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## Bad sleep 'dramatically' alters body

*A run of poor sleep can have a potentially profound effect on the internal workings of the human body, say UK researchers.*

By James Gallagher Health and science reporter, BBC News

The activity of hundreds of genes was altered when people's sleep was cut to less than six hours a day for a week. Writing in the journal PNAS, the researchers said the results helped explain how poor sleep damaged health.

Heart disease, diabetes, obesity and poor brain function have all been linked to substandard sleep.

What missing hours in bed actually does to alter health, however, is unknown.

So researchers at the University of Surrey analysed the blood of 26 people after they had had plenty of sleep, up to 10 hours each night for a week, and compared the results with samples after a week of fewer than six hours a night.

More than 700 genes were altered by the shift. Each contains the instructions for building a protein, so those that became more active produced more proteins - changing the chemistry of the body.

Meanwhile the natural body clock was disturbed - some genes naturally wax and wane in activity through the day, but this effect was dulled by sleep deprivation.

Prof Colin Smith, from the University of Surrey, told the BBC: "There was quite a dramatic change in activity in many different kinds of genes." Areas such as the immune system and how the body responds to damage and stress were affected.

Prof Smith added: "Clearly sleep is critical to rebuilding the body and maintaining a functional state, all kinds of damage appear to occur - hinting at what may lead to ill health. "If we can't actually replenish and replace new cells, then that's going to lead to degenerative diseases."

He said many people may be even more sleep deprived in their daily lives than those in the study - suggesting these changes may be common.

Dr Akhilesh Reddy, a specialist in the body clock at the University of Cambridge, said the study was "interesting".

He said the key findings were the effects on inflammation and the immune system as it was possible to see a link between those effects and health problems such as diabetes.

The findings also tie into research attempting to do away with sleep, such as by finding a drug that could eliminate the effects of sleep deprivation.

Dr Reddy said: "We don't know what the switch is that causes all these changes, but theoretically if you could switch it on or off, you might be able to get away without sleep. "But my feeling is that sleep is fundamentally important to regenerating all cells."

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## Surgery prices are elusive

*University of Iowa study finds 13-fold price difference among U.S. hospitals for prostate cancer surgery*

Let's say you're buying a car. You have a wealth of data at your fingertips, from safety information to performance, to guide your decision.

The same is not as true in health care, especially if you're pricing procedures. A new study from the University of Iowa compared the cost of prostate cancer surgery at 100 hospitals throughout the United States. The quote for the procedure, the researchers found, varied from \$10,100 to \$135,000, a 13-fold range. (The average price was nearly \$35,000, more than double the Medicare reimbursement.) Only 10 of the hospitals that provided cost information divulged anesthesia and surgeon costs, key criteria to consider when pricing a surgical procedure. Moreover, just three hospitals provided a hard copy of the charges, further complicating a patient's ability to compare costs, the study found.

"Such variability in pricing can produce significant confusion for consumers who are accustomed to the rules of free-market economics, which equate higher fees with higher quality," write the UI researchers, in the journal Urology.

"Unfortunately, in health care, this has not been found to be true."

Prostate disease is a major health concern in the U.S. It accounts for 28 percent of all new cancer diagnoses in men and nearly \$12 billion in treatment costs, according to the American Cancer Society. About 138,000 prostate cancer surgeries are performed yearly, according to government figures. Yet despite the commonness of the disease and the frequency of surgeries, getting a reliable, accurate quote is hard to come by.

Part of that is due to the system itself. What hospitals charge for a procedure don't reflect the actual costs, says Bradley Erickson, assistant professor in urology at the UI and corresponding author on the study. Think of the hospital's quote as the opening salvo in a negotiation - a give-and-take primarily with the health insurance provider over how much the hospital gets reimbursed. In that scenario, the higher the quote, the more room there is to negotiate, and thus arguably the more the hospital could get reimbursed.

"These (hospital) charges don't mean anything," Erickson notes. "There's no weight behind them."

What that all means is the consumer is working with inflated figures, at best, which puts them "at a significant disadvantage," Erickson says. Even more, the researchers learned there is precious little information about how well hospitals perform prostate cancer surgeries, as they report outcome data mostly only to government agencies.

That lack of transparency is "a huge problem," Erickson says. "It doesn't really incentivize any place to improve outcomes, because no one is holding us individually accountable for it."

That could be worrisome to health-care consumers who may face higher deductibles under the Affordable Care Act, Erickson notes.

"We're not ready for it (pricing transparency), because most hospitals can't tell you how much they charge," he says. "And the ones that do aren't based on reality."

Among the study's other findings:

*70 of the 100 hospitals surveyed provided some pricing*

*Of that number, nearly half (33) said they'd discount the procedure, to as much as 80 percent, for pre-pay or promptly paying patients*

*Academic medical centers charged 52 percent more, on average, than nonacademic centers (The UI's estimate was \$31,000, below the mean in the survey; the UI also offered a 25 percent discount for pre-paying patients.)*

*Hospitals in the northeast U.S. charged most (at \$40,802 on average), while hospitals in the South charged the least (\$30,305 on average)*

*Hospitals in the Midwest were the most likely to provide estimates and to offer discounts*

*There was little price difference at centers either when city population is factored or rankings as compiled by U.S. News and World Report*

The prostate-cancer surgery costs survey follows a UI study, published last year in JAMA Internal Medicine, which found hip replacement costs at hospitals nationwide ranged more than ten-fold, from \$11,100 to \$125,798. The reason, those researchers found, are largely due to the lack of transparency and knowledge how hospitals set their prices.

It also corroborates findings from the Centers for Medicare and Medicaid Services, which reported wide price differences for a variety of medical procedures across the U.S.

In a separate editorial comment in the journal, the authors, from the University of Montreal and Harvard Medical School, write: "The discrepancy in pricing highlights the substantial incongruity between the actual costs of a surgical procedure and the hospital charges. It would be highly implausible that the exact same procedure is 13 times more expensive to deliver at one hospital relative to another."

*Scott Pate, a UI medical student now at the University of Kansas, is the first author on the study, first published in March. Contributing authors include Matthew Uhlman, Jaime Rosenthal, and Peter Cram.*

*There was no outside funding for the study.*

<http://bit.ly/1xO2IPj>

**The first vertebrate sexual organs evolved as an extra pair of legs**  
*We humans use the euphemism for sex that "we like to get a leg over" but the first jawed vertebrates – the placoderms – they liked to get a leg in.*

They were the first back-boned creatures to evolve male genital organs, or claspers, supported by a bony internal skeleton.

What's even more peculiar is that, unlike the cartilaginous claspers of modern sharks, which are a modified part of the pelvic fin, our new research has shown that in placoderms they were basically a separate set of paired appendages.



*A bull male Eastmanosteus placoderm. Placoderms were the first creatures to evolve paired reproductive organs with a bony skeleton called claspers. Brian Choo & John Long, Flinders University.*

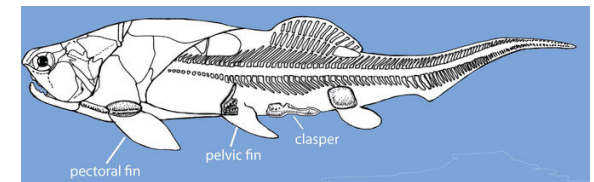
### The reign of the placoderms

Placoderms had thick bony plates enveloping the head and trunk regions. They ruled the seas, rivers and lakes of the world for 70 million years, becoming extinct around 360 million years ago. Placoderms were the world's first megapredators, with ancient behemoths such as Dunkleosteus reaching the same size as today's Great White Shark.

They were also the first vertebrate animals on Earth to have a complex form of sexual reproduction – copulation – where males fertilised the females internally rather than just spawning in water.

To achieve this, the males bore bony paired structures – the claspers – which were previously thought to be similar to the cartilaginous claspers of modern sharks.

For many years placoderms were thought of as "shark-like fishes" and so their anatomy was routinely interpreted using sharks as a model. This approach has shadowed the secret of their true evolutionary significance for almost the past century.

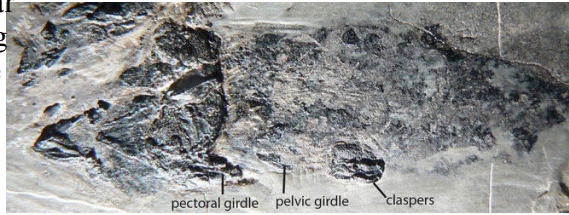


*The skeleton of placoderm Coccosteus, showing the bony claspers situated well behind the pelvic fins. John Long, Flinders University.*

### Hints of hidden genitals

The first hint that placoderm fishes were sexually dimorphic (meaning males look different to females) was seen in the different pelvic fins by English palaeontologist [David M.S. Watson](#) in the 1930s. He studied a placoderm fish called *Rhamphodopsis* that lived around 390 million years ago in Scotland.

In the 1960s Norwegian palaeontologist Tor Ørvig studied a similar kind of placoderm (a ptyctodontid) named *Ctenurella* and went one step further. He identified the strange structures near the pelvic fins as claspers, implying they were intromittent or insertable organs. Nonetheless, just identifying these structures doesn't mean the fishes actually used them to internally fertilise the females.



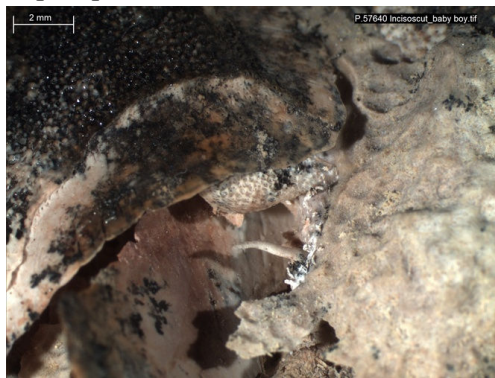
*A male placoderm, Rhamphodopsis, head towards the left, showing the bony claspers well behind the position of the pelvic girdle and fin. John Long, Flinders University.*

The first hard evidence that placoderms really did copulate was when our team announced in 2008 that we had found [complete embryos](#) in perfectly preserved fossil specimens from the Gogo Formation of Western Australia. These were found in just one group of placoderms called [ptyctodontids](#), which showed sexual differences in the pelvic region.

We found further embryos in the largest group of placoderms – the arthrodiirens – [in 2009](#) and later that same year identified the first male copulatory organs [in this group](#).

### Evidence there all the time

Our new study shows that many other common species of placoderm also had similar complex reproductive organs. The evidence was sitting in museum collections around the world but not noticed until one of us (Kate Trinajstić) went searching for and found them.



*A tiny clasper (white rod, centre bottom) from an unborn (embryonic) baby boy placoderm, Incisoscutum, from the Gogo site, Western Australia. Zerina Johanson, Natural History Museum, London.*

Our research has shown that the mating organs of the ancient placoderms were rather complex. The review of the reproductive structures in placoderms produced many new examples which showed an unusual pattern emerging.

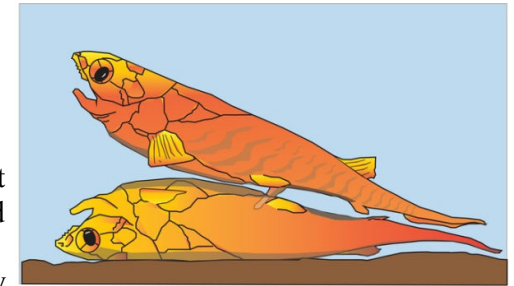
One specimen even showed an unborn embryo with a tiny clasper developed, so we could tell it was a male. Unlike the claspers of modern sharks and rays that are a part of the paired pelvic fins, the claspers and female basal plates in placoderms were not at all connected to that fin.

Instead they developed as an extra pair of limbs further down the body.

This discovery implies that the first vertebrates did not conform to the typical [tetrapod](#)-like pattern of having just two pairs of paired limbs (arms, or pectoral fins, and legs, or pelvic fins) that typifies the basic jawed vertebrate body pattern from fishes through to mammals.

The implications of this study mean that the similar looking male claspers in placoderms and sharks are actually not the same structures, but most likely evolved independently.

As the bony placoderm claspers were not rigidly fixed to the pelvic fin, they would have been able to rotate forwards, so the earliest sexual mating position was likely to have been a missionary one.



*How placoderms such as Incisoscutum probably mated. John Long, Flinders University.*

The claspers in placoderms can now be regarded as a [serial homologue](#) or gradual development of the other paired appendages - an extra pair of legs, so to speak.

The mechanism for how this happens is clear. Certain homeobox ([hox](#)) genes control the repetition of structures such as limbs (as in the [sonic hedgehog gene](#)) and the position of them on the body axis (the hox genes [tbx4](#), [tbx5](#)).

In the case of placoderms, the zone of competence to form paired appendages was much enlarged compared to modern vertebrates, and extended beyond the pelvic fins, enabling an extra pair of structures to develop.

In sharks the pelvic fins became elongated and [modified as claspers](#) using a different set of hox genes ([hoxd13](#)). This new discovery implies that the so-called primitive way of vertebrate reproduction – spawning in water – changed dramatically to copulation almost as soon as vertebrates had the right tools for the job.

[Jaws](#) appeared around the same time as claspers in placoderms, and so might also have been connected to this early reproductive behaviour in some way.

In addition to aiding in the capture of prey, feeding and ventilation, jaws may also have been utilised for holding on to a partner whilst mating, as many sharks do today (video, above). Clearly we don't know the full story yet. There is still a lot more to discover about this fascinating group of ancient extinct fishes.

[http://www.eurekalert.org/pub\\_releases/2014-06/sonm-dit060814.php](http://www.eurekalert.org/pub_releases/2014-06/sonm-dit060814.php)

### **Depression in the elderly linked to Alzheimer's risk**

#### ***Molecular imaging study suggests late-life depression and beta-amyloid plaque in the brain could tip-off hastened development of the deadly dementia***

St. Louis, Mo. – Many people develop depression in the latest stages of life, but until now doctors had no idea that it could point to a build up of a naturally occurring protein in the brain called beta-amyloid, a hallmark of Alzheimer's disease. In fact, late-life depression could become a major risk factor for developing Alzheimer's faster than others, according to research unveiled at the Society of Nuclear Medicine and Molecular Imaging's 2014 Annual Meeting.

Alzheimer's disease is a currently incurable neurodegenerative disease with marked protein aggregates including beta-amyloid and tau. The disease begins developing years before noticeable cognitive decline and memory loss. Depression has been proven to have its own neurodegenerative effects on the brain, but here researchers have found an undeniable connection between beta-amyloid in depressed elderly patients with cognitive deficits and advancement to Alzheimer's disease. They were able to prove this using molecular imaging data from a global dementia imaging database.

"Our results clearly indicate that mild cognitively impaired subjects with depressive symptoms suffer from elevated amyloid-levels when compared with non-depressed individuals," said the study's principal scientist Axel Rominger, MD, from the department of nuclear medicine at the University of Munich in Germany. "The combination of elevated amyloid-levels and coexisting depressive symptoms constitute a patient population with a high risk for faster progression to Alzheimer's disease."

The study involved 371 patients with mild cognitive impairment who underwent PET imaging with the radiotracer F-18 florbetapir and magnetic resonance imaging (MRI) chosen retrospectively from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database, which includes data from at least 55 research centers across the U.S. and Canada now readily available to more than 2,500 researchers worldwide. Results showed that mild cognitive impaired patients with depressive symptoms had higher amyloid deposition than non-depressed controls as indicated by the binding of the radiotracer to amyloid particularly in the frontal cortex and the anterior and posterior cingulate gyrus of the brain, both involved in mood disorders such as depression.

"Therapeutic options for Alzheimer's disease are still limited and therefore the identification and understanding of contributing risk factors that influence the disease are crucial in ongoing research as they offer the possibilities for future medical intervention," said co-author and fellow researcher Matthias Brendel.

Additionally, knowing the risk could help patients make necessary lifestyle changes and prepare their families.

Alzheimer's disease is the most prevalent form of dementia. It is estimated that 44.4 million people are living with dementia worldwide. This number is expected to increase to approximately 75.6 million in 2030 and 135.5 million in 2050, according to 2013 data from the Alzheimer's Disease International.

*Scientific Paper 87: Matthias Brendel, Eva Kalinowski, Andreas Delker, Peter Bartenstein, Axel Rominger, Dept. of Nuclear Medicine, University of Munich, Munich, Germany, "Subsyndromal late life depression is associated with amyloid accumulation in mild cognitive impairment," SNMMI's 61th Annual Meeting, June 7, 2014, St. Louis, Missouri.*

[http://www.eurekalert.org/pub\\_releases/2014-06/ru-trc060814.php](http://www.eurekalert.org/pub_releases/2014-06/ru-trc060814.php)

### **To recover consciousness, brain activity passes through newly detected states**

#### ***Anesthesia makes otherwise painful procedures possible by derailing a conscious brain, rendering it incapable of sensing or responding to a surgeon's knife. But little research exists on what happens when the drugs wear off.***

"I always found it remarkable that someone can recover from anesthesia, not only that you blink your eyes and can walk around, but you return to being yourself. So if you learned how to do something on Sunday and on Monday, you have surgery, and you wake up and you still know how to do it," says Alexander Proekt, a visiting fellow at Rockefeller University, in Don Pfaff's Laboratory of Neurobiology and Behavior, and an anesthesiologist at Weill Cornell Medical College. "It seemed like there ought to be some kind of guide or path for the system to follow."

The obvious explanation is that as the anesthetic washes out of the body, electrical activity in the brain gradually returns to its conscious patterns. However, new research by Proekt and colleagues suggests the trip back is not so simple. "Using statistical analysis, our research shows that the recovery from deep anesthesia is not a smooth, linear process. Instead, there are dynamic 'way stations' or states of activity the brain must temporarily occupy on the way to full recovery," Pfaff says. "These results have implications for understanding how someone's ability to recover consciousness can be disrupted by, for example, brain injury."

Proekt, along with for postdoc Andrew Hudson, now an assistant professor in anesthesiology at the University of California, Los Angeles, and Diany Paola Calderon, a research associate in the lab, put rats "under" using the common medical and veterinary anesthetic isoflurane. As the rats recovered, the team monitored the electrical potential outside neurons, known as local field potentials (LFPs), in particular parts of the brain known, from previous electrophysiological and pharmacological studies, to be associated with wakefulness and anesthesia.

These recordings gave them a sensitive handle on the activities of whole groups of neurons in particular parts of the thalamus and cortex.

In the awake brain, of both humans and rats, neurons generate electrical voltage that oscillates. Many of these oscillations together form a signal that appears as a squiggly line on a recording of brain activity, such as an LFP. When someone is asleep, under anesthesia, or in a coma, these oscillations occur more slowly, or at a low frequency. When he or she is awake, they speed up. The researchers examined the recordings from the rats' brains to figure out how the electrical activity in these regions changed as they moved from anesthetized to awake.

"Recordings from each animal wound up having particular features that spontaneously appeared, suggesting their brain activity was abruptly transitioning through particular states," Hudson says. "We analyzed the probability of a brain jumping from one state to another, and we found that certain states act as hubs through which the brain must pass to continue on its way to consciousness." While the electrical activity in all the rats' brains passed through these hubs, the precise path back to consciousness was not the same each time, the team reports today in the Proceedings of the National Academy of Sciences.

"These results suggest there is indeed an intrinsic way in which the unconscious brain finds its way back to consciousness. The anesthetic is just a tool for severely reducing brain activity in a way in which we can control," Hudson says.

In other scenarios, including coma caused by brain injury or neurological disease, the disruption to brain activity cannot be controlled, making these states much more difficult to study. However, the team's results may help explain what is going on in these cases. "Maybe a pathway has shut down, or a brain structure that was key for full consciousness is no longer working. We don't know yet, but our results suggest the possibility that under certain circumstances, someone may be theoretically capable of returning to consciousness but, due to the inability to transition through the hubs we have identified, his or her brain is unable to navigate the way back," Calderon says.

[http://www.eurekalert.org/pub\\_releases/2014-06/ps-5od060914.php](http://www.eurekalert.org/pub_releases/2014-06/ps-5od060914.php)

### **55-year old dark side of the moon mystery solved**

*Astrophysicists think they know why no "face" exists on farside of the moon*

The Man in the Moon appeared when meteoroids struck the Earth-facing side of the moon creating large flat seas of basalt that we see as dark areas called maria. But no "face" exists on farside of the moon and now, Penn State astrophysicists think they know why.

"I remember the first time I saw a globe of the moon as a boy, being struck by how different the farside looks," said Jason Wright, assistant professor of astrophysics.

"It was all mountains and craters. Where were the maria? It turns out it's been a mystery since the fifties."

This mystery is called the Lunar Farside Highlands Problem and dates back to 1959, when the Soviet spacecraft Luna 3 transmitted the first images of the "dark" side of the moon back to Earth. It was called the dark side because it was unknown, not because sunlight does not reach it. Researchers immediately noticed that fewer "seas" or maria existed on this portion of the moon that always faces away from Earth.

Wright, Steinn Sigurdsson, professor of astrophysics and Arpita Roy, graduate student in astronomy and astrophysics, and lead author of the study, realized that the absence of maria, which is due to a difference in crustal thickness between the side of the moon we see and the hidden side, is a consequence of how the moon originally formed. The researchers report their results in today's (June 9) Astrophysical Journal Letters.

The general consensus on the moon's origin is that it probably formed shortly after the Earth and was the result of a Mars-sized object hitting Earth with a glancing, but devastating impact. This Giant Impact Hypothesis suggests that the outer layers of the Earth and the object were flung into space and eventually formed the moon. "Shortly after the giant impact, the Earth and the moon were very hot," said Sigurdsson.

The Earth and the impact object did not just melt; parts of them vaporized, creating a disk of rock, magma and vapor around the Earth. "The moon and Earth loomed large in each others skies when they formed," said Roy.

The geometry was similar to the rocky exoplanets recently discovered very close to their stars, said Wright. The moon was 10 to 20 times closer to Earth than it is now, and the researchers found that it quickly assumed a tidally locked position with the rotation time of the moon equal to the orbital period of the moon around the Earth. The same real estate on the moon has probably always faced the Earth ever since. Tidal locking is a product of the gravity of both objects.

The moon, being much smaller than Earth cooled more quickly. Because the Earth and the moon were tidally locked from the beginning, the still hot Earth -- more than 2500 degrees Celsius -- radiated towards the near side of the moon. The far side, away from the boiling Earth, slowly cooled, while the Earth-facing side was kept molten creating a temperature gradient between the two halves.

This gradient was important for crustal formation on the moon. The moon's crust has high concentrations of aluminum and calcium, elements that are very hard to vaporize.

"When rock vapor starts to cool, the very first elements that snow out are aluminum and calcium," said Sigurdsson.

Aluminum and calcium would have preferentially condensed in the atmosphere of the cold side of the moon because the nearside was still too hot. Thousands to millions of years later, these elements combined with silicates in the moon's mantle to form plagioclase feldspars, which eventually moved to the surface and formed the moon's crust, said Roy. The farside crust had more of these minerals and is thicker.

The moon has now completely cooled and is not molten below the surface. Earlier in its history, large meteoroids struck the nearside of the moon and punched through the crust, releasing the vast lakes of basaltic lava that formed the nearside maria that make up the man in the moon. When meteoroids struck the farside of the moon, in most cases the crust was too thick and no magmatic basalt welled up, creating the dark side of the moon with valleys, craters and highlands, but almost no maria.

*The NASA Astrobiology Institute and the Pennsylvania State Astrobiology Research Center supported this work.*

[http://www.eurekalert.org/pub\\_releases/2014-06/hfhs-atm060914.php](http://www.eurekalert.org/pub_releases/2014-06/hfhs-atm060914.php)

**Antiviral therapy may prevent liver cancer in hepatitis B patients**  
*Researchers have found that antiviral therapy may be successful in preventing hepatitis B virus from developing into the most common form of liver cancer, hepatocellular carcinoma (HCC).*

DETROIT – That was the finding of a study published in the May issue of Clinical Gastroenterology and Hepatology. Investigators from Henry Ford Health System in Detroit, Geisinger Health System in Danville, Pa., and Kaiser Permanente in Honolulu, Hawaii and Portland, Ore. participated in the study, along with investigators from the Centers for Disease Control and Prevention in Atlanta. According to the first-of-its-kind analysis of more than 2,600 adult participants with hepatitis B, those treated with antiviral therapy had a significantly lower occurrence of HCC during a five-year follow up period.

Overall, 3 percent of patients developed HCC during the study's timeframe. But patients who received antiviral therapy were 60 percent less likely to develop HCC than untreated patients.

"The results of this study allow us to reassure our patients that we are not just treating their viral levels, but that antiviral therapy may actually lessen their chance of developing liver cancer," said the study's lead investigator, Henry Ford Health System's Stuart C. Gordon, M.D., who worked closely with Henry Ford Senior Scientist Mei Lu in Detroit.

HCC accounts for the most liver cancers in the United States, typically occurs in people age 50 or older and is more common in men. If the cancer cannot be removed, it is usually fatal in three to six months. In most cases, HCC is caused by

scarring in the liver – cirrhosis – which can be a result of alcohol abuse, hepatitis B or C, chronic inflammation of the liver or an iron overload.

"This study was one of the first to address antiviral therapy and its efficacy in preventing hepatitis B from developing into liver cancer," said Joseph Boscarino, Ph.D., senior scientist and investigator for the Geisinger site. "With this information, clinicians can begin to prescribe antiviral therapy for hepatitis B patients with the goal of preventing a common and dangerous form of cancer."

<http://www.bbc.com/news/health-27760736>

**Aspirin 'not best' for preventing strokes**

*Doctors are being told not to routinely prescribe aspirin for a common heart condition that increases stroke risk.*

**By Michelle Roberts Health editor, BBC News online**

Guidelines from the National Institute of Health and Care Excellence (NICE) are set to recommend other drugs instead for patients with an irregular heartbeat, called atrial fibrillation. Warfarin or similar blood-thinning medicine is best, says NICE in draft advice to be finalised this month.

The advice will affect hundreds of thousands of patients. But experts say most doctors already follow the advice to prescribe blood-thinners other than aspirin and that the guidelines are "playing catch-up" - this is the first time they will have been updated since they were first issued in 2006.

**Stroke prevention**

Atrial fibrillation (AF) is the most common heart rhythm problem, affecting up to 800,000 people - roughly one in 100 - in the UK. In AF, the heart cannot work as well as it should and blood clots can form, which, in turn, increases the risk of a stroke.

Aspirin has been used for years to help protect patients from strokes, but mounting evidence suggests the drug's benefits are too small compared with other treatments. The NICE guidelines for England and Wales look set to say that although daily aspirin might still be beneficial for some patients, most should be offered something else as well or instead. According to its draft advice, NICE says warfarin or a newer type of oral anticoagulant is often best.

The British Heart Foundation said most doctors were already doing this.

Prof Peter Weissberg, medical director at the British Heart Foundation, said:

"Strokes caused by atrial fibrillation are both common and preventable but only if the abnormal heart rhythm is identified in the first place and if effective drugs are given to prevent blood-clot development.

"The revised NICE guidance reflects accumulating evidence that warfarin and the newer anticoagulants are much more effective than aspirin at preventing strokes.

"This does not mean that aspirin is not important and effective at preventing heart attacks and strokes in other circumstances. Patients who are unclear on whether or not they should continue to take aspirin should speak to their doctor." Prof Peter Elwood, an expert at Cardiff University, warned it could be unsafe to suddenly stop taking aspirin. "If aspirin is to be stopped, it should be stopped gradually," he said.

### Do I have atrial fibrillation (AF)?

*An irregular pulse could be a sign that you have AF*

*It will feel erratic, and beats may be variable in strength*

*AF is most common in people aged over 55*

*If you think you might have AF, you should get yourself checked out by a doctor*

*Often, the underlying cause is not found, but AF is more common in people with high blood pressure and heart disease*

[http://www.eurekalert.org/pub\\_releases/2014-06/nios-sts061014.php](http://www.eurekalert.org/pub_releases/2014-06/nios-sts061014.php)

### Snowballs to soot: The clumping density of many things seems to be a standard

*Particles of soot floating through the air and comets hurtling through space have at least one thing in common: 0.36.*

That, reports a research group at the National Institute of Standards and Technology (NIST), is the measure of how dense they will get under normal conditions, and it's a value that seems to be constant for similar aggregates across an impressively wide size range from nanometers to tens of meters.\*

NIST hopes the results will help in the development of future measurement standards to aid climate researchers and others who need to measure and understand the behavior of aerosols like carbon soot in the atmosphere.

Soot comes mostly from combustion and is considered the second biggest driver of global warming, according to NIST chemist Christopher Zangmeister.

It is made up of small round particles of carbon about 10 or 20 nanometers across. The particles stick together randomly in short chains and clumps of a half dozen or more spheres. These, in turn, clump loosely together to form larger, loose aggregates of 10 or more which over a few hours will compact into a somewhat tighter ball which is atmospheric soot.

The interesting question for chemists studying carbon aerosols is how tight? How dense?

Among other things, the answer relates to the balance of climate effects from soot: heating from light absorption versus cooling from light reflection.

The maximum packing density of objects is a classic problem in mathematics, which has been fully solved for only the simplest cases.

The assumed density in models of atmospheric soot is 0.74, which is the maximum packing density of perfect spheres, such as billiard balls, in a given space.

But when Zangmeister's team made measurements of the packing density of actual soot particles, the figure they got was 0.36.

"We figured, man, we've got to be wrong, we're off by a factor of two," Zangmeister recalls, but "a bunch more measurements" convinced them that 0.36 was correct. Why?

Enter the summer help. Two students, one in college and one in high school, who were working with Zangmeister's group last summer were set to the task of modeling the packing question with little 6 mm plastic spheres sold for pellet guns. They glued thousands of random combinations of spheres together in clumps of from 1 to 12 spheres, and then filled every available size of graduated cylinders and hollow spheres with their assemblies, over and over, and over.

Their charted results, as a function of clump size, form a curve that levels off at ... 0.36.

It gets better. Inspired by a book on the solar system he was reading with his son, Zangmeister checked NASA's literature.

Comets are formed very much the same way as soot particles, except out of dust and ice, and they're a lot bigger.

NASA's measurements on a collection of 20 comets estimate that packing density at between 0.2 and 0.4. So 0.36 may be an all-purpose value.\*\*

NIST's interest in the nature of soot particles is driven by a desire to imitate them, according to Zangmeister.

"It's amazing how much uncertainty there is in optical measurements of particles in the atmosphere. The reason for this uncertainty is rooted in something really important to NIST: there are no real methods for calibrations. You can calibrate any CO2 measurement using one of our Standard Reference Materials for CO2 in air, but there's no such thing as a bottle of standard aerosol or a standard aerosol generator. That's really at the heart of what we're trying to do: make a black material that simulates carbon that you can put into an aerosol and know it will come out the same way every time. It's a real materials chemistry project."

The agency is working with the National Research Council of Canada and Environment Canada on the project.

*\*C.D. Zangmeister, J.G. Radney, L.T. Dockery, J.T. Young, X. Ma, R. You and M.R. Zachariah., The packing density of rigid aggregates is independent of scale. PNAS Early Edition. Published online June 9, 2014. doi:10.1073/pnas.1403768111.*

*\*\*0.36 is also very close to the reported values for compacted silicon dioxide monomers (ceramics industry) and pharmaceutical powders made from "microscale random aggregates."*

[http://www.eurekalert.org/pub\\_releases/2014-06/uoc--ho060614.php](http://www.eurekalert.org/pub_releases/2014-06/uoc--ho060614.php)

## 'Trust hormone' oxytocin helps old muscle work like new, study finds

### *Researchers have discovered that oxytocin is indispensable for healthy muscle maintenance and repair*

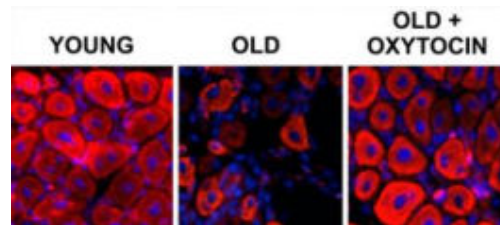
Berkeley - Researchers at the University of California, Berkeley, have discovered that oxytocin -- a hormone associated with maternal nurturing, social attachments, childbirth and sex -- is indispensable for healthy muscle maintenance and repair, and that in mice, it declines with age.

The new study, to be published Tuesday, June 10, in the journal Nature Communications, presents oxytocin as the latest treatment target for age-related muscle wasting, or sarcopenia.

A few other biochemical factors in blood have been connected to aging and disease in recent years, but oxytocin is the first anti-aging molecule identified that is approved by the Food and Drug Administration for clinical use in humans, the researchers said. Pitocin, a synthetic form of oxytocin, is already used to help with labor and to control bleeding after childbirth. Clinical trials of an oxytocin nasal spray are also underway to alleviate symptoms associated with mental disorders such as autism, schizophrenia and dementia.

"Unfortunately, most of the molecules discovered so far to boost tissue regeneration are also associated with cancer, limiting their potential as treatments for humans," said study principal investigator Irina Conboy, associate professor of bioengineering. "Our quest is to find a molecule that not only rejuvenates old muscle and other tissue, but that can do so sustainably long-term without increasing the risk of cancer."

Conboy and her research team say that oxytocin, secreted into the blood by the brain's pituitary gland, is a good candidate because it is a broad range hormone that reaches every organ, and it is not known to be associated with tumors or to interfere with the immune system.



*On the left is healthy muscle tissue from a young mouse. The ability of muscle to repair itself decreases with age, as evidenced by the middle image of old muscle tissue, which shows a lower density of muscle fibers, increased scar tissue and inflammation. The addition of oxytocin to the blood of old mice rapidly rejuvenates the old muscle, as shown in the image on the right. Photos by Wendy Cousin and Christian Elabd, UC Berkeley.*

### A happy hormone

Oxytocin is sometimes referred to as the "trust hormone" because of its association with romance and friendship. It is released with a warm hug, a grasped hand or a loving gaze, and it increases libido. The hormone kicks into high gear during and after childbirth, helping new mothers bond with and breastfeed their new babies.

"This is the hormone that makes your heart melt when you see kittens, puppies and human babies," said Conboy, who is also a member of the Berkeley Stem Cell Center and of the California Institute for Quantitative Biosciences (QB3). "There is an ongoing joke among my research team that we're all happy, friendly and trusting because oxytocin permeates the lab."

The researchers pointed out that while oxytocin is found in both young boys and girls, it is not yet known when levels of the hormone start to decline in humans, and what levels are necessary for maintaining healthy tissues.

Christian Elabd and Wendy Cousin, both senior scientists in Conboy's lab, were co-lead authors on this study.

Previous research by Elabd found that administering oxytocin helped prevent the development of osteoporosis in mice that had their ovaries removed to mimic menopause.

### Extra oxytocin more beneficial for the old

The new study determined that in mice, blood levels of oxytocin declined with age. They also showed that there are fewer receptors for oxytocin in muscle stem cells in old versus young mice.

To tease out oxytocin's role in muscle repair, the researchers injected the hormone under the skin of old mice for four days, and then for five days more after the muscles were injured. After the nine-day treatment, they found that the muscles of the mice that had received oxytocin injections healed far better than those of a control group of mice without oxytocin.

"The action of oxytocin was fast," said Elabd. "The repair of muscle in the old mice was at about 80 percent of what we saw in the young mice."

Interestingly, giving young mice an extra boost of oxytocin did not seem to cause a significant change in muscle regeneration.

"This is good because it demonstrates that extra oxytocin boosts aged tissue stem cells without making muscle stem cells divide uncontrollably," Cousin added.

The researchers also found that blocking the effects of oxytocin in young mice rapidly compromised their ability to repair muscle, which resembled old tissue after an injury.

The researchers also studied mice whose gene for oxytocin was disabled, and compared them with a group of control mice. At a young age, there was no significant difference between the two groups in muscle mass or repair efficiency



after an injury. It wasn't until the mice with the disabled oxytocin gene reached adulthood that signs of premature aging began to appear.

"When disabling other types of genes associated with tissue repair, defects appear right away either during embryonic development, or early in life," said Conboy.

"To our knowledge, the oxytocin gene is the only one whose impact is seen later in life, suggesting that its role is closely linked to the aging process."

#### **Future treatment options**

Cousin noted that oxytocin could become a viable alternative to hormone replacement therapy as a way to combat the symptoms of both female and male aging, and for long-term health. Hormone therapy did not show improvements in agility or muscle regeneration ability, and it is no longer recommended for disease prevention because research has found that the therapy's benefits did not outweigh its health risks. In addition to healthy muscle, oxytocin is predicted to improve bone health, and it might be important in combating obesity.

Conboy said her lab plans to examine oxytocin's role in extending a healthy life in animals, and in conserving its beneficial anti-aging effects in humans.

She noted that there is a growing circle of scientists who believe that aging is the underlying cause of a number of chronic diseases, including Parkinson's and Type 2 diabetes.

"If you target processes associated with aging, you may be tackling those diseases at the same time," said Conboy. "Aging is a natural process, but I believe that we can meaningfully intervene with age-imposed organ degeneration, thereby slowing down the rate at which we become progressively unhealthy."

*Funding from the SENS Research Foundation, the National Institute on Aging and the California Institute for Regenerative Medicine helped support this research.*

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#### **Bacteria help explain why stress, fear trigger heart attacks**

*Scientists believe they have an explanation for the axiom that stress, emotional shock, or overexertion may trigger heart attacks in vulnerable people.*

WASHINGTON, DC - Hormones released during these events appear to cause bacterial biofilms on arterial walls to disperse, allowing plaque deposits to rupture into the bloodstream, according to research published in published today in mBio®, the online open-access journal of the American Society for Microbiology.

"Our hypothesis fitted with the observation that heart attack and stroke often occur following an event where elevated levels of catecholamine hormones are released into the blood and tissues, such as occurs during sudden emotional shock or stress, sudden exertion or over-exertion" said David Davies of Binghamton University, Binghamton, New York, an author on the study.

Davies and his colleagues isolated and cultured different species of bacteria from diseased carotid arteries that had been removed from patients with atherosclerosis. Their results showed multiple bacterial species living as biofilms in the walls of every atherosclerotic (plaque-covered) carotid artery tested.

In normal conditions, biofilms are adherent microbial communities that are resistant to antibiotic treatment and clearance by the immune system. However, upon receiving a molecular signal, biofilms undergo dispersion, releasing enzymes to digest the scaffolding that maintains the bacteria within the biofilm. These enzymes have the potential to digest the nearby tissues that prevent the arterial plaque deposit from rupturing into the bloodstream.

According to Davies, this could provide a scientific explanation for the long-held belief that heart attacks can be triggered by a stress, a sudden shock, or overexertion

To test this theory they added norepinephrine, at a level that would be found in the body following stress or exertion, to biofilms formed on the inner walls of silicone tubing.

"At least one species of bacteria - *Pseudomonas aeruginosa* - commonly associated with carotid arteries in our studies, was able to undergo a biofilm dispersion response when exposed to norepinephrine, a hormone responsible for the fight-or-flight response in humans," said Davies. Because the biofilms are closely bound to arterial plaques, the dispersal of a biofilm could cause the sudden release of the surrounding arterial plaque, triggering a heart attack.

To their knowledge, this is the first direct observation of biofilm bacteria within a carotid arterial plaque deposit, says Davies. This research suggests that bacteria should be considered to be part of the overall pathology of atherosclerosis and management of bacteria within an arterial plaque lesion may be as important as managing cholesterol.

[http://www.eurekalert.org/pub\\_releases/2014-06/eaog-fft060914.php](http://www.eurekalert.org/pub_releases/2014-06/eaog-fft060914.php)

#### **From today, the Earth is around 60 million years older -- and so is the moon**

*Giant impact between Earth's ancestor and a planet-sized body occurred around 40 million years after the start of solar system formation*

Sacramento, CA - Work presented today at the Goldschmidt Geochemistry Conference in Sacramento, California shows that the timing of the giant impact between Earth's ancestor and a planet-sized body occurred around 40 million years after the start of solar system formation. This means that the final stage of Earth's formation is around 60 million years older than previously thought.

Geochemists from the University of Lorraine in Nancy, France have discovered an isotopic signal which indicates that previous age estimates for both the Earth and the Moon are underestimates. Looking back into "deep time" it becomes more difficult to put a date on early Earth events. In part this is because there is little "classical geology" dating from the time of the formation of the Earth – no rock layers, etc. So geochemists have had to rely on other methods to estimate early Earth events. One of the standard methods is measuring the changes in the proportions of different gases (isotopes) which survive from the early Earth. Guillaume Avice and Bernard Marty analysed xenon gas found in South African and Australian quartz, which had been dated to 3.4 and 2.7 billion years respectively. The gas sealed in this quartz is preserved as in a "time capsule", allowing Avice and Marty to compare the current isotopic ratios of xenon, with those which existed billions of years ago. Recalibrating dating techniques using the ancient gas allowed them to refine the estimate of when the earth began to form. This allows them to calculate that the Moon-forming impact is around 60 million years (+/- 20 m. y.) older than had been thought.

Previously, the time of formation of the Earth's atmosphere had been estimated at around 100 million years after the solar system formation. As the atmosphere would not have survived the Moon-forming impact, this revision puts the age up to 40 million years after the solar system formation (so around 60 million years older than previously thought).

According to Guillaume Avice:

"It is not possible to give an exact date for the formation of the Earth\*. What this work does is to show that the Earth is older than we thought, by around 60 my.

"The composition of the gases we are looking at changes according to the conditions they are found in, which of course depend on the major events in Earth's history. The gas sealed in these quartz samples has been handed down to us in a sort of "time capsule". We are using standard methods to compute the age of the Earth, but having access to these ancient samples gives us new data, and allows us to refine the measurement".

The xenon gas signals allow us to calculate when the atmosphere was being formed, which was probably at the time the Earth collided with a planet-sized body, leading to the formation of the Moon. Our results mean that both the Earth and the Moon are older than we had thought".

Bernard Marty added

"This might seem a small difference, but it is important. These differences set time boundaries on how the planets evolved, especially through the major collisions in deep time which shaped the solar system".

*\*The oldest rocks of the solar system have been dated to 4,568 my ago, so the Earth is younger than that.*

### Abstract

*The age of the Earth-Moon system revisited using xenon isotope systematics*

*G. AVICE\* AND B. MARTY*

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*Recently, xenon trapped in fluid inclusions of Archean samples from North Pole, Pilbara (Australia) was found to be isotopically intermediate between cosmochemical endmembers (chondritic or solar) and the atmosphere [1, 2]. These results have been interpreted as resulting from prolonged loss of Xe atoms from the atmosphere to the outer space, that lasted at least until the end of the Archean eon [3]. Archean samples analysis together with modeling could help to put further constraints on the early history of the Earth-Moon system. We have analyzed noble gases (Xe, Kr and Ar) in fluid inclusions contained in quartz veins from the Barberton greenstone belt (South Africa) in order to (i) check if this noble gas fractionation represents, or not, a worldwide signature of the Archean atmosphere, (ii) get a more precise isotope analysis of Archean noble gases, and (iii) investigate the Xe isotopic evolution through geological periods of time. The Archean ( $\approx 3.2$  Ga) Xe isotope ratios, analyzed with a permil precision, indicate an isotopic fractionation of  $1.0 \pm 0.1$  ‰ in favor of the lighter isotopes for the Archean atmosphere relative to the modern one. These results confirm the fractionated state of the archean atmospheric xenon, as a result of prolonged Xe escape from the atmosphere through time. A model has been built to reproduce the temporal evolution of the isotopic composition of atmospheric xenon after a major impact and to take into account the addition of radiogenic/fissiogenic Xe atoms from extinct radioactivities ( $^{129}\text{I}$ ,  $^{244}\text{Pu}$  and  $^{238}\text{U}$ ). It permits to put constraints on the I-Pu- Xe age of the Earth-Moon system. The model reproduces with <1% the Xe isotopic compositions of the Archean and the modern atmospheres. It also resolves the unexplained atmospheric under-abundance of Xe isotopes from the fission of  $^{244}\text{Pu}$ . When corrected for prolonged loss, I-Pu-Xe ages of the Earth-Moon system are reconciled and shift from 70-100 Ma as previously thought, to  $40 \pm 20$  Ma after CAI.*

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### Herpes infected humans before they were human

***The virus originated in chimpanzees, jumping into humans 1.6 million years ago***

Researchers at the University of California, San Diego School of Medicine have identified the evolutionary origins of human herpes simplex virus (HSV) -1 and -2, reporting that the former infected hominids before their evolutionary split from chimpanzees 6 million years ago while the latter jumped from ancient chimpanzees to ancestors of modern humans – Homo erectus – approximately 1.6 million years ago.

The findings are published in the June 10 online issue of *Molecular Biology and Evolution*.

"The results help us to better understand how these viruses evolved and found their way into humans," said Joel O. Wertheim, PhD, assistant research scientist at the UC San Diego AntiViral Research Center and lead author of the study.

"Animal disease reservoirs are extremely important for global public health. Understanding where our viruses come from will help guide us in preventing future viruses from making the jump into humans."

Approximately two-thirds of the human population is infected with at least one herpes simplex virus. The viruses are most commonly presented as cold sores on the mouth or lips or blisters on the genitals.

"Humans are the only primates we know of that have two herpes simplex viruses," said Wertheim. "We wanted to determine why."

The researchers compared the HSV-1 and HSV-2 gene sequences to the family tree of simplex viruses from eight monkey and ape host species. Using advanced models of molecular evolution, the scientists were able to more accurately estimate ancient viral divergence times.

This approach allowed them to determine when HSV-1 and HSV-2 were introduced into humans with far more precision than standard models that do not account for natural selection over the course of viral evolution.

The genetics of human and primate herpes viruses were examined to assess their similarity. It became clear that HSV-1 has been present in humans far longer than HSV-2, prompting the researchers to further investigate the origins of HSV-2 in humans.

The viral family tree showed that HSV-2 was far more genetically similar to the herpes virus found in chimpanzees.

This level of divergence indicated that humans must have acquired HSV-2 from an ancestor of modern chimpanzees about 1.6 million years ago, prior to the rise of modern humans roughly 200,000 years ago.

"Comparing virus gene sequences gives us insight into viral pathogens that have been infecting us since before we were humans," said Wertheim.

*Co-authors include Martin D. Smith and Sergei L. Kosakovsky Pond, UC San Diego; Davey M. Smith, UC San Diego and Veterans Affairs San Diego Healthcare System; Konrad Scheffler, UC San Diego and Stellenbosch University, South Africa.*

*Funding for this research came from the University of California Laboratory Fees Research Program (grant 12-LR-236617), the National Institutes of Health (grants DA034978 and GM093939), the Bioinformatics and Information Technologies Core of the UC San Diego Center for AIDS Research (P30 AI036214), and the Department of Veterans Affairs.*

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## **New paper suggests High Tibet was cradle of evolution for cold-adapted mammals**

***Extinct Tibetan fox, a likely ancestor of today's Arctic fox, is latest animal paleontologist team believes used Tibet as 'training ground' for ice age***

For the last 2.5 million years, our planet has experienced cold and warm, millennia-long cycles that collectively have become known as the Ice Age. During cold periods, continental-scale ice sheets blanketed large tracts of the northern hemisphere. As the climate warmed up, these colossal glaciers receded, leaving Yosemite-like valleys and other majestic geologic features behind. The advance and retreat of the ice sheets also had a profound influence in the evolution and geographic distribution of many animals, including those that live today in the Arctic regions.

A new study published in the *Proceedings of the Royal Society B: Biological Sciences* identifies a newly discovered 3- to 5-million-year-old Tibetan fox from the Himalayan Mountains, *Vulpes qiuzhudingi*, as the likely ancestor of the living Arctic fox (*Vulpes lagopus*), lending support to the idea that the evolution of present-day animals of the Arctic region is intimately connected to ancestors that first became adapted for life in cold regions in the high altitude environments of the Tibetan Plateau.

The paper's lead author is Xiaoming Wang, of the Natural History Museum of Los Angeles County (NHM). Co-authors are Zhijie Jack Tseng (University of Southern California), Qiang Li (Chinese Academy of Sciences), Gary T. Takeuchi (Page Museum at the La Brea Tar Pits), and Guangpu Xie (Gansu Provincial Museum). These writers, on a team with other geologists and paleontologists and led by Wang, uncovered the fossil specimens in the Zanda Basin in southern Tibet in 2010.

In addition to the arctic fox, the team also uncovered extinct species of a woolly rhino, three-toed horse, Tibetan bharal (also known as blue sheep), chiru (Tibetan antelope), snow leopard, badger, as well as 23 other mammals.

The origin of the cold-adapted Pleistocene megafauna has usually been sought either in the arctic tundra or in the cool steppes elsewhere. But the team's new fossil assemblage boosts an alternative scenario, which the authors call the "out of Tibet" hypothesis. It argues that some of the Ice Age megafauna (which in North America include the woolly mammoth, saber-toothed cat, giant sloths, and others) used ancient Tibet as a "training ground" for developing adaptations that allowed them to cope with the severe climatic conditions. These Tibetan ancestors were thus pre-adapted to cold climates during the Ice Age (2.6-.01 million years ago).

Tibet, according to Wang, is a rich but grueling location for paleontological fieldwork. Fifteen summer seasons, and a good deal of luck, have honed his team's success. The expeditions involve a one-week journey to Lhasa, then a four-day drive into the remote "layer cake" sediments of the Zanda Basin - a drive made in old model Land Cruisers known to get stuck in streams.

At more than 14,000-foot elevation, it's difficult to breathe, water freezes overnight in camps, and the team members disband every morning to walk alone in search of fossils. Wang and his team have trained their eyes to search for ancient lake margins, where the megafauna they're interested in are often found. They alternate camp nights with nights in town, so they keep their strength up for a couple of weeks. "There are a lot of challenges," Wang said, "but in paleontological terms, it is a relatively unexplored environment. Our efforts are rewriting a significant chapter of our planet's recent geological history."



***This is a map of Pliocene Tibetan fox localities (red stars), Ice Age (late Pleistocene) arctic fox localities (yellow circles), and extant arctic fox (*Vulpes lagopus*) distribution, showing the connection between these two regions (red arrow), probably during the Ice***

***Age.*** Natural History Museum of Los Angeles County

[http://www.eurekaalert.org/pub\\_releases/2014-06/p-mlt060314.php](http://www.eurekaalert.org/pub_releases/2014-06/p-mlt060314.php)

### **Moles linked to risk for breast cancer**

***Cutaneous nevi, commonly known as moles, may be a novel predictor of breast cancer, according to two studies published in this week's PLOS Medicine.***

Jiali Han and colleagues from Indiana University and Harvard University, United States, and Marina Kvaskoff and colleagues from INSERM, France, report that women with a greater number of nevi are more likely to develop breast cancer. The researchers reached these conclusions by using data from two large prospective cohorts— the Nurses' Health Study in the United States, including 74,523 female

nurses followed for 24 years, and the E3N Teachers' Study Cohort in France, including 89,902 women followed for 18 years.

In the Nurses' Health Study, Han and colleagues asked study participants to report the number of nevi >3mm on their left arm at the initial assessment. They observed that women with 15 or more nevi were 35% more likely to be diagnosed with breast cancer than women who reported no nevi, corresponding to an absolute risk of developing breast cancer of 8.48% in women with no nevi and 11.4% for women with 15 or more nevi. In a subgroup of women, they observed that postmenopausal women with six or more nevi had higher blood levels of estrogen and testosterone than women with no nevi, and that the association between nevi and breast cancer risk disappeared after adjustment for hormone levels.

In the E3N Study, including mostly teachers, Kvaskoff and colleagues asked study participants to report whether they had no, a few, many, or very many moles. They observed that women with "very many" nevi had a 13% higher breast cancer risk than women reporting no nevi, although the association was no longer significant after adjusting for known breast cancer risk factors, especially benign breast disease or family history of breast cancer, which were themselves associated with nevi number.

These studies do not suggest that nevi cause breast cancer, but raise the possibility that nevi are affected by levels of sex hormones, which may be involved in the development of breast cancer. The findings do suggest that the number of nevi could be used as a marker of breast cancer risk, but it is unclear whether or how this information would improve risk estimation based on established risk factors. The accuracy of the findings is limited by the use of self-reported data on nevus numbers. Moreover, these findings may not apply to non-white women given that these studies involved mostly white participants.

In a linked Perspective, Barbara Fuhrman and Victor Cardenas discuss the potential implications of the findings from these studies. They say: "Additional studies should be carried out to investigate melanocytic nevi and other cutaneous features in association with the risks of breast cancer and other estrogen-related proliferative diseases. It is our hope that this research will provide etiologic insights and test practical uses of nevi and related phenotypes for their potential utility in breast cancer risk assessment."

*Funding:* The Nurses' Health Study cohort is supported by NIH grants CA87969 and CA49449 (<http://www.nih.gov/>). 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:* Zhang M, Zhang X, Qureshi AA, Eliassen AH, Hankinson SE, et al. (2014)

*Association between Cutaneous Nevi and Breast Cancer in the Nurses' Health Study: A*

*Prospective Cohort Study.* [PLoS Med 11\(6\): e1001659. doi:10.1371/journal.pmed.1001659](http://dx.doi.org/10.1371/journal.pmed.1001659)

[http://www.eurekalert.org/pub\\_releases/2014-06/afps-itl061114.php](http://www.eurekalert.org/pub_releases/2014-06/afps-itl061114.php)

**It's the last bite that keeps you coming back for more**  
*Memory for that last bite of a steak or chocolate cake may be more influential than memory for the first bite*

Your memory for that last bite of a steak or chocolate cake may be more influential than memory for the first bite in determining when you want to eat it again, according to research published in *Psychological Science*, a journal of the Association for Psychological Science.

Our memories for foods are often vivid, especially when we experience foods that are terrifyingly bad or delightfully good. The findings from this research shed light on how memories for food are formed and how they guide our decisions about how soon we're willing to eat a food again.

"Research has told us a lot about factors that influence what foods people want to consume, but less is known about factors that influence when they want to consume a particular food again," explains researcher and lead author Emily Garbinsky of the Stanford University Graduate School of Business.

"Companies profit not only from the sale of food items but also from how frequently those particular items are sold, and the impact of eating both healthy and unhealthy foods on people's health is determined not only by how much they eat but how often those foods are eaten," says Garbinsky. "As such, it seemed important to get a better understanding of what influences the amount of time that passes until consumption is repeated."

Garbinsky and colleagues Carey Morewedge of the Boston University School of Management and Baba Shiv of the Stanford University Graduate School of Business investigated the question in a series of studies.

In one study, the researchers asked 134 undergraduate students to sample 3 flavors of Nut Thin crackers and then choose one to eat. They were then given a specific number of crackers and were asked to rate how much they enjoyed each one after they ate it. The results revealed that students who had eaten the larger portion (15 crackers) reported significantly lower enjoyment at the end than those who had eaten the smaller portion (3 crackers).

These findings replicate previous findings on "sensory-specific satiety": Each bit of food is less pleasant than the one before it. Thus, the bigger the portion, the less enjoyment you get out of the last few bites.

More importantly, participants' enjoyment of the last cracker (manipulated by portion size) seemed to influence how soon the students wanted to eat the crackers again: Participants who ate a small portion typically opted to receive a giveaway box of Nut Thins sooner than did participants who ate the larger portion.

These results suggest that the most recent tastes experienced in the last few bites of a given food drive our decisions about when to eat that food again, a finding that they researchers replicated in a second study.

Garbinsky and colleagues hypothesized that this so-called "recency effect" might be explained by memory interference induced by the repetitiveness of eating:

"A glass of juice, bowl of ice cream, or bag of potato chips contains many units of very similar stimuli that are consumed one sip or bite at a time until the entire portion has been eaten," they write. So, if we take a lot of bites of the same food in succession, our memory for the last bites may interfere with our ability to accurately remember the initial bites of that food.

Garbinsky and colleagues were able to eliminate this memory interference by reminding participants of their previous ratings as they continued to consume and rate a glass of juice. These participants were more accurate in remembering how much they enjoyed the first ounce of juice and they opted to receive a giveaway container of juice sooner than did the participants who rated each ounce of juice without being reminded of their previous ratings. The fact that memory for the last few bites seems to drive our decisions about when to eat a food again may be particularly relevant in places like the United States, where portion sizes tend to be larger and are likely to result in lower end enjoyment:

*"This finding is important in that it suggests that large portions may be somewhat detrimental to companies because they extend the amount of time that passes until repeat consumption occurs," says Garbinsky. "And it's also important to the public, as eating too much of a favorite - or healthy - food may increase the delay until one wants to eat it again."*

The studies do suggest that certain strategies – such as thinking back to the first few bites – could be used to encourage consumers to eat a food again soon. But, as tantalizing as these insights may be, Garbinsky cautions that more research is needed to investigate whether the findings translate to real-world settings, in which consumers have more control over deciding what and how much they eat.

All data and materials can be accessed at <http://stanford.edu/~emilyg47/cv.html>. The complete Open Practices Disclosure for this article can be found at <http://pss.sagepub.com/content/by/supplemental-data>.

<http://phys.org/news/2014-06-scientists-weed-pesky-poison-ivy.html>

**Scientists weed out pesky poison ivy with discovery of killer fungus**  
*John Jelesko and Matt Kasson have discovered a natural fungus that kills poison ivy.*

Much to the chagrin of gardeners, hikers, and virtually anyone enjoying the outdoors, one of the hazards of summer is picking up an itchy poison ivy rash. But researchers in the Virginia Tech College of Agriculture and Life Sciences have

found an effective way to kill poison ivy using a naturally occurring fungus that grows on the fleshy tissue surrounding the plant's seed, potentially giving homeowners and forest managers the ability to rid landscapes of the pernicious pest. Their findings could make the maddening itch of the summer season a thing of the past for the untold millions who are allergic to the plant. The study was published this week in the journal *Plant Disease* and is a first of its kind on a plant that affects millions but has had surprisingly little research done on it.

John Jelesko, an associate professor of plant pathology, physiology, and weed science, began studying the plant after experiencing a nasty poison ivy rash himself while doing some yard work. Much to his surprise, there was scant research focused on the plant itself. Most of the work was centered on urushiol, the rash-causing chemical found in the plant's oils. Urushiol is extremely potent. Only one nanogram is needed to cause a rash, and the oil can remain active on dead plants up to five years.

But rather than focusing on urushiol, Jelesko set about studying ways to kill the plant itself. He worked with Matt Kasson on the project, a senior research associate in the same department.

"This poison ivy research has the potential to affect the untold millions of people who are allergic to poison ivy," said Jelesko, a Fralin Life Science Institute faculty member. "We have the makings of a nonchemical way to control an invasive plant that can be used by homeowners and others who manage outdoor sites."

Their work is especially valuable in light of the fact that a 2006 study showed that as the planet warms, poison ivy is predicted to grow faster, bigger, and more allergenic, causing much more serious reactions that could send an increasing number of people to the doctor for prescription medications. "When poison ivy can't be treated with over-the-counter treatments and requires an outpatient visit, then we are talking about a public health concern that is very real," said Kasson. The research team discovered the killer fungus in their initial attempts to generate microbe-free poison ivy seedlings to use in their studies. Jelesko noticed that not only were some of the seeds failing to germinate, but on the seedlings that did germinate, there was a blight wiping out the young seedlings. Jelesko enlisted the help of Kasson to isolate what he suspected was a fungus causing disease in the plants. The team discovered that the fungus was growing on all the plants that died and the seeds that didn't germinate.

The fungus caused wilt and chlorophyll loss on the seedlings just by placing it at the junction of the main stem and root collar of the plant at three weeks post-inoculation. At seven weeks post-inoculation, all but one of the plants had died. Though herbicides are available to kill poison ivy, Jelesko and Kasson said that if this fungus were developed into a commercial application, it would not only be

more effective than its chemical counterparts, but also have the benefit of being completely natural.

"We have to keep in mind that the chemicals used to control poison ivy are general herbicides, meaning that they will affect and probably kill many other plant species, so their use in large areas is not always practical," said Thomas Mitchell, associate professor of fungal biology and molecular genetics at Ohio State University who is familiar with the research but not affiliated with it. "This work shows promise for an alternative approach to the use of chemicals and has great potential as a biological control alternative. This type of approach, using native pathogens to control noxious and invasive plants, is gaining more much deserved recognition." Kasson, whose research is funded by the U.S. Department of Agriculture Forest Service, believes it would be relatively simple to develop a soil granular to spread on top of poison ivy-infested areas in yards and recreational areas such as campgrounds to naturally infect the plants and kill them.

After Kasson successfully isolated the fungus in pure culture from infected plants, a DNA analysis revealed that the fungus - *Colletotrichum fioriniae* - is also widely known as an insect pathogen that kills an invasive bug that infests and kills hemlock trees.

In all of the natural world, only humans are allergic to poison ivy and its itch-inducing oil, urushiol. "Humans appear to be uniquely allergic to urushiol," said Jelesko. "Goats eat it, deer eat it, and birds eat the seeds, all to no ill effects."

Jelesko and Kasson have filed for a patent disclosure of their current findings, and say that this research just scratches the surface of possible avenues for the study of poison ivy.

*More information: "First Report of Seedling Blight of Eastern Poison Ivy (Toxicodendron radicans) by Colletotrichum fioriniae in Virginia." M. T. Kasson, J. R. Pollok, E. B. Benhase, and J. G. Jelesko, Plant Disease 2014 98:7, 995-995. dx.doi.org/10.1094/PDIS-09-13-0946-PDN*

<http://www.bbc.com/news/world-asia-27758640>

### Malaysia swarmed by giant moths

*Swarms of giant moths have descended on Malaysia, invading homes and even disrupting a national football match.*

By Heather Chen BBC News

Thousands of the furry insects, with a wing span of up to 16cm (6in), interrupted a semi-finals match at the Darul Makmur Stadium last week. Over 800 sightings were also reported in neighbouring Singapore last month, sparking intense online debate. The *Lyssa Zampa* tropical moth, which is also known as the Laos brown butterfly, is native to South East Asia.

Biology lecturer N Sivasothi said that while the moth sightings appear to be "unprecedented", it is not a new phenomenon. "

The moths are actually present during other times of the year but in very small numbers, so they are usually not noticed by people," Mr Sivasothi said, adding that the creatures typically emerge between April and August every year.

Ecologist Anuj Jain said moths' use of light for navigation often causes them to head to built-up areas.

"Their tendency to emigrate in search of new uneaten host plants attracts these moths to light in urban city areas," he said.

Experts said that while people suffering from asthma may be sensitive to hairs on their wings, the nocturnal creatures do not pose any threat.



*While harmless to many, people suffering from asthma may be sensitive to fine hairs on moths*

"The moths are harmless and the public has nothing to be afraid of," said Lena Chan, Director of the National Biodiversity Centre at the National Parks Board in Singapore.

"There is no need for people to protect themselves against these moths as they do not cause any allergies or diseases. In fact, they are important pollinators and are beautiful to watch."

Many Malaysians and Singaporeans however, took to the internet to share their moth encounters and to upload photographs of the winged creatures.

Although many seemed to welcome the arrival of the furry insects, others remained cautious.

"In China, moths are viewed as symbols of death as they represent the souls of deceased loved ones," said Chinese astrologer Cindy Wu. "It is therefore considered a serious taboo to kill moths or disturb them."

[http://www.eurekalert.org/pub\\_releases/2014-06/nu-wtb061114.php](http://www.eurekalert.org/pub_releases/2014-06/nu-wtb061114.php)

### **What's the best way for toddlers to acquire verb meaning?**

#### *How verbs are 'packaged' in sentences is key*

EVANSTON, Ill. - New research is shedding light on what kind of sentences are best at facilitating the growth of toddlers' vocabularies.

A new study conducted at Northwestern University provides evidence that toddlers can learn verbs after hearing them only twice.

Sandra R. Waxman, Louis W. Menk Professor of Psychology at Northwestern University and Sudha Arunachalam, formerly a postdoctoral fellow at Northwestern, note that previous studies have shown that children as young as two years of age can successfully learn novel verbs after they've heard the verb many times while looking at a corresponding visual scene.

However, Waxman said, the key to the toddlers' success is how the verb is "packaged."

For example, if a dad says to his two-year-old toddler, "I see a boy, and a balloon. I see waving," and another dad says to his two-year-old toddler, "A boy is waving a balloon," is one of them more likely to learn the verb "waving" than the other? The researchers said yes.

Arunachalam, lead author of the study and currently assistant professor of speech and hearing sciences at Boston University, and Waxman, director of Northwestern's Project on Child Development, looked into which of these ways of introducing novel verbs is most helpful to toddlers.

In a series of experiments, toddlers were introduced to six different novel verbs presented in one or two sentences of varying complexity.

Some heard the verb in a single sentence that also included two nouns such as, "A boy is gonna pilk a balloon! Let's see!"

Others heard the verb in simpler constructions in which the familiar nouns were mentioned in one sentence and the new verb in another, such as "Let's see a boy and a balloon. Let's see pilking!"

Then, both groups watched a short video clip of a boy waving a balloon.

Afterwards, the toddlers were shown two different pictures -- one with the same object, but a different action being performed on it (e.g., tapping the balloon), and one with the target action being performed on a new object (e.g., waving a rake). The toddlers were asked to point to "pilking."

Only the toddlers who heard the verb in the same sentence with both nouns (e.g., "The boy is waving a balloon") were able to successfully identify the target action.

"The results offer two insights," Arunachalam said.

"First, by age two, toddlers have the remarkable ability to learn new verbs with very little exposure and apply them in novel contexts. Second, presenting the verbs in complete sentences supports the toddlers' abilities to do so.

These findings highlight the positive impact that rich communication can have on two-year-olds' burgeoning linguistic abilities."

*"Let's See a Boy and a Balloon: Argument Labels and Syntactic Frame in Verb Learning" will be published in Language Learning and Development.*

[http://www.eurekalert.org/pub\\_releases/2014-06/uow-gfi060914.php](http://www.eurekalert.org/pub_releases/2014-06/uow-gfi060914.php)

## Genes found in nature yield 1918-like virus with pandemic potential

*An international team of researchers has shown that circulating avian influenza viruses contain all the genetic ingredients necessary to underpin the emergence of a virus similar to the deadly 1918 influenza virus.*

MADISON - Searching public databases, the researchers, led by Yoshihiro Kawaoka of the University of Wisconsin-Madison, identified eight genes from influenza viruses isolated from wild ducks that possessed remarkable genetic similarities to the genes that made up the 1918 pandemic flu virus. The 1918 or "Spanish flu" pandemic was one of recorded history's most devastating outbreaks of disease, resulting in an estimated 40 million deaths worldwide.

The new work was published today (June 11, 2014) in the journal *Cell Host and Microbe*. It shows that "there are gene pools in nature that have the potential to cause a severe pandemic in the future," says Kawaoka, an international authority on influenza and the senior author of the new report.

To assess the risk posed by a virus that could acquire all eight of the 1918-like genes, the team used reverse genetics methods to generate a virus that differed from the 1918 virus by only 3 percent of the amino acids that make the virus proteins.

The resulting virus was more pathogenic in mice and ferrets than an ordinary avian flu virus, but was not as pathogenic as the 1918 virus and it did not transmit in ferrets via respiratory droplets, the primary mode of flu transmission.

Since pandemic risk escalates when a virus becomes transmissible, Kawaoka's group then conducted additional experiments to determine how many changes would be required for the avian 1918-like virus to become transmissible in ferrets, a well-accepted model for influenza transmission studies. The researchers identified seven mutations in three viral genes that enabled the pathogen to transmit as efficiently as the 1918 virus.

The resulting virus, composed of genetic factors circulating in wild and domesticated birds, demonstrates that the genetic ingredients for a potentially deadly and pandemic pathogen exist in nature and could combine to form such a virus, according to Kawaoka.

The new study is important because it shows the potential risk of circulating strains of avian influenza viruses, Kawaoka explains.

Knowing what genes to look for, he says, can help predict the likelihood of an emerging strain of pandemic flu and, importantly, help scientists devise strategies for countering such a pathogen.

Critically, the research provides additional insight and evidence for the mechanisms responsible for adaptation of avian influenza viruses to mammals. One mutation in the novel transmissible 1918-like avian virus, for example, is responsible for increased virus growth in mammalian cells. Mutations in hemagglutinin, a protein found on the surface of influenza viruses that binds to host cells, alter the protein's stability, a change that could potentially enhance the virus's ability to infect the upper respiratory tract of humans.

The same mechanisms were associated with effective transmission of H5N1 avian viruses, as reported in an earlier study, and the newly emergent H7N9 virus infecting humans in China also seems to possess some of the same qualities. A key finding of the new study, notes Kawaoka, is that sera from individuals vaccinated with the current seasonal influenza vaccine (which protects against 2009 H1N1 influenza, a related virus) reacted with the novel transmissible 1918-like avian virus. That discovery suggests that protection against a potential pandemic threat exists in the currently available vaccine. In addition, the team showed that the novel transmissible virus is expected to be sensitive to the antiviral medication oseltamivir.

The transmission studies were conducted under specially designed high-containment conditions, using commensurate biosafety practices, at UW-Madison with approval of the university's Institutional Biosafety Committee.

The draft manuscript was reviewed by the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH), in keeping with the institute's implementation of the United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern.

"The point of the study was to assess the risk of avian viruses currently circulating in nature," explains Kawaoka, who, in addition to his appointment as a professor in the UW-Madison School of Veterinary Medicine, holds a faculty position at the University of Tokyo. "We found genes in avian influenza viruses quite closely related to the 1918 virus and, to evaluate the pandemic potential should such a 1918-like avian virus emerge, identified changes that enabled it to transmit in ferrets.

"With each study, we learn more about the key features that enable an avian influenza virus to adapt to mammals and become transmissible," says Kawaoka.

"Eventually, we hope to be able to reliably identify viruses with significant pandemic potential so we can focus preparedness efforts appropriately."

*The research described in this document was funded by grants from the National Institute of Allergy and Infectious Diseases Public Health Service research grants, by RO1 AI080598, and R56 AI099275, by ERATO (Japan Science and Technology Agency), and by the Strategic Basic Research Programs of Japan Science and Technology Agency.*



<http://bit.ly/1pSXx6X>

## Oldest Handmade Skull Attributed to Leonardo da Vinci

*Researchers believe they have found Leonardo Da Vinci's "sorrow stone" - a creepy, miniature skull crafted in great anatomical detail.*

Jun 11, 2014 06:25 PM ET // by Rossella Lorenzi

Missing a lower jaw, the early 16th century artifact was found by a German couple in 1987 in an antique shop.

"It is a small, naturalistic looking, deformed skull of a more than 50-year-old-male and it is made of a partially hollowed stone like material," wrote independent Belgian researcher Stefaan Missinne in the Wiener Medizinische Wochenschrift, a medical journal published in Vienna.

Milky white with small, brownish-yellow stains, the tiny artifact features remarkable detail. "Detailed eye sockets lead to the inside of the cranium and allow for a 'view' of the inside, which is anatomically abnormal," Missinne said.



**Photo: The miniature skull attributed to Leonardo Da Vinci. Credit: Dr. K.Becker**

According to French skull expert Roger Saban, the object resembles an anatomic drawing known as RL 19057. Housed in the Royal Collection in Windsor Castle, the unpublished drawing shows a similar deformed skull missing a lower jaw. Despite the extraordinary level of detail, the drawing and the skull both feature the same small anatomical errors, further strengthening the link with Leonardo.

Chemical analysis showed the artifact was made from an agate-based mixture of quartz and gypsum. Leonardo invented this mixture, which he called "mitioni," between 1503 and 1509. No one else is known to have experimented with this material, which was likely sourced in a mine near Volterra in Tuscany.

The size of the artifact matches Florentine measurement units that were used in the Renaissance. "The origin of the skull, leads, therefore, to Florence," Missinne said. Contemporary writings such as those in the inventory of Da Vinci's assistant Salai confirm Leonardo's possession of a detailed miniature skull made from mitioni. The skull dates to about 1508, Missinne said, when Leonardo was 56. Missinne believes the aging artist, who was prone to being melancholic, used the skull as his personal sorrow stone.

"The skull was exhibited several times, the last being in Leoben, Austria, and not one negative reaction was expressed on its attribution to Leonardo," Missinne said.

[http://www.eurekalert.org/pub\\_releases/2014-06/uoc-nff061014.php](http://www.eurekalert.org/pub_releases/2014-06/uoc-nff061014.php)

## New fossil find pinpoints the origin of jaws in vertebrates

*First time gill arches have been seen so early in the fossil record*

A key piece in the puzzle of the evolution of vertebrates has been identified, after the discovery of fossilised fish specimens, dating from the Cambrian period (around 505 million years old), in the Canadian Rockies. The fish, known as *Metaspriggina*, shows pairs of exceptionally well-preserved arches near the front of its body. The first of these pairs, closest to the head, eventually led to the evolution of jaws in vertebrates, the first time this feature has been seen so early in the fossil record.

Fish fossils from the Cambrian period are very rare and usually poorly preserved. This new discovery shows in unprecedented detail how some of the earliest vertebrates developed – the starting point of a story which led to animals such as later fish species, but also dinosaurs and mammals such as horses and even ourselves. The findings are published in the 11 June edition of the journal *Nature*. Fossils of *Metaspriggina* were recovered from several locations including the Burgess Shale site in Canada's Rocky Mountains, one of the richest Cambrian fossil deposits in the world. These fossils shed new light on the Cambrian 'explosion', a period of rapid evolution starting around 540 million years ago, when most major animal phyla originated.

Previously, only two incomplete specimens of *Metaspriggina* had been identified. During expeditions conducted by the Royal Ontario Museum in 2012, 44 new Burgess Shale fossils were collected near Marble Canyon in Kootenay National Park in British Columbia, which provide the basis for this study.

Researchers from the University of Cambridge and the Royal Ontario Museum/University of Toronto used these fossils, along with several more specimens from the eastern United States, to reclassify *Metaspriggina* as one of the first vertebrates.



**Left: This is an illustration of *Metaspriggina* swimming. Drawing by: Marianne Collins. © Conway Morris and Caron. Right: This is a fossil of *Metaspriggina* from Marble Canyon - head to the left with two eyes, and branchial arches at the top. Photo by: Jean-Bernard Caron © ROM. Credit: Left: Drawing by: Marianne Collins. © Conway Morris and Caron.**

**Right: Photo by: Jean-Bernard Caron © ROM.**

The fossils, which date from 505 million years ago, also show clearly for the first time how a series of rod-like structures, known as the gill or branchial arches, were

arranged in the earliest vertebrates. These arches have long been known to have played a key role in the evolution of vertebrates, including the origin of jaws, and some of the tiny bones in the ear which transmit sound in mammals. Until now, however, a lack of quality fossils has meant that the arrangement of these arches in the first vertebrates had been hypothetical.

Vertebrates first appear in the fossil record slightly earlier than these finds, but pinpointing exactly how they developed is difficult. This is because fossils of such animals are rare, incomplete and open to varying interpretations, as they show soft tissues which are difficult to identify with complete certainty.

The new fossils of *Metaspriggina* are remarkably well-preserved. The arrangement of the muscles shows these fish were active swimmers, not unlike a trout, and the animals saw the world through a pair of large eyes and sensed their surrounding environment with nasal structures.

"The detail in this *Metaspriggina* fossil is stunning," said lead author Professor Simon Conway Morris of Cambridge's Department of Earth Sciences. "Even the eyes are beautifully preserved and clearly evident."

But it is the branchial arches which makes this discovery so important. Previously, they were thought to exist as a series of single arches, but *Metaspriggina* now shows that they in fact existed in pairs. The anteriormost pair of arches is also slightly thicker than the remainder, and this subtle distinction may be the very first step in an evolutionary transformation that in due course led to the appearance of the jaw. "Once the jaws have developed, the whole world opens," said Professor Conway Morris. "Having a hypothetical model swim into the fossil record like this is incredibly gratifying."

"Obviously jawed fish came later, but this is like a starting post – everything is there and ready to go," said the paper's co-author Dr Jean-Bernard Caron, Curator of Invertebrate Palaeontology at the Royal Ontario Museum and an associate professor in the Departments of Earth Sciences and Ecology & Evolutionary Biology at the University of Toronto. "Not only is this a major new discovery, one that will play a key role in understanding our own origins, but Marble Canyon, the new Burgess Shale locality itself has fantastic potential for revealing key insights into the early evolution of many other animal groups during this crucial time in the history of life."

David Wilks, Member of Canadian Parliament for Kootenay-Columbia, noted, "The Government of Canada is excited about this incredible fossil find. As an international leader in conservation and steward of the Burgess Shale, Parks Canada is pleased to provide its research partners with access to the fossils. Their remarkable discoveries inform the work we do to share this rich natural history

through our popular guided hikes, and to protect this important Canadian heritage in a national park and UNESCO World Heritage Site."

"A primitive fish from the Cambrian of North America" in the journal *Nature*, published on June 11, 2014. DOI # is 10.1038/nature13414 [http://www.nature.com/search/adv\\_search](http://www.nature.com/search/adv_search)

[http://www.eurekalert.org/pub\\_releases/2014-06/uop-gdb061114.php](http://www.eurekalert.org/pub_releases/2014-06/uop-gdb061114.php)

## **Gum disease bacteria selectively disarm immune system, Penn study finds**

### ***Periodontitis bacteria cause dysbiosis through a sophisticated, two-prong manipulation of the human immune system***

The human body is comprised of roughly 10 times more bacterial cells than human cells. In healthy people, these bacteria are typically harmless and often helpful, keeping disease-causing microbes at bay. But, when disturbances knock these bacterial populations out of balance, illnesses can arise. Periodontitis, a severe form of gum disease, is one example.

In a new study, University of Pennsylvania researchers show that bacteria responsible for many cases of periodontitis cause this imbalance, known as dysbiosis, with a sophisticated, two-prong manipulation of the human immune system.

Their findings, reported in the journal *Cell Host & Microbe*, lay out the mechanism, revealing that the periodontal bacterium *Porphyromonas gingivalis* acts on two molecular pathways to simultaneously block immune cells' killing ability while preserving the cells' ability to cause inflammation. The selective strategy protects "bystander" gum bacteria from immune system clearance, promoting dysbiosis and leading to the bone loss and inflammation that characterizes periodontitis. At the same time, breakdown products produced by inflammation provide essential nutrients that "feed" the dysbiotic microbial community. The result is a vicious cycle in which inflammation and dysbiosis reinforce one another, exacerbating periodontitis.

George Hajishengallis, a professor in the Penn School of Dental Medicine's Department of Microbiology, was the senior author on the paper, collaborating with co-senior author John Lambris, the Dr. Ralph and Sallie Weaver Professor of Research Medicine in the Department of Pathology and Laboratory Medicine in Penn's Perelman School of Medicine. Collaborators included Tomoki Maekawa and Toshiharu Abe of Penn Dental Medicine.

Work by Hajishengallis's group and collaborators had previously identified *P. gingivalis* as a "keystone pathogen." Drawing an analogy from the field of ecology, in which a species such as a grizzly bear is thought of as a keystone species because of the influence it has over a number of other species in the community, the idea suggests that, although *P. gingivalis* may be relatively few in number in the mouth,

their presence exerts an outsized pull on the overall microbial ecosystem. Indeed, the team has shown that, although *P. gingivalis* is responsible for instigating the process that leads to periodontitis, it can't cause the disease by itself.

"Scientists are beginning to suspect that keystone pathogens might be playing a role in irritable bowel disease, colon cancer and other inflammatory diseases," Hajishengallis said. "They're bugs that can't mediate the disease on their own; they need other, normally non-pathogenic bacteria to cause the inflammation."

In this study, they wanted to more fully understand the molecules involved in the process by which *P. gingivalis* caused disease.

"We asked the question, how could bacteria evade killing without shutting off inflammation, which they need to obtain their food," Hajishengallis said.

The researchers focused on neutrophils, which shoulder the bulk of responsibility of responding to periodontal insults. Based on the findings of previous studies, they examined the role of two protein receptors: C5aR and Toll-like receptor-2, or TLR2. Inoculating mice with *P. gingivalis*, they found that animals that lacked either of these receptors as well as animals that were treated with drugs that blocked these receptors had lower levels of bacteria than untreated, normal mice. Blocking either of these receptors on human neutrophils in culture also significantly enhanced the cells' ability to kill the bacteria. Microscopy revealed that *P. gingivalis* causes TLR2 and C5aR to physically come together.

"These findings suggest that there is some crosstalk between TLR2 and C5aR," Hajishengallis said. "Without either one, the bacteria weren't as effective at colonizing the gums."

Further experiments in mice and in cultured human neutrophils helped the researchers identify additional elements of how *P. gingivalis* operates to subvert the immune system. They found that the TLR2-C5aR crosstalk leads to degradation of the protein MyD88, which normally helps clear infection. And in a separate pathway from MyD88, they discovered that *P. gingivalis* activates the enzyme PI3K through C5aR-TLR2 crosstalk, promoting inflammation and inhibiting neutrophils' ability to phagocytose, or "eat," invading bacteria.

Inhibiting the activity of either PI3K or a molecule that acted upstream of PI3K called Mal restored the neutrophils' ability to clear *P. gingivalis* from the gums.

"*P. gingivalis* uses this connection between C5aR and TLR2 to disarm and dissociate the MyD88 pathway, which normally protects the host from infection, from the proinflammatory and immune-evasive pathway mediated by Mal and PI3K," Hajishengallis said.

Not only does the team's discovery open up new targets for periodontitis treatment, it also suggests a bacterial strategy that could be at play in other diseases involving dysbiosis.

*Additional co-authors included Jennifer L. Krauss and Ravi Jotwani of the University of Louisville, who were former members of the Hajishengallis lab; Martha Triantafilou and Kathy Triantafilou of Cardiff University School of Medicine; Ahmed Hashim and Michael A. Curtis of Queen Mary University of London; and Shifra Hoch and Gabriel Nussbaum of Hebrew University.*

*The research was supported by the National Institutes of Health, European Commission and Medical Research Council.*

<http://bit.ly/1mVLfXb>

## **Two giant planets may cruise unseen beyond Pluto**

*The monsters are multiplying.*

17:30 11 June 2014 by Nicola Jenner

Just months after astronomers announced hints of a giant "Planet X" lurking beyond Pluto, a team in Spain says there may actually be two supersized planets hiding in the outer reaches of our solar system.

When potential dwarf planet 2012 VP113 was discovered in March, it joined a handful of unusual rocky objects known to reside beyond the orbit of Pluto. These small objects have curiously aligned orbits, which hints that an unseen planet even further out is influencing their behaviour. Scientists calculated that this world would be about 10 times the mass of Earth and would orbit at roughly 250 times Earth's distance from the sun.

Now Carlos and Raul de la Fuente Marcos at the Complutense University of Madrid in Spain have taken another look at these distant bodies. As well as confirming their bizarre orbital alignment, the pair found additional puzzling patterns. Small groups of the objects have very similar orbital paths. Because they are not massive enough to be tugging on each other, the researchers think the objects are being "shepherded" by a larger object in a pattern known as orbital resonance.

### **Planet shepherd**

For instance, we know that Neptune and Pluto are in orbital resonance – for every two orbits Pluto makes around the sun, Neptune makes three. Similarly, one group of small objects seems to be in lockstep with a much more distant, unseen planet. That world would have a mass between that of Mars and Saturn and would sit about 200 times Earth's distance from the sun.

Some of the smaller objects have very elongated orbits that would take them out to this distance. It is unusual for a large planet to orbit so close to other bodies unless it is dynamically tied to something else, so the researchers suggest that the large planet is itself in resonance with a more massive world at about 250 times the Earth-sun distance – just like the one predicted in the previous work.

Observing these putative planets will be tricky. The smaller bodies are on very elliptical orbits and were only spotted when they ventured closest to the sun. But

the big planets would have roughly circular orbits and would be slow moving and dim, making them tough for current telescopes to see. "It's not at all surprising that they haven't been found yet," says Carlos.

"As there are only a few of these extremely distant objects known, it's hard to say anything definitive about the number or location of any distant planets," says Scott Sheppard at the Carnegie Institution for Science in Washington DC, one of the discoverers of 2012 VP113. "However, in the near future we should have more objects to work with to help us determine the structure of the outer solar system."

Reference: [arxiv.org/abs/1406.0715](http://arxiv.org/abs/1406.0715)

[http://www.eurekalert.org/pub\\_releases/2014-06/elar-cum061114.php](http://www.eurekalert.org/pub_releases/2014-06/elar-cum061114.php)

### **Cranial ultrasound may replace temporal artery biopsy in diagnosis of giant cell arteritis**

*Non-invasive test more sensitive and equally specific compared to current gold standard*

A new study presented for the first time today at the European League Against Rheumatism Annual Congress (EULAR 2014), shows that cranial ultrasound has a greater sensitivity than temporal artery biopsy,\* and a comparable specificity in the diagnosis of Giant Cell Arteritis (GCA).<sup>1</sup>

Giant Cell Arteritis (GCA), a condition in which medium and large arteries mainly in the head and neck, become inflamed and narrowed, can cause blindness due to occlusion of the artery supplying the back of the eye. It is therefore essential that a prompt, accurate diagnosis of GCA is made and treatment with high dose steroids started as soon as possible. Currently there are no 100% accurate diagnostic tests for GCA. Patients typically present with severe headache and scalp tenderness located to one or both sides of the forehead. However, GCA can be difficult to distinguish from other less serious causes of headache.

In this study, cranial ultrasound was the strongest predictor for a diagnosis of GCA when results were evaluated against a confirmed clinical diagnosis at three months. In contrast, the existing American College of Rheumatology (ACR) criteria that include TAB,† when used alone, were insufficiently specific to accurately predict or exclude the diagnosis of GCA at three months. Relying on ACR criteria alone would therefore be leaving patients at risk of missing out on potentially sight-saving steroid treatment, or of being treated with high dose steroids unnecessarily. "Although temporal artery biopsy (TAB) has historically been considered the 'gold standard' diagnostic test for GCA, the exciting results of this new study suggest cranial ultrasound may soon replace TAB in the assessment of patients with a suspected diagnosis of GCA in routine clinical practice," said lead author Dr Adam Croft from the Centre for Translational Inflammation Research, University of Birmingham, UK.

"Patients with symptoms and signs of GCA can now be offered a much simpler, more accurate diagnostic test. The high predictive accuracy of cranial ultrasound over temporal artery biopsy indicated that temporal artery biopsy may now be unnecessary, particularly where clinical suspicion of GCA is high or quite low," Dr Croft added.

Out of a total of 87 patients who underwent cranial ultrasound for suspected GCA, 36 patients (41%) had a confirmed clinical diagnosis at the three month follow-up. Of the 30 patients who had a positive cranial ultrasound, 29 (96%) went on to have a confirmed diagnosis of GCA at three months. Of the 36 patients with more than three ACR criteria†, only 21 (58%) had a diagnosis of GCA confirmed at three months.

"Being able to reliably confirm the diagnosis is important not just to ensure those patients with GCA receive high-dose steroids to help prevent blindness, but also to prevent patients who don't have GCA continuing high-dose steroid therapy unnecessarily. High doses of steroids can cause a variety of unpleasant side effects including weight gain, infection risk, osteoporosis and fracture risk, high blood pressure, diabetes, cataracts," Dr Adam Croft explained.

When compared to clinical diagnosis at three months, the sensitivity of cranial ultrasound was 81%, specificity 98%, positive likelihood ratio 41, negative likelihood ratio 0.2, positive predictive value of 97% and negative predictive value of 88%. In contrast, when compared to clinical diagnosis at three months TAB had a sensitivity of 53%, specificity 100%, positive likelihood ratio 2.3, negative likelihood ratio 0.2, positive predictive value of 100% and negative predictive value of 47%. Over the last 25□ years, GCA has been found to be the most common type of vasculitis in Europe and North America, especially in people aged >70 years. GCA mainly affects white individuals, and it almost exclusively occurs in subjects aged >50 years. The cause of giant cell arteritis is unclear; however, it is thought that a combination of genetic and environmental factors, such as an infection may be responsible.<sup>2</sup> Prompt treatment of GCA with high dose steroids is essential to prevent permanent loss of vision. In one study, 14% permanently lost vision because of GCA, and in 94% of these patients the visual deficit developed before steroid therapy for GCA was begun.<sup>3</sup>

In this study, all patients undergoing cranial ultrasound between January 2005 and July 2013 were identified and clinical data obtained from electronic records, and, if necessary primary care providers. ACR criteria for GCA were used to classify patients.

Ultrasound reports were independently classified according to whether there was evidence of an arteritis or not. Explicit ultrasound features of GCA, such as a halo sign were not required to make this determination. The relationship between the

ACR criteria alone or in combination with ultrasound and a final clinical diagnosis of GCA (made after a minimum of three-month follow-up) was analysed. A clinical diagnosis of GCA after three months of follow up served as the gold standard. The sensitivity and specificity of cranial ultrasound and of TAB were examined against this gold standard.

**Abstract Number: OP0056**

<sup>1</sup>Croft A, Thompson N, Duddy M. et al. Can we replace temporal artery biopsy with cranial ultrasound for the diagnosis of giant cell arteritis? A retrospective cohort study of the diagnostic utility of ultrasound in routine clinical practice. EULAR 2014; Paris: Abstract OP0056 2 Gonzalez-Gay MA, Vazquez-Rodriguez TR, Lopez-Diaz MJ, et al. Epidemiology of giant cell arteritis and polymyalgia rheumatica. Arthritis Rheum. 2009; 61(10):1454-61 3 Aiello PD, Trautmann JC, McPhee TJ, et al. Visual prognosis in giant cell arteritis. Ophthalmology. 1993 Apr;100(4):550-5

\* minor procedure performed under local anaesthetic to remove a sample of one of the scalp arteries † Three or more of the following: age ≥ 50; new onset headache; tenderness or reduced pulsation of the temporal artery; elevated blood erythrocyte sedimentation rate; and positive TAB

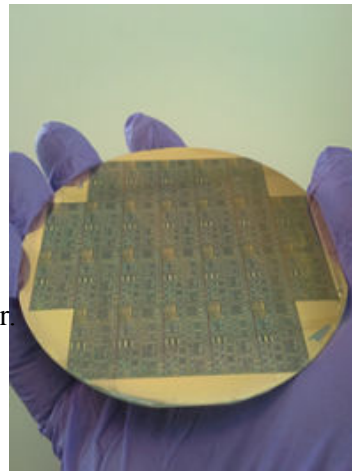
<http://bit.ly/1puZ9WN>

## Researchers design circuits capable of functioning at temperatures greater than 650 degrees Fahrenheit

### Integrated circuits that can survive at temperatures greater than 350 degrees Celsius

Phys.org - Engineering researchers at the University of Arkansas have designed integrated circuits that can survive at temperatures greater than 350 degrees Celsius – or roughly 660 degrees Fahrenheit. Their work, funded by the National Science Foundation, will improve the functioning of processors, drivers, controllers and other analog and digital circuits used in power electronics, automobiles and aerospace equipment – all of which must perform at high and often extreme temperatures.

"This ruggedness allows these circuits to be placed in locations where standard silicon-based parts can't survive," said Alan Mantooth, Distinguished Professor. "The circuit blocks we designed contributed to superior performance of signal processing, controllers and driver circuitry. We are extremely excited about the results so far."



*The silicon-carbide wafer contains more 1000 individual circuits.*

The research is critical because one-third of all power produced in the United States passes through some kind of power electronic converter or motor drive before it reaches the end user. Circuits developed by the University of Arkansas team will enable tight integration of control in the tough environmental conditions these applications demand. They will also improve electrical efficiency while simultaneously reducing the overall size and complexity of these systems.

The researchers worked with silicon carbide, a semiconducting material that is more rugged than conventional materials used in electronics. Silicon carbide is able to withstand extremely high voltage and is a good thermal conductor, meaning it can operate at high temperatures without requiring extra equipment to remove heat. The research team, led by Mantooth and Jia Di, professor of computer engineering, achieved the higher performance by combining silicon carbide with wide temperature design techniques. In the world of power electronics and integrated circuits, their work represents the first implementation of a number of fundamental analog, digital and mixed-signal blocks, such as a phase-locked loop using a complimentary-style silicon carbide technology. A phase-locked loop, or PLL, is a control system that generates an output signal whose phase is related to the phase of an input signal. Such a function is critical in a number of circuit applications such as signal synchronization, frequency synthesis, and modulation and demodulation schemes.

The research was part of the National Science Foundation's Building Innovation Capacity program, which is designed to partner university and industry research to build intellectual collaborations so that innovations flow from ideas to solid research results, company prototypes and products. The University of Arkansas and two Fayetteville technology firms, Ozark Integrated Circuits and Arkansas Power Electronics International, form the basis for this innovation ecosystem. Raytheon is also a key partner.

Ozark Integrated Circuits is commercializing the circuit technology. Arkansas Power Electronics International focuses on using the circuits in power applications. The research funding was awarded to Arkansas Circuit Design Center, which is comprised of two laboratories, one directed by Mantooth and one by Di. The Arkansas Circuit Design Center supports the mission of the University of Arkansas' National Center for Reliable Electric Power Transmission, which is funded as part of the federal government's focus on research and development on smart grid and renewable technologies. The center is one of only a few university-based research centers investigating electronic systems to make the nation's power grid more reliable and efficient. The U.S. Department of Energy has funded the center since 2005 because of the university's research expertise in advanced power electronics

and long-term investigation of silicon carbide. Mantooth is executive director of the center.

Arkansas Power Electronics International specializes in advanced, high-performance electronics for a variety of customers and applications, including the defense, aerospace and hybrid/electric vehicle markets. Ozark Integrated Circuits is a semiconductor company that develops integrated circuits for remote sensing and actuation under extreme environmental conditions.

<http://phys.org/news/2014-06-evidence-oceans-deep-earth.html>

### New evidence for oceans of water deep in the Earth

#### *Evidence for potentially oceans worth of water deep beneath the United States*

Researchers from Northwestern University and the University of New Mexico report evidence for potentially oceans worth of water deep beneath the United States. Though not in the familiar liquid form - the ingredients for water are bound up in rock deep in the Earth's mantle - the discovery may represent the planet's largest water reservoir.

The presence of liquid water on the surface is what makes our "blue planet" habitable, and scientists have long been trying to figure out just how much water may be cycling between Earth's surface and interior reservoirs through plate tectonics.

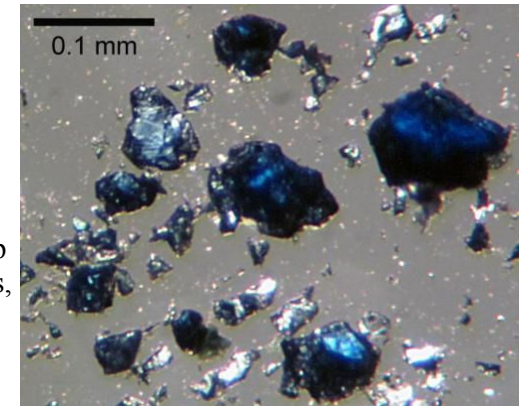
Northwestern geophysicist Steve Jacobsen and University of New Mexico seismologist Brandon Schmandt have found deep pockets of magma located about 400 miles beneath North America, a likely signature of the presence of water at these depths. The discovery suggests water from the Earth's surface can be driven to such great depths by plate tectonics, eventually causing partial melting of the rocks found deep in the mantle. The findings, to be published June 13 in the journal *Science*, will aid scientists in understanding how the Earth formed, what its current composition and inner workings are and how much water is trapped in mantle rock. "Geological processes on the Earth's surface, such as earthquakes or erupting volcanoes, are an expression of what is going on inside the Earth, out of our sight," said Jacobsen, a co-author of the paper. "I think we are finally seeing evidence for a whole-Earth water cycle, which may help explain the vast amount of liquid water on the surface of our habitable planet. Scientists have been looking for this missing deep water for decades."

Scientists have long speculated that water is trapped in a rocky layer of the Earth's mantle located between the lower mantle and upper mantle, at depths between 250 miles and 410 miles. Jacobsen and Schmandt are the first to provide direct evidence that there may be water in this area of the mantle, known as the "transition zone," on a regional scale. The region extends across most of the interior of the United States.

Schmandt, an assistant professor of geophysics at the University of New Mexico, uses seismic waves from earthquakes to investigate the structure of the deep crust and mantle. Jacobsen, an associate professor of Earth and planetary sciences at Northwestern's Weinberg College of Arts and Sciences, uses observations in the laboratory to make predictions about geophysical processes occurring far beyond our direct observation.

The study combined Jacobsen's lab experiments in which he studies mantle rock under the simulated high pressures of 400 miles below the Earth's surface with Schmandt's observations using vast amounts of seismic data from the USArray, a dense network of more than 2,000 seismometers across the United States.

Jacobsen's and Schmandt's findings converged to produce evidence that melting may occur about 400 miles deep in the Earth. H<sub>2</sub>O stored in mantle rocks, such as those containing the mineral ringwoodite, likely is the key to the process, the researchers said.



*Fragments of the blue-colored mineral called ringwoodite, synthesized in the laboratory.*

*This mineral is thought to exist in the mantle at depths between about 500 and 700 km depth. The laboratory-grown material can include a significant amount of water in its crystal structure (i.e. not in liquid form), but it was unknown whether or not water in the form of hydrated minerals such as ringwoodite can persist to 700 km depth. New evidence from experiments and from analysis of seismic waves passing through 700 km reveal that the layer of the Earth's mantle from 410 to 660 km depth, which geophysicists call the transition zone, may contain a significant amount of H<sub>2</sub>O in the form of hydrated ringwoodite. Steve Jacobsen / Northwestern University*

"Melting of rock at this depth is remarkable because most melting in the mantle occurs much shallower, in the upper 50 miles," said Schmandt, a co-author of the paper. "If there is a substantial amount of H<sub>2</sub>O in the transition zone, then some melting should take place in areas where there is flow into the lower mantle, and that is consistent with what we found."

If just one percent of the weight of mantle rock located in the transition zone is H<sub>2</sub>O, that would be equivalent to nearly three times the amount of water in our oceans, the researchers said. This water is not in a form familiar to us - it is not liquid, ice or vapor. This fourth form is water trapped inside the molecular structure of the minerals in the mantle rock. The weight of 250 miles of solid rock creates

such high pressure, along with temperatures above 2,000 degrees Fahrenheit, that a water molecule splits to form a hydroxyl radical (OH), which can be bound into a mineral's crystal structure.

Schmandt and Jacobsen's findings build on a discovery reported in March in the journal *Nature* in which scientists discovered a piece of the mineral ringwoodite inside a diamond brought up from a depth of 400 miles by a volcano in Brazil. That tiny piece of ringwoodite - the only sample in existence from within the Earth - contained a surprising amount of water bound in solid form in the mineral.

"Whether or not this unique sample is representative of the Earth's interior composition is not known, however," Jacobsen said. "Now we have found evidence for extensive melting beneath North America at the same depths corresponding to the dehydration of ringwoodite, which is exactly what has been happening in my experiments."

For years, Jacobsen has been synthesizing ringwoodite, colored sapphire-like blue, in his Northwestern lab by reacting the green mineral olivine with water at high-pressure conditions. (The Earth's upper mantle is rich in olivine.) He found that more than one percent of the weight of the ringwoodite's crystal structure can consist of water - roughly the same amount of water as was found in the sample reported in the *Nature* paper.

"The ringwoodite is like a sponge, soaking up water," Jacobsen said. "There is something very special about the crystal structure of ringwoodite that allows it to attract hydrogen and trap water. This mineral can contain a lot of water under conditions of the deep mantle."

For the study reported in *Science*, Jacobsen subjected his synthesized ringwoodite to conditions around 400 miles below the Earth's surface and found it forms small amounts of partial melt when pushed to these conditions. He detected the melt in experiments conducted at the Advanced Photon Source of Argonne National Laboratory and at the National Synchrotron Light Source of Brookhaven National Laboratory.

Jacobsen uses small gem diamonds as hard anvils to compress minerals to deep-Earth conditions. "Because the diamond windows are transparent, we can look into the high-pressure device and watch reactions occurring at conditions of the deep mantle," he said. "We used intense beams of X-rays, electrons and infrared light to study the chemical reactions taking place in the diamond cell."

Jacobsen's findings produced the same evidence of partial melt, or magma, that Schmandt detected beneath North America using seismic waves. Because the deep mantle is beyond the direct observation of scientists, they use seismic waves - sound waves at different speeds - to image the interior of the Earth.

"Seismic data from the USArray are giving us a clearer picture than ever before of the Earth's internal structure beneath North America," Schmandt said. "The melting we see appears to be driven by subduction - the downwelling of mantle material from the surface."

The melting the researchers have detected is called dehydration melting. Rocks in the transition zone can hold a lot of H<sub>2</sub>O, but rocks in the top of the lower mantle can hold almost none. The water contained within ringwoodite in the transition zone is forced out when it goes deeper (into the lower mantle) and forms a higher-pressure mineral called silicate perovskite, which cannot absorb the water. This causes the rock at the boundary between the transition zone and lower mantle to partially melt.

"When a rock with a lot of H<sub>2</sub>O moves from the transition zone to the lower mantle it needs to get rid of the H<sub>2</sub>O somehow, so it melts a little bit," Schmandt said.

"This is called dehydration melting." "Once the water is released, much of it may become trapped there in the transition zone," Jacobsen added.

Just a little bit of melt, about one percent, is detectable with the new array of seismometers aimed at this region of the mantle because the melt slows the speed of seismic waves, Schmandt said.

*More information: Dehydration melting at the top of the lower mantle, Science, 2014.*

[www.sciencemag.org/lookup/doi/10.1126/science.1253358](http://www.sciencemag.org/lookup/doi/10.1126/science.1253358)

[http://www.eurekalert.org/pub\\_releases/2014-06/bmj-uoc061014.php](http://www.eurekalert.org/pub_releases/2014-06/bmj-uoc061014.php)

### **Use of cement in partial hip replacement linked to risk of death** ***Relatively rare, but significant enough to warrant action; and concerns first raised in 2009***

The use of cement in partial hip replacement surgery may be linked to a risk of death - often occurring within minutes - finds research published in the online journal *BMJ Open*.

The risk is relatively rare. But the alarm was first sounded in 2009, and most of the cases that have come to light have occurred since that date, say the authors, who include the former chief medical officer for England. This suggests that measures to reduce the risks are not being acted on widely enough, they say.

They base their findings on an analysis of cases submitted between 2005 and 2012 to the National Reporting and Learning System (NRLS) - a database of patient safety incidents associated with the delivery of healthcare across the NHS in England and Wales.

All the cases involved sudden and severe deterioration among patients undergoing partial hip replacement, known as hemiarthroplasty, for fractured neck of femur (broken hip), and associated with the use of cement to help hold the artificial hip joint in place. This sudden deterioration is referred to as bone cement implantation

syndrome or BCIS for short. In each of the cases in this study, it caused either death; cardiac arrest, where the heart stops beating; or periarrest - severe deterioration in the patient's condition.

Between 2005 and 2012, the NRLS received 62 reports of BCIS, equivalent to one incident for every 2900 hemiarthroplasties performed for fractured neck of femur, indicating that it is a rare occurrence.

In 2012, 22,000 people in the UK underwent partial hip replacement for a fractured neck of femur, although not all these would have involved the use of cement.

But in 41 of the cases reported to the NRLS the patient died, and in most (80%), this was on the operating table. A further 14 patients had a heart attack but were resuscitated; and seven sustained a periarrest from which they recovered.

In most cases (55 out of 62; 89%), these events occurred within minutes of the cement being inserted. A further 39 cases of hip surgery associated with BCIS were also reported to the NRLS during this period, but were not included because it was not clear whether the procedures specifically related to partial hip replacement for fractured neck of femur.

In 2009, the now defunct National Patient Safety Agency raised the alarm about the use of cement and associated patient harm during hemiarthroplasty and issued guidance to the NHS on how to minimise the risks.

Fifty one of the 62 cases were reported to the NRLS after this date, possibly because of heightened awareness in the wake of the guidance, say the researchers. But the fact that deaths are continuing to occur "clearly shows that the implementation of mitigation measures set out in the alert was suboptimal, or that their effectiveness is suboptimal, or both," they write.

In an accompanying podcast, lead researcher Dr Paul Rutter emphasises that the risk of BCIS remains rare, but not so rare that orthopaedic surgeons don't need to know about it, or what steps they need to take to reduce it.

*What is the risk of death or severe harm due to bone cement implantation syndrome among patients undergoing hip hemiarthroplasty for fractured neck of femur? A patient safety surveillance study doi 10.1136/bmjopen-2014-004853*

[http://www.eurekalert.org/pub\\_releases/2014-06/osu-fpt061214.php](http://www.eurekalert.org/pub_releases/2014-06/osu-fpt061214.php)

### **Findings point toward one of first therapies for Lou Gehrig's disease**

***Researchers have determined that a copper compound known for decades may form the basis for a therapy for amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease.***

CORVALLIS, Ore. – In a new study just published in the Journal of Neuroscience, scientists from Australia, the United States (Oregon), and the United Kingdom showed in laboratory animal tests that oral intake of this compound significantly

extended the lifespan and improved the locomotor function of transgenic mice that are genetically engineered to develop this debilitating and terminal disease.

In humans, no therapy for ALS has ever been discovered that could extend lifespan more than a few additional months. Researchers in the Linus Pauling Institute at Oregon State University say this approach has the potential to change that, and may have value against Parkinson's disease as well.

"We believe that with further improvements, and following necessary human clinical trials for safety and efficacy, this could provide a valuable new therapy for ALS and perhaps Parkinson's disease," said Joseph Beckman, a distinguished professor of biochemistry and biophysics in the OSU College of Science.

"I'm very optimistic," said Beckman, who received the 2012 Discovery Award from the OHSU Medical Research Foundation as the leading medical researcher in Oregon.

ALS was first identified as a progressive and fatal neurodegenerative disease in the late 1800s and gained international recognition in 1939 when it was diagnosed in American baseball legend Lou Gehrig. It's known to be caused by motor neurons in the spinal cord deteriorating and dying, and has been traced to mutations in copper, zinc superoxide dismutase, or SOD1. Ordinarily, superoxide dismutase is an antioxidant whose proper function is essential to life.

When SOD1 is lacking its metal co-factors, it "unfolds" and becomes toxic, leading to the death of motor neurons. The metals copper and zinc are important in stabilizing this protein, and can help it remain folded more than 200 years.

"The damage from ALS is happening primarily in the spinal cord and that's also one of the most difficult places in the body to absorb copper," Beckman said.

"Copper itself is necessary but can be toxic, so its levels are tightly controlled in the body. The therapy we're working toward delivers copper selectively into the cells in the spinal cord that actually need it. Otherwise, the compound keeps copper inert."

"This is a safe way to deliver a micronutrient like copper exactly where it is needed," Beckman said.

By restoring a proper balance of copper into the brain and spinal cord, scientists believe they are stabilizing the superoxide dismutase in its mature form, while improving the function of mitochondria. This has already extended the lifespan of affected mice by 26 percent, and with continued research the scientists hope to achieve even more extension.

The compound that does this is called copper (ATSM), has been studied for use in some cancer treatments, and is relatively inexpensive to produce.

"In this case, the result was just the opposite of what one might have expected," said Blaine Roberts, lead author on the study and a research fellow at the University of Melbourne, who received his doctorate at OSU working with Beckman.



"The treatment increased the amount of mutant SOD, and by accepted dogma this means the animals should get worse," he said. "But in this case, they got a lot better. This is because we're making a targeted delivery of copper just to the cells that need it.

"This study opens up a previously neglected avenue for new disease therapies, for ALS and other neurodegenerative disease," Roberts said.

*Other collaborators on this research include OSU, the University of Melbourne, University of Technology/Sydney, Deakin University, the Australian National University, and the University of Leeds in the United Kingdom.*

*Funding has been provided by the Australian National Health and Medical Research Council, the U.S. National Institutes of Health, the Linus Pauling Institute and other groups in Australia and Finland.*

<http://bit.ly/1luX21K>

## The Snowy, Barren Arctic Actually Contains a Sophisticated Network of Inuit Trails

*Compiled from accounts over the past 200 years, a new atlas documents a network of trails stretching across the Arctic*

By [Mary Beth Griggs](#)

Back before 19th century explorers came to the Arctic with their fancy equipment, [Inuit trails](#) crossed the treacherous landscape. These trails connected communities—by boat, by foot, by sled—with each other and with the resources they needed to survive. Now, researchers have put together a database of trails from all over the Arctic, pulling together historical notes and maps from the 19th and 20th centuries into [an atlas](#).

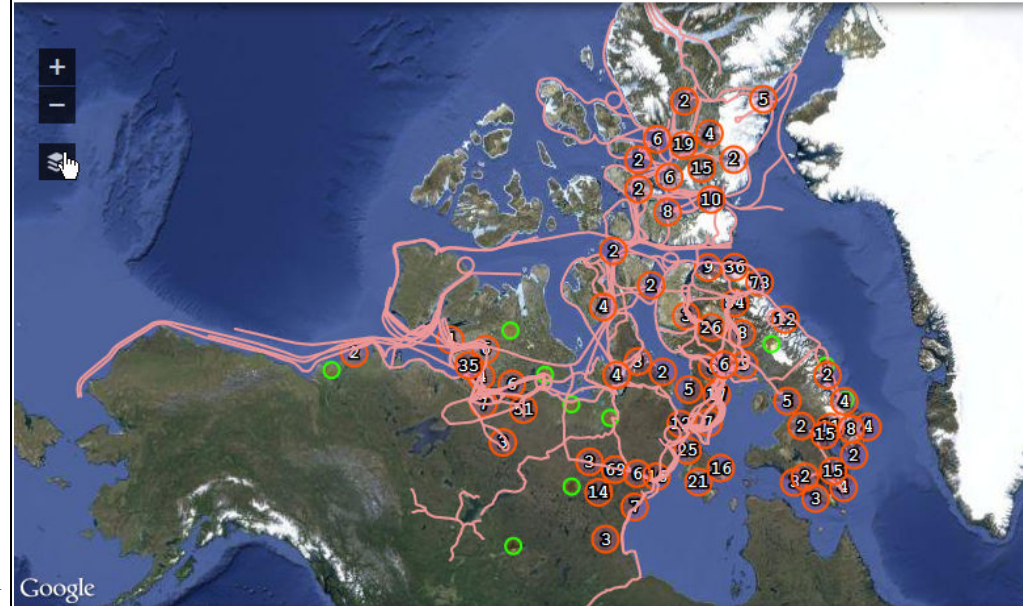
[Pan Inuit Trails](#) explains:

This Atlas focuses on historical written evidence of Inuit presence in most of the Canadian Arctic. It contains a selection of material obtained from hundreds of published and unpublished documents produced by explorers, ethnographers and other visitors who were in contact with Inuit during the early contact period or shortly before Inuit moved to permanent settlements. A very significant proportion of those trails and place names are still used today.

The resulting trails look a bit like pink silly-string sprayed onto the Arctic, but they're hugely important. In the past, they kept people alive. "Where migration routes are involved, being at the right place on the right day could be critical for hunting and survival," [the atlas points out](#). Today, they also provide a record showing how people have long settled in this area.

The researchers have included not only the trails, but geographic features and [place names](#), and even images of the [maps](#) that they pulled the information from. Still, the atlas [isn't intended](#) to be used for navigation. Instead, the database is meant to show

how the Inuit people remained connected from Greenland to Alaska, in some of the harshest conditions on earth. Its creators note that the original maps that they used to build the atlas weren't always to scale. So, don't head up to Canada and try to follow the paths.



<http://bit.ly/1p4OdUr>

## Radio Signals from Jupiter Could Aid in the Search for Extraterrestrial Life on Its Moons

*Radio Signals from Jupiter Could Aid Search for Life*

A new study reveals that radio signals generated from Jupiter could help researchers scan its giant moons for extraterrestrial life.

Powerful radio signals that Jupiter generates could be used to help researchers scan its giant moons for oceans that could be home to extraterrestrial life, according to a recent study submitted to the journal *Icarus*.

Jupiter, the largest planet in the Solar System, possesses 67 known moons, including three giant icy moons that might possess liquid oceans underneath their frozen surfaces. Astrobiologists want to investigate Europa, Ganymede and Callisto for extraterrestrial life, as there is life virtually wherever there is liquid water on Earth.

Of Jupiter's three largest icy moons, Europa, which is roughly the size of Earth's moon, is favored as having the greatest potential to sustain life. Magnetic readings

captured by NASA's Galileo spacecraft provided compelling hints that it has an ocean, and radio scans by the probe suggest a water-rich layer beneath the surface between 50 to 105 miles (80 to 170 kilometers) thick. Recent findings even suggest its ocean could be loaded with enough oxygen to support millions of tons worth of marine life.

Scientists would like to analyze Europa's ocean directly, perhaps with missions to bore into Europa's icy shell using heat to melt through the ice, whirling blades to clear away rocks, and robot subs to explore the ocean. However, it remains uncertain how thick this shell is, complicating any plans to penetrate it. Models of its thickness, based on the amount of heat the shell receives from the Sun and Europa itself, predict it to be roughly 18 miles (30 kilometers) thick. In contrast, analyses of the Galileo spacecraft's data suggest the shell is no more than 9 miles (15 kilometers) thick, and maybe as little as 2.5 miles (4 kilometers) thick. Ice-penetrating radar is currently the most promising technique to directly confirm the existence of any ocean hidden within Jupiter's icy moons. Radar works by transmitting radio signals, detecting any radio signals that reflect back, and analyzing these signals to deduce details about what they reflected off of, much like how a person might use a flashlight to illuminate objects hidden in the dark. Ice and ground-penetrating radar systems look for signals that indicate buried objects and boundaries between layers. In Europa's case, this means looking for the boundaries between the icy crust and any hidden ocean, and between such an ocean and Europa's rocky core.

To detect these oceans with ice-penetrating radar, low-frequency signals of less than 30 megahertz are needed to overcome radio wave absorption by the ice, as well as the unpredictable scattering of radio waves by the crinkled surfaces of these moons. The low-frequency radio waves that researchers would like to use are decametric, meaning they have wavelengths tens of meters long.

One problem with attempting ice-penetrating decametric radar on Jupiter's moons has to do with the powerful decametric radio bursts coming from Jupiter itself. Altogether, these signals are more than 3,000 times stronger than any leaking into the Solar System from the rest of the galaxy.

Jupiter's decametric waves come from clouds of electrically charged particles trapped in Jupiter's magnetic field. To overcome Jupiter's loud radio signals, a mission probing Jupiter's moons would need a relatively strong transmitter, a massive device that might be difficult to power and fit aboard the limited confines of a spacecraft.

"If one were to treat the source for Jupiter's decametric emission as a transmitter, it is roughly producing the equivalent of a megawatt," said lead study author Andrew Romero-Wolf, a physicist at NASA's Jet Propulsion Laboratory. "It is certainly

possible to generate a signal of that strength on Earth, but doing it in the vicinity of Jupiter is an entirely different challenge."

Instead of carrying a transmitter onboard a spacecraft to overpower Jupiter's radio signals, researchers now suggest using the giant planet's decametric radio waves to scan its moons.

"We can build our own transmitters to search for subsurface oceans with ice-penetrating radar, but when Jupiter is active, the radio emission is blinding to ice-penetrating radar," said Romero-Wolf. "The technique we are developing could not only provide a solution to that problem, it could turn it into a strength."

All the mission would then need are very low-power systems to detect radio signals reflected by the moons and any oceans lurking within them.

"The great strength of this technique is that it doesn't need a transmitter, just a receiver," Romero-Wolf said. "A scanning system for subsurface oceans in icy moons potentially already exists. All we have to do is go there and listen."

The strategy that Romero-Wolf and his colleagues developed involves placing a spacecraft between Jupiter and one of its icy moons. The probe would then monitor decametric emissions from Jupiter as well as echoes of those signals reflected off the icy moon. "The technology to do this is readily available and requires no major developments," Romero-Wolf said.

By comparing the signals from Jupiter with the echoes from its moon, the researchers can determine the thickness of the moon's icy shell and the depth of its ocean.

"I think this is one of those cases where a confluence of natural effects provides us with a probe for great science," Romero-Wolf said. "Jupiter not only hosts icy moons which could contain subsurface oceans, it is also an extremely bright radio emitter at decametric wavelengths. At these wavelengths, ice happens to be fairly transparent, providing a window to view subsurface oceans."

This strategy, where one analyzes both distant radio emissions and their echoes, is known as interferometric reflectometry. It was first applied by the Dover Heights radio observatory near Sydney, Australia, in the 1940s and was conceived due to the limited resources astronomers had available when the observatory first started out, not unlike the situation faced by designers of deep space probes.

Earth's atmosphere can interfere with traditional optical astronomy that focuses on visible light people can see with their eyes. However, the atmospheres of these icy moons are thin and are not expected to attenuate the decametric radio signal significantly.

"Europa does have an ionosphere, a layer of free electrons, which can distort the radio signal," Romero-Wolf said. "However, this is also fairly small, and not expected to have a big impact on our ability to probe the ice layer."

The scientists now plan to make more detailed estimates of how well their radio strategy might detect hidden oceans in Jupiter's icy moons. For instance, they are hoping to make observations from Earth of Jupiter's decametric radio emissions as they reflect off the icy moon surfaces.

"Our initial estimates indicate that this may be possible — the measurements would be close to the sensitivity of current ground-based radio observatories," Romero-Wolf said. "If we can get this to work, it could provide valuable information about the surface properties of the moons." He added that there are limitations to the technique.

"Unambiguous observation of a subsurface ocean or liquids in the ice of Europa is only the first step towards identifying the possibility for life," he said. "What we are proposing will not be able to tell us whether there are living organisms in Europa, but it could provide strong evidence for that possibility."

Publication: Submitted to *Icarus*

PDF Copy of the Study: [A Passive Probe for Subsurface Oceans and Liquid Water in Jupiter's Icy Moons](#)

<http://bit.ly/1jqHyYv>

## Did Super-Sized Animals Live Long Before Dinosaurs?

*Megamastax amblyodus* likely the earliest vertebrate apex predator in the fossil record

Jun 12, 2014 11:00 AM ET // by Jennifer Viegas

It's generally believed that Earth's earliest animals were not very big, but discovery of a huge new fish that lived around 423 million years ago has scientists rethinking what life was like close to 200 million years before the first dinosaurs emerged.

The fish, named Big Mouth Blunt Tooth (*Megamastax amblyodus*), is described in the latest issue of *Scientific Reports*. For its time, the toothy and lobe-finned fish was in the number one spot on the food chain.

"At 1 meter (3.3 feet) in length or greater, it was vastly larger than any other animal," lead author Brian Choo told *Discovery News*, adding that Big Mouth was "likely the earliest vertebrate (backboned) apex predator in the fossil record."



Recreation of *Megamastax amblyodus*. Brian Choo

Choo, a paleontologist at the Chinese Academy of Sciences and Flinders University, and his colleagues analyzed Big Mouth's remains, which were unearthed at the

Kuanti Formation in Yunnan, southwestern China. During the fish's lifetime, a period known as the Silurian, this region was part of the South China Sea. It is where the marine ancestors of all jawed animals, including humans, first evolved. Equipped with both piercing and crushing teeth, Big Mouth likely preyed upon hard-shelled moving species, such as mollusks and armored fishes. The second largest animal at the time, *Guiyu oneiros* -- aka Ghost Fish, was a mere one-third of Big Mouth's size. Why then was Big Mouth so big?

One reason, according to the researchers, is that competition among fish appears to have been fierce. Co-author Min Zhu explained, "During the Silurian period, the South China Sea, then at the equator, was the cradle of early jawed vertebrates, thus the ecological competition among these creatures was very intense."

Another reason is that Big Mouth probably had plenty of oxygen. Modern fish are generally worse off in low oxygen conditions, and big fish require more oxygen than small ones, Choo said. Big Mouth therefore could not have existed unless sufficient oxygen was present.

This has major implications because, as it stands, there are two major theories about what Earth's oxygen level was like during the Silurian. One holds that near-modern oxygen levels occurred around 420 million years ago, while another holds that they did not occur until 20 million years later. Big Mouth provides strong evidence that near-modern oxygen levels occurred at least 420 million years ago, which Choo said was "a likely byproduct of the spread of plants on land."

"There was life on land during the Silurian, but it certainly wasn't nearly as diverse as today," he continued. "There would have been a variety of low-growing primitive plants growing in moist areas. While there were no trees, there was a towering organism called *Prototaxites*, possibly a giant fungus, which grew up to 8 meters (26.3 feet) tall."

The only animals on land were backbone-less ones, such as huge sea scorpions that scuttled along the beaches and swamps. There were no flying animals at this time, and sharks weren't around yet either. If additional Big Mouth-sized (or larger) animals did exist, they were probably other fish.

Paleontologist Per Ahlberg is a professor of evolutionary organism biology at Uppsala University. He recently saw the fossils for Big Mouth, and was impressed. "This is a remarkably large, and very early, lobe-finned fish," Ahlberg told *Discovery News*. "It underscores the extraordinary importance of the Silurian fish faunas of Yunnan for our understanding of early vertebrate evolution."

For a time, Big Mouth was Earth's largest supreme predator, but it would have been dwarfed by what was to come. Members of its group -- the lobe-finned fishes -- later evolved into limbed animals that settled on land. By 95 million years ago,

dinosaurs up to 130 feet tall, or roughly the height of a 13-story building, were in existence.

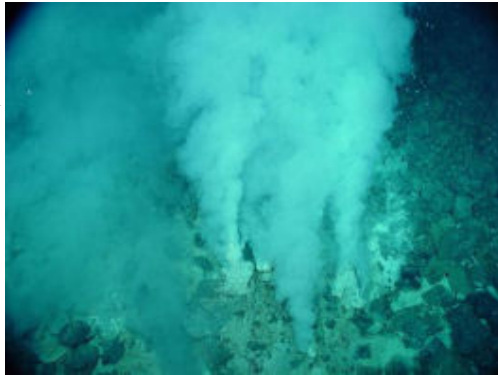
<http://phys.org/news/2014-06-energetic-life.html>

### The energetic origins of life

#### *A process by which natural ion gradients in alkaline hydrothermal vents, ignited the ongoing chemical reaction of life*

Phys.org -Imagination is perhaps the most powerful tool we have for creating the future. The same might be said when it comes to creating the past, especially as it pertains to origin of life. Under what conditions did the energetic processes of life first evolve? That question is the subject of a remarkable perspective piece just published in Science. Authors William Martin, Filipa Sousa, and Nick Lane come to the startling conclusion that the energy-harvesting system in ancient microbes can best be understood if it is viewed a microcosm of the larger-scale geochemical processes of the day. In particular, they imagine a process by which natural ion gradients in alkaline hydrothermal vents, much like the "Lost City" ecosystem still active in the mid-Atlantic today, ignited the ongoing chemical reaction of life.

When it comes to origin of life discussions the so-called "RNA World" often comes to mind. While fascinating, that set of ideas is not what is under discussion here. According to the authors, it's all about the acetogens, the methanogens, and the chemical transformations that were key to their evolution. These microorganisms synthesize ATP using electrons from H<sup>+</sup> to reduce CO<sub>2</sub>. In the process they generate either acetate or methane. The shared backbone in the energy metabolism of these microorganisms is the most primitive CO<sub>2</sub>-fixing pathway we know of—the acetyl-coenzyme A pathway. This pathway is generally referred to as the hub of metabolism as it links glycolytic energy production in the cell with oxidative energy production in its endosymbionts, the mitochondria.



*Alkaline hydrothermal vents, like the Lost City, may have been key to origins of life.*

Credit: commons.wikimedia.org

While most acetogens are classified as bacteria, the methanogens belong to kingdom Archaea. This domain was only recently classified as distinct from bacteria and eukaryotes in 1977 by the late Carl Woese. Methogens are key to a bold leap of thought primarily made by Martin, which has come to be known as the "hydrogen hypothesis". Martin had seen a slide at a lecture which showed clusters

of methogens inside eukaryotic cells nestled up right against hydrogenosomes, presumably feeding off the hydrogen they generate. Hydrogenosomes are similar to mitochondria in that they generate energy, but they are a paired-down version in that they do not contain any genome of their own.

Martin imagined that this cozy relationship he observed could have existed billions of years ago—only not as parasitic residents of a host eukaryotic cell, but rather as free residents at niche energy-producing locations within host earth. The host that then acquired what was to become the future mitochondrion was not a eukaryote with a fully-formed nucleus, but instead a prokaryotic and hydrogen-dependant methanogen. The future mitochondria then, was a facultative (as opposed to obligate) anaerobic eubacterium that in alternate incarnations also become the hydrogenosome.

The key feature and prediction of the theory is that the mitochondria created the nucleus, and therefore eukaryotes. This processes entailed massive transfer of most of the mitochondria's own genetic material to the host, which swelled the original genetic rank and congealed as chromosomes, simultaneously evolving the cytoskeletal provisions for a complicated division cycle. The theory also neatly explains the lack of mitochondria in several eukaryotes through their loss, rather than as a failure to ever acquire them. The bio-existential question of whether the host "stole" the genes from the symbiont, or whether the parasite donated them becomes one of relativity and viewpoint. It is the same dichotomy as whether to say engulf or infect, or perhaps whether the assorted neurotransmitter packages dispensed by neurons are wastes, gifts or irritants.

Few researchers have done more than co-author Nick Lane towards uncovering the role of mitochondria in nearly every major process of the cell. He has summed up many of these ideas in his book *Power, Sex, Suicide: Mitochondria and the Meaning of Life*. In it he observes many things that like the hydrogen hypothesis, are now becoming accepted reality. Of note, he maintains that using those few genes preserved as local copies in the mitochondrial genome, different regions of the cell can rapidly tailor their energy output. In the case of the [extended trees of neurons](#), this might also contribute to structural alterations and perhaps even memory.

As far as the origins of life, we need to turn back into the opposite direction now to try to un-create what might have happened prior to the eukaryotic merger, or at least led to it. In 2012 [Martin and Lane published](#) their thought-advances in imagining some of the geochemical processes which were later sped up, compacted, and made more efficient inside cells. These include how ion-gradients were set up at hydrothermal vents, bandied about, and later swapped H<sup>+</sup> ions for Na<sup>+</sup> ions as both the carriers and composers.

One such process they detail in their new paper is known as serpentinization. In this sequence of geochemical reactions, seawater percolating through submarine crust exothermically oxidizes Fe<sup>2+</sup> to Fe<sup>3+</sup> along with the release of H<sub>2</sub> and energy. Serpentinization taking place at the Lost City formation, for example, generates a strongly reducing environment (reducing CO<sub>2</sub>), and it also makes the effluent alkaline with a pH of around 10, essentially controlling the fluid composition of the vent. Natural proton gradients are spontaneously set up with the same magnitude and orientation as occurs inside modern autotrophes (self-nourishing, producing cells).

### What were the first ion-pumping mechanisms?

These vent features make them naturally chemiosmotic. In chemiosmosis, as also occurs in [mitochondria](#), ions flow down natural gradients which can potentially be harnessed to produce energy. In the case of life, which universally employs multi-tool pumps known as ATP-ases, this energy is deposited as phosphate bonds in ATP. If the primordial ATP-ase harnessed these alkaline vent gradients, a first step could have involved a simple H<sup>+</sup>/Na<sup>+</sup> antiporter. This kind of a device (now also protein-based like the ATP-ase) could have converted the initial vent gradient into the Na<sup>+</sup> gradient the acetogens and methanogens use today. These complexes still use iron-sulfur clusters and methyl groups as substrates, and could have enabled the emergence of free-living prokaryotes.

Our understanding of chemiosmosis today is still incomplete. The so-called "proton-motive force" which couples proton and electron transfer across nebulous barriers still defies exact quantification. The flow of electrons through proteins, and the membranes which house them, continues to be one of the most exciting areas both in the origins of life, and in the creatures later evolved.

*More information:* *Energy at life's origin*, *Science* 6 June 2014: Vol. 344 no. 6188 pp. 1092-1093. [DOI: 10.1126/science.1251653](https://doi.org/10.1126/science.1251653)

<http://www.medscape.com/viewarticle/826675>

### More Evidence Botox Works for Depression

*A single injection of cosmetic botulinum toxin (BTX), which is typically used to improve the appearance of facial wrinkles, may be an effective treatment for depression.*

Caroline Cassels

NEW YORK - In one of the first studies to suggest this, investigators at the Hannover Medical School in Germany found that treating the facial muscles involved in emotion with botulinum alleviates depressive symptoms.

"Our emotions are expressed by facial muscles, which in turn send feedback signals to the brain to reinforce those emotions. Treating facial muscles with botulinum

toxin interrupts this cycle," study investigator Prof. Tillmann Kruger said at a press conference here at the American Psychiatric Association's 2014 Annual Meeting.

### Novel Approach

According to the investigators, positive effects on mood have been observed in patients who have undergone BTX treatment for glabellar frown lines. A previous open case series showed that depression remitted or improved after such treatment. To confirm these results, Dr. Kruger and colleague M. Axel Wollmer, MD, from the Asklepios Clinic North Ochsenszoll in Hamburg, Germany, conducted a randomized, double-blind, placebo-controlled trial of BTX injection as an adjunctive treatment for major depression.

A total of 30 patients with high levels of chronic and treatment-resistant depression were enrolled in the study. Patients were randomly assigned to receive a single injection of BTX or a single injection of saline placebo.

The study's primary end point was a change from baseline in depressive symptoms, as measured by the 17-item Hamilton Depression Rating Scale (HAM-D17), during the 16-week study.

Six weeks after a single treatment, the BTX group experienced an average 47.1% reduction in HAM-D17 scores vs 9.2% in the placebo group.

The investigators found that the effect size was even larger at the end of the study and that treatment-dependent clinical improvement was also reflected in the Beck Depression Inventory and the Clinical Global Impressions Scale.

"This study shows that a single treatment of the glabellar region with botulinum toxin may shortly accomplish a strong and sustained alleviation of depression in patients who did not improve sufficiently on previous medication. It supports the concept that the facial musculature not only expresses but also regulates mood states," the investigators write.

Dr. Kruger said BTX may offer a "novel, effective, well-accepted, and economic therapeutic tool for the treatment of major depression."

These findings have since been replicated in 2 subsequent studies, one by Michelle Magid, MD, and colleagues, which was presented in March at the American Academy of Dermatology 72nd Annual Meeting and reported by Medscape Medical News at that time, and the other by Eric Finzi, MD, PhD, and colleagues, which was published in the May issue of *Journal of Psychiatric Research* and was also reported by Medscape Medical News.

Dr. Kruger reported that he and his colleagues are currently conducting a meta-analysis of the 3 randomized trials in an effort to "further corroborate this novel treatment approach." The researchers are also testing BTX's therapeutic potential in other psychiatric disorders.

Commenting on the study, press conference moderator Jeffrey Borenstein, MD, president and CEO of the Brain and Behavior Research Foundation in New York City and chair of the American Psychiatric Association's Council on Communications, said that pursuing new treatments for depression is "crucial." Dr. Borenstein added that he would like to see this line of research pursued in studies that include larger numbers of patients.

*Dr. Kruger, Dr. Wollmer, and Dr. Borenstein report no relevant financial conflicts of interest. American Psychiatric Association's 2014 Annual Scientific Meeting. Abstract NR3-030. Presented May 4, 2014.*

[http://www.eurekalert.org/pub\\_releases/2014-06/ps-roa061114.php](http://www.eurekalert.org/pub_releases/2014-06/ps-roa061114.php)

### **Rescue of Alzheimer's memory deficit achieved by reducing 'excessive inhibition'**

*Discovery also has potential for development as a novel diagnostic tool for Alzheimer's disease*

**Barbara K. Kennedy**

A new drug target to fight Alzheimer's disease has been discovered by a research team led by Gong Chen, a Professor of Biology and the Verne M. Willaman Chair in Life Sciences at Penn State University. The discovery also has potential for development as a novel diagnostic tool for Alzheimer's disease, which is the most common form of dementia and one for which no cure has yet been found. A scientific paper describing the discovery will be published in Nature Communications on 13 June 2014.

Chen's research was motivated by the recent failure in clinical trials of once-promising Alzheimer's drugs being developed by large pharmaceutical companies. "Billions of dollars were invested in years of research leading up to the clinical trials of those Alzheimer's drugs, but they failed the test after they unexpectedly worsened the patients' symptoms," Chen said.

The research behind those drugs had targeted the long-recognized feature of Alzheimer's brains: the sticky buildup of the amyloid protein known as plaques, which can cause neurons in the brain to die. "The research of our lab and others now has focused on finding new drug targets and on developing new approaches for diagnosing and treating Alzheimer's disease," Chen explained.

"We recently discovered an abnormally high concentration of one inhibitory neurotransmitter in the brains of deceased Alzheimer's patients," Chen said. He and his research team found the neurotransmitter, called GABA (gamma-aminobutyric acid), in deformed cells called "reactive astrocytes" in a structure in the core of the brain called the dentate gyrus. This structure is the gateway to hippocampus, an area of the brain that is critical for learning and memory.

Chen's team found that the GABA neurotransmitter was drastically increased in the deformed versions of the normally large, star-shaped "astrocyte" cells which, in a healthy individual, surround and support individual neurons in the brain.

"Our research shows that the excessively high concentration of the GABA neurotransmitter in these reactive astrocytes is a novel biomarker that we hope can be targeted in further research as a tool for the diagnosis and treatment of Alzheimer's disease," Chen said.

Chen's team developed new analysis methods to evaluate neurotransmitter concentrations in the brains of normal and genetically modified mouse models for Alzheimer's disease (AD mice).

"Our studies of AD mice showed that the high concentration of the GABA neurotransmitter in the reactive astrocytes of the dentate gyrus correlates with the animals' poor performance on tests of learning and memory," Chen said.

His lab also found that the high concentration of the GABA neurotransmitter in the reactive astrocytes is released through an astrocyte-specific GABA transporter, a novel drug target found in this study, to enhance GABA inhibition in the dentate gyrus.

With too much inhibitory GABA neurotransmitter, the neurons in the dentate gyrus are not fired up like they normally would be when a healthy person is learning something new or remembering something already learned.

Importantly, Chen said, "After we inhibited the astrocytic GABA transporter to reduce GABA inhibition in the brains of the AD mice, we found that they showed better memory capability than the control AD mice.

We are very excited and encouraged by this result, because it might explain why previous clinical trials failed by targeting amyloid plaques alone.

One possible explanation is that while amyloid plaques may be reduced by targeting amyloid proteins, the other downstream alterations triggered by amyloid deposits, such as the excessive GABA inhibition discovered in our study, cannot be corrected by targeting amyloid proteins alone.

Our studies suggest that reducing the excessive GABA inhibition to the neurons in the brain's dentate gyrus may lead to a novel therapy for Alzheimer's disease. An ultimate successful therapy may be a cocktail of compounds acting on several drug targets simultaneously."

*In addition to Chen, other members of the research team include Postdoctoral Scholar Zheng Wu and Graduate Researcher Ziyuan Guo at Penn State, and Marla Gearing at Emory University.*

*This research received support from the National Institutes of Health and Penn State University's Eberly College of Science Stem Cell Fund.*

[http://www.eurekalert.org/pub\\_releases/2014-06/eaog-ssm061014.php](http://www.eurekalert.org/pub_releases/2014-06/eaog-ssm061014.php)

## Studies show movements of continents speeding up after slow 'middle age'

*Two studies show that the movement rate of plates carrying the Earth's crust may not be constant over time.*

This could provide a new explanation for the patterns observed in the speed of evolution and has implications for the interpretation of climate models. The work is presented today at Goldschmidt 2014, the premier geochemistry conference taking place in Sacramento, California, USA.

The Earth's continental crust can be thought of as an archive of Earth's history, containing information on rock formation, the atmosphere and the fossil record. However, it is not clear when and how regularly crust formed since the beginning of Earth history, 4.5 billion years ago.

Researchers led by Professor Peter Cawood, from the University of St. Andrews, UK, examined several measures of continental movement and geologic processes from a number of previous studies. They found that, from 1.7 to 0.75 billion years ago (termed Earth's middle age), Earth appears to have been very stable in terms of its environment, with little in the way of crust building activity, no major fluctuations in atmospheric composition and few major developments seen in the fossil record. This contrasts markedly with the time periods either side of this, which contained major ice ages and changes in oxygen levels. Earth's middle age also coincides with the formation of a supercontinent called Rodinia, which appears to have been stable throughout this time.

Professor Cawood suggests this stability may have been due to the gradual cooling of the earth's crust over time. "Before 1.7 billion years ago, the Earth's crust would have been substantially hotter, meaning that continental plate movement may have been governed by different rules to those that operate today," said Professor Cawood. "0.75 billion years ago, the crust reached a point where it had cooled sufficiently to allow modern day plate tectonics to start working, in particular allowing subduction zones to form (where one plate of the crust moves under another). This increase in activity could have kick-started a myriad of changes including the break-up of Rodinia and changes to levels of key elements in the atmosphere and seas, which in turn may have induced evolutionary changes in the life forms present."

This view is backed up by work from Professor Kent Condie from New Mexico Tech, USA, which suggests the movement rate of the Earth's crust is not constant but may be speeding up over time. Professor Condie examined how supercontinents assemble and break up. "Our results challenge the view that the rate of plate

movement is stable over time," said Professor Condie. "The interpretation of data from many other disciplines such as stable isotope geochemistry, palaeontology and paleoclimatology in part rely on the assumption that the movement rate of the Earth's crust is constant."

Results from these fields may now need to be re-examined in light of Condie's findings. "We now urgently need to collect further data on critical time periods to understand more about the constraints on plate speeds and the frequency of collision between continental blocks," concluded Professor Condie.

### **ABSTRACTS:**

#### ***The origin of the continental crust and its impact on the Earth system***

*PETER A. CAWOOD<sup>1</sup>, CHRIS J. HAWKESWORTH<sup>1</sup> AND BRUNO DHUIME<sup>1,2</sup>, <sup>1</sup>Earth Sciences, University of St Andrews, UK, <sup>2</sup>Earth Sciences, University of Bristol, UK*

*The continental crust is the archive of Earth history and its record of rock units and events is heterogenous with distinctive peaks and troughs of ages for igneous crystallization, metamorphism, continental margins and mineralization. This temporal distribution is argued to largely reflect the different preservation potential of rocks generated in different tectonic settings, rather than fundamental pulses of activity, and the peaks of ages are linked to the timing of supercontinent assembly. In contrast there are other signals, such as the Sr isotope ratios of seawater, mantle temperatures, and redox conditions on the Earth, where the records are regarded as primary because they are not sensitive to the numbers of samples of different ages that have been analyzed. Models based on the U-Pb, Hf and O isotope ratios of detrital zircons suggest that at least ~60-70% of the present volume of the continental crust had been generated by 3 Ga. This volume contrasts markedly with the <10% of crust of that age apparently still preserved requiring ongoing recycling of early formed crust and subcontinental mantle lithosphere back into the mantle. Between 1.7 to 0.75 Ga, the tempo of Earth processes was characterized by environmental, evolutionary and lithospheric stability that contrasts with the dramatic changes in preceding and succeeding eras. The period is marked by a paucity of passive margins, an absence of a significant Sr anomaly in the paleoseawater record or in the epsilon Hf(t) in detrital zircon, a lack of orogenic gold and volcanic-hosted massive sulphide deposits, and an absence of glacial deposits and of iron formations. In contrast, anorthosites and kindred bodies are well developed and major pulses of Mo and Cu mineralization, including the world's largest examples of these deposits, are features of this period. These trends are attributed to the combined effects of lithospheric behaviour related to secular cooling of the mantle and a relatively stable continental assemblage that was initiated during assembly of the Nuna supercontinent by 1.7 Ga and continued until breakup of its closely related successor, Rodinia, around 0.75 Ga. Since ~0.75 Ga, modern plate tectonic processes have dominated the Earth system.*

#### ***Is there a secular change in supercontinent assemblies?***

*K. C. CONDIE<sup>1\*</sup>, S. A. PISAREVSKY<sup>2</sup> AND J. KORENAGA<sup>3</sup>, <sup>1</sup>New Mexico Tech, Socorro, NM 87801 USA <sup>2</sup>Curtin University, GPO Box U1987, Perth, WA 6845, Australia <sup>3</sup>Yale University, PO Box 208109, New Haven, CT 06520, USA*

High frequencies of craton collision occur during supercontinent assembly at 1800, 1100, 650-300 and <100 Ma and low rates during breakup at 2100, 1300-1200 (?), 750, and 200-100 Ma. Angular plate velocities as weighted by craton area range from 20 to 80 deg/100Myr with two peaks at 450- 350 Ma and 1100 Ma, both of which correlate with the initial stages of supercontinent assembly. The number of cratons decreases from  $\geq 15$  before 1900 Ma to  $< 10$  after this time. Orogens and passive margins show the same two cycles of ocean basin closing at 2700 to 2000 Ma and at  $\leq 2000$  Ma. The younger cycle shows decreasing durations of ocean basin closing until about 1000 Ma. Supercontinent assembly and breakup durations are 200-300 Myr and 100-200 Myr, respectively. Except for 1200-700 Ma, duration of ocean-basin closing is  $\leq 150$  Myr. Time-averaged plate speeds suggest more sluggish plate tectonics in the past, which is consistent with a possible increase in craton collision frequency in the last 1000 Myr. If Gondwana and Pangea are counted as stages of the same supercontinent, the supercontinent cycle has a period of about 500 Myr and there is no clear evidence for it speeding up or slowing down with time.

<http://www.medscape.com/viewarticle/826715?>

### FDA OKs Lymphoseek for Head and Neck Cancer

**The US Food and Drug Administration (FDA) has approved technetium 99m tilmanocept (Lymphoseek, Navidea Biopharmaceuticals) injection for identification of sentinel lymph nodes for head and neck cancer.**

Larry Hand

The radioactive diagnostic imaging agent was originally approved in 2013 to help identify lymph nodes nearest primary tumors for breast or skin cancer.

The new use gives physicians the option to perform less extensive lymph node surgery if a patient's sentinel nodes are negative for cancer.

"For some patients with head and neck cancer, removal and pathological examination of lymph nodes draining a primary tumor is an important diagnostic evaluation," Libero Marzella, MD, PhD, director of the Division of Medical Imaging Products in the FDA's Center for Drug Evaluation and Research, said in an FDA press release. "To use Lymphoseek, doctors inject the drug into the tumor area and later, using a handheld radiation detector, find the sentinel lymph nodes that have taken up Lymphoseek's radioactivity."

Researchers established Lymphoseek's safety and effectiveness in a clinical trial involving 85 patients with squamous cell carcinoma of the lip, oral cavity, and skin. After patients were injected with the diagnostic agent, surgeons removed suspected lymph nodes for pathologic examination and determined whether the cancer had spread through the lymphatic system.

Results showed that the Lymphoseek-guided sentinel lymph node biopsy accurately determined whether the cancer had spread through the lymphatic system, according to the FDA.

Researchers identified pain or irritation at the injection site as the most common adverse effects during the clinical trial.

Most head and neck cancers start in the squamous cells lining the moist surfaces inside the head and neck, according to the National Cancer Institute. Alcohol and tobacco use, as well as human papillomavirus infection, are risk factors for head and neck cancer.

[http://www.eurekalert.org/pub\\_releases/2014-06/uo-aw1061214.php](http://www.eurekalert.org/pub_releases/2014-06/uo-aw1061214.php)

### Arctic warming linked to fewer European and US cold weather extremes, new study shows

**Climate change is unlikely to lead to more days of extreme cold, similar to those that gripped the USA in a deep freeze last winter, new research has shown.**

The Arctic amplification phenomenon refers to the faster rate of warming in the Arctic compared to places further south. It is this phenomenon that has been linked to a spike in the number of severe cold spells experienced in recent years over Europe and North America.

However, new research by University of Exeter expert Dr James Screen has shown that Arctic amplification has actually reduced the risk of cold extremes across large swathes of the Northern Hemisphere.

The intriguing new study, published in leading scientific journal Nature Climate Change, questions growing fears that parts of Europe and North America will experience a greater number, or more severe, extreme cold days over the course of the next century.

Dr Screen, a Mathematics Research Fellow at the University of Exeter, said: "Autumn and winter days are becoming warmer on average, and less variable from day-to-day. Both factors reduce the chance of extremely cold days."

The idea that there was a link between Arctic amplification and extreme weather conditions became prevalent during the severe winter weather that plagued large areas of the United States in January 2014, leading to major transport disruption, power cuts and crop damage.

In his study, Dr Screen examined detailed climate records to show that autumn and winter temperature variability has significantly decreased over the mid-to-high latitude Northern Hemisphere in recent decades.

He found that this has occurred mainly because northerly winds and associated cold days are warming more rapidly than southerly winds and warm days.

Dr Screen said: "Cold days tend to occur when the wind is blowing from the north, bringing Arctic air south into the mid-latitudes. Because the Arctic air is warming so rapidly these cold days are now less cold than they were in the past."



Using the latest mathematical climate modelling, Dr Screen has also been able to show that these changes will continue in to the future, with projected future decreases in temperature variability in all seasons, except summer. 'Arctic amplification decreases temperature variance in northern mid-to-high-latitudes', by James Screen, is published in Nature Climate Change online, on Sunday, June 15.

*This research was financially supported by the UK Natural Environment Research Council.*

<http://www.scientificamerican.com/article/fusion-experiment-breakthrough/>

### **Fusion Experiment Breakthrough**

*In a first, the fuel released more energy than it absorbed*

**By David Biello**

Last September, under x-ray assault, the rapid implosion of a plastic shell into icy isotopes of hydrogen produced fusion at Lawrence Livermore National Laboratory's National Ignition Facility (NIF). This wasn't just a run-of-the-mill fusion reaction: it was the first one NIF has ever produced wherein the fuel released more energy than it absorbed.

The laboratory's 192 lasers have been pumping energy into a succession of tiny fuel pellets since 2010. In this instance, the scientists got the timing right. Instead of ramping up the lasers over the course of the blast, which lasts 20 trillionths of a second, Livermore physicist Omar Hurricane and his team started the blast at maximum intensity and then let it taper off.

That change made the fuel in the two-millimeter pellet hotter sooner—reaching temperatures of about 50 million degrees Celsius and pressures of 150 billion Earth atmospheres.

Such conditions enable fusion, and, in this case, the fusing fuel yielded nearly twice as much energy as the roughly 10,000 joules that triggered it. The results were published in February in Nature.

“This is closer than anyone's gotten before” to self-sustaining energy, Hurricane says. Yet scientists still have a lot of work to do. Although the fuel pellet yielded 17,000 joules of energy, the entire fusion experiment fell far short of breaking even. The NIF experiment required more energy to run than it generated; feeding the lasers alone required a burst of about 500 trillion joules.

Doing better than breaking even—or “ignition,” as the NIF folks put it—will require even more extreme pressures and other conditions. A source of nearly unlimited, clean energy is still decades away.

[http://www.eurekalert.org/pub\\_releases/2014-06/nu-dy-061214.php](http://www.eurekalert.org/pub_releases/2014-06/nu-dy-061214.php)

### **Delinquent youth -- especially girls -- more likely to die violently as adults**

*Delinquency in youth predicts much higher rate of being shot to death before age 30*

CHICAGO --- Delinquency in youth predicts a significantly higher rate of violent death in adulthood -- especially from firearms -- and females are among the most vulnerable, reports a new Northwestern Medicine® study.

Delinquent females died violently at nearly five times the rate of those in the general population, according to the study, while delinquent males died at three times general population rates.

Death rates in Hispanic males and females were five and nine times more than the general population rates, respectively.

This is the first large-scale study to look at death rates in delinquent females and adds new data on Hispanics, now the largest minority group in the U.S. The paper will be published June 16 in the journal Pediatrics.

In addition, violent death up to age 34 was predicted by three risk factors in adolescence: alcohol use disorder, selling drugs and gang involvement, according to the study.

"Our findings are shocking," said lead author Linda Teplin, the Owen L. Coon Professor of Psychiatry and Behavioral Sciences at Northwestern University Feinberg School of Medicine. "Death rates in our sample of delinquent youth, ages 15 to 19, are nearly twice those of troops in combat in wartime Iraq and Afghanistan."

"Early violent death is a health disparity," added Teplin. "Youth who get detained are disproportionately poor and disproportionately racial and ethnic minorities. We must address early violent death the same as any other health disparity."

The study used newly available data from the Northwestern Juvenile Project, a longitudinal study of 1,829 youth (1,172 males and 657 females, ages 10 to 18 years at baseline) who were detained at the Cook County Juvenile Temporary Detention Center in Chicago between 1995 and 1998. The authors interviewed participants and then followed them up using official death records up to 16 years after the initial interviews.

The youth in the study were randomly selected before their case was disposed, and had not yet been convicted of any crime.

Of the original participants, 111 died. Among those who died, 75 (68 percent) were victims of homicide of which 68 (91 percent) were killed with firearms. African

Americans were 4.5 times more likely to die from homicide than non-Hispanic whites.

"Prevention is key," Teplin said. "We need to reduce the likelihood that youth will become delinquent. And, if they are arrested and detained, we need interventions to reduce violence. Otherwise, perpetrators often become victims."

Many delinquent youth commit crimes because of untreated psychiatric problems. For example, they may abuse drugs to self-medicate for depression, and then sell drugs to afford them, Teplin noted.

"These youth may have fallen through the cracks of the health care system into the juvenile justice net," Teplin said. "We should avoid the stereotype that delinquent youth are just bad kids. Many are not hardened criminals; but once detained, they are on a path fraught with risk."

*Other Northwestern authors include Jessica A. Jakubowski, Karen M. Abram, Nichole D. Olson, Marquita L. Stokes and Leah J. Wely.*

*The study was supported in part by National Institute on Drug Abuse grants R01DA019380, R01DA022953 and R01DA028763 and National Institute of Mental Health grants R01MH54197 and R01MH59463, all of the National Institutes of Health; 1999-JE-FX-1001, 2005-JL-FX-0288 and 2008-JF-FX-0068 from the Office of Juvenile Justice and Delinquency Prevention; the Substance Abuse and Mental Health Services Administration, the Centers for Disease Control and Prevention and the Robert Wood Johnson Foundation.*

<http://www.bbc.com/news/health-27832220>

### **Washing chicken 'spreads infection'**

***Consumers are being warned to stop washing raw chicken as doing so increases the risk of food poisoning.***

An online survey of 4,500 UK adults by the Food Standards Agency (FSA) found 44% washed chicken before cooking.

But it warns this spreads campylobacter bacteria onto hands, work surfaces, clothing and cooking equipment, through the splashing of water droplets.

Campylobacter affects about 280,000 people in the UK each year but only 28% in the FSA survey had heard of it.

Only a third of them knew that poultry was the main source of the bacteria.

However 90% had heard of salmonella and E. coli.

The most commonly cited reasons for washing chicken were to remove dirt or germs, or because they had always done it.

### **Cross-contamination**

Campylobacter is the most common form of food poisoning in the UK.

The majority of cases come from contaminated poultry.

Symptoms include diarrhoea, stomach pains and cramps, fever, and generally feeling unwell.

Most people are only ill for a few days, but it can lead to long-term health problems, including irritable bowel syndrome and Guillain-Barre syndrome, a serious condition of the nervous system.

It can also kill. Those most at risk are children under five and older people.

FSA chief executive Catherine Brown said: "Although people tend to follow recommended practice when handling poultry, such as washing hands after touching raw chicken and making sure it is thoroughly cooked, our research has found that washing raw chicken is also common practice.

"That's why we're calling on people to stop washing raw chicken and also raising awareness of the risks of contracting campylobacter as a result of cross-contamination.

"Campylobacter is a serious issue. Not only can it cause severe illness and death, but it costs the economy hundreds of millions of pounds a year as a result of sickness absence and the burden on the NHS."

She said the FSA was also working with farmers and producers to try to reduce the rate of campylobacter in broiler chicken flocks and with slaughterhouses and processors to minimise the levels of contamination in birds.

<http://www.bbc.com/news/uk-wales-south-west-wales-27857569>

### **How WW1 changed emergency medicine**

***As the centenary of the start of the World War One draws nearer, BBC Wales is exploring how core roles in the modern British Army were first developed during the conflict.***

**By Charlotte Dubenskij BBC Wales**

From the introduction of gunners on tanks to signallers using radio communications, these technological advancements had far-reaching consequences on the war then and on today's battlefield.

Charlotte Dubenskij takes a present day Army first responder back in time, visiting a museum dedicated to probably WW1's most famous first-aider - the inventor of penicillin, Alexander Fleming.

It is a role L/Cpl Scott Haplin from Kidwelly in Carmarthenshire knows only too well. He has been a first responder for 1st The Queen's Dragoon Guards for three years.

In that time he has seen plenty of action as part of the Welsh Cavalry.

"On my last tour I was involved in an IED explosion when two men lost their lives. I helped the driver out of the vehicle, checked him over and made sure he got back safely for treatment," he said.

The role of a first responder is commonplace in the armed forces today, but it was only during World War One that it was realised medical expertise was needed closer to the action.

"Before the First World War there were only porters on the battlefield. These were men who picked up casualties and took them away from the battlefield to be treated," said military medical historian Dr Emily Mayhew.

"It was realised you needed expert stretcher bearers or first responders who had medical training and could treat the casualty, stop them bleeding and keep them alive until the next stage," she said.

Dr Mayhew says the introduction of the first responder is one of the great legacies of the conflict, but despite this she says the men were often abused by the other soldiers.

"When the battalions went forward, the stretcher bearers went with them. As they all wait in the front of the trenches to go over the top and fight, quite often the soldiers will abuse them saying, 'why don't you get a gun and fight?'

"They think it's bad luck to have them there.

"But when the soldiers go over the top and are injured, when the stretcher bearers get to them the soldiers apologise as they realise what their role is."

For L/Cpl Haplin that perception could not be more different today.

"Being a first responder I'm trusted by the soldiers I work with and they respect me as they know I'm there to help," he said.

As well as responding to injuries he also makes sure the soldiers he works with eat properly and are hydrated.

He carries a medical pouch containing re-hydration sachets, tourniquets and trauma bandages, and blood-stopping celox gauzes at all times.

The kit used today is a world away from that provided to stretcher bearers and field officers such as Fleming 100 years ago.

### 'Good war for medicine'

Kevin Brown, the curator of the Alexander Fleming Laboratory Museum, explained: "The men carried in their pockets this small metal tin.

"Inside it contains a number of small phials of pain relief such as pure ether, morphine and caffeine. Now at that point (WW1) it was thought the best treatment was morphia and cup of tea and a cigarette."

He describes World War One as being "a good war for medicine" with many advances in the field over the four-year conflict.

"The war saw a huge amount of innovative work on rehabilitation. Much of this was orchestrated by the British Army's expert on orthopaedics, the Welshman Sir Robert Jones," he said.

"This is the first time we see an emphasis on when the men get back home on getting them back to leading a normal life," he said. "Men who lost limbs were given prosthetics and trained in various crafts they could do to earn a living. Before the First World War they were ignored."

Other new inventions in the field of medicine included the Thomas Splint which is still used to stabilise fractured femurs to prevent infection and help knit the bones back together.

It was invented by another Welshman, Hugh Owen Thomas, who was also the uncle of Sir Robert Jones. When used in World War One it reduced mortality of compound fractures dramatically, reducing the number of soldiers who died.

"Looking back at the role then to what I do now, I think it would have been a lot harder," said L/Cpl Halpin.

But he says many of the ideas which were born in World War One are still being used on the modern battlefield. "As they say in the Army, if it ain't broke why fix it?"