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## **Inaccurate reporting jeopardizing clinical trials**

### ***Wide variety in how methods are reported and missing vital information about experiments limits accurate reproduction***

The team led by Dr Sheena Cruickshank of the Faculty of Life Sciences and Professor Andy Brass from the School of Computer Science analysed 58 papers on research into inflammatory bowel disease published between 2000 and 2014. They found a wide variety in how methods were reported and that vital information about experiments were missing, meaning they couldn't be accurately reproduced in animal or human models.

In several instances the gender of the animal used wasn't recorded which can have a bearing on the result as female mice have a stronger immune response to males. How the animals were housed will also impact on the results in experiments about the gut.

Dr Cruickshank says she was shocked at the lack of information provided in papers: "What our research has uncovered is that this lack of data makes it difficult to validate the experiment and the result. Crucially this is having an impact of the reproducibility of experiments, both in the animal model and when transferred to human trials."

The problem first became clear to the researchers when they were looking at building a knowledge base to help pull together research on inflammatory bowel disease (colitis). Working with computer scientists it became clear to the biologists that the data couldn't be understood by colleagues from different disciplines.

Professor Andy Brass says: "So much research is now being carried out across disciplines so it's vital that experiments can be understood by as many scientists as possible. Relying on the reader to make assumptions based on their own experience will only lead to errors, but this is what many papers are asking people to do when they come to replicate the research."

To address the issue the team have developed a critical checklist of what information should be included. It covers nine areas ranging from information about the animals, their housing condition, genetics, how colitis is induced, experiment design and monitoring. The checklist is included in their paper due to be published in the journal *Inflammatory Bowel Diseases*.

Dr Cruickshank explains: "Our checklist sounds like fairly basic information that should be in all papers. But over the past few years journals have asked for more and more abbreviated methods so information has stopped being included. Instead papers are focussed on the results and discussion and sometimes you

have to go back to a paper from the sixties to find the last time a particular method was accurately recorded."

Whilst the researchers have been critical of the method reporting they are keen to point out that their criticism doesn't mean the research isn't valid or accurate. The experiments may well be sound, but the lack of detail in how they're reported makes that judgement more difficult to make and the reproducibility much harder.

As an example Dr Cruickshank points to the test case for the Reproducibility Initiative which was published in the journal *PLOS One* in December last year. The team wanted to reproduce an experiment which had found that peptide hormones made naturally by cattle are efficient killers of the parasite *Leishmania major*. When they followed the reported methodology they had to up the dose by ten times to get the same result. But what had actually happened was that the original paper had not precisely described the molecules involved.

Moving forward the Manchester team is recommending the adoption of their checklist as a requirement for publication to improve the quality, comparability and standardization of studies into inflammatory bowel disease. They believe it will make the interpretation and translation of data to human disease more reliable and ultimately contribute to making clinical trials more successful.

*The paper "Quality of Methods Reporting in Animal Models of Colitis" will be published in the journal Inflammatory Bowel Diseases.*

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## **More detailed findings confirm that coffee protects against breast cancer recurrence**

### ***A number of research studies have shown that coffee helps to protect against breast cancer.***

A new study led by Lund University, has confirmed that coffee inhibits the growth of tumours and reduces the risk of recurrence in women who have been diagnosed with breast cancer and treated with the drug tamoxifen.

The study, which is a follow-up of the results the researchers obtained two years ago, was carried out at Lund University and Skåne University Hospital, in collaboration with researchers in the UK.

"Now, unlike in the previous study, we have combined information about the patients' lifestyle and clinical data from 1090 breast cancer patients with studies on breast cancer cells. The study shows that among the over 500 women treated with tamoxifen, those who had drunk at least two cups of coffee a day had only half the risk of recurrence of those who drank less coffee or none at all", explain

researchers Ann Rosendahl and Helena Jernström, who obtained the results in collaboration with Jeff Holly and his research team at University of Bristol.

"The study also shows that those who drank at least two cups of coffee a day had smaller tumours and a lower proportion of hormone-dependent tumours. We saw that this was already the case at the time of diagnosis."

In the cell study, the researchers looked more closely at two substances that usually occur in the coffee drunk in Sweden - caffeine and caffeic acid.

"The breast cancer cells reacted to these substances, especially caffeine, with reduced cell division and increased cell death, especially in combination with tamoxifen. This shows that these substances have an effect on the breast cancer cells and turn off signalling pathways that the cancer cells require to grow."

The researchers have demonstrated both in breast cancer patients and at cell level that coffee appears to reinforce the effect of treatment with tamoxifen, but emphasise the importance of taking prescribed medication. "They are incredibly important, but if you like coffee and are also taking tamoxifen, there is no reason to stop drinking it. Just two cups a day is sufficient to make a difference."

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### **Common back problems may be caused by evolution of human locomotion**

*A common spinal disease could be the result of some people's vertebrae sharing similarities in shape to a non-human primate, according to research published in the open-access journal BMC Evolutionary Biology*

A common spinal disease could be the result of some people's vertebrae, the bones that make up the spine, sharing similarities in shape to a non-human primate. The research, published in the open access journal BMC Evolutionary Biology, suggests that the relatively quick evolution of the ability to walk on two legs may have had a substantial impact on modern human health.

Humans are more commonly afflicted with spinal disease than non-human primates, and one widely discussed explanation for this is the stress placed on the spine by bipedal locomotion. This research backs up this theory.

A widespread cause of back pain, 'intervertebral disc herniation', has prevalence rates ranging from 20% to 78%, depending on the population. It is caused by the prolapse of a gelatinous substance inside the disc, and when the herniation is vertically directed it is often characterised by protrusions of cartilage called 'Schmorl's nodes'. Researchers studied the vertebrae of humans, chimpanzees and orangutans to examine links between vertebral shape, locomotion, and the appearance of vertical disc herniation in humans.

Postdoctoral researcher Kimberly Plomp from Simon Fraser University, Canada, said: "Our study is the first to use quantitative methods to uncover why humans are so commonly afflicted with back problems compared to non-human primates. The findings have potential implications for clinical research, as they indicate why some individuals are more prone to back problems. This may help in preventative care by identifying individuals, such as athletes, who may be at risk of developing the condition."

The researchers compared 141 human vertebrae, 56 chimpanzee vertebrae (a knuckle-walking primate), and 27 orangutan vertebrae (a climbing primate that uses all four feet which are modified as hands) and found significant differences in their shape. They say this could be explained by the different modes of locomotion and contributes to the understanding of the human evolution of bipedalism.

Of the human vertebrae they studied, 54 had 'Schmorl's nodes', the skeletal indicators of vertical disc herniation. The researchers found that human vertebrae with Schmorl's nodes shared more similarities in shape with chimpanzee vertebrae than the healthy human vertebrae shared with those non-human primates.

This suggests that vertical disc herniation preferentially affects human individuals with vertebrae that are towards the ancestral end of the range of human shape variation. These individuals may therefore be less well-adapted for bipedalism and suffer more from load-related spinal disease.

The authors say their findings could be used for interpreting medical scans of spinal disease. This could help clinicians investigate an individual's vertebral shape and predict their susceptibility to intervertebral disc herniation.

The identification of an ancestral vertebral shape that influences the occurrence of a common spinal disease in humans also supports the idea that the relatively quick evolution of bipedalism may have had a substantial impact on modern human health.

The authors note several study limitations such as small sample sizes, and including humans that are derived from Medieval and Post-Medieval English populations. Future research will include larger sample sizes and multiple human populations from different ancestral backgrounds. It will also include the analysis of CT scans of living individuals in order to study horizontal herniations that do not leave evidence on the bone, and focus on capturing the 3D shape of human and non-human primate data to capture vertebral elements that have been missed in the present study.

The research team included Mark Collard from Simon Fraser University, Darlene Weston from the University of British Columbia, Una Strand Viðarsdóttir from the University of Iceland, and Keith Dobney from the University of Aberdeen.

Kimberly A Plomp, Una Strand Vidarsdottir, Darlene A Weston, Keith Dobney and Mark Collard *The ancestral shape hypothesis: an evolutionary explanation for the occurrence of intervertebral disc herniation in humans*

*BMC Evolutionary Biology* 2015 doi: 10.1186/s12862-015-0336-y

<http://www.bbc.com/news/health-32453192>

### **HIV home test kit goes on sale in UK**

***The first legally approved HIV self-test kit that allows people to get a result in 15 minutes at home has gone on sale in England, Scotland and Wales.***

By Smitha Mundasad Health reporter, BBC News

Unlike other kits, these tests do not need to be sent off to a lab to get the results. It works by detecting antibodies on a small drop of blood, which are often only detectable three months after the infection is caught. Experts warn that any positive tests must be reconfirmed at clinics. Charities hope it will reduce some of the 26,000 people estimated to have undiagnosed HIV in the UK.

#### **Testing lines**

An early diagnosis allows people to get treatment quickly and can prevent serious complications. And individuals successfully treated for HIV are less likely to pass the infection on. This new "do-it-yourself" test is made by company Bio Sure UK and can be bought online. It works in a similar way to a pregnancy test, measuring levels of antibodies - proteins made in response to the virus - in a person's blood.

The device analyses a small droplet of blood, taken from the finger-tip using a lancet. Two purple lines appear if it is positive. The company recommends attending sexual health clinics for advice and further blood tests if both lines appear. And even if the test is negative experts say it does not mean people are definitely virus free - especially if exposure occurred within the last three months.

The three-month window period, between the moment someone catches the infection and the time it can take for antibodies to develop, means the kit is not reliable during this time.

#### **Quick access**

Charities have welcomed the test and hope it will encourage more people to get checks - particularly those reluctant to go to clinics in the first instance.

Dr Rosemary Gillespie, chief executive at Terrence Higgins Trust, said: "We campaigned for a long time to secure the legalisation of HIV self-test kits which happened in April 2014, so it is great to see the first self-test kits being approved. "However, it is important to make sure people can get quick access to support when they get their result."

Shaun Griffin, also at the charity, said: "At the moment there are funding challenges throughout the NHS, including for sexual health services. "It is absolutely critical that people have access to HIV tests and advice they need."

Free HIV tests are available across the NHS. In Northern Ireland ministers are considering legal changes to allow the sale of home testing kits.

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

### **The first complex life on Earth got eaten to extinction**

***The very first mass extinction of complex life forms had a biological cause***

13:05 27 April 2015 by Jeff Hecht

Strange and largely immobile organisms made of tubes were the first complex life on Earth. Appearing 579 million years ago, they thrived on the seafloor for some 37 million years, then vanished – becoming a curiosity we know only from faint impressions in the sandstone fossil record.

What made them die out? New fossil evidence from Namibia suggests that the Ediacarans, as these creatures are known, had their world turned upside by an explosion of life forms at the beginning of the Cambrian period 541 million years ago. Some of these may have evolved to eat their enigmatic predecessors and to bioengineer the environment in ways that left little hope for the passive Ediacarans.

If so, the very first mass extinction of complex life forms had a biological cause, unlike the big five mass extinctions which are thought to be environmentally driven – kicked off by widespread volcanic eruptions that poisoned the oceans or a massive meteorite strike, for example.

The disappearance of the Ediacarans from the fossil record has long troubled biologists. Leading theories are a catastrophic mass extinction, that Ediacarans got eaten or had their habitat destroyed by newly evolved animals, or no longer left fossils because of a change in ocean conditions.

#### **No signature**

But a careful search by Marc Laflamme of the University of Toronto in Mississauga and colleagues threw up no geochemical signatures of low-oxygen conditions or other turmoil to support the idea of an environmentally driven mass extinction. And given that soft-bodied Cambrian animals are fossilised within rocks like the famed Burgess Shale, it seems unlikely that the conditions

simply didn't allow any surviving Ediacarans to leave a fossil trace in the Cambrian period.

That suggests that by the time the Cambrian explosion of species reached full force, the Ediacarans were gone, says Simon Darroch of the Smithsonian Institution in Washington DC. He will detail the team's evidence next week at the Joint Assembly of the American Geophysical Union in Montreal, Canada.

Their search took them to southern Namibia, where outcrops stretching over a large area expose fossils covering the crucial few million years when the Ediacarans disappeared and the new animals of the Cambrian appeared.

The deposits showed a vastly increased number of trace fossils from Cambrian animals, showing they had already evolved and were breaking up sediment and disturbing the Ediacaran environment.

### **Eco engineers**

"Modern animals are ecosystem engineers. They alter the environment, burrow into sediments and prey on each other," says Darroch. So he looked for interactions between the two groups.

If these animals wiped out the Ediacarans, Darroch reasoned, fossils of the most recent Ediacaran communities should hint that they were struggling. By a number of measures, such as low species richness, he found the Namibian fossil communities did indeed "look very stressed". For example, he found traces in the latest Ediacaran fossils very similar to those left by sea anemones, which are predatory. "So there probably were predators in the late Ediacaran," he says.

All of this adds up to pretty robust evidence, he says, that the new species ate the old ones or destroyed their habitat.

However there was no cold, hard stop for everything Ediacaran, says Jim Gehling of the South Australian Museum in Adelaide, who has been studying Australian deposits of the same age. "Clearly there was an extinction of the big fleshy things stuck on the seafloor," he says.

But he adds that although many of those Ediacarans were so strange that their biology makes little sense to us today, there is evidence that some of them did evolve movement and ways of ingesting food like modern animals, so may have given rise to life forms that evolved later.

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### **Oil or fat?**

#### ***Saturated fatty acids might directly damage heart***

Olive oil is universally considered a much healthier alternative to meat fat. Plant-derived oils (such as olive oil, canola oil, and vegetable oil) largely consist of unsaturated fatty acids, whereas animal fat is richer in the saturated ones.

After a typical meal, carbohydrates are the primary source of energy production by the heart. Under fasting conditions, however, free fatty acids become the major energy producer. Saturated fat in a diet is known to be detrimental to heart health, but its impact on the cardiac muscle has been studied only recently.

Interestingly, while saturated fatty acids are toxic to cells, unsaturated fatty acids are not only harmless but also provide protection against the damage done by saturated fatty acids. Studies conducted on many cell lines have indicated that saturated fatty acids can cause cell death involving the "endoplasmic reticulum stress (ER stress)", a cellular process known to be involved in the development of many diseases. A new paper, "Saturated fatty acids induce endoplasmic reticulum stress in primary cardiomyocytes", just published in open access in "Endoplasmic Reticulum Stress in Diseases" by De Gruyter Open shows that there are striking differences in the accumulation of saturated and unsaturated fatty acids in cardiac muscle cells, and that saturated fatty acids induce the death of these cells through the ER stress. In stark contrast, unsaturated fatty acids protect the same cells from such damage.

A research group from the Montreal Heart Institute in Canada, led by Dr. Nicolas Bousette, evaluated the impact of palmitate and oleate on cellular fatty acid absorption, triglyceride synthesis, intracellular lipid distribution, ER stress, and cell death in primary cardiomyocytes. This is the first time that such phenomena were observed in cells directly derived from the heart, validating a critical role for saturated fatty acids in the development of heart diseases. Given a primary role for lipid metabolism in the development of type II diabetes, the current finding might suggest a probable role for saturated fatty acids in the development of heart conditions among diabetic patients. The current results and future research in this direction might improve our understanding on the possible connection between intracardiomyocyte lipid accumulation and the development of diabetic cardiomyopathy. [The article is available fully in open access to read, download and share on De Gruyter Online](http://www.eurekalert.org/pub_releases/2015-04/qmuo-bun042715.php)

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### **Bumblebees use nicotine to fight off parasites**

***Bees infected with a parasite were more likely to consume nicotine-laced nectar than uninfected ones***

Researchers from Queen Mary University of London (QMUL) and Royal Holloway, University of London (RHUL), gave bumblebees the option to choose between a sugar solution with nicotine in it and one without. Those bees infected with the *Crithidia bombi* parasite were more likely to go for the nicotine-laced nectar than those that weren't infected.

Infected bumblebees that consumed nicotine delayed the progress of the infection for a few days, showing lower levels of parasites than those that had not. However, it did not increase the life expectancy of those bees, meaning that the direct benefits of nicotine for the bee colony remain to be identified.

Consuming nicotine also had negative effects, appearing to suppress the appetite of infected bees much like smoking does in humans. Healthy bees that consumed nicotine also showed shorter lifespans than those that did not consume any.

Bees are not the only species known to use nicotine to fight parasites, with house sparrows using cigarette butts in their nests to ward off mites.

Dr David Baracchi from the School of Biological and Chemical Sciences at QMUL, co-author of the research, said:

"While it's clear that there is some benefit to nicotine consumption for parasite-infected bees, a key challenge now is to discover exactly how such natural medication limits the impact of the disease on the bees' society.

"Given the stresses placed on worldwide bee populations by disease, understanding how the bees themselves fight infection is key."

*Bibliographical information: 'Weak and contradictory effects of self-medication with nectar nicotine by parasitized bumblebees' by Baracchi D, Brown MJF and Chittka L. is published by F1000Research 2015, 4:73 (doi: 10.12688/f1000research.6262.1)*

[http://www.eurekalert.org/pub\\_releases/2015-04/ucl-cos042715.php](http://www.eurekalert.org/pub_releases/2015-04/ucl-cos042715.php)

## **Chemistry of seabed's hot vents could explain emergence of life**

***Hot vents on the seabed could have spontaneously produced the organic molecules necessary for life, according to new research by UCL chemists.***

The study shows how the surfaces of mineral particles inside hydrothermal vents have similar chemical properties to enzymes, the biological molecules that govern chemical reactions in living organisms. This means that vents are able to create simple carbon-based molecules, such as methanol and formic acid, out of the dissolved CO<sub>2</sub> in the water.

The discovery, published in the journal *Chemical Communications*, explains how some of the key building blocks for organic chemistry were already being formed in nature before life emerged - and may have played a role in the emergence of the first life forms. It also has potential practical applications, showing how products such as plastics and fuels could be synthesised from CO<sub>2</sub> rather than oil.

"There is a lot of speculation that hydrothermal vents could be the location where life on Earth began," says Nora de Leeuw, who heads the team. "There is a lot of CO<sub>2</sub> dissolved in the water, which could provide the carbon that the chemistry of living organisms is based on, and there is plenty of energy, because

the water is hot and turbulent. What our research proves is that these vents also have the chemical properties that encourage these molecules to recombine into molecules usually associated with living organisms."

The team combined laboratory experiments with supercomputer simulations to investigate the conditions under which the mineral particles would catalyse the conversion of CO<sub>2</sub> into organic molecules. The experiments replicated the conditions present in deep sea vents, where hot and slightly alkaline water rich in dissolved CO<sub>2</sub> passes over the mineral greigite (Fe<sub>3</sub>S<sub>4</sub>), located on the inside surfaces of the vents. These experiments hinted at the chemical processes that were underway. The simulations, which were run on UCL's Legion supercomputer and HECToR (the UK national supercomputing service), provided a molecule-by-molecule view of how the CO<sub>2</sub> and greigite interacted, helping to make sense of what was being observed in the experiments. The computing power and programming expertise to accurately simulate the behaviour of individual molecules in this way has only become available in the past decade.

"We found that the surfaces and crystal structures inside these vents act as catalysts, encouraging chemical changes in the material that settles on them," says Nathan Hollingsworth, a co-author of the study. "They behave much like enzymes do in living organisms, breaking down the bonds between carbon and oxygen atoms. This lets them combine with water to produce formic acid, acetic acid, methanol and pyruvic acid. Once you have simple carbon-based chemicals such as these, it opens the door to more complex carbon-based chemistry."

Theories about the emergence of life suggest that increasingly complex carbon-based chemistry led to self-replicating molecules - and, eventually, the appearance of the first cellular life forms. This research shows how one of the first steps in this journey may have occurred. It is proof that simple organic molecules can be synthesised in nature without living organisms being present. It also confirms that hydrothermal vents are a plausible location for at least part of this process to have occurred.

The study could also have a practical applications, as it provides a method for creating carbon-based chemicals out of CO<sub>2</sub>, without the need for extreme heat or pressure. This could, in the long term, replace oil as the raw material for products such as plastics, fertilisers and fuels. This study shows, albeit on a very small scale, that such products, which are currently produced from non-renewable raw materials, can be produced by more environmentally friendly means. If the process can be scaled up to commercially viable scales, it would not only save oil, but use up CO<sub>2</sub> - a greenhouse gas - as a raw material.

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## Neurons constantly rewrite their DNA

### *DNA regulatory tags must be cut out and replaced to allow neurons to function*

Johns Hopkins scientists have discovered that neurons are risk takers: They use minor "DNA surgeries" to toggle their activity levels all day, every day. Since these activity levels are important in learning, memory and brain disorders, the researchers think their finding will shed light on a range of important questions. A summary of the study will be published online in the journal *Nature Neuroscience* on April 27.

"We used to think that once a cell reaches full maturation, its DNA is totally stable, including the molecular tags attached to it to control its genes and maintain the cell's identity," says Hongjun Song, Ph.D., a professor of neurology and neuroscience in the Johns Hopkins University School of Medicine's Institute for Cell Engineering. "This research shows that some cells actually alter their DNA all the time, just to perform everyday functions."

***These are images of mouse neurons from the hippocampal region of the brain. Levels of the surface receptor GluR1, orange, are shown in unmodified neurons, left, and in those with increased levels of Tet3, right.*** Huimei Yu, Johns Hopkins Medicine

This DNA alteration is called DNA demethylation. Methyl groups are regulatory tags that are permanently bound to cytosines, the C's in DNA's four-letter alphabet. Removing them is a multistep process that requires excising a tagged cytosine from the long string of paired "letters" that make up a chromosome and, ideally, replacing it with an untagged cytosine. Because the process involves making a cut into DNA, it leaves the DNA somewhat vulnerable to mutations, so most cells use the process sparingly, mostly for correcting errors. But recent studies had turned up evidence that mammals' brains exhibit highly dynamic DNA modification activity - more than in any other area of the body - and Song's group wanted to know why all this risky business was going on in such a vulnerable tissue as the brain.

The main job of neurons is to communicate with other neurons through connections called synapses. At each synapse, an initiating neuron releases chemical messengers, which are intercepted by receptor proteins on the receiving neuron. Neurons can toggle the "volume" of this communication by adjusting the activity level of their genes to change the number of their messengers or receptors on the surface of the neuron. When Song's team added various drugs to neurons taken from mouse brains, their synaptic activity - the volume of their communication - went up and down accordingly. When it was

up, so was the activity of the Tet3 gene, which kicks off DNA demethylation. When it was down, Tet3 was down too.

Then, they flipped the experiment around and manipulated the levels of Tet3 in the cells. Surprisingly, when Tet3 levels were up, synaptic activity was down; when Tet3 levels were down, synaptic activity was up. So do Tet3 levels depend on synaptic activity, or is it the other way around?

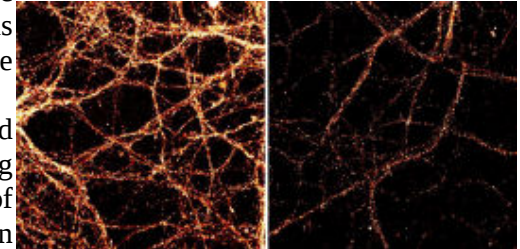
Another series of experiments showed them that one of the changes occurring in neurons in response to low levels of Tet3 was an increase in the protein GluR1 at their synapses. Since GluR1 is a receptor for chemical messengers, its abundance at synapses is one of the ways neurons can toggle their synaptic activity.

The scientists say they have discovered another mechanism used by neurons to maintain relatively consistent levels of synaptic activity so that neurons can remain responsive to the signaling around them. If synaptic activity increases, Tet3 activity and base excision of tagged cytosines increases. This causes the levels of GluR1 at synapses to decrease, in turn, which decreases their overall strength, bringing the synapses back to their previous activity level. The opposite can also happen, resulting in increasing synaptic activity in response to an initial decrease. So Tet3 levels respond to synaptic activity levels, and synaptic activity levels respond to Tet3 levels.

Song says: "If you shut off neural activity, the neurons 'turn up their volume' to try to get back to their usual level and vice versa. But they can't do it without Tet3."

Song adds that the ability to regulate synapse activity is the most fundamental property of neurons: "It's how our brains form circuits that contain information." Since this synaptic flexibility seems to require mildly risky DNA surgery to work, Song wonders if some brain disorders might arise from neurons losing their ability to "heal" properly after base excision. He thinks this study brings us one step closer to finding out.

*Other authors of the report include Huimei Yu, Yijin Su, Jaehoon Shin, Chun Zhong, Junjie Guo, Yi-lan Wen and Guo-li Ming of the Johns Hopkins University School of Medicine; and Fuying Gao, Daniel Geschwind and Giovanni Coppola of the University of California, Los Angeles.*



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### **Most women don't know female-specific stroke signs**

#### ***National survey: Women are largely unaware of many symptoms and risks of strokes***

COLUMBUS, Ohio - A national survey released today by The Ohio State University Wexner Medical Center shows that most women don't know the risks or symptoms females face when it comes to having a stroke.

The survey of 1,000 women released in time for Stroke Awareness Month in May found that only 11 percent of women could correctly identify pregnancy, lupus, migraine headaches and oral contraception or hormone replacement therapy as female-specific stroke risks.

**[VIDEO: Most women don't know female-specific risks or important symptoms when it comes to having a stroke, according to a survey released by The Ohio State University Wexner Medical Center](#)**

The survey also found that only 10 percent were aware that hiccups combined with atypical chest pain are among the early warning signs of a stroke in women when accompanied by or followed by typical stroke symptoms. Stroke is the third leading cause of death for women, according to the National Stroke Association.

"I think we have a ways to go when it comes to educating women about stroke and their unique risk factors," said Dr. Diana Greene-Chandos, a neurologist and director of neuroscience critical care at Ohio State's Wexner Medical Center. "Things like pregnancy, hormone replacement therapy and even something as trivial as a case of the hiccups can all play an important role when it comes to strokes in women, and we need to be more aware of it."

Some risk factors are the same for both women and men, including smoking, not exercising or having a blood pressure higher than 140/90. Other stroke risk factors for men and women include having a hemoglobin A1C of more than 7 if you are already diabetic, or 5.7 if not; as well as having a LDL cholesterol of less than 100 if you are without additional stroke risks, or less than 70 with additional stroke risks, particularly diabetes, she said.

Online assessments are available to help evaluate your risk for stroke, said Greene-Chandos, including a simple pen-and-paper test created by Ohio State's stroke experts that can be downloaded here.

"Women and men should really on focus keeping their blood pressure under 140/90, because having high blood pressure consistently puts people at risk for having a stroke," said Greene-Chandos, who is part of the team of stroke experts at Ohio State's Wexner Medical Center's Comprehensive Neurovascular Stroke Center.

But symptoms of stroke can be different for women, and may include hiccups, dizziness that is not classic vertigo, headaches, atypical chest pain and/or numbness of the entire body with one side being more numb than the other.

"Women may have more headaches with their strokes. They actually can have hiccups with a little bit of chest pain with their stroke symptoms, sometimes sending them down the pathway of looking for either heart disease or indigestion," said Greene-Chandos, who is also a member of Ohio State's Neurological Institute. "Pregnancy also increases their risk of stroke, particularly in the final months and the immediate period after delivering the child."

Recognizing a stroke quickly and seeking medical help immediately is crucial. Treatment with a clot-busting drug is only consistently an option within three hours of the onset of the stroke.

"Women do not think they are going to have a stroke. They think of it as a man's disease," said Greene-Chandos. "You have to know when you are having a stroke, you have to recognize that it's a stroke and you have to get to the emergency room and receive the medication. Women shouldn't ignore their symptoms or hope they will go away because they may lose their opportunity to receive acute treatment."

Each year, about 795,000 Americans suffer a new or recurrent stroke and more than 137,000 people die from stroke. About 60 percent of stroke deaths occur in females, and 40 percent in males, according to the American Heart Association (AHA) and American Stroke Association (ASA).

The number of people having strokes is rising each year, in part because of the aging population. Every 40 seconds someone has a stroke in the United States, and stroke kills someone in the United States about every four minutes, according to AHA/ASA.

The Ohio State survey also found that nearly half of all women said they don't know what problems females face after stroke. In addition to nerve damage and problems swallowing, depression is common among women and often keeps them from getting the rehab that is vital to their recovery, Greene-Chandos said.

"The more you use your brain, the better you'll do in your recovery after a stroke," Greene-Chandos said. "And overall for our society, we need to reduce our stress levels. Whatever it is that you can do that makes you happy and calm each day, make sure that you dedicate some time to doing it."

[http://www.eurekalert.org/pub\\_releases/2015-04/sp-hsc042415.php](http://www.eurekalert.org/pub_releases/2015-04/sp-hsc042415.php)

### **High-pitched sounds cause seizures in old cats**

#### ***Information from 96 cats reveals that some cats do indeed suffer from audiogenic reflex seizures***

When the charity International Cat Care asked veterinary neurologists at Davies Veterinary Specialists, UK, for help with several enquiries it had received regarding cats having seizures, seemingly in response to certain high-pitched sounds, the answer was that the problem was not documented and little, if anything, was known about it.

Mark Lowrie and Laurent Garosi from Davies Veterinary Specialists and Robert Harvey from the UCL School of Pharmacy, London, decided to investigate, and compiled a questionnaire for owners to complete. Working with International Cat Care, and using the interest generated by the media, the story went worldwide (dubbed 'Tom and Jerry syndrome' after the cartoon character Tom who has a strong startle reflex and often reacts with involuntary jerks to sound stimuli). They received hundreds of replies from across the globe from people who had noticed the same problem in their cats in response to certain types of sound. These owners had also found that their local vets had no information at all about it, and often did not believe that a sound had triggered the seizure!

Now the resulting paper, entitled 'Audiogenic reflex seizures in cats', has been published in the *Journal of Feline Medicine and Surgery*\* and has pulled together information from 96 of these cats, looking at the type and duration of seizure and the triggering sound. It reveals that some cats do indeed suffer from audiogenic reflex seizures - those which are consistently caused by sounds (this is also recognised in people).

Certain sounds induced 'absences' (non-convulsive seizures), myoclonic seizures (brief, shock-like jerks of a muscle or a group of muscles), or generalised tonic-clonic seizures. This last category is what most people think of as a 'seizure', with the cat losing consciousness and its body stiffening and jerking, often for several minutes. The new syndrome has been termed feline audiogenic reflex seizures (FARS).

The investigation found that FARS occurred in pedigree and non-pedigree cats, but that among the pedigrees, the Birman breed was over-represented. This is

also a problem of older cats - the average age of seizure onset was 15 years, with cats ranging in age from 10 to 19 years.

The most commonly reported triggers for FARS were the sound of crinkling tin foil (82 cats), a metal spoon clanging in a ceramic feeding bowl (79 cats), chinking or tapping of glass (72 cats), crinkling of paper or plastic bags (71 cats), tapping on a computer keyboard or clicking of a mouse (61), clinking of coins or keys (59), hammering of a nail (38) and even the clicking of an owner's tongue (24). Other, less common triggers were the sound of breaking the tin foil from packaging, mobile phone texting and ringing, digital alarms, Velcro, stove igniting ticks, running water, a dog jangling its collar as it scratched, computer printer, firewood splitting, wooden blocks being knocked together, walking across a wooden floor with bare feet or squeaky shoes and, in one case, the short, sharp scream of a young child.

Avoiding the sounds could reduce the seizures, although owners reported that it was sometimes difficult to avoid certain sounds, and the loudness of the sound also seemed to increase the severity of seizures.

This study has defined a previously unreported syndrome by using a carefully screened questionnaire and medical records. The geriatric nature of this condition is such that it may be overlooked in older cats, which may potentially suffer from other concurrent conditions. The hope is that publication of the paper will raise awareness among vets in practice about this syndrome. Meanwhile, work is ongoing to identify the genetic basis of this disorder and the team is now also working on a paper about treatment of these cases.

Lead author, Mark Lowrie, says: 'We have been overwhelmed by the response to our work. A second study is soon to be published suggesting that levetiracetam is an excellent choice of medication in managing this condition. Our experience is that it can completely rid a cat of these sound-induced seizures, including the myoclonic twitches - one owner reported that levetiracetam had 'truly been a miracle drug for my cat'.

Claire Bessant, Chief Executive of International Cat Care, summed up: 'How wonderful to be able to go back to those worried owners who came to us for help with a problem previously unrecognised by the veterinary profession with not only an explanation for their cats' behaviours, but a way to help them as well.'

*The study can be read for free here:*

<http://jfm.sagepub.com/content/early/2015/04/27/1098612X15582080.full.pdf+html>

\*Lowrie M, Bessant C, Harvey RJ, Sparkes A and Garosi L. Audiogenic reflex seizures in cats. *J Feline Med Surg. Epub ahead of print 27 April 2015. DOI: 10.1177/1098612X15582080.*



<http://nyti.ms/1I59KRy>

## Admitted to Your Bedroom: Some Hospitals Try Treating Patients at Home

*When Martin Fernandez came into Mount Sinai Hospital's emergency room one recent afternoon, with high fever and excruciating abdominal pain, he and his family were asked an unexpected question.*

By Daniela J. Lamas, M.D. April 27, 2015

Mr. Fernandez, 82, would have to be officially admitted to receive intravenous antibiotics for his urinary tract infection. But he could stay at Mount Sinai, or he could receive treatment at home.

If he chose to be hospitalized at home, doctors and nurses would visit daily. He would receive lab draws and intravenous medications, even X-rays or ultrasound scans if he needed them. The costs to him would be no greater than if he were physically in the hospital. In three or four days, he would be discharged - and he would not have to go anywhere.

For Mr. Fernandez, a retired house painter from Venezuela who lives with his wife on Manhattan's Upper West Side, the choice was clear. He was hospitalized at his daughter's apartment, just a couple blocks away, a few hours later.

He had a urinary catheter, but Mr. Fernandez could still wear his own clothes during the day and his pajamas at night. His wife and his daughter cooked him meals of arepas, vegetables and black beans, and served them to him in bed.

"Hospitals help you, but there's so much noise that you can't sleep and you're lonely," said Mr. Fernandez's daughter, Ana Vanessa Fernandez. "Here, there was no timing for visitors. There was no curfew. It's like being at home, but the hospital is home with you."

Under pressure to reduce costs while improving quality, a handful of hospital systems have embarked on an unusual experiment: They are taking the house call to the extreme, offering hospital-level treatment at home to patients like Mr. Fernandez who in the past would have been routinely placed in a hospital room. And as awareness spreads of the dangers that hospitalization may pose, particularly to older adults, patients are enthusiastically seizing the opportunity.

"I always laugh when people say, 'Do you really think you're as good as a hospital?'" said Dr. Melanie Van Amsterdam, the lead physician for Presbyterian Healthcare Services Hospital at Home program in Albuquerque. "Have you been to the hospital? For many of these patients, it's a little scary."

Dr. Bruce Leff noticed that back in the late 1980s while making house calls to homebound patients, part of his primary care training at Johns Hopkins

University School of Medicine. When some of his patients fell ill, they simply refused to go to a hospital.

He understood why: He had seen firsthand the delirium, infections and deconditioning that too often land older patients in nursing homes after hospitalization. "Being in the hospital could be toxic," said Dr. Leff, a geriatrician who is now a professor of medicine at Johns Hopkins.

So Dr. Leff and his colleagues had an idea. What if patients could be hospitalized in their own beds?

Some patients need the moment-to-moment monitoring that only a hospital can provide. The first task was to determine which common conditions required admission but could be treated with technologies placed in the home. These would be patients who clearly needed to be hospitalized, but who weren't going to need the intensive care unit. Intravenous medications and X-rays can be readily adapted for the home; ventilators cannot.

Dr. Leff and his colleagues settled on four diagnoses that could be treated without the patient's being physically in the hospital: heart failure, exacerbations of emphysema, certain types of pneumonia, and a bacterial skin infection called cellulitis.

"I'm a doctor. I can talk to a patient, I can examine a patient, I can bring home oxygen and IV meds and fluids, I can do home X-rays. I can do quite a bit," Dr. Leff said. "We felt that it could be done, and the hypothesis was that by doing so, we could reduce harm."

With a grant from the John A. Hartford Foundation, Dr. Leff and his team offered outpatient hospital-level care to nearly 150 patients with these four diagnoses who would otherwise have been treated at one of three hospitals, and compared those patients with a similar group who were hospitalized in the usual way. They called their program "Hospital at Home."

The findings, published in *The Annals of Internal Medicine*, were promising. Offered the opportunity, most patients agreed to be treated at home. They were hospitalized for shorter periods, and their treatments cost less. They were less likely to develop delirium or to receive sedative medications, and no more likely to return to the emergency room or be readmitted.

The results caught the interests of hospital systems nationwide. But payers were less enthusiastic. When it comes to fee-for-service Medicare, there are no existing payment systems even now to reimburse hospital-level care provided in the home.

But systems like the Veterans Affairs and Presbyterian Healthcare Services, in Albuquerque, were not so constrained. Presbyterian has its own health plan and

so, not limited by the lack of fee-for-service reimbursement, began offering a hospital-at-home option in 2008.

Dr. Van Amsterdam started out as the program's only full-time doctor. She spent hours trolling hospital records for patients who might be eligible for the new program: sick enough to require a hospital stay, but not so sick that they might need to go to an I.C.U.

Some of the patients she approached said no. One man did not want visitors because he had big dogs at home, she recalled. Another said that if he felt short of breath at night, he would prefer to be in a hospital. But more than 90 percent agreed.

Today, as she drives through New Mexico, Dr. Van Amsterdam finds herself delivering a different kind of care from what she did years ago as a doctor in a hospital.

"The hospital system is one where you get more information from the computer than you do from your own ears, eyes and nose," she said. "I rely far more on my physical exam skills to take care of these patients. You get a lot more comfortable with uncertainty, I think."

Even with the most careful admitting criteria, the unexpected happens. Dr. Van Amsterdam and her team have had to move patients to the hospital for worsening medical conditions, sometimes by calling 911. Still, it is an infrequent occurrence: only 2.5 percent of these patients must be moved into the traditional hospital.

The challenge of knowing which patients are appropriate for hospitalization at home bothers Dr. Bruce Vladeck, a health care consultant and former administrator of the Health Care Financing Administration.

"I think in order to make this work in a way that makes clinical and ethical sense, you really have to be careful about evaluating your patients on the front end," said Dr. Vladeck, who is a member of the advisory committee for Mount Sinai's continuing program. "And you have to be prepared to change your mind."

At Mount Sinai - whose program is funded by a nearly \$10 million grant from the Centers for Medicare and Medicaid Services - hospitalization at home is called "mobile acute care," but the principle is the same.

Patients with a set of specified diagnoses, expanded from Dr. Leff's earlier work, are approached in the emergency department after the emergency doctor has decided they need to be admitted.

Those with worrisome vital signs - heart rate too high, blood pressure too low - are not eligible. Nor are patients without electricity or running water at home, or

without space at home for oxygen or intravenous supplies, should they be needed - a pertinent question for residents in Manhattan apartments.

To measure the costs of patients who are hospitalized at home, patients will be followed for one month after their home hospital stay, during which they are eligible for services ranging from health coaching to home doctor visits.

The team at Mount Sinai will collaborate with Dr. Leff and his colleagues at Johns Hopkins to compare outcomes to a similar group of patients who are hospitalized and to measure patient satisfaction.

Even for Mount Sinai, whose house calls program has been around for two decades, bringing the key elements of the hospital to a Manhattan apartment hasn't been easy. A well-meaning family member of one of the first patients in the program decided to store her intravenous antibiotics in the freezer, rendering them unusable.

But before gearing up to enroll their first patient this past November, the Mount Sinai team arranged a complex system of backups. Patients have 24-hour physician and nurse coverage, and an arrangement with emergency medical service providers ensures that rather than reflexively transport all patients to the hospital if they are called, the providers will deliver all the care they can at home.

"I am very confident that we're going to be able to show that patients want to be home, that we can do this safely, and that we can do this with savings," said Dr. Linda DeCherrie, an associate professor of geriatrics and palliative care medicine at Mount Sinai and clinical director of the new program.

The trend toward taking hospital patients out of the hospital "will continue to evolve and get tested, but I think this will see its day," Dr. Leff said.

In the past two years, he has received calls from at least a hundred system administrators eager to learn more about how to hospitalize patients in their homes.

"My sense is that over time, hospitals will become places that you go only to get really specialized, really high-tech care," he said.

On a recent night, Mary Hull sat in her living room in Albuquerque, waiting for her doctor to check on her. Ms. Hull, 43, had been admitted to the hospital, at home, a few days before being treated with intravenous antibiotics for a skin infection on her leg and abdomen.

A portable X-ray machine had arrived. She was receiving daily lab draws. A nurse visited three times a day. She hadn't even needed to find someone to watch her cat.

"I'm hoping to be discharged soon," Ms. Hull said. "But I guess it doesn't matter much. I'm home."

[http://www.eurekalert.org/pub\\_releases/2015-04/tl-ttp042415.php](http://www.eurekalert.org/pub_releases/2015-04/tl-ttp042415.php)

## **The Lancet Psychiatry: Childhood bullying has worse effects on mental health in young adulthood than being maltreated**

*Being bullied in childhood has a greater negative impact on teenager's mental health than being maltreated*<sup>[1]</sup>, according to new research published in *The Lancet Psychiatry journal*.

The findings show that individuals who are bullied in childhood are around five times more likely to experience anxiety (odds ratio 4.9) and are nearly twice as likely to report more depression and self-harm at age 18 (odds ratio 1.7) than children who are maltreated.

The study, led by Professor Dieter Wolke from the University of Warwick, UK, is the first of its kind to directly compare the effects of maltreatment (by adults) and peer bullying in childhood on mental health outcomes (ie, anxiety, depression, self-harm, suicidal tendencies) in young adulthood.

The findings come from the UK Avon Longitudinal Study of Parents and Children (ALSPAC) and the Great Smoky Mountain Studies in the USA (GSMS). The current study includes 4026 children from ALSPAC whose parents provided information on maltreatment between the ages of 8 weeks and 8.6 years, and their child's reports of bullying when they were aged 8, 10, and 13; and 1420 children from GSMS who reported information on maltreatment and bullying between the ages of 9 and 16.

The harmful effects of bullying remained even when other factors that are known to increase the risk of child abuse and bullying, including family hardship and the mental health of mothers, were taken into account.

According to Professor Wolke, "Until now, governments have focused their efforts and resources on family maltreatment rather than bullying. Since 1 in 3 children worldwide report being bullied, and it is clear that bullied children have similar or worse mental health problems later in life to those who are maltreated, more needs to be done to address this imbalance. Moreover, it is vital that schools, health services, and other agencies work together to tackle bullying."

[2]

Writing in a linked Comment, David Finkelhor and Corinna Jenkins Tucker from the University of New Hampshire, Durham, USA discuss the fragmented response to child maltreatment and the need for protection lobbies to join forces, saying that, "This new study illustrates the growing consensus that children are entitled to grow up free from violence, denigration, and non-consented sexual activity at the hands of both adults and young peers. That growing consensus

might be responsible for the fact that, if the epidemiological data are to be trusted, in spite of the fragmentations of response systems, the toll of some of these various scourges seems to be on the decline in the past 20 years."

The research is being presented at the Pediatric Academic Societies (PAS) annual meeting in San Diego, USA. Professor Wolke will also give a talk covering this research at The Times Cheltenham Science Festival, UK, in June.

*This study was funded by the Wellcome Trust, Medical Research Council, Economic and Social Research Council, National Institute of Mental Health, the National Institute on Drug Abuse, NARSAD (Early Career Award), and the William T Grant Foundation.*

<http://www.psmag.com/business-economics/rise-of-the-taxibot>

## **The Many Impacts of Autonomous Vehicles**

*New research points to the potential effect of self-driving cars on things like city space and public transit.*

Gregory Ferenstein

As the multi-pronged debate over autonomous vehicles rages on, a new study finds that self-driving cars could have some major urban implications, aside from the elimination of virtually all cars: Namely, they might help to create more open space.

Led by Luis Martínez of the International Transport Forum, researchers at the Paris-based Organization for Economic Cooperation and Development estimate that a fully automated fleet of self-driving vehicles will reduce cars on the road by 90 percent. The researchers estimate that with so-called shared ride vehicles - also called taxibots - "[n]early the same mobility can be delivered with 10% of the cars TaxiBots combined with high-capacity public transport could remove 9 out of every 10 cars in a mid-sized European city."

To arrive at their conclusions, the researchers simulated a city's worth of driving from a real dataset of vehicle trips in Lisbon, Portugal. They then estimated how many of those rides could be grouped together, measuring the impact on driving time, city space, and vehicle usage.

The first thing that would go, according to the study, is public transit. "For small and medium-sized cities, it is conceivable that a shared fleet of self-driving vehicles could completely obviate the need for traditional public transport," the researchers write.

As private and public cars are eliminated, parking spaces will follow suit. And eliminating those parking spaces, the researchers write, would free up the equivalent of 210 football fields for public use.

Not included in their estimates is how this would impact housing prices and retail goods. Here, it's helpful to turn to prior research, which shows that parking

spaces not only reduce the land available for building, but increase the costs of developing. Parking also impacts commerce; one Ph.D. student made waves when he determined that parking space costs get passed on to retail customers, bumping up prices about one percent. Additionally, the environmental research group, the Sightline Institute, estimated that free parking in the city bumps rental costs about \$246/month.

Meanwhile, in the real world, Uber has not shied away from making this futuristic scenario a reality. CEO Travis Kalanick has been quite public about his desire to create a fleet of self-driving cars. The company is now even spending some of its revenue on a new facility to develop that technology. "The reason Uber could be expensive is because you're not just paying for the car - you're paying for the other dude in the car," Kalanick explained.

Despite the money being funneled at Uber's new endeavor, it could be another decade or so before any product actually hits the road. However, Google's self-driving car czar, Chris Urmson, thinks they may be standard in about five years. Whichever tech giant is proven right, this still seems like a future that has implications far beyond who's behind - or not behind - the wheel.

[http://www.eurekalert.org/pub\\_releases/2015-04/afps-fti042715.php](http://www.eurekalert.org/pub_releases/2015-04/afps-fti042715.php)

### **Framing time in days instead of years could spur action toward goals**

*People starting to plan for retirement or other big goals should pull out a calculator and multiply the years ahead by 365.*

Measuring time in days instead of months, or months instead of years, can make future events seem closer and thus more urgent, according to new research published in *Psychological Science*, a journal of the Association for Psychological Science.

When units of time were manipulated to bring important events closer to the forefront psychologically, people reported that they should start to plan and save significantly earlier, even when future events were described as being tens of thousands of days away.

"This is a new way to think about reaching goals that does not require willpower and is not about having character or caring," explains psychological scientist and lead researcher Daphna Oyserman of the University of Southern California.

Oyserman and co-author Neil Lewis Jr. of the University of Michigan devised a series of seven studies using diverse methods to investigate the relationship between metrics of time and taking action to reach a goal.

First, the researchers assessed how changing the units of time might affect estimates of when an event would occur once preparations were underway.

In two studies, the researchers recruited a total of 162 participants (either online or on a college campus) and asked them to read six scenarios - three with time metrics and three without time metrics. For the time-metric scenarios, participants imagined that they were shopping, studying, or carrying out other tasks in preparation for various events - a birthday party, presentation, wedding, exam - and were asked to report how long it would be until those events occurred.

The results showed that when participants were primed to consider the time in the smaller of two possible units, the event seemed closer. Specifically, events seemed an average of 29.7 days sooner when considered in days instead of months and an average of 8.7 months sooner when considered in months instead of years.

A subsequent series of studies evaluated whether the time metric would influence participants' plans to take action and, if so, whether it was because the shifting metrics helped people to connect their future to their present selves. Adults in the United States were recruited to participate in an online study, yielding more than 1100 participants across four studies. In each study, the vast majority of participants had some college education.

The researchers primed participants with either one of two time metrics for three randomly assigned scenarios. Participants filled in the blank for when they should start saving, cued by units of either days or years to match the scenario given. For example, they were asked to say when they would start saving for college that started in either 18 years or in 6,570 days, for retirement starting in 30 years or in 10,950 days, or for retirement starting in 40 years or in 14,600 days.

The results showed that the time metric affected plans for action: Participants planned to start saving four times sooner in the "days" condition compared with the "years" condition, even after age, income and education were accounted for.

The data suggest that the critical factor underlying the effect was whether participants felt connected with their future selves, which fostered congruence between the future and the present.

Thus, if the future "us" is more like the present "us" (only older), it may help us put aside present-day rewards (spending) in favor of future rewards (saving).

The researchers conclude that people may be able to get themselves working toward goals earlier by using smaller time metrics to feel closer to their future

selves. When that happens, says Oyserman, "investing in the future does not seem like a sacrifice."

This particular trick of time, she adds, "may be useful to anyone needing to save for retirement or their children's college, to start working on a term paper or dissertation, pretty much anyone with long-term goals or wanting to support someone who has such goals."

The team is continuing to study ways to make the future feel closer in order to influence other kinds of outcomes, including environmentally responsible behaviors.

*All materials have been made publicly available via Open Science Framework and can be accessed at <https://osf.io/8qkia/>. The complete Open Practices Disclosure for this article can be found at <http://pss.sagepub.com/content/by/supplemental-data>. This article has received the badge for Open Materials. More information about the Open Practices badges can be found at <https://osf.io/tvyxz/wiki/view/> and <http://pss.sagepub.com/content/25/1/3.full>.*

*For more information about this study, please contact: Daphna Oyserman at [daphna.oyserman@gmail.com](mailto:daphna.oyserman@gmail.com). The article abstract is available online: <http://pss.sagepub.com/content/early/2015/04/23/0956797615572231.abstract>*

*The APS journal Psychological Science is the highest ranked empirical journal in psychology. For a copy of the article "When Does the Future Begin?: Time Metrics Matter, Connecting Present and Future Selves" and access to other Psychological Science research findings, please contact Anna Mikulak at 202-293-9300 or [amikulak@psychologicalscience.org](mailto:amikulak@psychologicalscience.org).*

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## **Scientists discover salty aquifer, previously unknown microbial habitat under Antarctica**

### ***Discovery of a vast network of unfrozen salty groundwater that may support previously unknown microbial life deep under the coldest***

HANOVER, N.H. - Using an airborne imaging system for the first time in Antarctica, scientists have discovered a vast network of unfrozen salty groundwater that may support previously unknown microbial life deep under the coldest, driest desert on our planet. The findings shed new light on ancient climate change on Earth and provide strong evidence that a similar briny aquifer could support microscopic life on Mars.

The study appears in the journal Nature Communications. It is available through open access. A PDF of the study, photos and video also are available on request. The scientists used SkyTEM, an airborne electromagnetic sensor, to detect and map otherwise inaccessible subterranean features. The system uses an antennae suspended beneath a helicopter to create a magnetic field that reveals the subsurface to a depth of about 1,000 feet. Because a helicopter was used, large

areas of rugged terrain could be surveyed. The SkyTEM team was funded by the National Science Foundation and led by researchers from the University of Tennessee, Knoxville, and Dartmouth College, which oversees the NSF's SkyTEM project.

"These unfrozen materials appear to be relics of past surface ecosystems and our findings provide compelling evidence that they now provide deep subsurface habitats for microbial life despite extreme environmental conditions," says lead author Jill Mikucki, an assistant professor at UTK. "These new below-ground visualization technologies can also provide insight on glacial dynamics and how Antarctica responds to climate change."

Co-author Dartmouth Professor Ross Virginia is SkyTem's co-principal investigator and director of Dartmouth's Institute of Arctic Studies. "This project is studying the past and present climate to, in part, understand how climate change in the future will affect biodiversity and ecosystem processes," Virginia says. "This fantastic new view beneath the surface will help us sort out competing ideas about how the McMurdo Dry Valleys have changed with time and how this history influences what we see today."

The researchers found that the unfrozen brines form extensive, interconnected aquifers deep beneath glaciers and lakes and within permanently frozen soils. The brines extend from the coast to at least 7.5 miles inland in the McMurdo Dry Valleys, the largest ice-free region in Antarctica. The brines could be due to freezing and/or evaporation of a large ancient lake or much older ocean deposits. The findings show for the first time that the Dry Valleys' lakes are interconnected rather than isolated; connectivity between lakes and aquifers is important in sustaining ecosystems through drastic climate change, such as lake dry-down events. The findings also challenge the assumption that parts of the ice sheets below the pressure melting point are devoid of liquid water.

In addition to providing answers about the biological adaptations of previously unknown ecosystems that persist in the extreme cold and dark of the Antarctic winter, the new study could help to scientists to understand whether similar conditions might exist elsewhere in the solar system, specifically beneath the surface of Mars, which has many similarities to the Dry Valleys. Overall, the Dry Valleys ecosystem - cold, vegetation-free and home only to microscopic animal and plant life - resembles, during the Antarctic summer, conditions on the surface on Mars.

SkyTEM produced images of Taylor Valley along the Ross Sea that suggest briny sediments exist at subsurface temperatures down to perhaps -68°F, which is considered suitable for microbial life. One of the studied areas was lower

Taylor Glacier, where the data suggest ancient brine still exists beneath the glacier. That conclusion is supported by the presence of Blood Falls, an iron-rich brine that seeps out of the glacier and hosts an active microbial ecosystem.

Scientists' understanding of Antarctica's underground environment is changing dramatically as research reveals that subglacial lakes are widespread and that at least half of the areas covered by the ice sheet are akin to wetlands on other continents. But groundwater in the ice-free regions and along the coastal margins remains poorly understood.

*Co-authors on the paper include researchers from the University of Tennessee-Knoxville, Dartmouth College, University of California-Santa Cruz, University of Illinois at Chicago, Louisiana State University, University of Wisconsin, Aarhus University in Denmark and Sorbonne Universités, UPMC University in France.*

*Available to comment are UTK Assistant Professor Jill Mikucki at [jmikucki@utk.edu](mailto:jmikucki@utk.edu) and Dartmouth Professor Ross Virginia at [Ross.A.Virginia@dartmouth.edu](mailto:Ross.A.Virginia@dartmouth.edu).*

<http://bit.ly/1bpqL18>

### **Antarctica's Blood Falls are a sign of life below ground**

***Antarctica's Blood Falls are well named. There, the white tongue of the Taylor Glacier is stained crimson, as if the ice itself has been wounded.***

16:00 28 April 2015 by Colin Barras

The iron in the water – which oxidises to give the falls their vivid red colour – comes from the weathering of the bedrock beneath the ice, a process enhanced by microbial action.

"This unique feature is much more than a curiosity – it is a portal into the Antarctic subsurface, a hint at what lies beneath," says Jill Mikucki at the University of Tennessee in Knoxville.

We already know that there is liquid water – and life – in some of the lakes beneath Antarctica's ice. Blood Falls is a sign of something else: that the ground, too, holds liquid water, and that it may have extensive microbial activity. The falls are perhaps the only place where this groundwater comes to the surface. They flow just a few times a decade, possibly driven by changes in the weight of the ice above. Now a study by Mikucki and her colleagues has found this groundwater could be surprisingly extensive. They used an electromagnetic sensor attached to a helicopter to map electrical resistivity in the relatively ice-free Taylor Valley, to the east of Blood Falls.

Resistivity shoots up by several orders of magnitude when soil water freezes. So by looking for areas of the valley where resistivity readings were low, the team could map the extent of the sub-surface water. Their results revealed large bodies of liquid in ground 185 metres below the surface, forming aquifers that

stretch down the valley and apparently into the Ross Sea, a deep bay of the Southern Ocean.

"This may be the most different of all liquid water reservoirs on Earth since it is not directly replenished by infiltrating rainwater or seasonal snowmelt," says Slawek Tulaczyk at the University of California, Santa Cruz. "It certainly is the least understood component of hydrological system on our planet, because it is hidden beneath either permafrost or the ice sheet."

"It is becoming clear that water stored in the unfrozen ground beneath the Antarctic Ice Sheet comprises a very large groundwater reservoir," says Poul Christoffersen at the University of Cambridge, who wasn't involved in the research. "But we don't know much about this reservoir."

Tulaczyk says that there is no reason why similar groundwater bodies should not exist elsewhere beneath Antarctica.

The groundwater is cold, deep and twice as salty as seawater, but the water streaming out of Blood Falls, which teems with microbes, tells us that it is unlikely to be lifeless. "The fact that the [water] contains metabolically active micro-organisms that appear to be suited to life in a dark, cold brine supports the idea that life should persist throughout the subsurface," says Mikucki.

If so, those microbes could be fuelling life in the Southern Ocean. By breaking down iron-containing rocks they might be dumping as much as 170 million kilograms of iron into the ocean each year, according to the researchers' estimates, helping to explain why marine productivity is seasonally very high near to the coast.

However, we don't yet know whether this happens, cautions Mark Moore at the University of Southampton, UK – the iron might simply react and be lost where the groundwater meets the sea.

*Journal reference: Nature Communications, DOI: 10.1038/ncomms7831*

[http://www.eurekalert.org/pub\\_releases/2015-04/uoo-rpr042815.php](http://www.eurekalert.org/pub_releases/2015-04/uoo-rpr042815.php)

### **Research prompts rethink of enzyme evolution**

***New research by scientists at New Zealand's University of Otago suggests a need for a fundamental rethink of the evolutionary path of enzymes, the proteins vital to all life on Earth.***

Enzymes catalyse a vast array of biologically relevant chemical reactions even in the simplest living cells.

Biochemist Dr Wayne Patrick says that people tend to imagine evolution as a slow and steady march from barely functional life forms in the primordial soup, towards a modern-day pinnacle of near perfection.

"When it comes to enzyme evolution, this is also the textbook version of the events occurring at the molecular level; a smooth and steady trajectory, from barely functional primordial catalysts to the highly active and specific enzymes that we observe today. However, upon closer examination, the reality appears quite different."

In an article appearing in the UK Journal of the Royal Society Interface, Dr Patrick, his PhD student Matilda Newton and their collaborator Professor Vic Arcus (Waikato), summarise experimental data that challenges the prevailing thinking. "We discuss examples in which enzymes have evolved with lightning speed - over years, rather than eons - and provide evidence that many enzymes were better catalysts in the ancient past than they are today."

One example of extraordinarily rapid evolution is the emergence of enzymes that modern-day bacteria use to break down human-made antibiotics and pesticides, he says.

"Studying the complexities of enzyme evolution not only provides fundamental knowledge about how life emerged from the primordial soup, but also gives insights into designing proteins with biomedical and biotechnological applications."

Dr Patrick and colleagues at the Department of Biochemistry's Laboratory for Enzyme Engineering and Evolution are currently pursuing such applications. Their work includes collaborating with leading biotechnology company LanzaTech, which has a microbe that can grow by using harmful gases from industrial plants such as steel mills and oil refineries.

The Otago researchers are engineering enzymes to put into this microbe so it can produce useful raw materials that would otherwise have to be made from petroleum. "This is a great example of the ways in which really fundamental research - carried out with a grant from the Marsden Fund of New Zealand - can translate into applied outcomes in unexpected ways," Dr Patrick says.

[http://www.eurekalert.org/pub\\_releases/2015-04/aaft-pol042415.php](http://www.eurekalert.org/pub_releases/2015-04/aaft-pol042415.php)

### **Pneumonectomy or lobectomy?**

***Study shows that surgeon's experience may be a contributing factor for non-small cell lung cancer patients, presentation at 95th AATS Annual Meeting has important implications for long-term outcomes***

For patients in the early stage of non-small cell lung cancer, surgical resection yields optimal outcomes. Prior investigations have shown that different resection procedures have very different outcomes, with pneumonectomy associated with three-fold higher mortality than other resection types. While it is understandable that pathological and physiological factors influence a surgeon's choice of

surgery for a particular patient, the results presented in this study suggest that physician discomfort with the operative complexities of a procedure may lead to selection of a technique associated with less favorable outcomes.

Seattle, WA, April 28, 2015 - Researchers at McMaster University (Hamilton, ON) explored whether a surgeon's expertise influences procedural choice. The results of a new study of more than 8000 non-small cell lung cancer (NSCLC) patients undergoing surgical resection by 124 physicians showed that surgeons who perform more surgeries are less likely to perform high-risk pneumonectomies. Christian J. Finley, MD, MPH, will be presenting the results of this research at the 95th AATS Annual Meeting in Seattle, WA on April 28, 2015.

For patients in the early stages of NSCLC, lung surgery is associated with the best long-term survival. However, surgical and long-term outcomes vary depending on the choice of resection procedure. For example, removal of the whole lung (pneumonectomy) is associated with significantly higher morbidity and mortality rates compared to procedures in which smaller amounts of the lung are removed (lobectomies or sub-lobar resections), but can be less technically challenging than other procedures.

"If a surgeon with high surgical volumes is less likely to perform higher risk pneumonectomy procedures than one with lower volumes, this may translate to a significant reduction in adverse events. Surgeon volume should be considered an important component in how care is delivered in this population," explained Dr. Finley, who is affiliated with the Department of Surgery, St. Joseph's Healthcare Hamilton, McMaster University.

The researchers analyzed information on patients who underwent any pulmonary resection for primary NSCLC during 2004-2011 from an Ontario population-based database. They looked at patient demographics, co-morbidities, year of surgery, and institutional and surgical factors. All surgeons were trained as general thoracic surgeons. The volume of cases per surgeon per year was used as a surrogate for experience.

The resections were performed by 124 physicians at 45 institutions. Of the 8070 patients, 842 (10.4%) underwent pneumonectomy, 6212 (77.0%) underwent lobectomy, and 1002 (12.4%) wedge resection. The 90-day mortality was 12.6% for pneumonectomy, compared to 3.9% for lobectomy and 5.7% for wedge resection.

Odds ratios based on regression models for the three procedures revealed that physician volume was predictive of selecting pneumonectomy (OR 0.91, 95% CI 0.83 - 1.00, p=0.04). In fact, for each additional 10-unit increase in physician

volume, the risk of performing a pneumonectomy decreased by 9.1% ( $p=0.04$ ). As surgical volume increased, the number of wedge resections also decreased while the number of lobectomies increased. Other factors predictive of pneumonectomy were patient age, year of procedure, patient gender, and patient co-morbidities. No association was found between surgical volume and disease stage.

Variables, such as tumor biology and location, disease stage, and patient-specific factors such as age, pulmonary function and general health, are commonly taken into account when determining whether a patient with NSCLC will undergo surgery and what kind of surgery. "Only over the past decade have surgeon-specific factors such as experience, training, and volume been identified and examined as other important determinants of outcomes in lung cancer patients," noted Dr. Finley. "This study possibly provides more evidence that surgeries are more likely to be successful if they are performed by surgeons who have a high annual case volume."

[http://www.eurekalert.org/pub\\_releases/2015-04/uow-rsb042815.php](http://www.eurekalert.org/pub_releases/2015-04/uow-rsb042815.php)

### **Research shows brain differences in children with dyslexia and dysgraphia**

#### ***No scientific support for use of single category of learning disability to qualify students with written language challenges for special education services***

University of Washington research shows that using a single category of learning disability to qualify students with written language challenges for special education services is not scientifically supported. Some students only have writing disabilities, but some have both reading and writing disabilities.

The study, published online in *NeuroImage: Clinical*, is among the first to identify structural white matter and functional gray matter differences in the brain between children with dyslexia and dysgraphia, and between those children and typical language learners.

The researchers say the findings underscore the need to provide instruction tailored to each of these specific learning disabilities, though that is currently not mandated under federal or state law.

"This shows that there's a brain basis for these different disabilities," said co-author Virginia Berninger, a psychologist who heads the UW Learning Disabilities Center, funded by the National Institute of Child Health and Human Development. "So they require different diagnoses, and different instruction. We've got to start acknowledging this."

The study involved 40 children in grades 4 to 9, including 17 diagnosed with dyslexia - persisting difficulty with word reading and spelling - and 14 diagnosed with dysgraphia, persisting difficulty with handwriting, along with nine typical language learners. The children were asked to write the next letter in the alphabet following a letter they were shown, to write the missing letter in a word spelling, to rest without any task, and to plan a text about astronauts.

The children used a fiber-optic pen developed at the UW that allowed researchers to record their writing in real time while their active brain connections were measured with functional magnetic resonance imaging, or fMRI.

The three groups differed from each other in written language and cognitive tasks. The control group had more white matter connections, which facilitate functional connections in gray matter for language processing and cognitive thinking.

By contrast, children with dyslexia and dysgraphia showed less white matter connections and more functional connections to gray matter locations - in other words, their brains had to work harder to accomplish the same tasks.

"Their brains were less efficient for language processing," said lead author Todd Richards, a UW professor of radiology.

The results, Berninger said, show that the two specific learning disabilities are not the same because the white matter connections and patterns and number of gray matter functional connections were not the same in the children with dyslexia and dysgraphia - on either the writing or cognitive thinking tasks.

Federal law guarantees a free and appropriate public education to children with learning disabilities, but does not require that specific types of learning disabilities are diagnosed, or that schools provide evidence-based instruction for dyslexia or dysgraphia. Consequently, the two conditions are lumped together under a general category for learning disabilities, Berninger said, and many schools do not recognize them or offer specialized instruction for either one.

"There's just this umbrella category of learning disability," said Berninger. "That's like saying if you're sick you qualify to see a doctor, but without specifying what kind of illness you have, can the doctor prescribe appropriate treatment?"

"Many children struggle in school because their specific learning disabilities are not identified and they are not provided appropriate instruction," Berninger said. Recent UW research published in February in *Computers & Education* shows that computerized instruction has tremendous potential to help time-strapped



teachers in regular classrooms provide such instruction for children with dyslexia and dysgraphia, but only if they are correctly diagnosed.

"Dyslexia and dysgraphia are not the only kinds of learning disabilities. One in five students in the United States may have some kind of a specific learning disability," Berninger said. "We just can't afford to put 20 percent of children in special education classes. There just aren't the dollars."

Other co-authors are Thomas Grabowski, director of the UW Integrated Brain Imaging Center; Peter Boord, a UW senior fellow in radiology; UW research scientists Katie Askren, Paul Robinson and Kevin Yagle; UW undergraduate students Desiree Gulliford, Zoe Mestre and Olivia Welker; and William Nagy, a professor of education at Seattle Pacific University.

[http://www.eurekalert.org/pub\\_releases/2015-04/hcfa-wch042815.php](http://www.eurekalert.org/pub_releases/2015-04/hcfa-wch042815.php)

### **Water could have been abundant in the first billion years**

#### *How soon after the Big Bang could water have existed?*

Not right away, because water molecules contain oxygen and oxygen had to be formed in the first stars. Then that oxygen had to disperse and unite with hydrogen in significant amounts. New theoretical work finds that despite these complications, water vapor could have been just as abundant in pockets of space a billion years after the Big Bang as it is today.

"We looked at the chemistry within young molecular clouds containing a thousand times less oxygen than our Sun. To our surprise, we found we can get as much water vapor as we see in our own galaxy," says astrophysicist Avi Loeb of the Harvard-Smithsonian Center for Astrophysics (CfA).

The early universe lacked elements heavier than hydrogen and helium. The first generation of stars are believed to have been massive and short-lived. Those stars generated elements like oxygen, which then spread outward via stellar winds and supernova explosions. This resulted in "islands" of gas enriched in heavy elements. Even these islands, however, were much poorer in oxygen than gas within the Milky Way today.

The team examined the chemical reactions that could lead to the formation of water within the oxygen-poor environment of early molecular clouds. They found that at temperatures around 80 degrees Fahrenheit (300 Kelvin), abundant water could form in the gas phase despite the relative lack of raw materials.

"These temperatures are likely because the universe then was warmer than today and the gas was unable to cool effectively," explains lead author and PhD student Shmuel Bialy of Tel Aviv University.

"The glow of the cosmic microwave background was hotter, and gas densities were higher," adds Amiel Sternberg, a co-author from Tel Aviv University.

Although ultraviolet light from stars would break apart water molecules, after hundreds of millions of years an equilibrium could be reached between water formation and destruction. The team found that equilibrium to be similar to levels of water vapor seen in the local universe.

"You can build up significant quantities of water in the gas phase even without much enrichment in heavy elements," adds Bialy.

This current work calculates how much water could exist in the gas phase within molecular clouds that will form later generations of stars and planets. It doesn't address how much water would exist in ice form (which dominates within our galaxy) or what fraction of all the water might actually be incorporated into newly forming planetary systems. *This joint project was carried out as part of the Raymond and Beverly Sackler Tel Aviv University - Harvard Astronomy Program.*

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

### **Monkeys Can Hack Each Other's Grammar**

#### *Campbell's monkeys add suffixes to alarm calls to indicate specific threats, and Diana monkeys tune in for their own benefit*

By Rachel Nuwer

Language is one thing we do not share with other primates. While we humans have the ability to form words, our close relatives lack such finely tuned vocal control. Instead, like the majority of other animals, primates have evolved complex methods of conveying information, which range from grunts to body language to smell.



*A Diana monkey, perhaps tuning in to the distress calls of fellow primates. Michele Constantini/PhotoAlto/Corbis*

Now it seems that some species of monkey not only adjust the meanings of their calls using a simple grammatical trick, but other species know how to "translate" those calls to hack their neighbors' predator warning system.

The finding hints at a universal system of communication among some monkeys that includes some of the basic tools of human language.

Several years ago, researchers discovered that wild Campbell's monkeys can alter the meaning of their "krak," "hok" and "boom" calls by adding suffixes. Just as adding the suffix "-dom" to the word "king" creates "kingdom," the monkey's suffixes help indicate specific threats.

"Krak" means a leopard is present, for example, while "krak-oo" indicates unspecified danger, such as a falling branch or another troop of monkeys

encroaching on the caller's territory. "This is the first time that we can demonstrate that these sequences convey something about the environment or an event the monkey has witnessed," Klaus Zuberbuehler, a professor at the University of St Andrews, commented when the findings were announced.

Now, Zuberbuehler and several international colleagues have delved deeper into that discovery. As they report this week in Proceedings of the Royal Society B, they found that another species, the Diana monkey, has tapped into the suffixed system of communication. Diana monkeys not only recognize the Campbell's monkeys' danger calls, but they know which call corresponds to which type of danger.

To reveal these secret monkey ways, the researchers traveled to Ivory Coast and conducted field experiments in Tai National Park, the largest tropical forest in West Africa. They sought out 42 wild groups of Diana monkeys and then played one-minute clips of Campbell's monkeys making "krak" or "krak-oo" alarm calls. Some of the calls were natural, while others had been digitally edited, either taking off the "oo" suffix or adding it on.

From their previous work, the team knew that Campbell's monkeys respond more strongly to "krak" calls than to "krak-oo" calls. This makes sense, given that leopards are the monkeys' natural predator, while a falling branch or neighboring troop may pose less of a threat.

The Diana monkeys likewise responded to the "krak" calls more intensely. When they thought a leopard was nearby, they gave significantly more of their own alarm calls than when they heard a general "krak-oo" call.

They also remained on high alert for longer and made fewer social calls following the "krak" alarm. These findings held true for both natural and edited clips, meaning it's most likely the "oo" suffix - not some special intonation on the "krak" - that marks the distinction between a leopard and a general disturbance.

To the best of the researchers' knowledge, this is the first time that scientists have demonstrated experimentally that wild, untrained animals use suffixation to communicate with one another in the natural world.

The result suggests "that basic features of human speech ... can evolve independently in species that are not so closely related to humans," the authors write.

The researchers plan to investigate whether other animals have developed similarly refined species-to-species communication hacks, which they strongly suspect is the case.

[http://www.eurekalert.org/pub\\_releases/2015-04/acs-tad042915.php](http://www.eurekalert.org/pub_releases/2015-04/acs-tad042915.php)

### **Transforming all donated blood into a universal type** *An efficient way to transform A and B blood into a neutral type that can be given to any patient*

Every day, thousands of people need donated blood. But only blood without A- or B-type antigens, such as type O, can be given to all of those in need, and it's usually in short supply. Now scientists are making strides toward fixing the situation. In ACS' Journal of the American Chemical Society, they report an efficient way to transform A and B blood into a neutral type that can be given to any patient.

Stephen G. Withers and colleagues note that currently, blood transfusions require that the blood type of the donor match that of the recipient. If they aren't the same, a patient can suffer serious side effects, and could even die. The exception is the universal-donor blood type O, which can be given to anyone because it doesn't have the A or B antigens that could provoke an immune reaction. For years, scientists have been searching for a way to convert types A and B into type O. They found that some enzymes from bacteria can clip the sugars off red blood cells that give blood its "type." But the enzymes are not very efficient. Withers' team wanted to see if they could boost the enzymes' activity.

The researchers tweaked one of those enzymes and improved its ability to remove type-determining sugars by 170-fold, rendering it antigen-neutral and more likely to be accepted by patients regardless of their blood type. In addition to blood transfusions, the researchers say their advance could potentially allow organ and tissue transplants from donors that would otherwise be mismatched.

*The authors acknowledge support from the Canadian Blood Services, the Canadian Institutes of Health Research, Health Canada and the Michael Smith Foundation for Health Research.*

[http://www.eurekalert.org/pub\\_releases/2015-04/sfu-sfa042915.php](http://www.eurekalert.org/pub_releases/2015-04/sfu-sfa042915.php)

### **Study finds ancient clam beaches not so natural** *Northwest Coast Indigenous people were farmers who cultivated productive clam gardens to ensure abundant and sustainable clam harvests*

Casting a large interdisciplinary research net has helped Simon Fraser University archaeologist Dana Lepofsky and 10 collaborators dig deeper into their findings about ancient clam gardens in the Pacific Northwest to formulate new perspectives.

Lepofsky's research team has discovered that Northwest Coast Indigenous people didn't make their living just by gathering the natural ocean's bounty.

Rather, from Alaska to Washington, they were farmers who cultivated productive clam gardens to ensure abundant and sustainable clam harvests.

In its new paper published by American Antiquity, Lepofsky's team describes how it isolated novel ways to date the stone terraces that created clam beaches. These beaches are certainly more than 1,000 years old and likely many thousands of years older. The researchers identified many places where people built gardens on bedrock - creating ideal clam habitats where there were none before. This, the researchers concluded, clearly challenges the notion that First Nations were living in wild, untended environments.

"We think that many Indigenous peoples worldwide had some kind of sophisticated marine management, but the Pacific Northwest is likely one of the few places in the world where this can be documented," says Lepofsky. "This is because our foreshores are more intact than elsewhere and we can work closely with Indigenous knowledge holders."

The researchers, who worked with First Nations linguistic data, oral traditions and memories, geomorphological surveys, archaeological techniques and ecological experiments, belong to the Clam Garden Network. It's a coastal group interested in ancient clam management. "Understanding ancient marine management is relevant to many current issues," says Lepofsky.

Her team is comparing clam garden productivity to that of modern aquaculture and assessing whether the shell-rich beaches of clam gardens help buffer against increasing ocean acidification. The team will also build experimental clam gardens, applying many of the traditional cultivation techniques learned from First Nations collaborators as a means of increasing food production and food security today.

This latest study is on the heels of one done a year ago by Lepofsky and her collaborators. The original three-year study published in PLOS ONE found that these ancient gardens produced quadruple the number of butter clams and twice the number of littleneck clams as unmodified clam beaches. It was the first study to provide empirical evidence of the productivity of ancient Pacific Northwest clam gardens and their capacity to increase food production. The Tula Foundation, Parks Canada, the Social Sciences and Humanities Research Council and Wenner Gren, among other groups, are funding the team's studies.

#### **Key highlights of new study:**

*Northwest Coast Indigenous peoples from Alaska to Washington State managed clam beaches in a variety of ways. These included replanting of small clams and building rock terrace walls at the low-low tide line to create clam gardens.*

*Northwest Coast First Nations language terms indicate clam gardens were built in specific places by rolling the rocks for two purposes. One was to create rock-walled terraces ideal for clam growth. Another was to clear the beaches of unwanted rubble that would limit clam habitat.*

*The researchers developed novel ways to date the clam gardens and their preliminary excavations revealed that many date to more than 1,000 years ago.*

*Working on these clam gardens posed some logistical challenges since many are only visible for about 72 daylight hours per year.*

*Extensive air and ground surveys revealed that clam gardens can be found from Alaska to Washington State, but in some places, such as the Gulf Islands, recent rising sea level obscures the rock walls. In some areas, clam gardens made possible the dense ancient First Nations settlements that dot our coastline.*

[http://www.eurekalert.org/pub\\_releases/2015-04/icl-upp042815.php](http://www.eurekalert.org/pub_releases/2015-04/icl-upp042815.php)

#### **Urine profiles provide clues to how obesity causes disease**

*Scientists have identified chemical markers in urine associated with body mass, providing insights into how obesity causes disease.*

Being overweight or obese is associated with higher risk of heart disease, stroke, diabetes and cancer, but the mechanisms connecting body fat and disease are not well understood.

The new study, led by Imperial College London, shows that obesity has a 'metabolic signature' detectable in urine samples, pointing to processes that could be targeted to mitigate its effects on health. The findings are published in Science Translational Medicine.

Urine contains a variety of chemicals known as metabolites, from a vast range of biochemical processes in the body. Technologies that analyse the metabolic makeup of a sample can therefore offer huge amounts of information that reflects both a person's genetic makeup and lifestyle factors.

The Imperial researchers analysed urine samples from over 2,000 volunteers in the US and the UK. They found 29 different metabolic products whose levels correlated with the person's body mass index, and how they fit together in a complex network that links many different parts of the body.

Some of these metabolites are produced by bacteria that live in the gut, highlighting the potentially important role these organisms play in obesity. Altered patterns of energy-related metabolites produced in the muscles were also identified as being linked to obesity.

Professor Jeremy Nicholson, Director of the MRC-NIHR National Phenome Centre at Imperial College London and a senior author of the study said: "Obesity has become a huge problem all over the world, threatening to overwhelm health services and drive life expectancy gains into reverse. Tackling

it is an urgent priority and it requires us to have a much better understanding of how body fat and other aspects of biology are related. These findings provide possible starting points for new approaches to preventing and treating obesity and its associated diseases."

Professor Paul Elliott, Head of the Department of Epidemiology and Biostatistics at Imperial, said: "Our results point to patterns of metabolic markers in the urine associated with obesity. It may be possible to identify non-obese people who have such patterns in their urine profile. These people could be at risk of developing obesity and metabolic diseases, and might benefit from personalised preventative interventions."

*P. Elliott et al. 'Urinary Metabolic Signatures of Human Adiposity.' Science Translational Medicine, 2015. Sci. Transl. Med. 7, 285ra62 (2015).*

<http://bit.ly/1DMmJ2D>

### Laptops of the Future May Not Have Space Bars

*A recent Google patent points to a time when trackpads replace the trusty key*

By Erin Blakemore

It's been a mainstay of the keyboard for decades. But is Google about to press delete on the trusty space bar? According to Quartz's Mike Murphy, the answer could well be yes.

Murphy reports that Google recently obtained a patent for a "spacebar integrated with trackpad." The design does away with the space bar entirely, using a trackpad in its place. The idea is simple: instead of tapping a key to make a space, users would tap a trackpad to create a space while typing. When using the trackpad as an ordinary mouse, a tap would equal a mouse click.

Why ditch the space bar? Murphy and others speculate that the move to ditch the bar is the company's latest move in the light laptop wars. As ultralight laptops get ever thinner, Google and its competitors are looking for ways to reduce component weights and increase portability.

Murphy reports that the company's Chromebook, which relies heavily on cloud-based storage, could benefit from a space bar-free design.

The space bar wasn't always second nature for typists. This typewriting manual from the 1890s warns stenographers to practice using the space bar "so it becomes a fixed habit," calling for a whopping three spaces between sentences.

So when will the space bar disappear from keyboards altogether? Don't count on it any time soon, says Google.

The company tells Murphy that "prospective product announcements should not necessarily be inferred from our patents."

<http://nyti.ms/1QbQh2I>

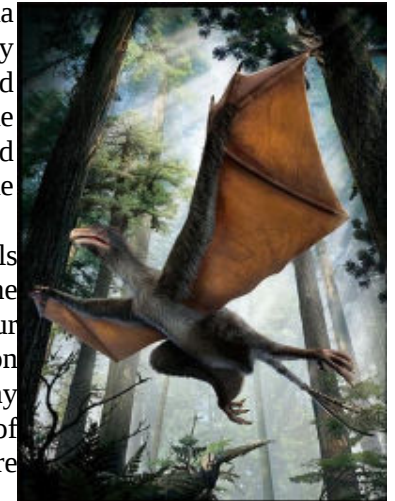
### Small Jurassic Dinosaur May Have Flown Without Feathers

*One of presumably many experiments in early flight that failed the test of time and was eventually abandoned*

By JOHN NOBLE WILFORD APRIL 29, 2015

Over the last two decades, scientists in China have paraded one surprising dinosaur discovery after another, enough to rewrite textbooks and even impress dinophile first graders. Some of the smaller newfound creatures, it turns out, had feathers, which shifted expert thinking to the dinosaurian origin of birds.

Now a discovery of 160-million-year-old fossils in northeastern China, reported Wednesday in the journal *Nature*, calls attention to a dinosaur species that may have tried to take to the air on featherless wings. It was one of presumably many experiments in early flight that failed the test of time and was eventually abandoned. Scientists are not even sure how it was supposed to work.



*Bat-like Yi qi is the flying dinosaur this forest deserves. Dinostar Co. Ltd*

After studying findings by a Chinese-led team of paleontologists, Kevin Padian, an American dinosaur authority, said he could only think that the attempted flight innovations "have just gone from the strange to the bizarre."

The fossil remains belonged to a previously unknown species of an obscure group of small dinosaurs, related to primitive birds such as the famous *Archaeopteryx*. It had feathers, but they seemed too insubstantial to be useful in flight. Then the scientists said they recognized the unusually long rodlike bone extending from each of the two wrists: curving structures possibly supporting an aerodynamic membrane.

Sure enough, patches of membrane tissue were detected along the bone supports. So, the scientists concluded, their specimen must have had wings somewhat like those of bats or flying squirrels. Nothing like this had been found before in dinosaurs.

The research team, led by Xu Xing of the Institute of Vertebrate Paleontology and Paleoanthropology in Beijing and Zheng Xianoting of Linyi University in Shandong Province, named the specimen *Yi qi* (pronounced "ee chee"), meaning "strange wing" in Mandarin.

“No other bird or dinosaur has a wing of the same kind,” Dr. Xu said in a statement issued by the Beijing institute. “We don’t know if Yi qi was flapping or gliding, or both, but it definitely evolved a wing that is unique in the context of the transition from dinosaurs to birds.”

Yi qi belongs to a group of carnivorous dinosaurs found so far only in Chinese fossil beds, and the few related species had no apparent flight capabilities. The group is called scansoriopterygids. In an aside, Dr. Xu said Yi qi may be the shortest name ever given to a dinosaur.

In a commentary in Nature, Dr. Padian, a paleontologist at the University of California, Berkeley, who was not part of the discovery team, said the examination of the fossils, found by a farmer in Hebei Province, had been meticulous “to be sure none of its elements had been faked or restored.”

He said the researchers wisely did not commit themselves to whether this animal could flap its wings or glide, or both, or neither. No evidence presented so far, he added, showed that Yi qi had the ability for powered flight. The preservation of the wing membrane was incomplete, and there is still uncertainty about the configuration of this wing support apparatus.

Also, most of the dinosaur’s body below the rib cage is missing. This leaves unanswered the important question of whether the animal’s tail created lift or drag in any kind of powered flight. Other discoveries will have to be made.

“We are left in a quandary,” Dr. Padian concluded. This dinosaur has a strange wing structure, he said, “that looks like it could have been used in flight, borne by an animal that otherwise shows no such tendencies.” And so far, he continued, “there is no other possible explanation for the function of this structure.”

Dr. Zheng, an author of the journal report, noted that Yi qi lived in the Jurassic Period, in the middle of the Age of Dinosaurs and early in the evolution of flight on the line to birds. “It reminds us,” he said, “that the early history of flight was full of innovation, not all of which survived.”

<http://nyti.ms/1JJYt>

## **Rubella Has Been Eliminated From the Americas, Health Officials Say**

***Rubella, a disease with terrible consequences for unborn children, has finally been eliminated from the Americas, a scientific panel set up by global health authorities announced Wednesday.***

By [DONALD G. McNEIL Jr.](#) APRIL 29, 2015

The disease, also known as [German measles](#), once infected millions of people in the Western Hemisphere. In a 1964-65 outbreak in the United States, 11,000

fetuses were miscarried, died in the womb or were aborted, and 20,000 babies were born with defects. “Although it has taken some 15 years, the fight against rubella has paid off,” said Dr. Carissa F. Etienne, director of the Pan American Health Organization, which made the [announcement](#) in conjunction with the United States [Centers for Disease Control and Prevention](#), Unicef and the United Nations Foundation. “Now, with rubella under our belt, we need to roll up our sleeves and finish the job of eliminating [measles](#), as well.”

The Americas region is the first World Health Organization region to eliminate rubella. The European region - which includes Eastern Europe, Russia and Central Asia - hopes to follow next. Some regions are still not close enough to set firm target dates, so there is no chance that the disease will be eliminated worldwide before 2020, said Dr. Susan E. Reef, team lead for rubella at the C.D.C.’s global [immunization](#) division, who joined in the announcement.

Around the world, about 120,000 children are born each year with severe [birth defects](#) attributed to rubella. Two other diseases were first eliminated in the Americas: [smallpox](#) in 1971, and [polio](#) in 1994. [Smallpox](#) is now eliminated worldwide. [Polio](#) is nearly gone, but has clung on stubbornly for decades; almost all remaining cases originate in Pakistan.

Although rubella usually produces only a relatively mild rash and [fever](#) in children and adults, it is devastating to fetuses in the first trimester; many are born deaf, blind from [cataracts](#) and with severe permanent brain damage.

The last endemic case in the Americas was confirmed in Argentina in 2009. It took six more years to declare the disease eliminated because its symptoms are harder to detect than, for example, polio, which causes [paralysis](#), or smallpox or [measles](#), which cause intense, easily diagnosable [rashes](#).

Public health authorities had to review 165 million records and do 1.3 million checks to see if any communities had rubella cases. All recent cases had to be genetically tested at the C.D.C. to confirm that they were caused by known imported strains of the virus, not by quietly circulating domestic ones.

As with measles, there is no cure for rubella, but the disease is prevented by a very effective vaccine. In the United States, the shot usually contains three vaccines and is known as M.M.R., for measles, [mumps](#) and rubella.

Measles cases in the United States [have surged recently](#) because some parents who believe, contrary to scientific evidence, that the [measles vaccine](#) causes [autism](#) do not let their children receive the shot.

Endemic measles was eliminated from the hemisphere in 2002, but imported cases can surge in pockets of unvaccinated children, as happened last year in an outbreak that began at Disneyland in California.

Rubella is less contagious than measles, and the vaccine for it is somewhat more effective, so the rare imported cases have not spread as rapidly. The rubella vaccine was first developed in 1969 by Dr. Maurice Hilleman, a prolific vaccine inventor.

In 1964-65, a strain of the virus from Europe caused an epidemic of an estimated 12.5 million cases across the country. Of the 20,000 infected infants born alive, 2,100 died soon after birth, 12,000 were deaf, 3,580 were blind, and 1,800 had permanent mental disabilities.

Perhaps the most famous American rubella victim was the actress Gene Tierney. In 1943, newly pregnant, she volunteered to be in a show at the Hollywood Canteen, a film-industry nightclub for American troops. She caught the disease that night, and her daughter Daria was born weighing only three pounds, deaf, with [cataracts](#) and with brain damage so severe that she never learned to speak. According to [Ms. Tierney's biography](#), two years later, at a tennis match, she met a fan, a former member of the Marine Corps Women's Reserve, who said she had slipped out of a rubella quarantine to go to the Canteen that night. "Everyone told me I shouldn't go, but I just had to," Ms. Tierney recalled the woman telling her. "You were always my favorite." Ms. Tierney wrote that she was too stunned to answer. Agatha Christie used that story as a plot device in "The Mirror Crack'd From Side to Side." In it, an actress murders the woman whose thoughtlessness destroyed her child.

The campaign to eliminate rubella in the Americas was formally declared by the Pan American Health Organization in 2003, but many countries had long suppressed their outbreaks through various campaigns. The island nations of the Caribbean began with a pilot program in the Bahamas in 1997, said Dr. Karen Lewis-Bell, a Jamaica-based Pan American Health Organization adviser.

By that time, most children were protected by [vaccinations](#) given in school, but many adult men were not because earlier campaigns had focused on vaccinating only girls starting at age 10 because they were in the highest-risk group.

Vaccination teams set up tables at shopping malls, construction sites, union halls, bus stops where workers returned from field labor, high schools, universities and any place where unvaccinated men could be reached.

By then, the campaign was conducted largely with M.M.R. shots, and men were told that the rubella component would protect their unborn children, and that the [mumps](#) component would prevent mumps complications, which in post-pubescent men include painful swollen testicles and sterility.

Not only did the men line up for the shot, "but they brought their wives and girlfriends to construction sites to get it," Dr. Lewis-Bell said.

As with all disease elimination campaigns, there were regular setbacks. For example, by 2006, confirmed cases in the Americas had dropped to fewer than 3,000. But in 2007, a surge in Argentina, Brazil and Chile pushed the hemisphere's count over 13,000. Most cases were in teenage boys and young men who had been skipped for vaccinations, as they previously had been in the Caribbean.

In the United States and Canada, routine childhood shots are relied on to prevent measles, rubella and mumps, but local mass vaccination campaigns are rolled out whenever there is a measles outbreak, and rubella protection increases as a consequence.

Since 2003, many other countries in the hemisphere have held an annual vaccination week in which as many as 60 million people may be vaccinated. [This year's](#) began on Saturday. Limited rubella outbreaks are still common in other wealthy countries. Japan [had 15,000 cases in 2013](#).

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### **Pancreatic cancer risk linked to weak sunlight**

#### ***UC San Diego epidemiologists suggest harm may come from low vitamin D***

Writing in the April 30 online issue of the Journal of Steroid Biochemistry and Molecular Biology, researchers at University of California San Diego School of Medicine report pancreatic cancer rates are highest in countries with the least amount of sunlight. Low sunlight levels were due to a combination of heavy cloud cover and high latitude.

"If you're living at a high latitude or in a place with a lot of heavy cloud cover, you can't make vitamin D most of the year, which results in a higher-than-normal risk of getting pancreatic cancer," said first author Cedric F. Garland, DrPH, adjunct professor in the Department of Family Medicine and Public Health and member of UC San Diego Moores Cancer Center.

"People who live in sunny countries near the equator have only one-sixth of the age-adjusted incidence rate of pancreatic cancer as those who live far from it. The importance of sunlight deficiency strongly suggests - but does not prove - that vitamin D deficiency may contribute to risk of pancreatic cancer."

Limited foods naturally contain vitamin D. Fatty fish, such as salmon and tuna, are good sources; beef liver, cheese and egg yolks provide small amounts. Vitamin D is often added as a fortifying nutrient to milk, cereals and juices, but experts say most people also require additional vitamin D to be produced by the body when skin is directly exposed to sunlight. Specifically, ultraviolet B radiation. Skin exposed to sunshine indoors through a window will not produce

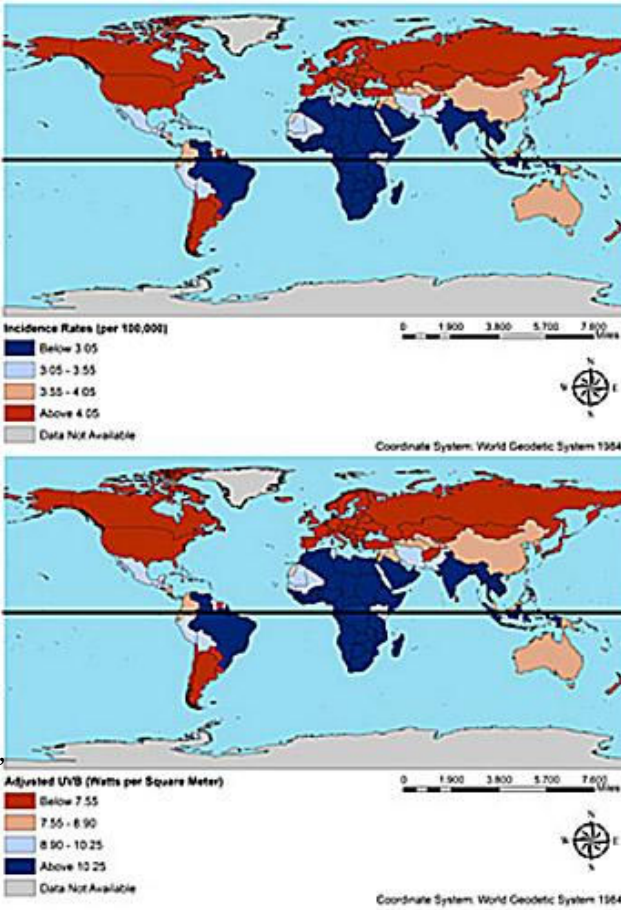
vitamin D. Cloudy skies, shade and dark-colored skin also reduce vitamin D production.

The UC San Diego team, led by Garland and Edward D. Gorham, PhD, associate professor, had previously shown that sufficient levels of a metabolite of vitamin D in the serum, known as 25-hydroxyvitamin D was associated with substantially lower risk of breast and colorectal cancer. The current paper is the first to implicate vitamin D deficiency with pancreatic cancer.

Researchers studied data from 107 countries, taking into account international differences and possible confounders, such as alcohol consumption, obesity and smoking. "While these other factors also contribute to risk, the strong inverse association with cloud-cover adjusted sunlight persisted even after they were accounted for," said Garland.

**Maps depict global incidence rates of pancreatic cancer (per 100,000) and ultraviolet B radiation (watts per square meter). UC San Diego School of Medicine**

UC San Diego researchers had previously identified an association of high latitude with a higher risk of pancreatic cancer. Garland said the new study advances that finding by showing that an estimate of solar ultraviolet B that has been adjusted for heavy cloud cover produces an even stronger prediction of risk of pancreatic cancer.



Pancreatic cancer is the 12th most common cancer in the world, according to World Cancer Research Fund International, with 338,000 new cases diagnosed annually. Incidence rates are highest in North America and Europe; lowest in Africa and Asia. It is the seventh most common cause of death from cancer. Coauthors of the study include Raphael E. Cuomo, Kenneth Zeng and Sharif B. Mohr, all at UC San Diego. Funding for this research came, in part, from UC San Diego Department of Family Medicine and Public Health.

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**Drug that can prevent the onset of diabetes is rarely used**  
**Metformin is inexpensive and effective for people with pre-diabetes, but few take it, UCLA research shows**

Few doctors are prescribing a low-cost drug that has been proven effective in preventing the onset of diabetes, according to a UCLA study. The study, published in the peer-reviewed journal *Annals of Internal Medicine*, found that only 3.7 percent of U.S. adults with pre-diabetes were prescribed metformin during a recent three-year period.

Metformin and lifestyle changes both can prevent the onset of diabetes, but people often struggle to adopt healthier habits, according to Dr. Tannaz Moin, the study's lead author and an assistant professor of medicine in the division of endocrinology at the David Geffen School of Medicine at UCLA and at VA Greater Los Angeles.

"Diabetes is prevalent, but pre-diabetes is even more prevalent and we have evidence-based therapies like metformin that are very safe and that work," Moin said. "Metformin is rarely being used for diabetes prevention among people at risk for developing it. This is something that patients and doctors need to be talking about and thinking about." It is estimated that about one-third of adults in the U.S. have pre-diabetes, which is marked by higher-than-normal blood sugar levels.

The American Diabetes Association in 2008 added metformin to its annual "Standards for Medical Care in Diabetes" guidelines for use in diabetes prevention for those at very high risk who are under age 60, are severely obese, or have a history of gestational diabetes.

Under the guidelines, metformin may also be considered for patients whose blood sugar is above normal but not yet in the diabetes range. The researchers examined data from 2010 to 2012 from UnitedHealthcare, the nation's largest

private insurer, for a national sample of 17,352 adults aged 19 to 58 with pre-diabetes. They also found:

***The prevalence of metformin prescriptions was 7.8 percent for severely obese patients.***

***Metformin prescriptions were nearly twice as high for women (4.8 percent) as for men (2.8 percent).***

***Among people with pre-diabetes, the prevalence of prescriptions for obese individuals was 6.6 percent, versus 3.5 percent for non-obese people.***

***Among people who had pre-diabetes and two other chronic diseases, 4.2 percent received prescriptions for metformin, versus 2.8 percent of people with pre-diabetes and no other chronic diseases.***

The reasons for the underuse of metformin are not clear, the researchers write, but they could include a lack of knowledge of the 2002 Diabetes Prevention Program Study, which showed that both lifestyle changes and metformin use can prevent or delay progression to diabetes among those with pre-diabetes, the fact that the drug does not have FDA approval for pre-diabetes and reluctance by patients and doctors to "medicalize" pre-diabetes.

"Identifying more effective ways to help people avoid diabetes is essential to individuals' lives and to society as a whole, which is why it was important to us to support this research," said Dr. Sam Ho, a co-author of the study and chief medical officer of Minnetonka, Minnesota-based UnitedHealthcare.

Potential limitations to the study included a lack of access to data on participation in lifestyle programs; possible misclassification of pre-diabetes and metformin use; the fact that the analysis focused on adults with commercial insurance, which could make the findings inapplicable to uninsured or older adults; and the researchers' inability to independently verify patients' eligibility to receive metformin under the American Diabetes Association guidelines.

*The study's co-authors are Jinnan Li, O. Kenrik Duru, Susan Ettner, Norman Turk and Carol Mangione of UCLA; and Abigail Keckhafer of UnitedHealthcare.*

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### **New origin theory for cells that gave rise to vertebrates**

***Discovery could be useful*** in regenerative medicine and understanding human diseases

The vivid pigmentation of zebras, the massive jaws of sharks, the fight or flight instinct and the diverse beaks of Darwin's finches. These and other remarkable features of the world's vertebrates stem from a small group of powerful cells, called neural crest cells, but little is known about their origin.

Now Northwestern University scientists propose a new model for how neural crest cells, and thus vertebrates, arose more than 500 million years ago.

The researchers report that, unlike other early embryonic cells that have their potential progressively restricted as an embryo develops, neural crest cells retain the molecular underpinnings that control pluripotency - the ability to give rise to all the cell types that make up the body.

"This study provides deep new insights into the evolutionary origins of humans and other vertebrates," said evolutionary molecular biologist Carole LaBonne, who led the research. "It also provides critical new information about the molecular circuitry of stem cells, including cancer stem cells."

Regenerative medicine scientists now have an updated framework for future studies aiming to harness the power of stem cells to treat human diseases and congenital defects, LaBonne said.

The study also turns conventional thought on its head. Previously, scientists thought neural crest cells had to evolve to gain their incredible properties, but the Northwestern work shows the power was there all along.

Researchers now can focus on the molecular mechanisms by which neural crest cells escaped having their potential restricted.

In a study using embryos from the frog *Xenopus*, a powerful model system used in studies of development, LaBonne and her team found that neural crest cells and the early pluripotent cells present in blastula embryos have surprising similarities, including shared expression of a key set of genes which work together to endow the cells with their unique properties.

The findings will be published today (April 30) as a Science Express article by the journal Science. The article also will be the cover story of the journal's June 19 issue.

"Neural crest cells never had their potential restricted at all," LaBonne said. "We believe a small population of early stem cells were set aside, so that when the time came, their immense developmental potential could be unleashed to create new features characteristic of vertebrates."

LaBonne is a professor of molecular biosciences in the Weinberg College of Arts and Sciences. She holds the Arthur Andersen Teaching and Research Chair and is co-leader of the Tumor Invasion and Metastasis program of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Acquisition of neural crest cells more than 500 million years ago led vertebrates to evolve and leave behind less complex life forms (simple aquatic filter feeders, much like today's sea squirts and lancelets).

With these cells, animals developed important new features such as a skull to house a complex brain, jaws for predation, a complex peripheral nervous system and many other cell types essential to the vertebrate body.



In their study, LaBonne and her research team studied the genetic toolkit that early embryonic cells use to promote pluripotency or "stemness" and compared it to the one used by neural crest cells.

They found that the toolkit used by neural crest cells also is used by pluripotent blastula cells, and they showed that it is essential for pluripotency in both cell types. The proteins that derive from this toolkit work together to enable a dizzying array of tissues to arise from a population of single cells.

One of these proteins, called Snail1, has been the focus of previous studies by LaBonne's lab. They and others had shown that Snail1 plays key roles in controlling not only the immense developmental potential of neural crest cells but also their capacity for migratory and invasive behavior.

Cancer cells co-opt the function of Snail1 and other neural crest regulatory proteins to allow the formation of cancer stem cells and mediate the process of metastasis, whereby cancer cells disperse throughout the body to form new tumors, LaBonne said.

Researchers therefore gain insights into Snail1's role in cancer by studying its function in the developing embryo.

In early blastula embryos, pluripotent cells were thought to exist only transiently; as an embryo develops, cells become restricted into categories of cells called germ layers and then into specialized cell types.

The Northwestern study suggests that not all cells get restricted at those early stages. Instead, neural crest cells may have evolved as a consequence of a subset of blastula cells retaining activity of the regulatory network underlying pluripotency.

The study underscores just how much remains to be discovered about embryonic development.

The human body has more than 10 trillion cells elaborately organized into tissues and organs that are intricate and highly complex, yet it all is self-assembled from a single cell, the fertilized egg.

"It's a fascinating process," LaBonne said. "One of the great frontiers in biology is understanding both how complexity is generated and how it evolves to create what Charles Darwin memorably called 'endless forms most beautiful.'"

*The title of the paper is "Shared Regulatory Programs Suggest Retention of Blastula-Stage Potential in Neural Crest Cells."*

*In addition to LaBonne, other authors of the paper are Elsy Buitrago-Delgado, Kara Nordin, Anjali Rao and Lauren Geary, all Ph.D. students in Northwestern's Interdisciplinary Biological Sciences Program, directed by LaBonne.*

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## **Did dinosaur-killing asteroid trigger largest lava flows on Earth?** ***New theory links impact to re-ignition of Deccan Traps lava flows 66 million years ago***

The asteroid that slammed into the ocean off Mexico 66 million years ago and killed off the dinosaurs probably rang the Earth like a bell, triggering volcanic eruptions around the globe that may have contributed to the devastation, according to a team of University of California, Berkeley, geophysicists.

Specifically, the researchers argue that the impact likely triggered most of the immense eruptions of lava in India known as the Deccan Traps, explaining the "uncomfortably close" coincidence between the Deccan Traps eruptions and the impact, which has always cast doubt on the theory that the asteroid was the sole cause of the end-Cretaceous mass extinction.

"If you try to explain why the largest impact we know of in the last billion years happened within 100,000 years of these massive lava flows at Deccan ... the chances of that occurring at random are minuscule," said team leader Mark Richards, UC Berkeley professor of earth and planetary science. "It's not a very credible coincidence."

Richards and his colleagues marshal evidence for their theory that the impact reignited the Deccan flood lavas in a paper to be published in *The Geological Society of America Bulletin*, available online today (April 30) in advance of publication.

While the Deccan lava flows, which started before the impact but erupted for several hundred thousand years after re-ignition, probably spewed immense amounts of carbon dioxide and other noxious, climate-modifying gases into the atmosphere, it's still unclear if this contributed to the demise of most of life on Earth at the end of the Age of Dinosaurs, Richards said.

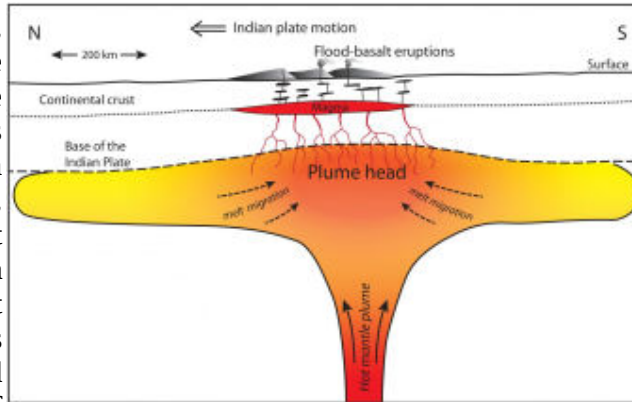
"This connection between the impact and the Deccan lava flows is a great story and might even be true, but it doesn't yet take us closer to understanding what actually killed the dinosaurs and the 'forams,'" he said, referring to tiny sea creatures called foraminifera, many of which disappeared from the fossil record virtually overnight at the boundary between the Cretaceous and Tertiary periods, called the KT boundary. The disappearance of the landscape-dominating dinosaurs is widely credited with ushering in the age of mammals, eventually including humans.

He stresses that his proposal differs from an earlier hypothesis that the energy of the impact was focused around Earth to a spot directly opposite, or antipodal, to the impact, triggering the eruption of the Deccan Traps. The "antipodal

focusing" theory died when the impact crater, called Chicxulub, was found off the Yucatán coast of Mexico, which is about 5,000 kilometers from the antipode of the Deccan traps.

### Flood basalts

Richards proposed in 1989 that plumes of hot rock, called "plume heads," rise through Earth's mantle every 20-30 million years and generate huge lava flows, called flood basalts, like the Deccan Traps. It struck him as more than coincidence that the last four of the six known mass extinctions of life occurred at the same time as one of these massive eruptions.



**Illustration of a hot mantle plume "head" pancaked beneath the Indian Plate. The theory by Richards and his colleagues suggests that existing magma within this plume head was mobilized by strong seismic shaking from the Chicxulub asteroid impact, resulting in the largest of the Deccan Traps flood basalt eruptions.** Mark Richards et al, UC Berkeley

"Paul Renne's group at Berkeley showed years ago that the Central Atlantic Magmatic Province is associated with the mass extinction at the Triassic/Jurassic boundary 200 million years ago, and the Siberian Traps are associated with the end Permian extinction 250 million years ago, and now we also know that a big volcanic eruption in China called the Emeishan Traps is associated with the end-Guadalupian extinction 260 million years ago," Richards said. "Then you have the Deccan eruptions - including the largest mapped lava flows on Earth - occurring 66 million years ago coincident with the KT mass extinction. So what really happened at the KT boundary?"

Richards teamed up with experts in many areas to try to discover faults with his radical idea that the impact triggered the Deccan eruptions, but instead came up with supporting evidence. Renne, a professor in residence in the UC Berkeley Department of Earth and Planetary Science and director of the Berkeley Geochronology Center, re-dated the asteroid impact and mass extinction two years ago and found them essentially simultaneous, but also within

approximately 100,000 years of the largest Deccan eruptions, referred to as the Wai subgroup flows, which produced about 70 percent of the lavas that now stretch across the Indian subcontinent from Mumbai to Kolkata.

Michael Manga, a professor in the same department, has shown over the past decade that large earthquakes - equivalent to Japan's 9.0 Tohoku quake in 2011 - can trigger nearby volcanic eruptions. Richards calculates that the asteroid that created the Chicxulub crater might have generated the equivalent of a magnitude 9 or larger earthquake everywhere on Earth, sufficient to ignite the Deccan flood basalts and perhaps eruptions many places around the globe, including at mid-ocean ridges.

"It's inconceivable that the impact could have melted a whole lot of rock away from the impact site itself, but if you had a system that already had magma and you gave it a little extra kick, it could produce a big eruption," Manga said.

Similarly, Deccan lava from before the impact is chemically different from that after the impact, indicating a faster rise to the surface after the impact, while the pattern of dikes from which the supercharged lava flowed - "like cracks in a soufflé," Renne said - are more randomly oriented post-impact.

"There is a profound break in the style of eruptions and the volume and composition of the eruptions," said Renne. "The whole question is, 'Is that discontinuity synchronous with the impact?'"

### Reawakened volcanism

Richards, Renne and graduate student Courtney Sprain, along with Deccan volcanology experts Steven Self and Loÿc Vanderkluysen, visited India in April 2014 to obtain lava samples for dating, and noticed that there are pronounced weathering surfaces, or terraces, marking the onset of the huge Wai subgroup flows. Geological evidence suggests that these terraces may signal a period of quiescence in Deccan volcanism prior to the Chicxulub impact. Apparently never before noticed, these terraces are part of the western Ghats, a mountain chain named after the Hindu word for steps.

"This was an existing massive volcanic system that had been there probably several million years, and the impact gave this thing a shake and it mobilized a huge amount of magma over a short amount of time," Richards said. "The beauty of this theory is that it is very testable, because it predicts that you should have the impact and the beginning of the extinction, and within 100,000 years or so you should have these massive eruptions coming out, which is about how long it might take for the magma to reach the surface."

Since the team's paper was accepted for publication, a group from Princeton University published new radioisotopic dates for the Deccan Traps lavas that are

consistent with these predictions. Renne and Sprain at UC Berkeley also have preliminary, unpublished dates for the Deccan lavas that could help solidify Richards' theory, Renne said.

*Co-authors of the paper, in addition to Richards, Renne, Manga and Sprain, are Walter Alvarez, a UC Berkeley professor emeritus of earth and planetary science and the co-ordinator of the dinosaur-killing asteroid theory; Stephen Self, an adjunct professor in the same department at UC Berkeley; Leif Karlstrom of the University of Oregon; Jan Smit of Vrije Universiteit in Amsterdam, the Netherlands; Loïc Vanderkluyzen of Drexel University in Philadelphia, Pennsylvania; and Sally A. Gibson of the University of Cambridge in the United Kingdom.*

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## **Even casual walking for an extra 2 minutes each hour may help prolong life**

***Replacing sedentary activity with light activity linked with improved survival***

### **Highlight**

***In an observational study that followed participants for an average of just under 3 years, a "trade-off" of sedentary activity with low-intensity activity was not beneficial, but a trade-off of 2 minutes/hour of sedentary activity with an equal amount of light-intensity activity was associated with 33% lower risk of dying in the general population and a 41% lower risk of dying in the individuals with chronic kidney disease.***

***Previous research suggests that sitting for long periods of time may increase the risk of disease and early death.***

Washington, DC - Casual walking for as little as an extra 2 minutes per hour throughout the day, rather than sitting, may have a significant benefit on longevity. The findings come from a study appearing in an upcoming issue of the Clinical Journal of the American Society of Nephrology (CJASN).

The Physical Activity Guidelines for Americans recommend at least 150 minutes of moderate intensity activity per week or 75 minutes of vigorous-intensity activity per week. Assuming 16 awake hours per day, achieving the currently recommended duration of moderate/vigorous activities would account for only 2% of the total awake time. This leaves considerable time for low-intensity activities - such as standing - or light-intensity activities - such as casual walking - that might provide additional benefits.

Srinivasan Beddhu, MD (University of Utah) and his colleagues analyzed information on 3626 participants in the 2003-2004 National Health & Nutrition Examination Survey to examine the relative importance of low- and light-intensity activities in the general population and in patients with chronic kidney disease (CKD). The average follow-up of participants was just under 3 years.

"We hoped to understand whether lower duration of sedentary activities with higher duration of low- or light-intensity activities is associated with survival benefit," explained Dr. Beddhu.

Using sophisticated statistical techniques, the researchers found that a "trade-off" of sedentary activity with low-intensity activity was not beneficial, but a trade-off of 2 minutes/hour of sedentary activity with an equal amount of light-intensity activity was associated with 33% lower risk of death in the general population and a 41% lower risk of death in the CKD population. The investigators noted that participants spent more than half the time in sedentary activities. Those with CKD were even more sedentary and spent more than two-thirds of the time in sedentary activities.

"Sitting for a long time strongly increases the risk of death. Our findings suggest that replacing sedentary duration with an increase in light activity might confer a survival benefit," said Dr. Beddhu.

*Study co-authors include Guo Wei, MS, Robin Marcus, PT, PhD, Michel Chonchol, MD, and Tom Greene, PhD.*

*Disclosures: The authors reported no financial disclosures.*

*The article, entitled "Light Intensity Physical Activities and Mortality in the US General Population and CKD Subpopulation," will appear online at <http://cjasn.asnjournals.org/> on April 30, 2015.*

[http://www.eurekalert.org/pub\\_releases/2015-04/si-sdk042415.php](http://www.eurekalert.org/pub_releases/2015-04/si-sdk042415.php)

## **Scientists discover key driver of human aging**

***Salk Institute findings on premature aging syndrome could lead to slowing or reversing the aging process***

LA JOLLA - A study tying the aging process to the deterioration of tightly packaged bundles of cellular DNA could lead to methods of preventing and treating age-related diseases such as cancer, diabetes and Alzheimer's disease, as detailed April 30, 2015, in Science.

In the study, scientists at the Salk Institute and the Chinese Academy of Science found that the genetic mutations underlying Werner syndrome, a disorder that leads to premature aging and death, resulted in the deterioration of bundles of DNA known as heterochromatin.

The discovery, made possible through a combination of cutting-edge stem cell and gene-editing technologies, could lead to ways of countering age-related physiological declines by preventing or reversing damage to heterochromatin.

"Our findings show that the gene mutation that causes Werner syndrome results in the disorganization of heterochromatin, and that this disruption of normal DNA packaging is a key driver of aging," says Juan Carlos Izpisua Belmonte, a

senior author on the paper. "This has implications beyond Werner syndrome, as it identifies a central mechanism of aging - heterochromatin disorganization - which has been shown to be reversible."

Werner syndrome is a genetic disorder that causes people to age more rapidly than normal. It affects around one in every 200,000 people in the United States. People with the disorder suffer age-related diseases early in life, including cataracts, type 2 diabetes, hardening of the arteries, osteoporosis and cancer, and most die in their late 40s or early 50s.

The disease is caused by a mutation to the Werner syndrome RecQ helicase-like gene, known as the WRN gene for short, which generates the WRN protein. Previous studies showed that the normal form of the protein is an enzyme that maintains the structure and integrity of a person's DNA. When the protein is mutated in Werner syndrome it disrupts the replication and repair of DNA and the expression of genes, which was thought to cause premature aging. However, it was unclear exactly how the mutated WRN protein disrupted these critical cellular processes.

In their study, the Salk scientists sought to determine precisely how the mutated WRN protein causes so much cellular mayhem. To do this, they created a cellular model of Werner syndrome by using a cutting-edge gene-editing technology to delete WRN gene in human stem cells. This stem cell model of the disease gave the scientists the unprecedented ability to study rapidly aging cells in the laboratory. The resulting cells mimicked the genetic mutation seen in actual Werner syndrome patients, so the cells began to age more rapidly than normal. On closer examination, the scientists found that the deletion of the WRN gene also led to disruptions to the structure of heterochromatin, the tightly packed DNA found in a cell's nucleus.

This bundling of DNA acts as a switchboard for controlling genes' activity and directs a cell's complex molecular machinery. On the outside of the heterochromatin bundles are chemical markers, known as epigenetic tags, which control the structure of the heterochromatin. For instance, alterations to these chemical switches can change the architecture of the heterochromatin, causing genes to be expressed or silenced.

The Salk researchers discovered that deletion of the WRN gene leads to heterochromatin disorganization, pointing to an important role for the WRN protein in maintaining heterochromatin. And, indeed, in further experiments, they showed that the protein interacts directly with molecular structures known to stabilize heterochromatin - revealing a kind of smoking gun that, for the first time, directly links mutated WRN protein to heterochromatin destabilization.

"Our study connects the dots between Werner syndrome and heterochromatin disorganization, outlining a molecular mechanism by which a genetic mutation leads to a general disruption of cellular processes by disrupting epigenetic regulation," says Izpisua Belmonte. "More broadly, it suggests that accumulated alterations in the structure of heterochromatin may be a major underlying cause of cellular aging. This begs the question of whether we can reverse these alterations - like remodeling an old house or car - to prevent, or even reverse, age-related declines and diseases."

Izpisua Belmonte added that more extensive studies will be needed to fully understand the role of heterochromatin disorganization in aging, including how it interacts with other cellular processes implicated in aging, such as shortening of the end of chromosomes, known as telomeres. In addition, the Izpisua Belmonte team is developing epigenetic editing technologies to reverse epigenetic alterations with a role in human aging and disease.

*Other authors on the paper include: Weiqi Zhang, Jingyi Li, Keiichiro Suzuki, Jing Qu, Ping Wang, Junzhi Zhou, Xiaomeng Liu, Ruotong Ren, Xiuling Xu, Alejandro Ocampo, Tingting Yuan, Jiping Yang, Ying Li, Liang Shi, Dee Guan, Huize Pan, Shunlei Duan, Zhichao Ding, Mo Li, Fei Yi, Ruijun Bai, Yayu Wang, Chang Chen, Fuquan Yang, Xiaoyu Li, Zimei Wang, Emi Aizawa, April Goebel, Rupa Devi Soligalla, Pradeep Reddy, Concepcion Rodriguez Esteban, Fuchou Tang and Guang-Hui Liu.*

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## **Viruses responsible for 50 percent of gastroenteritis cases can spread by air**

### ***Noroviruses can spread by air up to several meters from an infected person***

Quebec City - Noroviruses, a group of viruses responsible for over 50% of global gastroenteritis cases, can spread by air up to several meters from an infected person according to a new study by Université Laval researchers. The discovery, details of which are presented in the latest issue of *Clinical Infectious Diseases*, suggests that measures applied in hospitals during gastroenteritis outbreaks may be insufficient to effectively contain this kind of infection.

The team led by Caroline Duchaine, professor at Université Laval's Faculty of Science and Engineering and researcher at the Québec Heart and Lung Institute (IUCPQ) Research Centre, conducted the study at 8 hospitals and long-term care facilities affected by gastroenteritis outbreaks. Researchers gathered air samples at a distance of 1 meter from patients, at the doors to their rooms, and at nursing stations.

Noroviruses were found in the air at six of the eight facilities studied. The viruses were detected in 54% of the rooms housing patients with gastroenteritis, 38% of the hallways leading to their rooms, and 50% of nursing stations. Virus concentrations ranged from 13 to 2350 particles per cubic meter of air. A dose of 20 norovirus particles is usually enough to cause gastroenteritis.

According to Professor Duchaine, this previously unknown mode of norovirus propagation could explain why gastroenteritis outbreaks are so hard to contain: "The measures applied in hospital settings are only designed to limit direct contact with infected patients. In light of our results, these rules need to be reviewed to take into account the possibility of airborne transmission of noroviruses. Use of mobile air filtration units or the wearing of respiratory protection around patients with gastroenteritis are measures worth testing."

*In addition to Caroline Duchaine, the study's coauthors are: Laetitia Bonifait, Rémi Charlebois, Nathalie Turgeon, and Marc Veillette (Université Laval and IUCPQ); Allison Vimont and Julie Jean (Université Laval's Institute of Nutrition and Functional Foods); Yves Longtin (Jewish General Hospital and McGill University).*

<http://bit.ly/1E8080Q>

### **Birds Are in a Tailspin Four Years After Fukushima**

*Like the proverbial canary in a coalmine, avian abundances may paint a grim picture of the effects of nuclear disasters on wildlife*

By Ben Mirin

The first time Tim Mousseau went to count birds in Fukushima, Japan, radiation levels in the regions he visited were as high as 1,000 times the normal background. It was July 2011, four months after the Tohoku earthquake and subsequent partial meltdown at the Fukushima-Daiichi nuclear power plant, and the nation was still recovering from massive infrastructure damage. Still, when Mousseau and his research partner rented a car and drove up from Tokyo, they encountered little resistance on the road.

"I knew we had to get there and capture as best we could the early effects [of radioactive contamination] that nobody had really looked for," he remembers thinking after seeing news of the Fukushima disaster. "Ultimately we realized that our best possible approach for that first year was simply to start doing bird counts."

Now, after four years surveying bird populations in 400 sites around Fukushima-Daiichi, Mousseau and his team have assembled a grim portrait of the disaster's impact on local wildlife, using bird populations as a model system. Even though radioactivity has dropped throughout the region, their data show that bird species

and abundances are in sharp decline, and the situation is getting worse every year.

"At first only a few species showed significant signs of the radiation's effects," Mousseau says. "Now if you go down and around the bend maybe five or ten kilometers [from a safe zone] to where it's much, much hotter, it's dead silent. You'll see one or two birds if you're lucky."

Mousseau's team conducted almost 2,400 bird counts in total and gathered data on 57 species, each of which showed specific sensitivity to background radiation. Thirty of the species showed population declines during the study period, the team report in the March issue of the *Journal of Ornithology*. Among these, resident birds such as the carrion crow and the Eurasian tree sparrow demonstrated higher susceptibility than migratory species, which didn't arrive in the region until a few weeks after the partial meltdown in early March.

Nuclear accidents are rare in human history, so we have very little data about such radiation's direct effects on wildlife. Mousseau has spent the past 15 years drawing comparisons between nuclear events to help build up our knowledge base and fill in the gaps. For instance, while there are no official published records of the Chernobyl disaster's early impact on wildlife, plenty of work has been done in recent years to assess Chernobyl's ecosystem post-accident, from local birds to forest fungi.

When Mousseau returned to Fukushima in 2012, he began capturing birds in irradiated zones that had patches of bleach-white feathers. It was a familiar sign: "The first time I went to Chernobyl in 2000 to collect birds, 20 percent of the birds [we captured] at one particularly contaminated farm had little patches of white feathers here and there - some large, some small, sometimes in a pattern and other times just irregular."

His team thinks these white patches are the result of radiation-induced oxidative stress, which depletes birds' reserves of the antioxidants that control coloration in their feathers and other body parts. In Chernobyl, the patches have a high coincidence with other known symptoms of radiation exposure, including cataracts, tumors, asymmetries, developmental abnormalities, reduced fertility and smaller brain size. By 2013, the birds Mousseau was counting in Fukushima had white patches big enough to be seen through binoculars.

Presented together, Mousseau thinks such data sets on Chernobyl and Fukushima could offer significant evidence for radiation's prolonged, cumulative effects on wildlife at different stages after a nuclear disaster. But other experts have a completely different take on the available information.

"I'm not convinced about the oxidative stress hypothesis, full stop," says Jim Smith, editor and lead author of *Chernobyl: Catastrophe and Consequences* and an expert on pollution in terrestrial and aquatic ecosystems. "The radiation levels in both Fukushima and Chernobyl are currently low-dose, and the antioxidant capacity of a cell is way, way bigger than the oxidizing capacity of the radiation at those levels," he says. This would mean the white feather patches - and perhaps the overall bird declines - are being caused by something other than radiation.

Birds' feathers often change color as a byproduct of aging, much like our hair color changes as we get older. They also get replaced in molt cycles a few times a year and require new doses of melanin every time to retain their pigment. According to Yale evolutionary ornithologist Richard Prum, this opens the door for pigment mutations to occur quite regularly - whether or not a bird lives in or passes through a radiation zone.

"It's a bit like fixing a car: the problem may be obvious, but there are lots of moving parts," says Prum, who studies the evolution of avian plumage coloration. "Melanin stress can manifest in the same way - such as white feathers - under a variety of circumstances, and the causes behind it can be very diverse. Just this winter I saw four species with abnormal white pigmentation visit my feeder at home, but I'm not too worried about radiation levels in New Haven."

Prum says he had heard the ecosystem at Chernobyl was doing quite well, an opinion defended by Mousseau's critics. Back at the University of Portsmouth in the U.K., Smith primarily studies aquatic invertebrates, and in some of Chernobyl's most contaminated lakes he has actually observed increased levels of biodiversity following the accident.

"Many of the literature studies on animals find it difficult to distinguish between the early effects of high doses shortly after the accident and later effects of much lower subsequent doses," Smith says. "Plus some of them don't properly account for the ecosystem impacts of removal of humans."

Back in 2000, Robert Baker and Ron Chesser of Texas Tech University published a paper characterizing Chernobyl as a wildlife preserve, established thanks to the absence of humans since the accident. Both scientists have maintained that biodiversity and species abundance in Chernobyl and Fukushima are, in the long term, not adversely affected by radiation.

"Despite our best efforts, post-accident field studies aren't sufficient to give us a clear picture," says Chesser. "They offer no good controls, because we aren't working with data from before the accident." Chesser suggests that physiological

aberrations of the sort Mousseau has observed are not conclusive results of chronic radiation exposure. Instead, they reflect other sources of oxidative stress including reproduction, immune response to infection and disease and strenuous physical activity such as migration.

"All the evidence that I grew up with and read in the last 60 years tells me [Mousseau's findings] are probably wrong," Chesser says, explaining why he disputes radiation as the cause behind the bird declines in Japan. "I don't intend to cast aspersions on anyone, but if your evidence is really outside the norm, you better have some extraordinary data to back that up."

Mousseau acknowledges that his research methods deviate from those of "old-school radiation biologists," whose work has typically measured responses to radiation based on Geiger counter readings of individual animals. Not caring about the exact levels of radioactivity, as Mousseau says he does not, understandably ruffles some feathers.

"We're strictly motivated by measurements of ecological and evolutionary response," Mousseau says. "Our extraordinary evidence relates to these censuses, these massively replicated bionic inventories across a landscape scale and in both locations, and that has not been done in any rigorous way by any of these other groups."

"The data are not anecdotal, they're real and rigorous," he adds. "They're replicated in space and time. How you interpret them is up for grabs, and certainly a lot more experimentation needs to be done in order to better appreciate the mechanism associated with these declines." For their part, Mousseau's team hopes next to understand why different bird species in their data appear to demonstrate varying levels of radioactive sensitivity. They're headed to Chernobyl again next week, and back to Fukushima in July.

<http://wb.md/1QeiplT>

### **What Is Trichotillomania? And How Is It Treated?**

***An author's own struggles with trichotillomania, a condition in which patients uncontrollably pull out their hair***

**Bret S. Stetka, MD, Lindsey M. Muller, MS**

**Editor's Note:** *In her new book Life Is Tricky: Memoir of a Mental Health Therapist With a Mental Health Disorder, behavioral therapist Lindsey M. Muller, MS, writes about her own struggles with trichotillomania, a condition in which patients uncontrollably pull out their hair. The disorder is more common than you might think, and Medscape recently interviewed Ms Muller on what exactly trichotillomania is and how to manage it.*

### **Background**

**Medscape: What is trichotillomania?**

**Ms Muller:** According to the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5), the symptoms of trichotillomania are:

- **Recurrent pulling out of one's hair, resulting in hair loss;**
- **Repeated attempts to decrease or stop hair-pulling;**
- **The hair-pulling causes clinically significant distress or impairment in social, occupational, or other important areas of functioning;**
- **The hair-pulling or hair loss is not attributable to another medical condition (eg, a dermatologic condition); and**
- **The hair-pulling is not better explained by the symptoms of another mental disorder (eg, attempts to improve a perceived defect or flaw in appearance in body dysmorphic disorder).**

**Medscape: Can you briefly review the history of the condition? When was it first described, and how has understanding of it has evolved over the years?**

**Ms Muller:** The name of the disorder was coined by French dermatologist François Hallopeau in 1889 and comes from the Greek words *trich* (hair), *tillein* (to pull), and *mania* (madness). However, the disorder was not formally introduced as a disorder and added to the DSM-III-R until 1987.

Classification of the disorder has been vague and questioned by many researchers and clinicians; it has been conceptualized as an obsessive-compulsive spectrum disorder, anxiety disorder, and an impulse control disorder, and most recently it appears under "Obsessive-Compulsive and Related Disorders" in DSM-5. The understanding of the disorder as sometimes present without reported feelings of anxiety and with inclusion of a sensory processing component has greatly altered how the disorder is presented in various DSM versions. From the DSM-IV-TR to the DSM-5, the following changes were made:

- **Trichotillomania moved from the impulse control disorder category to the obsessive-compulsive and related disorders category;**
- **Criterion B, "an increasing sense of tension immediately before pulling out the hair or when attempting to resist the behavior" was removed; and**
- **Criterion C, "pleasure, gratification, or relief when pulling out the hair" was also removed.**

**Medscape: Whom does trichotillomania affect, and how widely?**

**Ms Muller:** The lifetime prevalence of trichotillomania is estimated to be between 1% and 4% of the overall population. It is expected that this percentage is probably higher owing to the shame and stigma associated with the disorder. Even with increased research and media exposure to shed light on this disorder,

many people are still unaware that there is a name for the behavior of hair-pulling.

With regard to gender distribution, the female-to-male ratio is 3 to 1. Again, this statistic is questionable, given that men may underreport symptoms because they shave to "manage" the behavior.

**Causes and Treatment****Medscape: Do we know anything about what causes trichotillomania? Are there associated risk factors?**

**Ms Muller:** The etiology of trichotillomania is still unknown. However, we do know there are various factors to consider. Neurobiological research via brain scans demonstrates the structure and functioning of persons with trichotillomania to differ from that of control participants, persons with attention-deficit/hyperactivity disorder (ADHD), persons with tic disorder, and persons with obsessive-compulsive disorder (OCD). There is a genetic component in some cases; we have identified families in which trichotillomania is diagnosed in parent and child, or siblings.

Personality traits (low tolerance to stress, perfectionism, low tolerance to anxiety) are apparent. Sensory processing, such as overstimulation or understimulation from an environmental or physical standpoint, is also relevant when discussing etiology. As in all other mental health disorders, there are exceptions. Additional areas of further research that have been reported include the relationship between pulling urges and sugar consumption, caffeine consumption, and lack of sleep.

Risk factors include family history; age (peak onset is most often between age 11 and 13 years); poor coping mechanisms for emotional regulation; premorbid mental health diagnoses, such as ADHD, OCD, tic disorder, an eating disorder, an anxiety disorder, or depressive disorder; and the personality traits mentioned above.

**Medscape: How is trichotillomania treated and managed?**

**Ms Muller:** Empirically validated treatment for trichotillomania includes cognitive-behavioral therapy (CBT) and acceptance and commitment therapy (ACT), which is the third wave of treatment approaches and a branch of CBT. ACT teaches patients to recognize, accept, and embrace urges without acting on them. Behavioral approaches, such as habit reversal, stimulus control, and awareness training, are also used and are efficacious.

Regarding medication, research is not overwhelmingly positive on prescribing medication for trichotillomania. Some patients benefit from use of a selective

serotonin reuptake inhibitor in conjunction with psychotherapy, whereas others do not.

There is no cure for trichotillomania, but freedom from it is possible by recognizing the behavior, increasing awareness of the thoughts and feelings driving the urges, understanding that urges are different from behaviors, breaking the habitual cycle of pulling with behavioral interventions, increasing positive coping skills, and incorporating sensory regulation methods.

#### **A Personal Account**

**Medscape: If you are comfortable doing so, can you tell us a bit about your own struggle with the condition?**

**Ms Muller:** I started with skin-picking and nail-biting from a young age (approximately 4). Over time, these behaviors subsided, and I began pulling my hair in seventh grade until 2008 (when I was 24 years old). It was a daily and constant struggle as I tried to fight the urges day after day. Each time, I would lose the fight. The more I focused on not pulling, the more I pulled.

I tried CBT, many medications, hypnosis, and wearing something on my head at all times. Each tactic seemed to work in the beginning (the placebo effect), but the results never lasted. It was frustrating and disheartening. I felt alone, ashamed, guilty, damaged, and lost.

In 2008, I found freedom from hair-pulling when I came to understand that pulling was a choice. I could not choose whether or not I had an urge, but I could choose what to do with that urge. I waited several years until I felt enough distance and separation from my own struggle before I opened my doors to patients.

**Medscape: Do you have any final thoughts for a clinician audience on how to approach this condition and discuss it with their patients?**

**Ms Muller:** For clinicians who may not be familiar with treatment of trichotillomania, it is important to recognize that this disorder is not treated like OCD, but requires specialized understanding and treatment approaches. And for all clinicians, I would like to share that trichotillomania is almost always a symptom of something else. Treating the behavior as "just a behavior, or just a habit" is not going to address what is underlying the behavior. To really make progress, the following questions should be explored and answered: "What is driving the urges? Where are they coming from?" When treating patients, I tend to view trichotillomania as a messenger or a red flag that something is out of alignment or has gone awry.

Finally, patients may get worse before they get better as personal experiences, deep-rooted emotions, and core beliefs are brought to the surface.

[http://www.eurekalert.org/pub\\_releases/2015-05/aafc-psu042915.php](http://www.eurekalert.org/pub_releases/2015-05/aafc-psu042915.php)

### **Prolonged statin use may lower risk of lung cancer death**

*Lung cancer patients who used statins in the year prior to a lung cancer diagnosis or after a lung cancer diagnosis had a reduction in the risk of death from the disease.*

**Chris Cardwell**

**Background:** Recently there has been much interest in the potential for exploring new therapeutic uses for existing drugs, in part, because existing medications are relatively inexpensive and have known side effect profiles, according to Cardwell. This study investigated whether lung cancer patients who received statins had improved cancer outcomes.

**How the Study Was Conducted:** Cardwell and colleagues used data from nearly 14,000 patients newly diagnosed with lung cancer between 1998 and 2009 from English cancer registry data. They gathered the patients' prescription records from the U.K. Clinical Practice Research Datalink and mortality data up to 2012 from the Office of National Statistics.

**Results:** Among patients who survived at least six months after a diagnosis, those who used statins after a lung cancer diagnosis had a statistically nonsignificant 11 percent reduction in lung cancer-specific deaths. Among those who used at least 12 prescriptions of statins there was a statistically significant 19 percent reduction in lung cancer-specific deaths, and among those who used lipophilic statins such as simvastatin there was a 19 percent reduction in lung cancer-specific deaths as well.

Among all patients in the study, those who used statins in the year before a lung cancer diagnosis had a statistically significant 12 percent reduction in lung cancer-specific deaths.

Cardwell noted that the outcomes were not different between non-small cell lung cancer patients and small cell lung cancer patients in this study.

**Author Comment:** In an interview, Cardwell said, "Our study provides some evidence that lung cancer patients who used statins had a reduction in the risk of death from lung cancer. The magnitude of the association was relatively small and, as with all observational studies, there is the possibility of confounding--meaning that simvastatin [a type of statin] users may have differed from simvastatin nonusers in other ways that could have protected them from death from cancer, for which we could not correct. However, this finding is worthy of further investigation in observational studies. If replicated in further observational studies, this would provide evidence in favor of conducting a randomized, controlled trial of simvastatin in lung cancer patients. We hope to



conduct a similar analysis in a large cohort of lung cancer patients from Northern Ireland."

*Funding & Disclosures: This study was funded by the Health and Social Care Research and Development Division of the Public Health Agency of Northern Ireland. Cardwell declares no conflicts of interest.*

[http://www.eurekalert.org/pub\\_releases/2015-04/mu-nri043015.php](http://www.eurekalert.org/pub_releases/2015-04/mu-nri043015.php)

### **New research into health benefits of coffee**

*New research has brought us closer to being able to understand the health benefits of coffee.*

Monash researchers, in collaboration with Italian coffee roasting company Illycaffè, have conducted the most comprehensive study to date on how free radicals and antioxidants behave during every stage of the coffee brewing process, from intact bean to coffee brew.

The team observed the behaviour of free radicals - unstable molecules that seek electrons for stability and are known to cause cellular and DNA damage in the human body - in the coffee brewing process. For the first time they discovered that under certain conditions coffee can act as an antioxidant, a compound found in foods that helps stabilise free radicals.

The findings, published in PLOS ONE, will lead to a deeper understanding of the brewing process, as well as the potential health benefits of coffee.

Chief Chemist of Illycaffè, Dr Luciano Navarini, approached Monash physicist Dr Gordon Troup, School of Physics and Astronomy, and his team in 2012 to conduct the research using state-of-the-art EPR (Electron Paramagnetic Resonance) Spectroscopy.

"Dr Troup was one of the first scientists to discover free radicals in coffee in 1988 and so it made sense for Illycaffè - a world-leading coffee roasting company actively involved in coffee research - to collaborate with Dr Troup and his team on this significant piece of research into free radical and antioxidant behaviour in coffee," Dr Navarini said.

"The most important aim of this research was to better understand the development of stable free radicals during the roasting process and the possible influence exerted by developed radicals on the well-documented coffee antioxidant properties. We also wanted to evidence possible coffee constituents as a source of antioxidant activity." Dr Troup worked with a team of researchers including Monash alumnus Dr Simon Drew from the University of Melbourne, who carried out the spectroscopy at the University of Melbourne.

"Our research studied both the Arabica coffee bean itself and what happens to its stable free radical and antioxidant properties during the brewing process," Dr

Troup said. "The findings provide a better understanding of the potential health benefits of coffee, as well as a deeper knowledge of the roasting process - ultimately leading to the highest quality cup of coffee."

[http://www.eurekalert.org/pub\\_releases/2015-05/iu-smo050115.php](http://www.eurekalert.org/pub_releases/2015-05/iu-smo050115.php)

### **Majority of older adults willing to be screened by telephone for dementia**

*2/3 of older adults were willing to undergo telephone screening for dementia*

INDIANAPOLIS -- Nearly two-thirds of older adults were willing to undergo telephone screening for dementia, according to a new study from the Indiana University Center for Aging Research and the Regenstrief Institute. Willingness to be screened by phone did not differ by sex, age or race.

The researchers found that the two most significant predictors of willingness to be screened by phone were belief in benefits of early knowledge of cognitive decline and having a friend or relative with Alzheimer's disease.

Screening for dementia is designed to detect problems requiring further diagnostic assessment.

"Older Primary Care Patients' Attitudes and Willingness to Screen for Dementia" appears in the peer reviewed, open access Journal of Aging Research. Patient willingness to be screened for dementia by phone was determined via a phone survey of older primary care patients. The 63 percent willingness rate was significant although lower than the 90 percent willingness rate of patients who were queried in face-to-face interviews as reported by IU Center for Aging Research and Regenstrief Institute researchers in a 2012 study.

"Despite rising incidence rates of Alzheimer's and other dementias, many individuals with cognitive impairment are not screened. They go unrecognized and thus never receive evaluation or diagnosis," said IU Center for Aging Research and Regenstrief Institute investigator Nicole Fowler, Ph.D., who led both studies. "Understanding patients' attitude about the risk and benefits of early identification of dementia is vital as we evaluate potential screening barriers and facilitators."

In 2013 the United States Preventive Services Task Force concluded that the evidence to routinely screen for dementia in primary care is insufficient due to a lack of studies evaluating the risks, benefits and patient perspectives of the value of dementia screening.

"Our study provides insight into what patients think about dementia screening," Dr. Fowler said. "In addition to informing policymakers and researchers, we should make community physicians and others outside the academic community

more aware of both the benefits of informing older adults about screening options for dementia and the willingness of this group to undergo screening either in person or by telephone."

Telephone screening is less burdensome to the patient and possibly to the physician's office, she noted. The 400 older adults in the study were patients of physicians affiliated with two large community health care systems. None of the patients had a dementia diagnosis and less than two percent reported being told by their physician that they suspected memory problems.

Dementia is an overall term for the wide range of symptoms associated with a decline in memory or other cognitive skills severe enough to reduce a person's ability to perform everyday activities. Alzheimer's disease, which is progressive, is the most common form of dementia.

*In addition to Dr. Fowler authors of the study are Anthony J. Perkins, M.S., Hilary A. Turchan, B.S., and Amie Frame, MPH, of the IU Center for Aging Research and the Regenstrief Institute; Patrick Monahan, Ph.D., and Sujuan Gao, Ph.D., of the IU School of Medicine and Malaz Boustani, M.D., MPH, of the IU Center for Aging Research, Regenstrief Institute and the IU School of Medicine. Dr. Boustani is also the chief operating officer of the Center for Health Innovation and Implementation Science.*

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[http://www.eurekalert.org/pub\\_releases/2015-05/acoe-ted050115.php](http://www.eurekalert.org/pub_releases/2015-05/acoe-ted050115.php)

### **The ER docs said 'stop smoking,' and they did!**

***An intervention in the emergency department designed to encourage tobacco cessation in smokers appears to be effective.***

WASHINGTON - Two and a half times more patients in the intervention group were tobacco-free three months after receiving interventions than those who did not receive the interventions, according to a study published online Friday in *Annals of Emergency Medicine* ("Successful Tobacco Dependence Treatment in Low-Income Emergency Department Patients: A Randomized Trial").

"Because approximately 20 million smokers visit emergency departments annually, this intervention has the potential to greatly reduce tobacco use among our patients," said lead study author Steven L. Bernstein, MD, of the Yale School of Medicine in New Haven, Conn. "Given that cigarette smoking is the leading cause of preventable death and illness in the United States, anything we can do to discourage smoking has value. The need is particularly acute in low-income populations like those we studied."

Researchers enrolled 778 patients who identified as smokers. They provided motivational interviewing, nicotine replacement and quitline referral for 386 of the patients. After three months, 12.2 percent of those patients were tobacco-free.

Of the control group, only 4.9 percent were tobacco-free. The three-month abstinence rate was biochemically verified. At one year, abstinence rates were statistically significant as well for the intervention group, at least according to self-reported rates.

"While a busy emergency department may not welcome the additional responsibility of tobacco-cessation counseling, sometimes we have to meet our patients where they are," said Dr. Bernstein. "Future research should focus on longer-term interventions, as well as mobile health technologies, such as texting."

<http://bit.ly/1Azz8XN>

### **You Don't Actually Need to Bury the Dead Immediately After an Earthquake**

***In fact, it may be healthy not to.***

**Francie Diep**

It's a persistent myth that the bodies of the dead after a natural disaster are a big health risk. Sadly, most of the people who die in disasters such as earthquakes or floods are healthy. That means their bodies aren't likely to hold disease that can spread to survivors. (The situation is different for disasters such as the Ebola outbreak in West Africa, during which dead bodies were a major transmitter of illness.)

Public health organizations have been trying for the last decade to get the message across that it's OK to leave bodies unburied after natural disasters, to give people time to identify their deceased loved ones, but as recently as 2013, officials in the Philippines buried people in mass graves following a typhoon there. There are many better ways to prevent disease outbreaks after natural disasters.

In fact, it may actually be better for public health to go about burials more slowly, as natural-disaster consultant Claude de Ville de Goyet argued in an op-ed published in the *Pan American Journal of Public Health* in 2004:

The inability to mourn a close relative, the lingering doubt on the whereabouts of the disappeared, and the legal limbo of the surviving spouse or child all contribute to the many potential mental health problems associated with disasters and the difficult rehabilitation process that follows.

Mental health is just as crucial as any other aspect of health following disasters. Giving survivors time to identify, mourn, and bury disaster victims in the same way that they would have, had their loved ones died in any other way, is an important part of the healing process.

[http://www.eurekalert.org/pub\\_releases/2015-05/uoca-sqt043015.php](http://www.eurekalert.org/pub_releases/2015-05/uoca-sqt043015.php)

**Study: Generic transplant drugs as good as brand name**  
**A University of Cincinnati (UC)-led research team has found that generic formulations of tacrolimus, a drug used post-transplant to lower the risk of organ rejection, are just as good as the name-brand version.**

CINCINNATI - The findings were presented Sunday, May 3, by lead investigator Rita Alloway, PharmD, UC research professor of medicine and director of transplant clinical research within the UC Department of Internal Medicine, and her study collaborators at the 2015 American Transplant Congress annual meeting in Philadelphia.

Funded by the U.S. Food and Drug Administration (FDA), the study was a prospective, blinded, six-way crossover study in kidney and liver transplant patients. It tested whether the two most disparate generics, based on potency, purity and dissolution ("Generic Hi" and "Generic Lo"), are bioequivalent to the drug tacrolimus (Prograf) in stable transplant patients.

The researchers analyzed a total of 70 patients who were transplanted at either University of Cincinnati Medical Center or The Christ Hospital (Cincinnati) transplant programs. Patients were given brand name tacrolimus or one of two generic versions.

"We found there to be essentially no difference in the formulations between the generics and brand-name version," says Alloway. "In other words, if you were on brand and switched to generic--and you take your medication as instructed--there should be no clinical consequence."

Alloway stresses, however, that despite their team's findings, patients are still encouraged to report any product concerns to the FDA.

The findings are important, says Alloway, because while more than 70 percent of tacrolimus dispensed is generic--with no consistent negative reports--physicians and patients still have concern over the use of generics post-transplant.

"Most immunosuppressant drugs require individualized dosing and careful management to ensure the proper blood concentrations are maintained," says Alloway. "Too high exposure to these drugs increases the risk of toxicity, over-immunosuppression and cancer in patients. Too low exposure may lead to rejection of the organ by the patient's immune system."

Alloway says it's these strict conditions that cause concern that the quality, pharmacokinetics and therapeutic efficacy of new drugs may differ from the branded, or innovator, product.

To analyze drug levels and pharmacokinetics as well as pharmacogenetics, Alloway collaborated with Uwe Christians, MD, PhD, professor of anesthesiology at the University of Colorado, and Sander Vinks, PharmD, PhD, UC professor of pediatrics and director of the Division of Clinical Pharmacology at Cincinnati Children's Hospital Medical Center.

"Drs. Christians and Vinks provided expertise in tacrolimus level analysis and pharmacokinetic-pharmacogenetic data analysis," says Alloway. "The study design incorporated the most sensitive and specific tacrolimus level analysis while evaluating different methods of bioequivalence data analysis."

Alloway and team will continue this important research through an FDA-funded study of patients who are at risk of experiencing lower concentrations and subsequent rejection episodes because they have been shown to require larger doses of tacrolimus to attain therapeutic blood concentrations.

Those data, Alloway says, "will allow us to characterize unique factors which may affect tacrolimus levels to identify if formulation has an effect in this enriched population."

*Prograf (tacrolimus) is manufactured by Astellas Pharma Inc. Alloway has received clinical research support from and has served on the advisory board to Astellas.*

*She also reports receiving clinical research grants from Novartis, Veloxis, Takeda, Onyx, GSK, Prolong, Bristol-Myers Squibb, Chiltern and Sanofi. She has served on the advisory boards of Veloxis, Sanofi and Amgen.*

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

## **Our Taste for Alcohol Goes Back Millions of Years**

### **Genetics research sheds light on a long human relationship**

February 3, 2015 | By Robert Martone

Alcohol has been part of human existence for millennia. Alcoholic beverages are an integral part of human culture. Like the wines consumed in Jewish and Christian rituals, these drinks have ceremonial and religious uses. Until the nineteenth century, beer, brandy, rum or grog was the drink of choice for sailors in lieu of stagnant water during long voyages. Alcohol is a social lubricant, an anesthetic and an antiseptic. It is one of the most widely used drugs in the world and has been manufactured since the advent of agriculture nearly 9000 years ago. How is it that this drug — an intoxicating poison — has become such a part of human existence?

A new study finds that our forebears acquired the capacity to digest alcohol some 10 million years ago, among a common ancestor to humans, chimpanzees and gorillas, and certainly well before we learned to manufacture it. This suggests that alcohol became part of the human diet much earlier than previously

thought, and in a manner that had significant implications for the survival of the human species.

Humans carry with them genetic signatures of their ancestral feeding habits. Genetic variants that make new food sources available can provide tremendous opportunities to those who possess them. The ability to consume milk, for example, is due to the “lactase persistence” variant of a gene which emerged around 7500 years ago among early Europeans. For those lacking the mutation, the lactose in milk is a mild poison, eliciting symptoms akin to those of dysentery. Similarly, the ability to digest alcohol may be a genetic signature of feeding pattern among human ancestors: this alcohol tolerance may have made it possible to eat over-ripe fruit that had fallen to the ground and begun to naturally ferment. Since few animals can tolerate alcohol, this would have provided our ancestors with an abundant food source for which there were few competitors. It may also have contributed to the move towards a terrestrial rather than arboreal existence.

The breakdown of alcohol after ingestion is a complex process that involves a number of different enzymes. Most of the alcohol that is ingested is broken down in the gut and liver. This study focused on the enzyme ADH4 because it is abundant in the gut and plays a major role in preventing ingested alcohol from entering the blood stream. ADH4 from human relatives as distant as the tree shrew were tested for their ability to digest alcohol. The form of ADH4 found in humans, gorillas and chimpanzees was found to be 40 fold more efficient at clearing alcohol than the form found in more primitive species. ADH4 also digests chemicals that plants produce in order to deter animals from feeding upon them. However, with the increase in ability to digest alcohol came a reduced ability to digest many of these other chemicals. This suggests that the food containing alcohol was more important.

While ADH4 is among the most important enzymes for the digestion of alcohol, it is not the only one. Another related enzyme, ADH3, also contributes to the breakdown of alcohol. Women typically have lower activity levels of this enzyme, leading them to have higher blood levels of alcohol than men after taking a high dose of alcohol. And ADH4 is not the only enzyme that may have helped humans adapt to the consumption of alcohol: a variant of a liver enzyme (ADH1B) with high activity in the breakdown of alcohol emerged among East Asian populations during the advent of rice cultivation, perhaps as an adaptation to rice fermentation. (Interestingly, other animals have adopted their own strategies: Using a different enzyme, a member of the tree shrew family is able

to consume fermented nectar from palm tree flowers — the equivalent of 10 -12 glasses of wine every day without obvious signs of intoxication.)

Because humans rely upon ADH4 as their primary means to digest alcohol, they are also susceptible to hangovers. ADH4 and similar enzymes digest alcohol by converting it into another chemical, acetaldehyde, which causes the skin flushing, headache and other symptoms of overindulgence. The modern consumption of alcohol has been characterized as an "evolutionary hangover," an adaptation to modest levels of alcohol in food sources which left humans prone to alcohol abuse once we learned how to manufacture it in highly concentrated forms. And, in fact, genetic variants of ADH4 have been linked to alcohol and drug dependence, although there are many other genes that may influence susceptibility to alcohol dependency. Regardless of the role ADH4 plays in alcohol addiction, it's clear that our complex relationship with alcohol dates back millions of year, and began, in fact, before we were even human.