantage of those tags, filtering the data to eliminate anything with poor positional certainty. Mostly, the emissions traced the outlines of our galaxy as you'd expect—there are plenty of energetic events taking place in binary star systems throughout the galaxy. But once the expected distribution of those normal events was accounted for, the center of our galaxy retained a spherical area of intense gamma ray emissions.



The distribution of gamma rays seen by Fermi (left) and the hot spot that remains after accounting for known sources (right). **Daylan et. al.**

The key feature of this hot spot of emissions is that it covers a very large area; it extends about 6,500 light years in all directions from the galaxy's central black hole. That's too far from the galactic bulge for there to be many stars present, and thus many normal source of gamma rays. So at the moment, there's no mundane process we know about that could be producing these gamma rays.
In contrast, the dense concentration of dark matter near the galactic core provides a good fit for the site of these emissions. Better yet, it behaves exactly as we expect some of the simpler options for dark matter should. "Excellent fits are found for dark matter that annihilates to bottom, strange, or charm quarks," the researchers' paper says, which means we don't have to postulate some sort of exotic decay process. And the apparent mass, 30-40 giga-electronvolts, is within the range that could easily produce the sort of behavior we see in our Universe.
Better yet, the frequency of collisions (as measured by a value called the "annihilation cross section") would produce a particle that stopped interacting with the known members of the Standard Model as things cooled down very early in the Universe's history. At that point, the amount of stuff that was "frozen out" as dark matter would be roughly the amount that we expect from the measurements of the cosmic microwave background.
So all the pieces seem to fall neatly into place, and the data is pretty compelling (the excess is present with a statistical significance of over 40 sigma). Does this mean we've finally nailed down dark matter?
Even the authors of the paper don't want to go there. "Given the frequency of such false alarms, we would be wise to apply a very high standard before concluding that any new signal is, in fact, the result of annihilating dark matter," they write. We'll have to wait for astronomers and particle physicists to mull over these new results. And even then, the radiation will only be compelling evidence; we're not likely to accept it until we can detect something on Earth. But by figuring out this many of its likely properties, the Fermi results could help us build a detector that's more likely to succeed. *The arXiv. Abstract number: 1402.6703 (About the arXiv).*

http://www.eurekalert.org/pub_releases/2014-04/uoc--bta040714.php#rssowlmlink

Breakthrough therapy allows 4 paraplegic men to voluntarily move their legs

Four young men who have been paralyzed for years achieved groundbreaking progress - moving their legs - as a result of epidural electrical stimulation of the spinal cord, an international team of life scientists reports today in the medical journal Brain.

The study, conducted by researchers from the University of Louisville, UCLA and the Pavlov Institute of Physiology, was funded in part by the Christopher and Dana Reeve Foundation and the National Institutes of Health. All four participants were classified as suffering from chronic, motor complete spinal cord injuries and were unable to move their lower extremities prior to the implantation of an epidural stimulator. The stimulator delivers a continuous electrical current to the participants' lower spinal cords, mimicking signals the brain normally transmits to initiate movement.

The research builds on an initial study, published in May 2011 in the journal The Lancet, that evaluated the effects of epidural stimulation in the first participant, Rob Summers of Portland, Ore., who recovered a number of motor functions as a result of the intervention.
Now, three years later, the key findings documented in Brain detail the impact of epidural stimulation in a total four participants, including new tests conducted on Summers. Summers was paralyzed after being struck by a vehicle, and the other three participants were paralyzed in auto or motorcycle accidents.
What is revolutionary, the scientists said, is that the second, third and fourth participants — Kent Stephenson of Mt. Pleasant, Texas; Andrew Meas of Louisville, Ky.; and Dustin Shillcox of Green River, Wyo. — were able to execute voluntary movements immediately following the implantation and activation of the stimulator.
The participants' results and recovery time were unexpected, which led researchers to speculate that some pathways may be intact post-injury and therefore able to facilitate voluntary movements.
"Two of the four subjects were diagnosed as motor and sensory complete injured with no chance of recovery at all," said lead author Claudia Angeli, a senior researcher with the Human Locomotor Research Center at Frazier Rehab Institute and an assistant professor at University of Louisville's Kentucky Spinal Cord Injury Research Center (KSCIRC). "Because of epidural stimulation, they can now voluntarily move their hips, ankles and toes. This is groundbreaking for the entire field and offers a new outlook that the spinal cord, even after a severe injury, has great potential for functional recovery."
In epidural stimulation, the electrical current is applied at varying frequencies and intensities to specific locations on the lumbosacral spinal cord, corresponding to the dense neural bundles that largely control the movement of the hips, knees, ankles and toes. With the participants, once the signal was triggered, the spinal cord reengaged its neural network to control and direct muscle movements.
When coupling the intervention with rehabilitative therapy, the impact of epidural stimulation intensified. Over the course of the study, the researchers noted that the participants were able to activate movements with less stimulation, demonstrating the ability of the spinal network to learn and improve nerve functions.
"We have uncovered a fundamentally new intervention strategy that can dramatically affect recovery of voluntary movement in individuals with complete paralysis, even years after injury," said Susan Harkema, a University of Louisville professor and rehabilitation research director at KSCIRC, Frazier Rehab Institute, director of the Reeve Foundation's NeuroRecovery Network and primary author of The Lancet article. "The belief that no recovery is possible and complete paralysis is permanent has been challenged."
Beyond regaining voluntary movement, the research participants have displayed a myriad of improvements in their overall health, including increases in muscle mass and regulation of their blood pressure, as well as reduced fatigue and dramatic improvements to their sense of well-being.
Additionally, all four men were able to bear weight independently, as reported by the team, which also includes UCLA's V. Reggie Edgerton and Yury Gerasimenko, professor and director of the laboratory of movement physiology at Russia's Pavlov Institute in St. Petersburg and a researcher in the UCLA Department of Integrative Biology and Physiology.
"This research brings up an amazing number of possibilities for how we can develop interventions that will help people recover movement they have lost," said Edgerton, a distinguished professor of integrative biology and physiology, neurobiology, and neurosurgery at UCLA and a co-author of the research. "The circuitry in the spinal cord is remarkably resilient. Once you get them up and active, many physiological systems that are intricately connected and that were dormant come back into play."

Providing hope for people living with paralysis

The study offers hope that clinical therapies can be developed to advance treatment for the nearly 6 million Americans living with paralysis, including nearly 1.3 million with spinal cord injuries.
The four paralyzed participants ranged in neurological level from C7–T5 and were at least two years post-injury at the time of the intervention. Two of them had been rated "A" on the American Spinal Injury Association's classification system, meaning they had absolutely no sensation or cognition below the site of their injury; the researchers were highly sceptical that these men would elicit any voluntary movement as a result of the intervention.
However, with the application of epidural stimulation, all four participants recovered voluntary control of their lower extremities, surprising the scientists, who believed at least some of the sensory pathway must be intact for epidural stimulation to be successful.
"With this study, the investigators show that their findings about a motor complete patient regaining movement, as published three years ago in The Lancet, were not an anomaly," said Susan Howley, executive vice president for research at the Reeve Foundation. "At the present time, other than standard medical care, there are no effective evidence-based treatments for chronic spinal cord injury. However, the implications of this study for

the entire field are quite profound, and we can now envision a day when epidural stimulation might be part of a cocktail of therapies used to treat paralysis."

Investing in epidural stimulation

The research was funded by the Reeve Foundation and the National Institutes of Health (RO1EB007615, P30 GM103507), the Leona M. and Harry B. Helmsley Charitable Trust, the Kessler Foundation, the University of Louisville, the Jewish Hospital and St. Mary's Foundation, the Frazier Rehab Institute and University Hospital.
"When we first learned that a patient had regained voluntary control as a result of the therapy, we were cautiously optimistic," said Roderic Pettigrew, director of the National Institute of Biomedical Imaging and Bioengineering, which provided support for the study. "Now that spinal stimulation has been successful in four out of four patients, there is evidence to suggest a large cohort of individuals, previously with little realistic hope of any meaningful recovery from spinal cord injury, may benefit from this intervention."
"This is a wake-up call for how we see motor complete spinal cord injury," said Edgerton, who has been conducting fundamental research in this area for 38 years and is a member of the Reeve Foundation's International Research Consortium on Spinal Cord Injury. "We don't have to necessarily rely on regrowth of nerves in order to regain function. The fact that we've observed this in four out of four people suggests that this is actually a common phenomenon in those diagnosed with complete paralysis."
The scientists are optimistic that the therapy intervention will continue to result in improved motor functions. In fact, based on observations from the research, there is strong evidence that with continued advancements of the epidural stimulator, individuals with complete spinal cord injuries will be able to bear weight independently, maintain balance and work towards stepping, the scientists said.
For more information about epidural stimulation studies and other spinal cord injury research, please visit http://chartingourcourse.org/research/victory.html.
For more information on the Reeve Foundation, visit http://www.christopherreeve.org/epi.

http://phys.org/news/2014-04-beloved-antiquity-greece-hot-left.html#rssowlmlink

Beloved in antiquity, Greece's hot springs left untapped

Hercules used them to regain his strength after his legendary labours, Hippocrates lauded their beneficial properties and even a famous Roman general, Sulla, said he owed his health to them.

Their praise was for hot springs, a medicinal resource known and appreciated in Greece since antiquity - though regrettably less so nowadays. "Greece invented the therapeutic use of hot springs thousands of years before the birth of Jesus Christ," says Zisis Aggelidis, a professor of hydrogeology at Thessaloniki's Aristotelio University.
In ancient Greece, healing temples known as Asclepieia - named after the god of medicine Asclepius - were popular with pilgrims.
Greece today has some 700 hot springs known to have curative properties, but just over 100 are accessible and even fewer are commercially exploited. Many are still free of charge to the public, out in nature with minimal facilities, even on popular tourist islands such as Santorini, Milos and Kos.
Evangelos Kyriazis, a barrel-chested man in his sixties, says he has not been to a doctor in years thanks to his local spa. Kyriazis' magic potion bubbles forth from a mountain in central Greece, near the town of Thermopylae. His self-styled treatment is to take 300 baths a year for half an hour in the sulphurous water, which has a temperature of between 30 and 40 degrees Celsius (86-104 Fahrenheit).
"It detoxifies and oxygenates the body, regulates pressure, dilates the blood vessels, relaxes the muscles, clears the lungs, strengthens the bones and relaxes the nervous system," says Kyriazis. "It even whitens the teeth."

'Hot gates'

Thermopylae, literally "hot gates" in Greek, has become synonymous with the ferocious battle in which 300 Spartans sacrificed themselves against overwhelming Persian odds in 480 BC.
Few today, however, associate Thermopylae with the hot springs Hercules frequented in Greek mythology, except a few locals and a small number of connoisseurs.
"These springs cured my aching knees and shoulder. The waters here are more natural than in Germany," says pensioner Alfred Weigel, who makes an annual pilgrimage from his native Bavaria for a dip here.
To the uninitiated, the site appears inauspicious, close to an abandoned petrol station and a derelict hotel. Bathers change in their car, and step over a wobbly wooden pallet to reach the springs. "We have an exceptional product but it is poorly used," sighs Markos Danas, secretary general of the union of Greek spa towns. He notes that across the country less than a dozen sites offer acceptable tourism infrastructure. "Hot springs are mostly run by local communities, and this has limited the scope of development," he adds.
Three of Greece's best-known spa towns are Loutraki in the Peloponnese, Kamena Vourla in central Greece and Edipsos, on the island of Evia.
The latter is known to posterity through the Greek biographer Plutarch as the site that cured Rome's Sulla.

For years much of the clientele were Greek pensioners on state-funded curative tours. However, in the wake of the economic crisis gripping the country for the past five years, demand has fallen dramatically.
The union of spa towns reports a 50-percent drop in paying customers since 2009.
The spa towns are now hoping an EU directive that authorises reimbursing citizens taking hot baths in other member states will revive interest. Greece's state privatisation agency last year also offered four hot springs in central Greece, including Thermopylae, for sale to private developers. But there were no takers - meaning more free visits for Evangelos and his fellow bathers in the foreseeable future.

http://www.bbc.com/news/health-26920528##rssowlmlink

Living organ regeneration 'first' by gene manipulation

An elderly organ in a living animal has been regenerated into a youthful state for the first time, UK researchers say.

By James Gallagher Health and science reporter, BBC News

The thymus, which is critical for immune function, becomes smaller and less effective with age, making people more susceptible to infection. A team at the University of Edinburgh managed to rejuvenate the organ in mice by manipulating DNA. Experts said the study was likely to have "broad implications" for regenerative medicine.
The thymus, which sits near the heart, produces T-cells to fight off infection. However, by the age of 70 the thymus is just a tenth of the size in adolescents.
"This has a lot of impacts later in life, when the functionality of the immune system decreases with age and you become more vulnerable to infection and less responsive to vaccines," one of the researchers, Dr Nick Bredenkamp, told the BBC.

Boosting

The team at the MRC Centre for Regenerative Medicine at the University of Edinburgh tried to regenerate the thymus of old mice. A gene, called Foxn1, naturally gets shut down as the thymus ages. So they tried to boost it back to youthful levels. A drug was used to increase the activity of the gene in elderly mice. The results, published in the journal Development, showed that boosting Foxn1 activity in elderly mice could give them the thymus of a much younger animal.
Dr Bredenkamp said: "We could regenerate the thymus using this method. It increases in size and makes more T-cells. It is almost completely regenerated. "The exciting thing really is the manner in which it is done. We've targeted a single gene and we've been able to regenerate an entire organ."

More youthful

It is not certain why the thymus shrinks with age. One theory is that it needs a lot of energy to run, which the body starts to divert towards reproduction during adolescence. Dr Bredenkamp argued that the technique could eventually be adapted to work in people, but it would need to be "very tightly controlled" to ensure the immune system did not then go into overdrive and attack the body.
It also raises the prospect that other organs in the body, such as the brain or heart, could be made more youthful by targeting a single gene.
Dr Rob Buckle, the head of regenerative medicine at the Medical Research Council, said: "One of the key goals in regenerative medicine is harnessing the body's own repair mechanisms and manipulating these in a controlled way to treat disease. "This interesting study suggests that organ regeneration in a mammal can be directed by manipulation of a single protein, which is likely to have broad implications for other areas of regenerative biology."

http://www.eurekalert.org/pub_releases/2014-04/tjnj-sec040314.php#rssowlmlink

Study examines criteria for 'choosing wisely' lists of least beneficial medical services

'Top 5' list of medical services that provide no overall benefit to patients in most situations

In the creation of lists by specialty societies of medical services deemed least beneficial (the "Choosing Wisely" initiative), inclusion was often justified by evidence suggesting no additional benefit with higher risk, higher cost, or both, compared with other options, according to a study in the April 9 issue of JAMA.
"Aiming to reduce wasteful medical care, the American Board of Internal Medicine Foundation's Choosing Wisely initiative asks leading physician specialty societies to create a 'Top 5' list of medical services that provide no overall benefit to patients in most situations. As of August 2013, 25 participating specialty societies had produced 1 or more Top 5 lists containing a total of 135 services," according to background information in the article.
Catherine Gliwa, B.A., and Steven D. Pearson, M.D., M.Sc., of the National Institutes of Health, Bethesda, Md., evaluated the role that evidence related to benefits, risks, and costs plays in selecting a service for the Top 5 lists. "As Choosing Wisely continues to grow, clarity on the evidentiary justifications for the lists will be crucial

for the overall credibility of the campaign," they write. Using information provided by the specialty societies, the authors created categories based on the level of certainty of evidence regarding risks and benefits, how the risks and benefits of the service compare with other alternatives, and the comparative cost or cost-effectiveness of the service.

Of the 135 services identified, 36 percent were for diagnosis or monitoring; 34 percent for treatment; and 30 percent for population screening. Most services were included in the Top 5 lists based on evidence that demonstrates equivalent but not superior benefit with higher risk or higher costs, or both, compared with other options. The second most common rationale was that there was not enough evidence to evaluate benefit for use of the service beyond the established indications, frequency, intensity, or dosage.

The authors assessed the rationales for selecting all 135 services. Overall, 49 percent mentioned greater risks to patients, 24 percent mentioned higher costs, 16 percent mentioned both greater risk and higher cost, and 42 percent mentioned neither. Of the 25 specialty societies, 60 percent had at least 1 service whose inclusion was justified in part by higher costs.

"Our data show that the issue of cost was almost always raised in the context of a service being judged as good as other options but more expensive. We believe that specialty societies should seek greater opportunities to include within their Top 5 lists services that offer only small incremental benefits at much higher prices," the authors write.

"Specialty societies can enhance trust in the Choosing Wisely campaign by defining more clearly the types of potentially wasteful medical care they seek to eliminate, and by providing a clear evidentiary justification for the selection of each service."

(doi:10.1001/jama.2013.285362; Available pre-embargo to the media at http://media.jamanetwork.com)

Editor's Note: This research was supported by the Intramural Research Program of the National Institutes of Health. The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

http://www.eurekalert.org/pub_releases/2014-04/ez-gpl040414.php#rssowlmlink

Glucosamine promotes longevity by mimicking a low-carb diet

Life-prolonging effect of a commonly used food supplement in worms and mice

Glucosamine has been freely available in drugstores for many decades. It is widely used to treat arthritis and to prevent joint degeneration. Moreover, glucosamine is known to delay cancer growth. In addition, glucosamine reduces metabolism of nutritive sugars, as was already shown some 50 years ago.

In 2007, Michael Ristow showed that too much nutritive sugar shortens the lifespan of roundworms, a widely studied model organism in ageing research. Conversely, impairing carbohydrate metabolism in these worms was capable of extending lifespan [reference 1]. Unfortunately, the method used in worms at that time unexpectedly appeared to be ineffective in rodents [reference 2], and hence was not studied further.

Extended lifespan by almost 10%

In the recently published study that was performed at ETH Zurich and four German research institutions, Ristow and his colleagues applied glucosamine to roundworms and found that they live around 5% longer than their untreated counterparts.

Next and most importantly, the researchers fed glucosamine to ageing mice in addition to their normal diet. The mice were 100 weeks of age, reflecting a comparative human age of approximately 65 years. A control group of mice received no glucosamine while otherwise receiving an identical diet. Feeding the supplement to mice extended their lifespan by almost 10%, reflecting around 8 additional years of human lifespan. Moreover, glucosamine improved glucose metabolism in elderly mice indicating protection from diabetes, a life-threatening disease most prevalent amongst the elderly.

Mimicking a low-carb diet

Additional analyses revealed that glucosamine feeding promotes the breakdown of amino acids in both worms and mice. Amino acids are key components of proteins, and they become preferentially metabolized in the absence of carbohydrates. As Ristow points out, "this reflects the metabolic state of a low-carb diet due to glucosamine supplementation alone – while these mice ingested the same amount of carbohydrates as their unsupplemented counterparts." This implies that glucosamine would mimic a low-carb diet in humans as well – without the necessity of reducing the uptake of carbohydrates in our daily diet.

Should we now start taking glucosamine supplements? Ristow replies: "This may be considered a valid option, and yes, I have started taking glucosamine myself." However, he points out that "diabetics should perform tight blood glucose control, especially during the first weeks." Interestingly, two recent epidemiological studies on more than 77,000 individuals suggest that intake of glucosamine supplements is associated with reduced mortality in humans [references 3, 4]. "Unlike with our longer living mice, such an association is no definite

proof of the effectiveness of glucosamine in humans", says Ristow. He continues, "But the chances are good, and since unlike with most other potentially lifespan-extending drugs there are no known relevant side effects of glucosamine supplementation, I would tend to recommend this supplement."

Original publication: Sandra Weimer et al.: D-Glucosamine supplementation extends lifespan of nematodes and of ageing mice. Nature Communications, 2014, doi: 10.1038/ncomms4563,

http://www.eurekalert.org/pub_releases/2014-04/si-srp040814.php#rssowlmlink

Scientists reveal potential link between brain development and breast cancer gene

Scientists at the Salk Institute have uncovered details into a surprising -- and crucial -- link between brain development and BRCA1, a gene whose mutation is tied to breast and ovarian cancer.

La Jolla—Scientists at the Salk Institute have uncovered details into a surprising—and crucial—link between brain development and a gene whose mutation is tied to breast and ovarian cancer. Aside from better understanding neurological damage associated in a small percentage of people susceptible to breast cancers, the new work also helps to better understand the evolution of the brain.

The research, published this month in PNAS, shows that the gene known as BRCA1 has a significant role in creating healthy brains in mice and may provide a hint as to why some women genetically prone to breast cancer experience brain seizures.

"Previously, people associated mutations or deletions of BRCA1 with breast and ovarian cancer," says Inder Verma, a professor in Salk's Laboratory of Genetics and American Cancer Society Professor of Molecular Biology. "Our paper goes beyond this link to explain the protective mechanism of BRCA1 in the brain."

Through a three–lab collaboration at the Salk Institute, which began over a water cooler conversation between adjacent lab researchers 10 years ago, the work has culminated in dramatic findings. The team found that eliminating BRCA1 in neural stems cells had profound effects: large swaths of brain were simply missing; the cortex, which typically has six layers, only developed two very rudimentary layers; the cerebellum, which is normally made up of many folds and creases, was almost completely smooth; and the olfactory bulb, which processes odor information, was severely disorganized and poorly developed. Neurons were dying rapidly shortly after forming, while ones that did last were often defective. In mouse models, this resulted in interference in balance, motor skills, and other core functions.

How exactly was the absence of BRCA1 leading to such a neural catastrophe? In a previous paper, the team showed that without the protein coded by the BRCA1 gene, DNA is not packaged properly, becoming fragile and more likely to break during DNA replication. In this new paper, the researchers reveal more about that mechanism, showing that without the protective ability of BRCA1, breaks in the DNA strands go unfixed, prompting the molecule ATM kinase to activate a cellular "suicide" pathway involving a protein called p53. This pathway helps to halt the replication of damaged cells and is important in cancer research.

"BRCA1 acts by conferring stability to the DNA and preventing it from breaking," says Carlos G. Perez–Garcia, a Salk researcher in the Molecular Neurobiology Lab. "BRCA1 is important for all healthy cells."

When the researchers eliminated both BRCA1 and p53, they found the neurons grew at a normal rate, but still disorderly, with cells pointed in the wrong direction.

"In this scenario, we recover a lot of neurons but there's still a lot of abnormalities, such as cells that are sideways and pointed the wrong direction," says Gerald Pao, who, along with Quan Zhu and Perez–Garcia, is a primary contributor to the paper and Salk researcher.

This observation led the team to propose that BRCA1 has an additional role in assisting neurons in orienting: the gene acts on the centromere of DNA—essentially an anchor for the chromosome arms essential in cell replication—to tell the new cell in which direction to grow, providing guidance in developing the brain's organized layers.

"It is remarkable that BRCA1 has such a significant effect on the brain, especially size. This work leads us to a better understanding of how to protect neurons," says Verma, who is also the Irwin and Joan Jacobs Chair in Exemplary Life Science. Because BRCA1 seems to regulate the centromere, studying the gene will help scientists to understand how mammalian brains have evolved over time.

"Now we have an explanation for why some patients with breast cancer also experienced brain seizures," adds Pao. This knowledge could potentially help identify breast cancer–susceptible patients predisposed to seizures and provide appropriate treatments.

This work was a collaboration among researchers in the labs of Inder Verma, Dennis O'Leary, holder of the Institute's Vincent J. Coates Chair in Molecular Neurobiology Fred Gage, holder of Salk's Vi and John Adler Chair for Research on Age–Related Neurodegenerative Disease.

http://www.medscape.com/viewarticle/823262?src=rss

Psychiatric Symptoms May Precede Cognitive Decline

Laird Harrison

Elders with nonpsychotic psychiatric symptoms run an increased risk for mild cognitive impairment (MCI), a new study shows.

Agitation, apathy, anxiety, irritability, and depression all independently correlated to cognitive impairment, whereas delusion and hallucination did not, the researchers found. "These baseline psychiatric symptoms were of similar or greater magnitude as biomarkers (genetic and structural MRI) in increasing the risk of incident mild cognitive impairment," the researchers, led by Yonas E. Geda, MD, Mayo Clinic in Scottsdale, Arizona, write. The study was published online April 4 in the *American Journal of Psychiatry*.

Key Psychiatric Symptoms

Individuals with MCI develop dementia at a rate of 10% to 15% per year, compared with 1% to 2% per year in the general population. Researchers are trying to determine who is at greatest risk so that they can develop targeted interventions. To see whether neuropsychiatric status correlates to MCI, investigators evaluated 1408 people with a median age of 79.3 years in Olmsted County, Minnesota.

Participants underwent a neurologic evaluation by a physician, a risk factor assessment by a nurse or study coordinator, and a neuropsychological test interpreted by a neuropsychologist.

After adjusting for age, sex, education, and medical comorbidity, the researchers found that several psychiatric symptoms were associated with a much greater risk for cognitive decline. The correlation was statistically significant for agitation, apathy, anxiety, irritability, and depression ($P < .0001$).

Table. Psychiatric Symptoms Predicting Mild Cognitive Impairment

	Agitation	Apathy	Anxiety	Irritability	Depression
Hazard ratio	3.06	2.26	1.87	1.84	1.63

Although nighttime behavior also correlated with MCI, there were missing data, so the investigators recommended interpreting the results with caution. Likewise, though euphoria and disinhibition were significant predictors, the analysis was based on a relatively small number of events.

Noncognitive Indicator of Neurodegeneration?

The researchers conducted secondary analyses to differentiate predicted amnestic or nonamnestic impairment. They found that euphoria, disinhibition, and nighttime behavior predicted nonamnestic impairment, but not amnestic impairment. On the other hand, depression predicted amnestic impairment, but not nonamnestic impairment, whereas apathy predicted both.

The strength of the psychiatric symptoms was similar to the strength of such factors as hippocampal volume, the investigators reported. It was also similar to the strength of apolipoprotein ε4, comorbid medical conditions, or demographic variables, such as education, as predictors.

The researchers speculated that psychiatric symptoms could be a noncognitive manifestation of the underlying neurodegenerative disorder that causes the cognitive impairment.

Alternatively, another neuropathology could cause both the cognitive and the psychiatric symptoms, they write. Or there could be some synergistic interaction between psychiatric symptoms and a biological factor, such as the apolipoprotein ε4 genotype.

The study was funded by the National Institutes of Health, the Mayo Clinic, the Robert Wood Johnson Foundation, the Robert H. and Clarice Smith and Abigail Van Buren Alzheimer's Disease Research Program, the European Regional Development Fund, and the Czech Ministry of Health. The researchers reported financial relationships to Allon Pharmaceuticals, Cephalon, GE Healthcare, Genentech, Janssen Alzheimer Immunotherapy, Merck, Pfizer, Roche, and various foundations.

Am J Psychiatry. Published online April 4, 2014. Abstract

http://www.medscape.com/viewarticle/822980?src=rss

Multivitamins: Time to Just Say No?

Hello. I'm Dr. Sandra Fryhofer. Welcome to Medicine Matters. The topic: multivitamins, help or harm?

Sandra Adamson Fryhofer, MD

There are 2 original studies,[1,2] a US Preventive Services Task Force (USPSTF) review,[3] and a provocative editorial,[4] all published in the Annals of Internal Medicine. Here is why it matters. Vitamins and supplements: It's a growing industry, with sales of $28 billion in 2010 alone, but are they helpful or harmful? Are they a waste of precious healthcare resources that could be better spent on more beneficial therapies?

Let's start with the heart. The first study [discussed in the Annals editorial] was a multicenter, double-blind, placebo-controlled, randomized trial that included more than 1700 patients aged 50 years or older.[1] All had recently suffered a heart attack. Patients were given either a multivitamin, multimineral mix, or a placebo and

were followed for nearly 3 years. The results: The extra vitamins didn't protect the heart. They did not seem to protect against secondary cardiovascular events.
Another study in the same Annals issue looked at the effect of vitamins on cognition.[2] This is from the Physicians' Health Study II and looked at nearly 6000 male physicians age 65 years and older and followed them for 12 years. Initial and intermittent cognitive assessments were conducted. The results: Vitamin use did not slow cognitive decline. There was no change in verbal memory scores or cognition between those who took them and those who didn't.
Also included in the Annals is the USPSTF review of 26 studies looking at the pros and cons of supplements and preventing heart disease, cancer, and death.[3] This blue-ribbon panel found insufficient evidence that vitamins were beneficial.
Now, the editorial.[4] Clear-spoken and direct: Enough is enough. Stop wasting money. Well-nourished adults don't need them. There is no clear benefit, and they might even be harmful. Don't use them to prevent chronic disease. The editorial specifically mentions beta-carotene, vitamin E, and high doses of vitamin A as being harmful. Beta-carotene increases risk for lung cancer in those who smoke. Vitamin E supplements have been linked to increases in all-cause mortality.
There was one exception: vitamin D. The editorial acknowledges that the role of vitamin D supplementation is an open area of investigation, especially in those who are vitamin D deficient. More study is needed. But even with vitamin D, there is no solid evidence that the benefits outweigh the harms.
There is one group that does need vitamin supplementation: women of childbearing potential. For them, folic acid supplementation is important because it prevents neural tube defects in their babies. Now you know.
For Medicine Matters, I'm Dr. Sandra Fryhofer.

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http://phys.org/news/2014-04-landscape-transition-zones-tornadoes.html#rssowlmlink

Landscape 'transition zones' may influence where tornadoes strike

Areas where landscape shifts from urban to rural or forest to farmland may have a higher likelihood of severe weather and tornado touchdowns, a Purdue University study says.

Phys.org - An examination of more than 60 years of Indiana tornado climatology data from the National Weather Service's Storm Prediction Center showed that a majority of tornado touchdowns occurred near areas where dramatically different landscapes meet - for example, where a city fades into farmland or a forest meets a plain. Forecasters and city planners may need to pay closer attention to these "transition zones" to better understand tornado risks, said Olivia Kellner, doctoral student in the Department of Earth, Atmospheric and Planetary Sciences and first author of the study.
"There are still many unanswered questions about tornado climatology, but what we're finding is that there may be a relationship between the Earth's surface and the atmosphere that contributes to where tornadoes tend to touch down," Kellner said.
An analysis of locations where tornadoes touched down between 1950 and 2012 revealed that 61 percent of tornado touchdowns occurred within 1 kilometer (about 0.62 mile) of urban areas while 43 percent of touchdowns fell within 1 kilometer of forest. Some tornadoes touched down in close proximity to both cities and forests.
Although highly populated urban areas can increase the number of tornado reports, the analysis showed a large percentage of touchdowns also occurred in low-population regions with significant changes in surface features. Kellner said the percentages suggest that certain locations may enhance the likelihood of tornado touchdowns. Increased "surface roughness" - an abrupt change in the height of land surface features - can stretch or squash a column of air, increasing the air's rate of spin, which could contribute to the formation of severe storms.
Dev Niyogi, Indiana's state climatologist and co-author of the study, said the possibility that land surface could affect the development of severe weather deserves further scrutiny.
"Forecasting and preparing for severe weather risks such as tornadoes are difficult and societally important tasks," he said. "We might need to pay more attention to areas where land surface features transition from rough to smooth, flat to sloped, or wet to dry. These changes in landscape may provide triggers for severe weather."

The study also found that tornado touchdowns in urban areas tend to occur at about 1 and 10 miles from the city center.
Kellner said these "rings" of increased tornado activity could be related to how cities are developed.
"Cities impact the surrounding climate in terms of regional airflow and temperature," she said. "The size of cities, what they're made of and the heat they produce are factors that could affect the microclimate."
Niyogi cautioned that every storm is unique and that a variety of factors influence storm intensity and the potential for severe weather. Identifying areas of high risk, however, could lead to city designs that would reduce the conditions associated with producing severe weather hazards such as tornadoes.
"As we continue to modify our landscapes, there will be many environmental and societal changes," he said. "But perhaps we have the potential to engineer cities to be more resilient to severe weather by thinking holistically about the way cities can be developed and how they affect local climate conditions."
According to the study, Indiana has a distinct spring tornado season with a majority of tornadoes occurring in June, May and July, respectively. Strong tornadoes with estimated wind speeds of more than 158 miles per hour occur most frequently in April and June. The total number of tornado days per year - days on which at least one tornado report is made - has not increased over time. The study also found that drought conditions and climate variations such as El Niño have some impact on Indiana tornado climatology.
More information: The paper "Land-surface Heterogeneity Signature in Tornado Climatology? An Illustrative Analysis over Indiana 1950-2012" was published in the American Meteorological Society's Earth Interactions journal and is available at journals.ametsoc.org/doi/abs/10.1175/2013EI000548.1

http://www.nature.com/news/bacterial-tricks-for-turning-plants-into-zombies-1.15011

Bacterial tricks for turning plants into zombies

Microbe deploys proteins that manipulate both the plant it infects and the insects that spread it.

Ed Yong

Many parasites commandeer the bodies of their hosts in order to spread. Examples of this include horsehair worms that reach water by forcing their cricket hosts to drown themselves, and liver flukes that drive infected ants to climb blades of grass, where cows can eat the insects, and so the flukes.
But parasites can turn plants into zombies, too — and a team of scientists from the John Innes Centre in Norwich, UK, has now discovered how they do it.
When plants are infected by parasitic bacteria called phytoplasmas, their flowers turn into leafy shoots, their petals turn green and they develop a mass of shoots called ‘witches’ brooms’. This transformation sterilizes the plant, while attracting the sap-sucking insects that carry the bacteria to new hosts.
“The plant appears alive, but it’s only there for the good of the pathogen,” says plant pathologist Saskia Hogenhout from the John Innes Centre in Norwich, UK. “In an evolutionary sense, the plant is dead and will not produce offspring.”
“Many might baulk at the concept of a zombie plant because the idea of plants behaving is strange,” says David Hughes, a parasitologist at Pennsylvania State University in University Park. “But they do, and since they do, why wouldn't parasites have evolved to take over their behaviour, as they do for ants and crickets?”

Dual control

Hogenhout’s team had previously shown that the bacteria manipulate their hosts by means of a single protein called SAP54. It interacts with the plant protein RAD23, which sends molecules destined for destruction to the cell’s waste-disposal centre — the proteasome. In this case, the targeted molecules are those that make flowers. The findings are published today in PLoS Biology1.
The same interaction between SAP54 and these plant proteins increased the plants' attraction for the leafhoppers that transmit phytoplasmas. The team found that leafhoppers lay more eggs on infected plants that had leaf-like flowers than on those with normal blooms. They also showed that even SAP54 alone, in the absence of the bacteria, could attract the insects. “The beauty of the paper is that the bacteria control both plant and insect at the same time with the same protein,” said Hughes. “That’s stunning.”
Hogenhout says that this discovery reveals a connection between a plant’s developmental program and its immune system — one that no one had suspected and that probably holds in many other species. She hopes that studying this connection will lead to new ways of simultaneously improving crop production and boosting resistance to pests.
She also wants to work out how other pathogens create zombie plants. The rust fungus Puccinia monoica, for example, sterilizes its hosts and transforms their leaves into bright yellow ‘pseudoflowers’. These fake flowers are loaded with fungal cells, and attract insect pollinators that spread the cells to uninfected hosts2. No one knows how it reprograms the host, says Hogenhout. “It would be so cool to find out.”
Nature doi:10.1038/nature.2014.15011

http://bit.ly/1iG4piY

Pharmaceutical giant Takeda to fight $6 billion damages ruling over hidden cancer risks

Takeda Pharmaceutical Co. said it would contest $6 billion in punitive damages imposed by a jury in the United States in a case that accused Japan's largest drugmaker of concealing cancer risks associated with its Actos diabetes drug.

San Francisco - Eli Lilly and Co., Takeda's co-defendant in the case, was ordered to pay $3 billion in punitive damages by the jury in Louisiana on Monday. It also awarded $1.48 million in compensatory damages.

The $9 billion in punitive damages awarded by the jury against Takeda and Eli Lilly exceed the $5 billion penalty that a jury in Alaska previously imposed on Exxon Mobil Corp. following the 1989 Exxon Valdez oil spill. Legal experts said it was unlikely such a large award would stand after challenges in court by both companies. Eli Lilly and Takeda have said they would dispute the verdict, which could include appeals to a higher court or filing motions asking the trial judge to set aside or reduce the verdict.

"Although there's no mathematical bright line" to determine how high is too high when it comes to punitive damage awards, federal appeals courts generally scrutinize the ratio of punitive to compensatory damages, preferring those that fall into the single-digit range, according to professor Catherine Sharkey, a tort law expert at New York University School of Law.

Punitive damages are meant to discourage companies from bad conduct. Compensatory damages are meant to pay victims for their actual losses. With a ratio of more than 6,100 to 1 of punitive to compensatory damages, the Actos award could be highly vulnerable. "It's definitely the case that the U.S. Supreme Court has signaled to lower courts that they should be restraining very large punitive awards," Sharkey added.

Lilly, which co-promoted Actos from 1999 to 2006, said in a press release it will be indemnified by Takeda for losses and expenses arising from the litigation under the terms of the companies' agreement.

Takeda's shares fell as much as 8.8 percent to an eight-month low in Tokyo trading after the verdict on Tuesday. Lilly shares fell 0.2 percent, or 12 cents per share, to $58.50 per share in New York Stock Exchange trading.

The massive award was met with "stunned silence" in the Lafayette, Louisiana, courtroom, plaintiffs' lawyer Mark Lanier said. Lanier acknowledged it was not certain whether the damages award would be sustained.

"Nobody has gone out and bought a new home," Lanier said. "This is a conservative judge and a conservative court and she's very 'balls and strikes.' We're not under any grand illusion." In 2008, the U.S. Supreme Court ruled that the Exxon Valdez award had been "excessive." The company was ultimately ordered to pay $500 million. That, and other rulings, have been read as limiting punitive damages in federal cases.

Lanier said the jury deliberated for only 70 minutes to deliver its verdict finding liability on all 14 questions, and 45 minutes longer to come out with the multibillion-dollar punitive damages. The allocation of liability for compensatory damages was 75 percent for Takeda and 25 percent for Lilly, according to the latter.

Takeda said judgments were entered in its favor in all three previous Actos trials, while this was the first federal case to be tried in a consolidated multidistrict litigation comprising more than 2,900 lawsuits. Last May, a U.S. judge nullified a separate jury verdict for $6.5 million against Takeda after ruling that the plaintiffs failed to offer any reliable evidence that Actos had caused cancer. Germany and France suspended use of the drug, a multibillion-dollar seller, in 2011 over concerns about a possible link to cancer.

http://www.eurekalert.org/pub_releases/2014-04/uoy-rsn040914.php#rssowlmlink

Researchers say Neanderthals were no strangers to good parenting

Archaeologists at the University of York are challenging the traditional view that Neanderthal childhood was difficult, short and dangerous.

A research team from PALAEO (Centre for Human Palaeoecology and Evolutionary Origins) and the Department of Archaeology at York offer a new and distinctive perspective which suggests that Neanderthal children experienced strong emotional attachments with their immediate social group, used play to develop skills and played a significant role in their society.

The traditional perception of the toughness of Neanderthal childhood is based largely on biological evidence, but the archaeologists, led by Dr Penny Spikins, also studied cultural and social evidence to explore the experience of Neanderthal children.

In research published in the Oxford Journal of Archaeology, they found that Neanderthal childhood experience was subtly different from that of their modern human counterparts in that it had a greater focus on social relationships within their group. Investigation of Neanderthal burials suggests that children played a particularly significant role in their society, particularly in symbolic expression.

The research team, which also included Gail Hitchens, Andy Needham and Holly Rutherford, say there is evidence that Neanderthals cared for their sick and injured children for months and often years. The study of

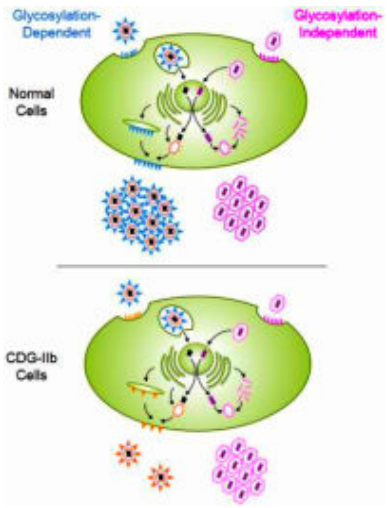
child burials, meanwhile, reveals that the young may have been given particular attention when they died, with generally more elaborate graves than older individuals.
Neanderthal groups are believed to have been small and relatively isolated, suggesting important implications for the social and emotional context of childhood. Living in rugged terrain, there will have been little selection pressure on overcoming the tendency to avoid outside groups with a consequent natural emotional focus on close internal connections.
Dr Spikins, who has a new book on why altruism was central to human evolutionary origins, How Compassion Made Us Human, (Pen and Sword) published later this year, said: "The traditional view sees Neanderthal childhood as unusually harsh, difficult and dangerous. This accords with preconceptions about Neanderthal inferiority and an inability to protect children epitomising Neanderthal decline.
"Our research found that a close attachment and particular attention to children is a more plausible interpretation of the archaeological evidence, explaining an unusual focus on infants and children in burial, and setting Neanderthal symbolism within a context which is likely to have included children.
"Interpretations of high activity levels and frequent periods of scarcity form part of the basis for this perceived harsh upbringing. However, such challenges in childhood may not be distinctive from the normal experience of early Palaeolithic human children, or contemporary hunter-gatherers in particularly cold environments. There is a critical distinction to be made between a harsh childhood and a childhood lived in a harsh environment."

http://www.eurekalert.org/pub_releases/2014-04/nioa-gdm040914.php#rssowlmlink

Genetic defect may confer resistance to certain viral infections

NIH study could offer clues for developing new antiviral treatments

A National Institutes of Health (NIH) study reports that a rare genetic disease, while depleting patients of infection-fighting antibodies, may actually protect them from certain severe or recurrent viral infections. Researchers found that HIV and influenza viruses replicate in the cells of people with congenital disorder of glycosylation type IIb (CDG-IIb) at a much lower rate than in healthy donor cells, creating fewer and less infectious viruses. The study, published in The New England Journal of Medicine, was led by Sergio Rosenzweig, M.D., Ph.D., director of the Primary Immune Deficiency (PID) Clinic at the NIH's National Institute of Allergy and Infectious Diseases (NIAID).
In the study, the researchers diagnosed CDG-IIb in two siblings with severe development issues who were referred to the NIAID PID Clinic though the NIH Undiagnosed Diseases Program. CDG-IIb is extremely rare, with only one other case reported. The genetic defect of the disease disrupts glycosylation, or the process of attaching sugars to proteins. As a result, proteins called gamma globulins, which include infection-fighting antibodies, are unstable and persist at low levels in the patients' blood.



Viruses (blue and pink) must use host cells (green) to create more viruses that spread infection (top panel). CDG-IIb patients have defective glycosylation, the process of adding sugars to proteins, resulting in poor production of viruses that depend on this process, such as HIV and influenza (bottom panel). The scientists also show that viruses coming from the patients' cells (orange) are less infectious because of changes to their outer shields. **NIAID**

Interestingly, some viruses, including HIV and influenza, depend on glycosylation to form protective shields. The researchers showed that these viruses were less able to replicate or create protective shields because of the glycosylation defects in CDG-IIb cells. In comparison, adenovirus, poliovirus and vaccinia virus, which either do not rely on glycosylation or do not form protective shields, replicated normally when added to both CDG-IIb and healthy cells. This study suggests that modulating aspects of host glycosylation may be a strategy to control certain viral infections.

MA Sadat, S Moir et al. Glycosylation, hypogammaglobulinemia and resistance to viral infections. NEJM DOI: 10.1056/NEJMoa1302846 (2014).

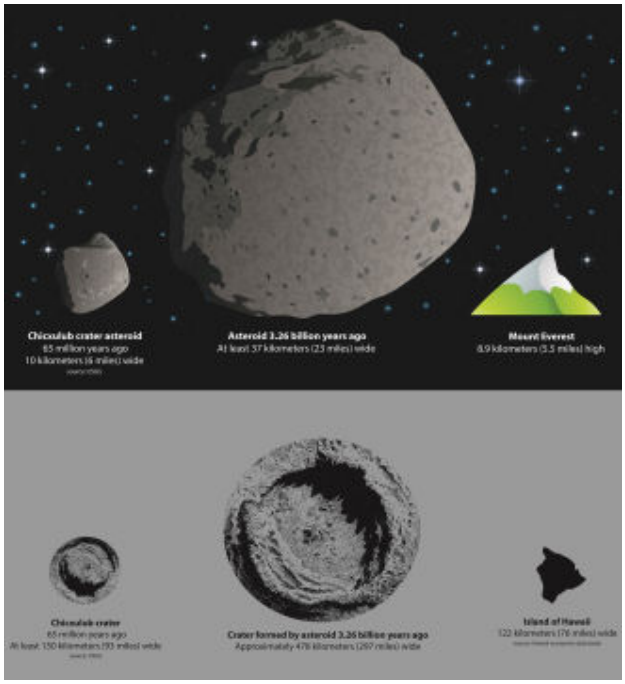
http://www.eurekalert.org/pub_releases/2014-04/agu-sra040914.php#rssowlmlink

Scientists reconstruct ancient impact that dwarfs dinosaur-extinction blast

Picture this: A massive asteroid almost as wide as Rhode Island and about three to five times larger than the rock thought to have wiped out the dinosaurs slams into Earth.

Washington, D.C. - The collision punches a crater into the planet's crust that's nearly 500 kilometers (about 300 miles) across: greater than the distance from Washington, D.C. to New York City, and up to two and a half times larger in diameter than the hole formed by the dinosaur-killing asteroid. Seismic waves bigger than any recorded earthquakes shake the planet for about half an hour at any one location – about six times longer than

the huge earthquake that struck Japan three years ago. The impact also sets off tsunamis many times deeper than the one that followed the Japanese quake.
Although scientists had previously hypothesized enormous ancient impacts, much greater than the one that may have eliminated the dinosaurs 65 million years ago, now a new study reveals the power and scale of a cataclysmic event some 3.26 billion years ago which is thought to have created geological features found in a South African region known as the Barberton greenstone belt. The research has been accepted for publication in Geochemistry, Geophysics, Geosystems, a journal of the American Geophysical Union.
The huge impactor – between 37 and 58 kilometers (23 to 36 miles) wide – collided with the planet at 20 kilometers per second (12 miles per second). The jolt, bigger than a 10.8 magnitude earthquake, propelled seismic waves hundreds of kilometers through the Earth, breaking rocks and setting off other large earthquakes. Tsunamis thousands of meters deep – far bigger than recent tsunamis generated by earthquakes -- swept across the oceans that covered most of the Earth at that time. "We knew it was big, but we didn't know how big," Donald Lowe, a geologist at Stanford University and a co-author of the study, said of the asteroid.
Lowe, who discovered telltale rock formations in the Barberton greenstone a decade ago, thought their structure smacked of an asteroid impact. The new research models for the first time how big the asteroid was and the effect it had on the planet, including the possible initiation of a more modern plate tectonic system that is seen in the region, according to Lowe.
The study marks the first time scientists have mapped in this way an impact that occurred more than 3 billion years ago, Lowe added, and is likely one of the first times anyone has modeled any impact that occurred during this period of the Earth's evolution.
The impact would have been catastrophic to the surface environment. The smaller, dino-killing asteroid crash is estimated to have released more than a billion times more energy than the bombs that destroyed Hiroshima and Nagasaki. The more ancient hit now coming to light would have released much more energy, experts said.
The sky would have become red hot, the atmosphere would have been filled with dust and the tops of oceans would have boiled, the researchers said. The impact sent vaporized rock into the atmosphere, which encircled the globe and condensed into liquid droplets before solidifying and falling to the surface, according to the researchers.
The impact may have been one of dozens of huge asteroids that scientists think hit the Earth during the tail end of the Late Heavy Bombardment period, a major period of impacts that occurred early in the Earth's history – around 3 billion to 4 billion years ago.



A graphical representation of the size of the asteroid thought to have killed the dinosaurs, and the crater it created, compared to an asteroid thought to have hit the Earth 3.26 billion years ago and the size of the crater it may have generated. A new study reveals the power and scale of the event some 3.26 billion years ago which scientists think created geological features found in a South African region known as the Barberton greenstone belt. **American Geophysical Union**

Many of the sites where these asteroids landed were destroyed by erosion, movement of the Earth's crust and other forces as the Earth evolved, but geologists have found a handful of areas in South Africa, and Western Australia that still harbor evidence of these impacts that occurred between 3.23 billion and 3.47 billion years ago. The study's co-authors think the asteroid hit the Earth thousands of kilometers away from the Barberton Greenstone Belt, although they can't pinpoint the exact location. "We can't go to the impact sites. In order to better understand how big it was and its effect we need studies like this," said Lowe. Scientists must use the geological evidence of these impacts to piece together what happened to the Earth during this time, Lowe said.
The study's findings have important implications for understanding the early Earth and how the planet formed. The impact may have disrupted the Earth's crust and the tectonic regime that characterized the early planet, leading to the start of a more modern plate tectonic system, according to the paper's co-authors.
The pummeling the planet endured was "much larger than any ordinary earthquake," said Norman Sleep, a physicist at Stanford University and co-author of the study. He used physics, models, and knowledge about the formations in the Barberton greenstone belt, other earthquakes and other asteroid impact sites on the Earth and

the moon to calculate the strength and duration of the shaking that the asteroid produced. Using this information, Sleep recreated how waves traveled from the impact site to the Barberton greenstone belt and caused the geological formations.
The geological evidence found in the Barberton that the paper investigates indicates that the asteroid was "far larger than anything in the last billion years," said Jay Melosh, a professor at Purdue University in West Lafayette, Indiana, who was not involved in the research.
The Barberton greenstone belt is an area 100 kilometers (62 miles) long and 60 kilometers (37 miles) wide that sits east of Johannesburg near the border with Swaziland. It contains some of the oldest rocks on the planet.
The model provides evidence for the rock formations and crustal fractures that scientists have discovered in the Barberton greenstone belt, said Frank Kyte, a geologist at UCLA who was not involved in the study. "This is providing significant support for the idea that the impact may have been responsible for this major shift in tectonics," he said.
Reconstructing the asteroid's impact could also help scientists better understand the conditions under which early life on the planet evolved, the paper's authors said. Along with altering the Earth itself, the environmental changes triggered by the impact may have wiped out many microscopic organisms living on the developing planet, allowing other organisms to evolve, they said. "We are trying to understand the forces that shaped our planet early in its evolution and the environments in which life evolved," Lowe said.

http://www.eurekalert.org/pub_releases/2014-04/asu-gco040914.php#rssowlmlink

Gusev Crater once held a lake after all, says ASU Mars scientist

If desert mirages occur on Mars, "Lake Gusev" belongs among them. This come-and-go body of ancient water has come and gone more than once, at least in the eyes of Mars scientists.

Tempe, Ariz. - Now, however, it's finally shifting into sharper focus, thanks to a new analysis of old data by a team led by Steve Ruff, associate research professor at Arizona State University's Mars Space Flight Facility in the School of Earth and Space Exploration. The team's report was just published in the April 2014 issue of the journal Geology.
The story begins in early 2004, when NASA landed Spirit, one of its two Mars Exploration Rovers, inside 100-mile-wide Gusev Crater. Why Gusev? Because from orbit, Gusev looked, with its southern rim breached by a meandering river channel, as if it once held a lake – and water-deposited rocks were the rover mission's focus.
Yet when Spirit began to explore, scientists found Gusev's floor was paved not with lakebed sediments, but volcanic rocks.
Less than two miles away however stood the Columbia Hills, 300 feet high. When Spirit drove up into them, it indeed discovered ancient rocks that had been altered by water. But to scientists' chagrin, no lake sediments were among them. Instead, scientists discovered evidence of hydrothermal activity, essentially hot springs like those in Yellowstone National Park.
But there's hope yet for Lake Gusev, thanks to a Columbia Hills rock outcrop dubbed Comanche. This outcrop is unusually rich in magnesium-iron carbonate minerals, a discovery made in 2010 that Ruff played a major role in making. While Comanche's carbonate minerals were originally attributed to hydrothermal activity, the team's new analysis points to a different origin.

Cool waters

Says Ruff, "We looked more closely at the composition and geologic setting of Comanche and nearby outcrops. There's good evidence that low temperature surface waters introduced the carbonates into Comanche rather than hot water rising from deep down."
Comanche started out as a volcanic ash deposit known as tephra that originally covered the Columbia Hills and adjacent plains. This material, Ruff explains, came from explosive eruptions somewhere within or around Gusev.
Then floodwaters entered the crater through the huge valley that breaches Gusev's southern rim. These floods appear to have ponded long enough to alter the tephra, producing briny solutions. When the brines evaporated, they left behind residues of carbonate minerals. As the lake filled and dried, perhaps many times in succession, it loaded Comanche and its neighbor rocks with carbonates.
"The lake didn't have to be big," Ruff explains. "The Columbia Hills stand 300 feet high, but they're in the lowest part of Gusev. So a deep, crater-spanning lake wasn't needed."
Today, the Columbia Hills rise as an island of older terrain surrounded by younger lava flows, Ruff says. "Comanche and a neighbor outcrop called Algonquin are remnants of the older and much more widespread tephra deposit. The wind has eroded most of that deposit, also carrying away much of the evidence for an ancient lake."

Return to Gusev?

Mars rover Spirit fell silent on a winter night in March 2010, and it has never been heard from since. Spirit left most of the Columbia Hills and other Gusev targets unexplored. Ruff says that as NASA evaluates landing sites for its new sample-collecting rover in 2020, Gusev Crater deserves serious consideration.

"Going back to Gusev would give us an opportunity for a second field season there, which any terrestrial geologist would understand," argues Ruff. "After the first field season with Spirit, we now have a bunch more questions and new hypotheses that can be addressed by going back."

Because the Mars 2020 rover mission will collect and cache samples for potential return to Earth, Ruff says, that makes going to an already visited site more important. "Scientifically and operationally it makes sense to go to a place which we know has geologically diverse – and astrobiologically interesting – materials to sample," Ruff argues. "And we know exactly where to find them."

http://www.medscape.com/viewarticle/823217?src=rss

Should POLICE Replace RICE as the Ankle Therapy of Choice?

The Wrong Therapy for Sprains and Strains?

Laird Harrison

Every now and then, a patient hobbles into the physical therapy offices of Eric Robertson, PT, DPT, still wearing a walking boot weeks after spraining an ankle.

"We kind of cringe," says Robertson, a spokesperson for the American Physical Therapy Association and an Assistant Professor of Physical Therapy at Regis University in Denver, Colorado.

Patients should start moving most sprained and strained joints soon after the injury, yet many doctors go too far in applying the "rest" part of the traditional prescription of rest, ice, compression, and elevation (RICE), says Robertson. "This RICE construct doesn't necessarily reflect modern science."

RICE appears all over the Internet and in self-care books and pamphlets -- wherever you can find advice about sprains and strains, including the Websites of the American Academy of Orthopaedic Surgeons (AAOS)[1] and the American College of Sports Medicine (ACSM).[2]

But the formula derives more from educated guessing than actual research. In recent years, a movement has grown to replace it with a more evidence-based approach. Even some defenders of RICE, such as AAOS spokesperson Barbara Bergin, MD, say RICE is not meant as a clinical guideline but more as a first-aid recommendation for laypeople.

A Problem That Affects Thousands of Patients

Sprains and strains may seem like a trivial problem. After all, they don't kill anyone and usually heal without much intervention. But in the United States alone, some 28,000 ankle injuries occur every day.[3] A recent systematic review in the *American Journal of Medicine* showed that only 35%-85% of sprained ankles heal in 3 years.[4]

Such statistics have focused increasing attention on therapy for sprains. A 2012 editorial published in the *British Journal of Sports Medicine* called for replacement of RICE with a different set of guidelines: protection, optimal loading, ice, compression, and elevation (POLICE).[5]

"Rest should be of limited duration and restricted to immediately after trauma," the authors wrote. "Longer periods of unloading are harmful and produce adverse changes to tissue biomechanics and morphology."

In 2013, the National Athletic Trainers Association (NATA) published some of the first official guidelines anywhere for ankle sprains.[6] Researchers for the organization spent 6 years combing through the literature and assigning letter grades from "A" to "C," from best to worst quality of the evidence behind each possible therapy. Most elements of RICE got a "C," yet lead author Thomas W. Kaminski, PhD, ATC, believes that many practitioners are still following the prescription too closely.

"I wish I could say that what we found is what is really being done in a clinical setting," says Kaminski, Professor of Kinesiology and Applied Physiology at the University of Delaware in Newark. "That's probably not the case."

Evidence Supports Early Movement, Not Rest

The NATA researchers found level "A" evidence supporting functional rehabilitation -- in other words, therapies that involve moving the ankle soon after the injury -- for ankle sprains of grade I (stretching and damage to ligament fibers) and grade II (partial tearing of the ligaments).

No one recommends forcing patients to walk on their sprained ankles right away. But some randomized controlled trials have shown that beginning range-of-motion exercises within a couple of days, followed by gradual loading, can get patients back on their feet more quickly.[6] Manipulation of the joint by trained therapists has also shown success in these trials.[6]

For grade III ankle sprains (complete ligament tear), Kaminski and colleagues found "B" level evidence for immobilizing the joint for 10 days.[6] After that, they recommend, patients should begin moving the joint. They also call for more conservative treatment of syndesmotic or "high" ankle sprains.
Which other therapies received an "A" for evidence? Balance training and nonsteroidal anti-inflammatory drugs (NSAIDs). That's it.
Designed to improve proprioception, balance training reduced the risk for reinjury in some clinical trials.
NSAIDs are more controversial. Kaminski recommends not using them for the first 48 hours after the injury because they might interfere with the benefits of inflammation during that period.
But just because evidence is lacking for the rest of the RICE prescription, advocates of a revision aren't ready to throw it out completely.

Rethinking RICE

Kaminski, for one, thinks ice, compression, and elevation still have a role to play. He's most skeptical of ice. "Maybe our European colleagues know something we don't," he says. "There is very little icing over there." On the other hand, "We do know it's a good pain reliever."
With no contradictory evidence at hand, he's willing to go along with the conventional wisdom behind compression and elevation: Compression can reduce the leaking of fluid through capillary into tissue spaces. And elevation can keep blood from pooling in the limb. "Extreme swelling adds days, if not weeks, to the healing," he says.
A similar line of thinking has convinced Stephen Rice, MD, PhD, former chair of the ACSM Health Science Policy Committee, to keep recommending ice, compression, and elevation for sprains and strains.
"I think nobody would make the argument that if you get a musculoskeletal injury you should just let it swell," says Rice, a pediatric sports medicine specialist at Jersey Shore University Medical Center in Neptune, New Jersey. "I've known for many years that we don't have the hard science, but I have nearly 40 years of experience that if you can control the swelling, people can return faster." He believes the therapy should start immediately. "I'm so aggressive with my icing, compression, and elevation that I don't worry about the anti-inflammatories," he says.
Barbara Bergin, the AAOS spokesperson, believes there's a lot of good in RICE as well. "You just can't beat rest, ice, compression, and elevation," she says. "But it's not a treatment guideline; it's an initial management guideline for the general public. You sprain your ankle and it's a Sunday afternoon and you don't want to have to go to the emergency room because you'll have to wait in line for hours, and you'll have to pay a lot, and your doctor will be in on Monday."
As for actual clinical guidelines, she says they can't be summed up in a single acronym. Every patient is different, and every therapy has to be designed for that individual, she says. In this respect, critics and defenders of RICE agree. It won't hurt and may help patients with self-care until they can get medical attention.
"RICE by itself is not necessarily too dangerous," says Eric Robertson. "But you should know that there is a better way."

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http://bit.ly/Rd0pzo

Dysentery parasite attacks gut by eating cells alive

It's a killer amoeba. More than 100,000 people die each year from amoebic dysentery, mostly in developing countries where sanitation is poor.

18:00 09 April 2014 by Chelsea Whyte

But only 10 per cent of people who carry the amoebic parasite ever show symptoms, leaving scientists mystified as to how it preys on the body. Now Katherine Ralston and William Petri of the University of Virginia, Charlottesville, have found that Entamoeba histolytica has a unique – and gruesome – strategy. It gnaws away at the gut wall, ripping and ingesting chunks off living cells, killing them in the process.

It's "purely malevolent", says Michael Blennerhassett of Queen's University in Ontario, Canada, because the amoeba aren't interested in the cells once they're dead. This suggests they don't need to eat them for the nutrients they contain, says Blennerhasset, who was not involved in the study. "This is a previously unsuspected method of attack."
Ralston and Petri labelled mouse intestines using fluorescent dyes, in order to follow their fate. Most amoebas kill cells by attaching themselves to them, but E. histolytica tears at its targets. "We saw that the amoeba ingested bites of the fluorescent membranes of the intestinal cells," says Ralston. "They are impressively ravenous."
If E. histolytica is constantly grazing throughout the gut, it may be able to lurk inside a host for years without wreaking enough damage to cause inflammation or disease.
"The way it samples bits and pieces of the cell suggests this may be going on all the time, and only when a certain balance is broken does the disease set in," says Kris Chadee, a microbiologist from the University of Calgary in Alberta, Canada. "The parasite needs to attach to the cell to rip off little pieces, so if you could get blocking antibodies in the place where it attaches, that would be a potential target for drug development."
Journal reference: Nature, DOI: 10.1038/nature13242

http://www.bbc.com/news/health-26954482##rssowlmlink

Tamiflu: Millions wasted on flu drug, claims major report

Hundreds of millions of pounds may have been wasted on a drug for flu that works no better than paracetamol, a landmark analysis has said.

By James Gallagher Health and science reporter, BBC News

The UK has spent £473m on Tamiflu, which is stockpiled by governments globally to prepare for flu pandemics. The Cochrane Collaboration claimed the drug did not prevent the spread of flu or reduce dangerous complications, and only slightly helped symptoms. The manufacturers Roche and other experts say the analysis is flawed. The antiviral drug Tamiflu was stockpiled from 2006 in the UK when some agencies were predicting that a pandemic of bird flu could kill up to 750,000 people in Britain. Similar decisions were made in other countries.

Analysis James Gallagher
Health and Science reporter, BBC News

"Does a drug work?" should be an easy question to answer. Yet after hundreds of millions of pounds, either down the drain or saving lives depending on your stance, this question is being asked of Tamiflu.
It stems from the way drugs are approved. Pharmaceutical companies conduct trials, some but not all of the data is made publicly available and regulators decide if it works. It is estimated that, entirely legally, half of clinical trials have never been reported and that favourable data is more likely to published.
The UK Public Accounts Committee said the lack of data available to researchers and doctors was "of extreme concern".
So the Tamiflu saga raises another important question - what other drugs are we using that might not work as well as we thought?

Hidden data

The drug was widely prescribed during the swine flu outbreak in 2009. Drug companies do not publish all their research data. This report is the result of a colossal fight for the previously hidden data into the effectiveness and side-effects of Tamiflu. It concluded that the drug reduced the persistence of flu symptoms from seven days to 6.3 days in adults and to 5.8 days in children. But the report's authors said drugs such as paracetamol could have a similar impact.
On claims that the drug prevented complications such as pneumonia developing, Cochrane suggested the trials were so poor there was "no visible effect".
Another justification for stockpiling was to slow the spread of the disease to give time for a vaccine to be developed. The report's authors said "the case for this is simply unproven" and "there is no credible way these drugs could prevent a pandemic". It also claimed that the drug had a number of side-effects, including nausea, headaches, psychiatric events, kidney problems and hyperglycaemia.
Carl Heneghan, Professor of Evidence-Based Medicine at the University of Oxford and one of the report's authors, told the BBC: "I think the whole £500m has not benefited human health in any way and we may have harmed people. "The system that exists for producing evidence on drugs is so flawed and open to misuse that the public has been misled."
Dr Tom Jefferson, a clinical epidemiologist and former GP, said: "I wouldn't give it for symptom relief, I'd give paracetamol."
The Cochrane Collaboration researchers have not placed the blame on any individual or organisation, instead saying there had been failings at every step from the manufacturers to the regulators and government.

'Wrong statistics'

However, there is disagreement about the findings and accusations that a simultaneous campaign to open up drug research is influencing the findings. The pharmaceutical company Roche said "we disagree with the overall conclusions" and warned they could "potentially have serious public health implications".
Its UK medical director, Dr Daniel Thurley, told the BBC News website: "The definitive piece of research stands as the randomised control trials, which were shared with the regulators, which led to them in 100 countries around the world approving Tamiflu for treatment and prevention of flu." He said the Cochrane group had used the wrong statistics, which "systematically underestimate the benefits" of the drug, and used "unorthodox" methods to analyse the side-effects. He concluded: "One of the challenges we have here is actually knowing what they've done."
Prof Wendy Barclay, who researches the influenza virus at Imperial College London, said reducing symptoms in children by 29 hours would be "pretty beneficial". She told the BBC: "Tamiflu works as well as any drug we have now or [that] is on the cards. "Yes, I think they should replenish the stockpile. What else can you do if a pandemic strikes? We won't have a vaccine for the first six months." She also questioned the validity of the research as it analysed the impact during seasonal flu: "If it works a little bit in season flu, the chances are they'll work quite a lot better in a pandemic situation and get more people back to school and work."
Kevin McConway, a professor of applied statistics at the Open University, said it was an "impressive" piece of work. He said: "It is a potential limitation of this study that the work has been carried out alongside campaigning on access to trial data. "The writers of the review have a clear position in this controversy, and, although I personally do generally agree with their position, I feel it does at times lead to some confusion between reporting the results of the review of these particular drugs and commenting on the general position on access to and use of unpublished data."
The Department of Health, which took the lead for the UK, said Britain was recognised as "one of the best prepared countries in the world for a potential flu pandemic" and "our stockpile of antivirals is a key part of this. "We regularly review all published data and will consider the Cochrane review closely."
The World Health Organization, which classes Tamiflu as an essential medicine, said: "We welcome a new and rigorous analysis of available data, and look forward to consideration of its findings after it appears."

http://nyti.ms/1kHeL80

A 'Code Death' for Dying Patients

Sadly, but with conviction, I recently removed breathing tubes from three patients in intensive care.

By JESSICA NUTIK ZITTER, M.D.

As an I.C.U. doctor, I am trained to save lives. Yet the reality is that some of my patients are beyond saving. And while I can use the tricks of my trade to keep their bodies going, many will never return to a quality of life that they, or anyone else, would be willing to accept.
I was trained to use highly sophisticated tools to rescue those even beyond the brink of death. But I was never trained how to unhook these tools. I never learned how to help my patients die. I committed the protocols of lifesaving to memory and get recertified every two years to handle a Code Blue, which alerts us to the need for immediate resuscitation. Yet a Code Blue is rarely successful. Very few patients ever leave the hospital afterward. Those that do rarely wake up again.
It has become clear to me in my years on this job that we need a Code Death.
Until the early 20th century, death was as natural a part of life as birth. It was expected, accepted and filled with ritual. No surprises, no denial, no panic. When its time came, the steps unfolded in a familiar pattern, everyone playing his part. The patients were kept clean and as comfortable as possible until they drew their last breath.
But in this age of technological wizardry, doctors have been taught that they must do everything possible to stave off death. We refuse to wait passively for a last breath, and instead pump air into dying bodies in our own ritual of life-prolongation. Like a midwife slapping life into a newborn baby, doctors now try to punch death out of a dying patient. There is neither acknowledgement of nor preparation for this vital existential moment, which arrives, often unexpected, always unaccepted, in a flurry of panicked activity and distress.
We physicians need to relearn the ancient art of dying. When planned for, death can be a peaceful, even transcendent experience. Just as a midwife devises a birth plan with her patient, one that prepares for the best and accommodates the worst, so we doctors must learn at least something about midwifing death.
For the modern doctor immersed in a culture of default lifesaving, there are two key elements to this skill. The first is acknowledgment that it is time to shift the course of care. The second is primarily technical.
For my three patients on breathing machines, I told their families the sad truth: their loved one had begun to die. There was the usual disbelief. "Can't you do a surgery to fix it?" they asked. "Haven't you seen a case like this where there was a miracle?"

I explained that at this point, the brains of their loved ones were so damaged that they would most likely never talk again, never eat again, never again hug or even recognize their families. I described how, if we continued breathing for them, they would almost definitely be dependent on others to wash, bathe and feed them, how their bodies would develop infection after infection, succumbing eventually while still on life support.
I have yet to meet a family that would choose this existence for their loved one. And so, in each case, the decision was made to take out the tubes.
Now comes the technical part. For each of the three dying patients, I prepped my team for a Code Death. I assigned the resident to manage the airway, and the intern to administer whatever medications might be needed to treat shortness of breath. The medical student collected chairs and Kleenex for the family.
I assigned myself the families. Like a Lamaze coach, I explained what death would look like, preparing them for any possible twist or turn of physiology, any potential movements or sounds from the patient, so that there would be no surprises.
Families were asked to wait outside the room while we prepared to remove the breathing tubes. The nurses cleaned the patients' faces with warm, wet cloths, removing the I.C.U. soot of the previous days. The patients' hair was smoothed back, their gowns tucked beneath the sheets, and catheters stowed neatly out of sight.
Then, the respiratory therapist cut the ties that secured the breathing tube around the patients' neck. As soon as the tubes were removed and airways suctioned, families were invited back into the room. The chairs had been pulled up next to the bed for them and we fell back into an inconspicuous outer circle to provide whatever medical support might be needed.
I stood in the back of the room, using hand motions and quietly mouthing one-word instructions to my team as the scene unfolded — another shot of morphine when breathing worsened, a quick insertion of the suction catheter to clear secretions. We worked like the well-oiled machine of any Code Blue team.
Of those three Code Death patients, one died in the I.C.U. within an hour of the breathing tube's removal. Another lived for several more days in the hospital, symptoms under watch and carefully managed. The third went home on hospice care and died there peacefully the next week, surrounded by family and friends.
I would argue that a well-run Code Death is no less important than a Code Blue. It should become a protocol, aggressive and efficient. We need to teach it, practice it, and certify doctors every two years for it. Because helping patients die takes as much technique and expertise as saving lives.
Jessica Nutik Zitter is an attending physician at Alameda County Medical Center in Oakland, Calif. She is board-certified in both critical-care and palliative-care medicine.

http://phys.org/news/2014-04-romania-ancient-tradition-bee-medicine.html#rssowlmlink

Romania keeps ancient tradition of bee medicine alive

Bee venom to combat multiple sclerosis, pollen for indigestion, honey to heal wounds—the humble bee has been a key source of alternative medicines since ancient times, and Romania is working to keep the tradition of "apitherapy" alive.

The tradition goes back to ancient Greece when Hippocrates applied honey to treat wounds, and the Romans saw pollen as "life-giving". In the past of India, China and Egypt, a resinous substance collected by bees from the buds of certain trees, known as "propolis", was popular as an antiseptic.
"The hive is the oldest and healthiest natural pharmacy," said Cristina Mateescu, director general of the Institute for Apicultural Research and Development in Bucharest.
Today in the wilderness of Romania's Carpathian mountains, honey bee products are still a familiar part of traditional medicine. "In my village, my great-grandmother was a healer and used products from beehives. She inspired me," Dr Mariana Stan told AFP. Having spent years as a conventional doctor, Stan now practises in Bucharest as a "apitherapist"—using bee products "which give slower but longer lasting and more profound results". In a country still infused with folk culture, several families continue to use propolis against sore throats, as well as honey and pollen to boost the immune system.

Apitherapy pioneer

Every town in Romania has its "plafar"—natural pharmacies selling products made from plants, honey, beeswax and propolis. "Romania is a pioneer of apitherapy, which it recognised very early as a component of scientific medicine," said US professor Theodor Charbuliez, head of the Apimondia Commission of Apitherapy, a group that brings together thousands of practitioners from around the world.
Modules on apitherapy have started to work their way into more conventional medical classes and extracts from propolis developed by the Apicultural institute into recognised medicines.
Founded in 1974, the institute employs 105 people who look after local bee colonies and sell around 30 approved products. A new range even seeks to treat cats and dogs with bee-related products.
Bucharest also boasts an Apitherapy medical centre, the world's first, which opened in 1984.

Scepticism remains among the regular medical community in the absence of scientific studies about the effects of bee venom, but many users are full of praise and welcome the cheap costs and environmentally friendly approach.
Doina Postolachi comes twice a week to the medical centre to receive injections of bee venom, or "apitoxin". The 34-year-old poet says the injections have allowed her to "rediscover hope" in her fight against multiple sclerosis. "For a year, I could no longer walk or get into my bath. My feet were stuck to the ground. But today, the venom treatment has given me back strength in my legs. I walk, I can take baths," she said.
She said she has never wanted any regular pharmaceutical treatments "which come with numerous side effects".

Bees do wonders

There has been mounting interest across the world in apitherapy. In 2013, Washington University in the US city of St Louis published a study on the efficacy of milittine, a toxin contained in bee venom, in countering the AIDS virus. In France, thousands of patients have benefited from bandages treated with honey at the abdominal surgery department of Limoges hospital. Bee products are also infiltrating the cosmetics industry, used in skin-toning and anti-wrinkle creams.
Part of the appeal rests with the natural and organic image of bee products. "In Romania, we have the chance to maintain an unspoiled nature," said Cornelia Dostetan, a member of the National Apitherapy Society.
Under Communism, poverty meant that pesticides were rarely used and the country has never shifted to large-scale monoculture forms of agriculture. The result is that Romania retains a great diversity of flora, said Dostetan.
Certified organic, the Romanian brand Apiland, a specialist in raw pollen, has launched its products in France and Italy. According to the last agricultural census in 2010, Romania counted 42,000 beekeepers and more than 1.3 million colonies of bees.
Postolachi says she looks on the bees with "immense gratitude". "These miniscule beings do wonders."

http://www.eurekalert.org/pub_releases/2014-04/sifm-pda041014.php#rssowlmlink

Planaria deploy an ancient gene expression program in the course of organ regeneration

Stowers team develops novel assay to identify genes controlling pharynx regeneration in flatworms

Kansas City, Mo - As multicellular creatures go, planaria worms are hardly glamorous. To say they appear rudimentary is more like it. These tiny aquatic flatworms that troll ponds and standing water resemble brown tubes equipped with just the basics: a pair of beady light-sensing "eyespots" on their head and a feeding tube called the pharynx (which doubles as the excretory tract) that protrudes from a belly sac to suck up food. It's hard to feel kinship with them.
But admiration is another thing, because many planaria species regenerate in wondrous ways—namely, when quartered they reconstruct themselves from the pieces. Sliced through the "waist", they regenerate the missing tail or head; bisected lengthwise, worms duplicate their mirror image. This capacity is not what's surprising, as biologists know that 30% of their body cells are stem cells. The question is, how do stem cells in a planaria fragment know how to generate what's missing?
In the April 15, 2014 issue of the online journal eLife, Stowers Institute for Medical Research Investigator Alejandro Sánchez Alvarado and colleagues address that issue by identifying genes worms use to rebuild an amputated pharynx. They report that near the top of the pharynx regeneration hierarchy is a master regulator called FoxA. These findings support an evolutionarily conserved role for FoxA proteins in driving construction of endoderm-derived organs and reveal how stem cells sense loss of a particular structure on a molecular level.
Mammals can deploy adult stem cells to replace skin or immune system cells, among others. But when it comes to re-creating entire structures, amphibian, fish and planarian species are the champs. "When mammals are severely injured, they just heal the wound and call it a day," says Sánchez Alvarado, who is also a Howard Hughes Medical Institute Investigator. "But if a salamander loses a limb, it will first heal the wound and then start assembling the missing parts. Right now, the mechanisms cells use to realize what structure is missing and then restore it remain completely mysterious."
To unravel the mystery, the team conducted two "screens". First, they amputated the worm pharynx, which prohibits feeding for about a week as planaria rebuild a new one. Around day 3 post-amputation, the team conducted microarray analysis to identify any gene switched on by amputation and amassed about 350 candidates. To test them, they then fed inhibitory RNAs designed to suppress expression of each gene separately to new batches of worms, repeated the amputations and observed whether worms regained feeding ability. That narrowed the list to 20 candidates that when lost hampered feeding and in most cases interfered with pharynx formation.

According to Carrie Adler, Ph.D., a postdoctoral fellow in the Sánchez Alvarado lab who led the study, analysis showed most of the 20 factors either had a generic function in stem cells (which was interesting but not what they were after) or were specifically required for pharynx regeneration. Among the latter, one factor showing a particularly robust effect was a DNA-binding protein called FoxA. "Targeting FoxA completely blocked pharynx regeneration but had no effect on the regeneration of other organs," says Adler.

High resolution microscopy analysis showed that stem cells ramped up FoxA expression soon after they converged on the amputation site. "Currently, we think that FoxA triggers a cascade of gene expression that drives stem cells to produce all of the different cells of the pharynx, including muscle, neurons, and epithelial cells," says Adler. "The next question is how FoxA gets stimulated in the first place in only some stem cells."

Researchers knew previously that during embryogenesis FoxA initiates formation of endoderm-derived organs in species as diverse as mouse and roundworms. The new work suggests that regenerating tissues exploit those evolutionarily ancient gene expression pathways. "Engulfing food is one thing that defines an animal," says Sánchez Alvarado. "This means that organisms from humans to flatworms use a common toolbox to build a digestive system, one that has been shared since animals became multicellular."

A fortuitous (in hindsight) setback facilitated the work. As a graduate student studying the roundworm C. elegans, Adler decided to test effects of roundworm anesthetics on flatworms. One, a sodium azide bath, put planaria to sleep but made their pharynxes drop off. Aghast, Adler soon realized that the azide solution (which planaria survived) left a uniform, minimally-destructive lesion. Thus was born the "selective chemical amputation method", allowing large-scale analysis and reliable quantification of results and freeing researchers from tedious hours at a dissecting microscope.

But why go to such trouble to pioneer regeneration research in small animal models? The answer is obvious to both Adler and Sánchez Alvarado. "Because regeneration is limited and difficult to study in humans and mice," Adler says. "Planaria have infinite capacity to regrow all organs. By understanding this enhanced ability we may learn how to accelerate mammalian regeneration."

Sánchez Alvarado concludes that the work cements planaria's place as a tractable model system to analyze regeneration or stem cell activity. "Planaria's simplicity is what makes it such a fruitful system to answer questions relevant to regeneration," he says. "If we used salamanders for these studies it would take 90 days to do an experiment. I want answers to these questions yesterday, not years from now."

Also contributing to the all-Stowers study were Genomics Scientist Chris Seidel, Ph.D., and Sean McKinney, Ph.D., of the Microscopy Center.

The Stowers Institute for Medical Research, the National Institutes of Health, and the Howard Hughes Medical Institute funded the study.

http://www.eurekalert.org/pub_releases/2014-04/cp-rft040314.php#rssowlmlink

Researchers find that influenza has an Achilles' heel

Flu epidemics cause up to half a million deaths worldwide each year, and emerging strains continually threaten to spread to humans and cause even deadlier pandemics.

A study published by Cell Press on April 10 in the journal Immunity reveals that a drug that inhibits a molecule called prostaglandin E2 (PGE2) increases survival rates in mice infected with a lethal dose of the H1N1 flu virus. The findings pave the way for an urgently needed therapy that is highly effective against the flu virus and potentially other viral infections.

"Drugs that specifically target PGE2 pathways have already been developed and tested in animals, so our results have excellent potential for clinical translation, not only for the treatment of influenza, but also other viral respiratory infections that interact with similar host immune pathways," says senior study author Maziar Divangahi of McGill University.

Despite the worldwide use of vaccination and other antiviral interventions, the flu virus remains a persistent threat to human health. To investigate molecular pathways that could be targeted by novel interventions, Divangahi and his team became interested in ibuprofen, which is commonly used to manage flu-like symptoms. By inhibiting a molecule called cyclooxygenase (COX), ibuprofen and other nonsteroidal anti-inflammatory drugs (NSAIDs) lower the production of prostaglandins—immune molecules that contribute to pain and fever. But COX inhibition has produced conflicting effects on immune responses and survival rates in animals infected with the flu virus, highlighting the importance of clarifying the role of prostaglandins in antiviral immunity.

In the new study, Divangahi and his team found that mice genetically engineered to lack PGE2 showed enhanced immune responses, lower viral levels in the lungs, and better survival rates following infection with a lethal dose of the H1N1 flu virus compared with infected mice that were not genetically modified. Similarly,

mice treated with a compound that inhibits PGE2 showed enhanced antiviral immunity and survival rates following infection with a lethal dose of the flu virus compared with untreated mice.
"We believe that previous studies produced conflicting results because COX inhibition affects all prostaglandins, not just PGE2," Divangahi says. "Our findings suggest that different prostaglandins have different roles in antiviral immunity and that specific inhibition of PGE2 will be much more effective than NSAIDs at protecting against influenza infection."
Immunity, Coulombe et al.: "Targeted Prostaglandin E2 Inhibition Enhances Anti-Viral Immunity through Induction of Type I Interferon and Apoptosis in Macrophages."

http://www.eurekalert.org/pub_releases/2014-04/p-umt040314.php#rssowlmlink

Using mathematics to beat jetlag effectively

Our "internal clock" is predicted to shift more rapidly than previously thought.

In a study published in PLOS Computational Biology on April 10th, researchers present schedules of light exposure that may shift our circadian clock in the minimum time, simply by adjusting the timing of the beginning and end of each day. The authors calculated optimal schedules for thousands of different situations, and condensed their findings into four general principles of optimal circadian shifting.
"Overcoming jetlag is fundamentally a math problem and we've calculated the optimal way of doing it," said study author Danny Forger, of the University of Michigan, USA. "We're certainly not the first people to offer advice about this, but our predictions show the mathematically best and quickest ways to adjust across time zones."
The schedules presented are simple to follow, in that they involve only a single daily light exposure, and that they are predicted to produce the same results even in the presence of unpredictable factors.
The work could provide insights to help improve the health and quality of life for pilots and flight attendants as well as shift workers, which make up more than 10 percent of the American workforce. Based on their findings, the authors have created an app, 'Entrain', which is available for free via the Apple store.
Financial disclosure This work was supported by AFOSR grant FA9550-11-1-0165 and internal funds from the University of Michigan. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. ***Competing interests:*** *The authors have declared that no competing interests exist.*
Citation: Serkh K, Forger DB (2014) Optimal Schedules of Light Exposure for Rapidly Correcting Circadian Misalignment.
PLoS Comput Biol 10(3): e1003523.doi:10.1371/journal.pcbi.1003523

http://www.eurekalert.org/pub_releases/2014-04/jhm-gt040714.php#rssowlmlink

Getting to the root of Parkinson's disease

Working with human neurons and fruit flies, researchers at Johns Hopkins have identified and then shut down a biological process that appears to trigger a particular form of Parkinson's disease present in a large number of patients.

A report on the study, in the April 10 issue of the journal Cell, could lead to new treatments for this disorder.
"Drugs such as L-dopa can, for a time, manage symptoms of Parkinson's disease, but as the disease worsens, tremors give way to immobility and, in some cases, to dementia. Even with good treatment, the disease marches on," says Ted Dawson, M.D., Ph.D., professor of neurology and director of the Johns Hopkins Institute for Cell Engineering,
Dawson says the new research builds on a growing body of knowledge about the origins of Parkinson's disease, whose symptoms appear when dopamine-producing nerve cells in the brain degenerate. Further evidence for a role of genetics in Parkinson's disease appeared a decade ago when researchers identified key mutations in an enzyme known as leucine-rich repeat kinase 2, or LRRK2 — pronounced "lark2." When that enzyme was cloned, Dawson, together with his wife and longtime collaborator Valina Dawson, Ph.D., professor of neurology and member of the Institute for Cell Engineering, discovered that LRRK2 was a kinase, a type of enzyme that transfers phosphate groups to proteins and turns proteins on or off to change their activity.
Over the years, it was found that blocking kinase activity in mutated LRRK2 halted degeneration, while enhancing it made things worse. But nobody knew what proteins LRRK2 was acting on.
"For nearly a decade, scientists have been trying to figure out how mutations in LRRK2 cause Parkinson's disease," said Margaret Sutherland, Ph.D., a program director at the National Institute of Neurological Disorders and Stroke. "This study represents a clear link between LRRK2 and a pathogenic mechanism linked to Parkinson's disease."
Dawson went fishing for the right proteins using LRRK2 as bait. When his team began to identify those proteins, Dawson says they were surprised to discover that many were linked to the cellular machinery, like ribosomes, that make proteins. Nobody, says Dawson, suspected that LRRK2 might be involved at such a basic level as protein manufacture.

Unsure if they were right, the team then tested the proteins they identified to see which of them, if any, LRRK2 could add phosphate groups to. They came up with three ribosomal protein candidates — s11, s15 and s27. They then altered each ribosomal protein to see what would happen. It turned out that mutating s15 in a manner that blocked LRRK2 phosphorylation protected nerve cells taken from rats, humans and fruit flies from death. In other words, s15 appeared to be the much sought-after target of LRRK2, Dawson says.
"When you go fishing, you want to catch fish. We just happened to catch a big one," Dawson says.
With the protein now identified, Dawson's team is tackling further experiments to find out how excess protein production causes dopamine neurons to degenerate. And they want to see what happens when they block LRRK2 from phosphorylating the s15 protein in mice, to build on their findings from fruit flies and nerve cells grown in a dish.
"There's a big chasm between animal disease models and human treatments," says Ian Martin, Ph.D., a neuroscientist in Dawson's lab and the lead author on the paper. "But it's exciting. I think it definitely could turn into something real, hopefully in my lifetime."

Other authors on the paper include Jungwoo Wren Kim, Byoung Dae Lee, Hochul Kang, Jin-Chong Xu, Hao Jia, Jeannette Stankowski, Min-Sik Kim, Jun Zhong, Manoj Kumar, Shaida Andrabi, Yulan Xiong, Dennis Dickson and Akhilesh Pandey from the Johns Hopkins University School of Medicine and Zbigniew Wszolek of the Mayo Clinic.
The Johns Hopkins University is part of the Morris K. Udall Centers of Excellence for Parkinson's Disease. This work was supported by the National Institute of Neurological Disorders and Stroke (P50 NS038377 and P50 NS072187), the JPB Foundation, the Maryland Stem Cell Research Fund, the Adrienne Helis Malvin Medical Research Foundation and the Diana Helis Henry Medical Research Foundation.
Funding for a portion of the research described in this article was provided by Merck KGAA. Under a licensing agreement between Merck KGAA and The Johns Hopkins University, Dawson and the university shared fees received by the university on licensing of some of the reagents described in this article. Dawson was also a paid consultant to Merck KGAA. The terms of this arrangement are being managed by The Johns Hopkins University in accordance with its conflict of interest policies.

http://bit.ly/1gqwJYk

Engineered vaginas grown in women for the first time

Vaginas grown in a lab from the recipients' own cells have been successfully transferred to the body for the first time.

23:30 10 April 2014 by Catherine de Lange

The surgery was carried out on four women who were born without vaginal canals because of a rare condition. The women, who were teenagers at the time of the operation, now have fully functioning sexual organs.
"After the operation they were able to function normally. They had normal levels of desire, arousal, satisfaction and orgasm," says Anthony Atala at Wake Forest School of Medicine in North Carolina, who led the research. He published the results only after four to eight years had elapsed following surgery, enough time for him to be sure there were no long-term complications.

Video: ***Vagina grown in the lab from the recipient's own cells***

The four women had undeveloped vaginas because they all have a severe form of a condition called Mayer-Rokitansky-Küster-Hauser Syndrome (MKRH), which affects about 1 in 5000 women. They also had some abnormal development of the uterus, although they did have a vulva – the external part of the sex organ which includes the labia and the clitoris. They were not able to have penetrative sex or menstruate. One of the women was diagnosed after her menstrual blood had collected in her abdomen.
As well as having physical implications, a diagnosis of MKRH is also a huge psychological burden for women.

Maturity challenge

Building on techniques the group developed in the 1990s and perfected on rabbits, Atala and his colleagues removed a small part of the vulva from each woman and grew the cells in the lab. After about four weeks they had enough cells to begin to lay them on to a degradable scaffold one layer at a time "like the layers of a cake", he says. The challenge was how to get the cells to grow to the right level of maturity in the lab, says Atala. You need to make sure that the cells are mature enough so that when you implant them into the body, they can recruit other cells in the body to form tissue that includes nerves and blood vessels.
Working with surgeons at the Federico Gomez Children's Hospital of Mexico in Mexico City, Atala's team used MRI scans to calculate the appropriate shape and size of the scaffolds for each patient. After cells had established themselves on these scaffolds, surgeons created a cavity in the abdomen and inserted the engineered vagina. It was then stitched in place, connected at the top to the uterus.

The women used a stent for six weeks to make sure the structure maintained the right shape. The scaffold was made of a collagen matrix and degraded spontaneously over the months following surgery. In that time, the implanted cells matured into the normal tissue of the vaginal wall, including the right layers of muscle and epithelial cells (see video). The vagina was fully developed after six months, and the women were able to menstruate and have sex.

Better than a skin graft

Atala hopes that in the future, the technique could be used to treat not only women who have congenital vaginal defects but also those who have suffered damage through trauma – for instance, because of a car accident or cancer.

Currently it is possible to surgically create vaginas using grafts from either intestinal or skin tissue, but these can lead to severe complications. Skin cell grafts do not provide lubrication which causes pain during sex, and can thicken to the point where the vagina closes. Intestinal cells secrete mucus constantly, which is unhygienic and causes an unpleasant odour. Using the women's own cells from the vulva gets around these issues.

Knowing that the engineered tissue originates from the recipient's own body can be reassuring for them, says Sylvie Miot at the University of Basel, Switzerland, whose team has also successfully engineered new nostrils for patients who had to have skin cancers removed from their nose. Their findings are being published in the same issue of the Lancet. Both studies involved small numbers of patients, but they provide the first strong evidence that nerve and blood vessels can reconnect to large patches of bioengineered tissues directly inside the body.

Normal life

The findings also show that lab-engineered organs can grow to maturity healthily inside the body, says Martin Birchall at University College London. The women were aged between 13 and 18 years old when the surgery took place so their bodies were still developing. Birchall, who pioneered the first transplant of a human windpipe using the recipient's stem cells, calls the results "very meaningful".

One of the recipients, who wished to remain anonymous, said the treatment opened up new possibilities. "I truly feel fortunate, because I'll have a normal life – completely normal," she says. "It's important to let other girls that have the same problem know that it does not end knowing that you have the disease, because there is a treatment."

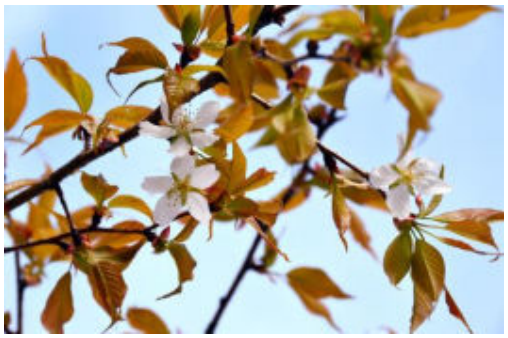
Two of the four women have a functional uterus, so the big question is whether they will be able to have children. "They haven't tried," says Atala, "but they can ovulate, so there is no reason to suspect that they cannot."

Journal references: The Lancet, DOI: 10.1016/S0140-6736(14)60542-0 and 10.1016/S01460544-4

http://phys.org/news/2014-04-cherry-tree-space-mystery-baffles.html#rssowlmlink

'Cherry tree from space' mystery baffles Japan

A cosmic mystery is uniting monks and scientists in Japan after a cherry tree grown from a seed that orbited the Earth for eight months bloomed years earlier than expected—and with very surprising flowers.



The four-year-old sapling - grown from a cherry stone that spent time aboard the International Space Station (ISS) - burst into blossom on April 1, possibly a full six years ahead of Mother Nature's normal schedule.

Its early blooming baffled Buddhist brothers at the ancient temple in central Japan where the tree is growing.

"We are amazed to see how fast it has grown," Masahiro Kajita, chief priest at the Ganjoji temple in Gifu, told AFP by telephone. "A stone from the original tree had never sprouted before. We are very happy because it will succeed the old tree, which is said to be 1,250 years old."

A cherry tree in bloom, grown from a cherry pit that spent time onboard the International Space Station (ISS), is shown at the Ganjoji temple in Gifu city, central Japan, April 3, 2014

The wonder pip was among 265 harvested from the celebrated "Chujo-hime-seigan-zakura" tree, selected as part of a project to gather seeds from different kinds of cherry trees at 14 locations across Japan.

The stones were sent to the ISS in November 2008 and came back to Earth in July the following year with Japanese astronaut Koichi Wakata, after circling the globe 4,100 times.

Some were sent for laboratory tests, but most were ferried back to their places of origin, and a selection were planted at nurseries near the Ganjoji temple.

By April this year, the "space cherry tree" had grown to around four metres (13 feet) tall, and suddenly produced nine flowers—each with just five petals, compared with about 30 on flowers of the parent tree. It normally takes about 10 years for a cherry tree of the similar variety to bear its first buds.
The Ganjoji temple sapling is not the only early-flowering space cherry tree.
Of the 14 locations in which the pits were replanted, blossoms have been spotted at four places. Two years ago, a young tree bore 11 flowers in Hokuto, a mountain region 115 kilometres (70 miles) west of Tokyo, around two years after it was planted. It was of a variety that normally only comes into flower at the age of eight.

Cosmic rays

The seeds were sent to the ISS as part of "an educational and cultural project to let children gather the stones and learn how they grow into trees and live on after returning from space," said Miho Tomioka, a spokeswoman for the project's organiser, Japan Manned Space Systems (JAMSS). "We had expected the (Ganjoji) tree to blossom about 10 years after planting, when the children come of age," she added.
Kaori Tomita-Yokotani, a researcher at the University of Tsukuba who took part in the project, told AFP she was stumped by the extra-terrestrial mystery. "We still cannot rule out the possibility that it has been somewhat influenced by its exposure to the space environment," she said.
Tomita-Yokotani, a plant physiologist, said it was difficult to explain why the temple tree has grown so fast because there was no control group to compare its growth with that of other trees. She said cross-pollination with another species could not be ruled out, but a lack of data was hampering an explanation.
"Of course, there is the possibility that exposure to stronger cosmic rays accelerated the process of sprouting and overall growth," she said. "From a scientific point of view, we can only say we don't know why."
Wakata is back aboard the ISS, where he is in command of the station. The astronaut took part in a video link-up on Thursday with Japanese Prime Minister Shinzo Abe and US Ambassador to Japan Caroline Kennedy, chatting about his daily life hundreds of kilometres above the Earth.

http://www.eurekalert.org/pub_releases/2014-04/mu-otg041114.php#rssowlmlink

Odds that global warming is due to natural factors: Slim to none

Statistical analysis rules out natural-warming hypothesis with more than 99 percent certainty

An analysis of temperature data since 1500 all but rules out the possibility that global warming in the industrial era is just a natural fluctuation in the earth's climate, according to a new study by McGill University physics professor Shaun Lovejoy.
The study, published online April 6 in the journal Climate Dynamics, represents a new approach to the question of whether global warming in the industrial era has been caused largely by man-made emissions from the burning of fossil fuels. Rather than using complex computer models to estimate the effects of greenhouse-gas emissions, Lovejoy examines historical data to assess the competing hypothesis: that warming over the past century is due to natural long-term variations in temperature.
"This study will be a blow to any remaining climate-change deniers," Lovejoy says. "Their two most convincing arguments – that the warming is natural in origin, and that the computer models are wrong – are either directly contradicted by this analysis, or simply do not apply to it."
Lovejoy's study applies statistical methodology to determine the probability that global warming since 1880 is due to natural variability. His conclusion: the natural-warming hypothesis may be ruled out "with confidence levels great than 99%, and most likely greater than 99.9%."
To assess the natural variability before much human interference, the new study uses "multi-proxy climate reconstructions" developed by scientists in recent years to estimate historical temperatures, as well as fluctuation-analysis techniques from nonlinear geophysics.
The climate reconstructions take into account a variety of gauges found in nature, such as tree rings, ice cores, and lake sediments. And the fluctuation-analysis techniques make it possible to understand the temperature variations over wide ranges of time scales.
For the industrial era, Lovejoy's analysis uses carbon-dioxide from the burning of fossil fuels as a proxy for all man-made climate influences – a simplification justified by the tight relationship between global economic activity and the emission of greenhouse gases and particulate pollution, he says. "This allows the new approach to implicitly include the cooling effects of particulate pollution that are still poorly quantified in computer models," he adds.
While his new study makes no use of the huge computer models commonly used by scientists to estimate the magnitude of future climate change, Lovejoy's findings effectively complement those of the International Panel on Climate Change (IPCC), he says. His study predicts, with 95% confidence, that a doubling of carbon-dioxide levels in the atmosphere would cause the climate to warm by between 2.5 and 4.2 degrees Celsius. That range is

more precise than – but in line with -- the IPCC's prediction that temperatures would rise by 1.5 to 4.5 degrees Celsius if CO2 concentrations double.
"We've had a fluctuation in average temperature that's just huge since 1880 – on the order of about 0.9 degrees Celsius," Lovejoy says. "This study shows that the odds of that being caused by natural fluctuations are less than one in a hundred and are likely to be less than one in a thousand. "While the statistical rejection of a hypothesis can't generally be used to conclude the truth of any specific alternative, in many cases – including this one – the rejection of one greatly enhances the credibility of the other."
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EMA: Don't Combine ARBs, ACE Inhibitors, and Direct Renin Inhibitors

No two drug classes that act separately on the renin-angiotensin system (RAS) should be used in combination, the European Medicines Agency (EMA) warned today[1].

Shelley Wood

LONDON, UK - According to the European drug regulator, angiotensin-receptor blockers (ARBs), ACE inhibitors, and direct renin inhibitors should not routinely be used in combination. In particular, patients with diabetic nephropathy should not be given an ARB with an ACE inhibitor, the agency concluded.
The recommendation from the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) comes after a 10-month review, first reported by **heart*wire*** last May. A final decision rests with the Committee for Medicinal Products for Human Use (CHMP), which typically adopts the PRAC recommendation.
"Where such combination (dual blockade) is considered absolutely necessary, it must be carried out under specialist supervision with close monitoring of kidney function, fluid and salt balance, and blood pressure," an EMA press release states. This includes the licensed use of the ARBs **candesartan** or **valsartan** as add-on therapy to ACE inhibitors in patients with heart failure in whom the combination is deemed necessary, the statement adds. "The combination of **aliskiren** (Tekturna, Novartis) with an ARB or ACE inhibitor is strictly contraindicated in those with kidney impairment or diabetes."
Concerns over the combined use of these drug classes stems from a large meta-analysis by Makani et al, with senior author **Dr Franz Messerli** (St Luke-Roosevelt Hospital, New York), published last year in *BMJ*. The analysis was a follow-up to a viewpoint Messerli published in 2009, calling for physicians to stop using dual RAS blockade in clinical practice, based on a signal of harm seen in the **ONTARGET** study.
Key risks of combining several RAS-acting agents include hyperkalemia, low blood pressure, and worsening of kidney function compared with using one of these medicines alone, without a corresponding improvement in the anticipated clinical benefits of enhanced BP lowering, the EMA statement notes.
The **2014 Evidence Based Guidelines for the Management of High Blood Pressure in Adults** (published by the majority of panel members from the **Eighth Joint National Committee**, but not officially the "JNC8 guidelines") specifically state that ACE inhibitors and ARBs should not be used in combination.
The US **Food and Drug Administration** (FDA), however, has not reviewed the concerns or issued any warnings on the combined use of these drug classes. By contrast, the **Canadian Heart and Stroke Foundation** issued a guideline alert back in 2009 advising patients to see their family physicians as soon as possible to get their treatment changed if they were taking both an ARB and an ACE inhibitor.
Back in 2012, both the FDA and EMA formally warned against the use of the direct renin inhibitor aliskiren in combination with an ACE inhibitor or ARB.
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http://www.scientificamerican.com/article/ohio-links-fracking-to-earthquakes-announces-tougher-rules/

Ohio Links Fracking to Earthquakes, Announces Tougher Rules

Recent small earthquakes in Ohio were likely triggered by fracking, state regulators said on Friday, a new link that could have implications for oil and gas drilling in the Buckeye State and beyond.

By Edward McAllister

New York (Reuters) - In the strongest wording yet from the state linking energy drilling and quakes, the Ohio Department of Natural Resources (ODNR) said that injecting sand, water and chemicals deep underground to help release oil and gas may have produced tremors in Poland Township last month.
The statement, in which the department announced stricter rules for oil and gas exploration in areas where seismic activity has occurred, comes after a steep rise in earthquakes in Ohio and other areas where intense drilling has taken place.

Most earthquakes occur naturally, but scientists have long linked some smaller tremors to oil and gas work underground, which can alter pressure points and cause shifts in the earth. Last month, drilling and fracking was suspended near the site of two earthquakes in Poland Township in the northeast of the state, 70 miles southeast of Cleveland, the first of which was magnitude 3.0, enough to be felt for miles around.

Earthquakes rattled residents in Oklahoma last weekend, the latest in a series that have put the state on track for record quake activity this year, which some seismologists say may be tied to oil and gas exploration.

"Regarding the seismic events in Poland Township, ODNR geologists believe the sand and water injected into the well during the hydraulic fracturing process may have increased pressure on an unknown microfault in the area," ODNR said in a statement.

Friday's statement could have impacts not just for a state where a drilling boom is under way, but in other regions where concerns have emerged about the impact of fracking on fault lines. The new rules require a company to install seismic monitors if it is drilling within three miles of a known fault or an area which has recently experienced quakes, the ODNR said. It is unclear how much drilling will be affected by the new rules.

Hilcorp Energy, the company that was drilling near the quakes in Poland Township in March, cannot resume operations until it submits a new plan convincing regulators that drilling is safe, an agency spokesman said. Hilcorp was not immediately available to comment.

The department had not previously linked earthquakes to fracking, which involves fracturing rock by creating a series of small blasts thousands of feet below the surface, but the new data gave it "reasonable certainty" that fracking was the cause, the agency spokesman said.

"It is significant that they have acknowledged that there is a connection between fracking and earthquakes," said Ray Beiersdorfer, professor of geology at Youngstown State University in Ohio.

The disposal of drilling wastewater in rockbed deep underground has been linked by geologists to earthquakes, sucah as the 4.0 magnitude one experienced on New Year's Eve 2011 in Youngstown, but opinion is divided about whether fracking itself can cause quakes, and if it can trigger more than just small tremors.

While there are concerns about the environmental impact of injecting chemical-laced water into the ground, including on freshwater supplies, they are spreading to include the effect on fault lines than run beneath the surface, often undetected.

Worries surrounding seismic activity emerged in Ohio in 2011 when a spate of small quakes followed the beginning of intensive drilling in the Utica shale. More than 800 wells have been drilled in the Ohio portions of the Utica and the Marcellus shales, two major gas deposits that have helped transform the U.S. energy market. Once a regular importer of gas from overseas, the United States is set to export gas for the first time to countries across the globe.

"The steps announced today to protect communities from seismic events are reasonable precautions," said Scott Anderson, a policy advisor at the Environmental Defense Fund. "Although there is much uncertainty regarding what causes earthquakes ... the state's decisive action is based on the best information available."

http://www.eurekalert.org/pub_releases/2014-04/uoth-hct041014.php#rssowlmlink

Hepatitis C treatment cures over 90 percent of patients with cirrhosis

Oral combination proves safe for patients who could not have interferon therapy

San Antonio, Texas - Twelve weeks of an investigational oral therapy cured hepatitis C infection in more than 90 percent of patients with liver cirrhosis and was well tolerated by these patients, according to an international study that included researchers from UT Medicine San Antonio and the Texas Liver Institute. Historically, hepatitis C cure rates in patients with cirrhosis (liver scarring) have been lower than 50 percent and the treatment was not safe for many of these patients.

Hepatitis C virus is the No. 1 driver of cirrhosis, liver transplants and liver cancer in the United States, noted Fred Poordad, M.D., lead author on the study, which was released Saturday by The New England Journal of Medicine in conjunction with Dr. Poordad's presentation of the data at the International Liver Congress in London. UT Medicine is the clinical practice of the School of Medicine at The University of Texas Health Science Center at San Antonio, where Dr. Poordad is a professor of medicine. He is vice president of the Texas Liver Institute in San Antonio.

Interferon previously was the only agent to show effectiveness against hepatitis C, but patients often relapsed and the therapy caused multiple side effects. The new regimen is interferon-free and consists of several agents — ABT-450/ritonavir, ombitasvir, dasabuvir and ribavirin. Twelve weeks after the last dose, no hepatitis C virus was detected in the bloodstream of 91.8 percent of patients who took the pills for 12 weeks. Among patients treated for 24 weeks, 95.9 percent were virus-free 12 weeks after the end of therapy.

"These are out-of-the-ballpark response rates, not on the same planet as interferon," Dr. Poordad said. "The reason this study is so profound is because interferon is not tolerated nor is it safe in many people with cirrhosis. Many of the patients with cirrhosis in this study were not even eligible to be treated with interferon."
One of those patients was retired San Antonio anesthesiologist Sergio Buentello, M.D. Diagnosed with hepatitis C infection 11 years ago, Dr. Buentello had treatment with side effects and no cure eight years ago. "My viral count came down, but never to zero," he said.
When Eric Lawitz, M.D., of the Texas Liver Institute told him of the possibility of treatment with the new therapy, Dr. Buentello said he was skeptical. But as for so many others, the therapy worked. "I feel very lucky to be living in this time, because I was almost resigned to the idea that I could never be cured," Dr. Buentello said. The study examined outcomes in 380 patients at 78 sites, including hospitals and centers in Spain, Germany, England, Canada and the U.S. The biopharmaceutical company AbbVie provided support.
Investigators are cataloging patient blood samples for three years after therapy and so far have noticed no long-term, late relapses, Dr. Poordad said. "Patients with advanced liver disease can now be cured of their hepatitis with a very well-tolerated and short regimen," he said. The combination medication regimen is expected to be on the market as early as the end of 2014 or very early 2015.

http://www.eurekalert.org/pub_releases/2014-04/eaft-gm041114.php#rssowlmlink

Gut microbiota may play a role in the development of alcoholic liver disease

Exciting new data presented today at the International Liver Congress™ 2014 shows that the gut microbiota has a potential role in the development of alcoholic liver disease (ALD).[1]

London, UK - Though an early stage animal model, the French study highlights the possibility of preventing ALD with faecal microbiota transplantation – the engrafting of new microbiota, usually through administering human faecal material from a healthy donor into the colon of a recipient.[2]
In the study, two groups of germ-free mice received gut microbiota transplants from human representatives; one set from a patient with severe alcoholic hepatitis, the other from a patient with a history of alcohol abuse but without alcoholic hepatitis. The two sets of germ-free mice were then fed a liquid alcoholic diet.
The group that received microbiota from the patient with severe alcoholic hepatitis developed a more severe liver injury and a higher disruption of the intestinal mucosa in direct comparison to the group that received microbiota from the patient without severe alcoholic hepatitis. The study also identified two Clostridium bacteria that were able to produce ethanol in vitro and that were systematically associated with intestinal microbiota associated liver injury.
EASL Scientific Committee Member Prof. Frank Lammert commented: "Among heavy drinkers, the severity of alcoholic liver disease does not strictly correlate with the amount of alcohol intake, meaning that other factors must be influencing its development."
"These findings provide first evidence for a causal role of gut microbiota in alcohol-induced inflammation, and open up new avenues for the treatment of alcoholic liver disease with potentially better patient outcomes." At present, intestinal microbiota is considered to constitute a "microbial organ": one that has pivotal roles in the body's metabolism as well as immune function. Therefore transplantation aims to restore gut functionality and re-establish the homoestasis of intestinal flora.
The study was developed by an INRA-Micalis and INSERM/Paris-South University/Antoine-Béclère hospital collaboration.
Disclaimer: the data referenced in this release is based on the submitted abstract. More recent data may be presented at the International Liver Congress™ 2014.
[1]. M. Llopis et al. Intestinal Dysbiosis Explains Inter-Individual Differences In Susceptibility To Alcoholic Liver Disease. Abstract presented at the International Liver Congress™ 2014
[2]. Khoruts A and Sadowsky MJ, Therapeutic transplantation of the distal gut microbiota. Mucosal Immunology 2011; 4: 4-7

http://bit.ly/1epqAwN

Japan orders slaughter of 112,000 chickens after H5 strain of bird flu detected

Japan has ordered the slaughter of some 112,000 chickens after officials confirmed Sunday bird flu infections at a poultry farm in the south.

Tokyo (AFP) - DNA tests confirmed the H5 strain of the virus at a farm in Kumamoto prefecture that kept 56,000 birds, after its owner reported Saturday a lot of sudden deaths among his poultry, the agriculture ministry said in a statement.
Officials also ordered the culling of another 56,000 birds at a separate farm run by the same owner after treating it as a location of possible infections, the ministry said.
It was the first confirmed outbreak of bird flu in Japan in three years.

The ministry has however been warning farmers about infection risks, citing the continued spread of the disease in Asia, including neighbouring South Korea.
Local authorities on Saturday banned movement of chickens from the two affected farms as well as other farms in their vicinities. Authorities were sanitising areas around the two farms and testing birds at other area farms.
Officials were also setting up areas to disinfect vehicles travelling on major roads around the affected farms to prevent the virus from spreading further.
The government will dispatch a team of officials and experts to identify the cause of the latest infections and to assist local authorities to take necessary measures.
Chief Cabinet Secretary Yoshihide Suga held a meeting with selected ministers, including Agriculture Minister Yoshimasa Hayashi, to discuss the outbreak.
"The government will take thorough measures to prevent wider infections," Suga told the meeting.

http://www.bbc.com/news/health-26986117##rssowlmlink

Why insurers should fund medical research

Financial belts are being tightened in many areas - including medical research. But scientists say funding for such work is crucial, for the UK's research industry as well as for patients.

By Dr John Moore-Gillon British Lung Foundation

In this week's Scrubbing Up, Dr John Moore-Gillon, a respiratory health expert and honorary medical adviser at the British Lung Foundation, suggests the solution in the case of the asbestos-related cancer, mesothelioma, could be to turn to the insurance industry - and that this could be a model for supporting other areas of research.
Each year, the insurance industry pays out hundreds of millions of pounds in compensation to people who have developed mesothelioma - a cancer of the outer covering of the lung - as a result of exposure to asbestos at work.
With the UK having the highest rates of mesothelioma in the world, it is estimated that these payments will cost the insurance industry in excess of £11bn over the coming years.
A far more profound cost is borne, though, by those actually living with this often very painful disease.
With no cure and little by way of effective treatments, mesothelioma can act with devastating speed.
Fewer than one in 10 sufferers are alive just three years after diagnosis, and many survive just a matter of months.

'Loose change'

Compensation can help a family cope financially, but nothing makes up for the loss of a loved one.
Well-funded medical research is essential if this situation is to improve - but such funding remains shamefully low, with that for mesothelioma lagging well behind levels invested in diseases, like skin cancer, that kill similar numbers of people.
With about 60,000 people expected to die of mesothelioma in the UK over the next 30 years unless new treatments are found, the need to address this funding shortfall is urgent.
But with public finances still tight, the key question is: how can we afford this extra investment without cutting back elsewhere?
One solution is to work with the insurance industry. If, each year, insurers invested in mesothelioma research just a tiny fraction of the amount they will end up paying out in compensation - for example, just 0.05% of that £11bn - it would absolutely transform mesothelioma research.
What is loose change for a multi-billion pound global industry could prove life-saving for thousands.
And what is more, as treatments improve, and more mesothelioma patients live healthy, fulfilling and economically productive lives, the amount of compensation insurers would have to pay out would fall.
It's a win-win situation that should save the industry money.

'An outstanding opportunity'

This principle of turning potential private sector beneficiaries into benefactors may sound unorthodox.
However, I believe such approaches to medical research funding will be crucial in future, not only to cope with the burgeoning health problems presented by our ageing population and modern lifestyle, but to ensure that diseases like mesothelioma aren't neglected.
Of course, it wouldn't address all our research-funding needs, across all disease areas.
And making it work will require a level of co-operation between politicians and industry that, frustratingly, we haven't yet seen for mesothelioma, even though both sides publicly support a deal.
However, with mesothelioma, we have an outstanding opportunity.
If government and industry pass this test, it may not only help the tens of thousands of people who will otherwise die of mesothelioma over the coming years it could also fundamentally change, in the long term, the way we think about funding medical research.

http://phys.org/news/2014-04-japan-stem-cell-body-splashes.html#rssowlmlink

Japan stem cell body splashes cash on luxury furniture

A publicly-funded research institute in Japan, already embattled after accusing one of its own stem cell scientists of faking data, has spent tens of thousands of dollars on designer Italian furniture, reportedly to use up its budget.

The respected Riken Institute, headed by Nobel chemistry laureate Ryoji Noyori, spent almost 10 million yen ($100,000) on two shopping sprees in March 2011 at Cassina Ixc., a maker and importer of top-range furniture, publicly-released information shows.

In its latest edition, Shukan Bunshun magazine cites a former Riken researcher as saying the lavish spending was part of a drive to use up its approximately 100 billion yen budget before the April 1 end of the fiscal year.

"When I was at the institute, it was having a tough time spending its budget within a fiscal year, so it would frequently do interior renovations," the researcher, who was not identified, was quoted as saying.

A Riken spokesman said the furniture was appropriate for a building that receives "guests from overseas".

"The building where the furniture is located was completed in February of that year, and the furniture was ordered to be on schedule for the completion of the new building," he said.

The luxurious furniture was purchased for the stem cell research and development facilities in western Kobe city, where under-fire Haruko Obokata is accused of fabricating data.

Obokata was feted as a modern-day Marie Curie after unveiling research that showed a simple way to re-programme adult cells to become a kind of stem cell, a breakthrough that could provide a ready supply of the base material for transplant tissue.

But Riken has since distanced itself from the study, which was published in the British journal Nature, after it came to light that some of Obokata's data was faulty.

The 30-year-old scientist has acknowledged errors, but defends her conclusions.

The scandal, which has played out emotively and very publicly as a David-and-Goliath tale of a lone young woman battling an establishment body, has tarnished the image of Riken, and prompted Japanese media to scrutinise the taxpayer-funded institute.