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## **Killer robot threat must be faced, say experts**

***116 founders of AI and robotics companies have called on the UN to ban lethal autonomous weapons, writes Michael Lucy.***

Now is the time to act to avoid a killer robot future, according to AI industry leaders and researchers.

Fears of killer robots doing the bidding of terrorists, despots and hackers have prompted leaders from the AI and robotics industries to call on the United Nations to ban the use of lethal autonomous weapons.

In an open letter published today 116 AI heavyweights from 26 countries, including Elon Musk (of Tesla, SpaceX and OpenAI fame) and Mustafa Suleyman (of Google's DeepMind), warn of an incipient "third revolution in warfare" and ask the UN to "find a way to protect us all from these dangers".

Lethal autonomous weapons are weapons that can operate without human supervision and possess some degree of "decision-making" ability, including the ability to choose their targets. By turning the astounding technical developments in machine learning and robotics made in recent years to the task of killing, they threaten to "permit armed conflict to be fought at a scale greater than ever, and at timescales faster than humans can comprehend", the letter says.

A similar open letter was signed by thousands of AI and robotics researchers in 2015. In December 2016, 123 countries at the UN came to a unanimous decision to begin a round of formal discussions of this kind of weaponry. 19 countries have already called for an outright ban. Toby Walsh, a professor of AI at the University of New South Wales who was one of the organisers of the letter, says we stand at a crossroads in the development of AI. While it can be used to help us tackle social problems such as inequality, climate change and economic crisis, it could also be turned to the industrialisation of war. "We need to make decisions today choosing which of these futures we want," says Walsh.

The letter was released at the International Joint Conference on Artificial Intelligence 2017 in Melbourne, Australia, the world's biggest AI conference.

<http://bit.ly/2viNikw>

## **Licorice is a hot trend in hot flashes, but could interact with medications**

***Scientists caution that licorice could pose a health risk by interacting with medications***

Washington - Licorice roots have a diverse and flavorful history, having been used in ancient Egyptian times as a tea and in traditional Chinese medicines, all the way to today as a flavoring agent and as an ingredient in some licorice candies. Some women now take licorice extracts as supplements to treat hot flashes and other menopausal symptoms. But scientists caution that the substance could pose a health risk by interacting with medications.

The researchers are presenting their results today at the 254th National Meeting & Exposition of the American Chemical Society (ACS). ACS, the world's largest scientific society, is holding the meeting here through Thursday. It features nearly 9,400 presentations on a wide range of science topics.

"Concerns about the risk of stroke and breast cancer associated with conventional hormone therapy are prompting women to seek alternatives," Richard B. van Breemen, Ph.D., says. "Some take botanical dietary supplements, such as licorice, to treat menopausal symptoms like hot flashes."

But just because a substance is sold as a supplement in a health food store doesn't mean it is completely safe for all people to take. And on its own, even as a candy, licorice can be harmful in some cases. The U.S. Food and Drug Administration recommends that licorice not be eaten in large amounts during one sitting, and warns that excessive consumption can lead to irregular heart rhythm and muscle fatigue.

"Consuming too much licorice can be harmful, but in our lab, we wondered whether the small amounts in dietary supplements might

also cause problems by interfering with drug metabolism or transportation," says van Breemen, who is at the University of Illinois at Chicago. "The liver has enzymes that process medications, and if these enzymes are induced or inhibited, the drugs will either be processed too quickly or too slowly, respectively." He points out that these changes could pose a significant safety risk to those who take a daily licorice dietary supplement along with other medication.

Van Breemen's team analyzed how three types of licorice -- two North American species, *Glycyrrhiza uralensis* and *G. inflata*, and a European species called *G. glabra* -- affected liver enzymes involved in drug metabolism. They found that all three species inhibit several of these enzymes. Only *G. uralensis* and *G. inflata* extracts were found to induce some of these enzymes. Therefore, the researchers say that *G. uralensis* and *G. inflata* are more likely to interfere with drug metabolism when compared to *G. glabra*.

Consumers would have a difficult time using this information, however, because most supplements don't list the species on their labels. But the researchers are using this knowledge to develop their own licorice therapy that would be safe and effective for women experiencing menopausal symptoms, such as hot flashes. They plan to start clinical trials on their *G. glabra*-based supplements next year.

*Van Breemen's work was funded by the National Institutes of Health.*

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## **Antarctic salt-loving microbes provide insights into evolution of viruses**

***UNSW Sydney scientists studying microbes from some of the saltiest lakes in Antarctica have discovered a new way that the microbes can share DNA that could help them grow and survive.***

The research, based on 18 months of water sampling in remote Antarctic locations, including during the extreme cold of winter, could throw light on the evolutionary history of viruses.

The team unexpectedly discovered one strain of the Antarctic salt-loving microbes contained plasmids - small molecules of DNA which

can replicate independently in a host cell, and which often contain genes useful to an organism.

"Unlike viruses, which encase themselves in a protective protein coat, plasmids usually move around by cell to cell contact, or as a piece of naked DNA," says research team leader, UNSW scientist Professor Rick Cavicchioli.

"But the plasmids that we found in the Antarctic microbes were masquerading as viruses. They produced proteins which went into the host's membrane, which then allowed the membrane to bud off containing the plasmid DNA.

"The budded membranes, called membrane vesicles, allowed the plasmids to infect microbes of the same species that did not have any plasmids present, and then replicate themselves in the new host," he says.

Study first author Dr Susanne Erdmann says: "This is the first time this mechanism has been documented. And it could be an evolutionary forerunner to some of the more structured protective coats that viruses have developed to help them spread and become successful invaders.

"This finding suggests some viruses may have evolved from plasmids," she says.

The study, by Dr Erdmann, Dr Bernhard Tschitschko, Dr Ling Zhong, Associate Professor Mark Raftery and Professor Cavicchioli, is published in the journal *Nature Microbiology*.

The Antarctic microbes studied by the researchers are called haloarchaea and are known to be promiscuous, swapping DNA readily between themselves. They can survive in Deep Lake, a 36-metre deep lake that is so salty it remains in liquid form down to a temperature of minus 20 degrees. The lake, which is about five kilometres from Australia's Davis Station, was formed about 3500 years ago when the Antarctic continent rose, isolating a section of ocean.

Haloarchaea microbes containing the plasmids were isolated from very rare water samples collected from the Rauer Islands about 35 kilometres further away.

"We also discovered that the plasmids could take some of the DNA from the host microbe, integrate it into their own DNA, produce membrane vesicles around themselves, and then go off and infect other cells," says Professor Cavicchioli. "The findings are therefore relevant to Antarctic science as well as biology as a whole."

*Key research on the plasmid proteins was carried out in the Bioanalytical Mass Spectrometry Facility at UNSW's Mark Wainwright Analytical Centre.*

<http://bit.ly/2w17n1A>

## Have flowers devised the ultimate weapon of distraction?

### *Nectar not just a 'come on' to bees, it's a honeytrap*

Nectar, the high-energy 'honey' produced by flowers, might be a brilliant distraction technique to help protect a flower's reproductive parts, according to new research.

Rather than merely providing a 'come-on' to bees and other insects to attract them to pollinate the flower, nectar could be playing a much more subtle and entrancing role.

Scientists from across the world have studied the part played by herbivores, such as sawflies, which eat petals and nectar, on an iris found in the Himalayas. They are now confident that a visiting insect which feasts on the nectar and the gland which produces it, and makes merry, is playing into the hands of the flower and ensuring it survives and thrives.

Scientists at the universities of Wuhan, China; Calgary, Canada; Portsmouth, UK; and at the Fairylake Botanical Garden in Shenzhen, China, have published their findings in *Biology Letters*.

Scott Armbruster, Professor of Ecology and Evolution at the University of Portsmouth, and one of the authors, said: "Contrary to the accepted wisdom, the role of nectar seems in this instance to not be just about attracting and rewarding pollinating insects.

"It seems nectar and nectaries, the glands which produce it, attract herbivores that would otherwise feed on other flower parts. Thus the nectar and nectaries may be acting as a decoy. Like nectar thieves and robbers, the herbivores we observed have a high energy demand, and

because nectar is rich in nutrients, it appears flowers are using it as a distraction, to keep herbivores away from critical reproducing parts of the flower, which are also edible.

"They are sacrificing their nectar and nectaries for the greater goal of maintaining other floral parts that are critical for attracting pollinators, and hence being pollinated."

The researchers studied *Iris bulleyana*, with showy, large, colourful petals, which conventional wisdom says are a means of attracting the attention of bees and other pollinators.

Nearly all (98 per cent) of the flowers studied in natural conditions were damaged by herbivores, but in 85 per cent of the flowers, damage was restricted to just the nectaries, suggesting nectar was being sacrificed to protect more critical parts of the plant. The researchers saw sawflies 'frequently' using the flower as a mating site during which all the nectar and nectaries were eaten, mainly by female sawflies, causing no damage to the stamen and stigma, the reproductively critical parts of the flower.

Even though colourful - and edible - petals play no direct role in producing seeds or pollen, they do attract the interest and attention of pollinating insects, such as bees. When sawfly herbivores grazed on the petals, damaging them, fewer pollinators visited the flower, meaning its chances of reproduction plummeted. By offering up a decoy of calorie-rich nectar, the herbivores were distracted enough to not damage the petals or other parts of the flower critical to its chances of being pollinated.

Professor Armbruster said: "The results are clear that floral tissues with a higher reproductive importance are essentially protected through the presence of sacrificial parts, the nectaries and nectar."

Most previous research has examined either plant-herbivore or plant-pollinator relationships, and this is thought to be one of the first studies to examine both relationships together in a flower with abundant nectar and showy petals.

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## Newly developed nomograms provide accurate predictions for patients with oropharyngeal cancer

### *Nomograms provide accurate prediction of overall survival and progression-free survival for patients with oropharyngeal cancer*

PHILADELPHIA, Pa. -- NRG Oncology researchers recently developed and validated a nomogram that can predict 2-year and 5-year overall survival (OS) and progression-free survival (PFS) for patients with local-regionally advanced oropharyngeal squamous cell carcinoma (OPSCC) treated primarily with radiation-based therapy. This nomogram was developed with data from clinical trials NRG Oncology/RTOG 0129 and 0522. Results were published online in the *Journal of Clinical Oncology* on August 4, 2017.

A nomogram is a graphic depiction of models that can be utilized to estimate the numeric probability of death, disease progression, or other events for a particular patient. Validated nomograms can be advantageous in determining social or biological factors that could be associated with survival. NRG Oncology's validated nomogram for prediction of survival in oropharyngeal cancer can be found on the NRG Oncology website under the Resources tab.

"Nomograms offer the ability to personalize survival estimates for patients based upon a host of factors that are clinically relevant when we meet patients," stated Carole Fakhry, MD, the study's lead author and an associate professor in the Department of Otolaryngology Head and Neck Surgery at John Hopkins University.

Researchers developed and validated the nomograms for OS and PFS using a derivation cohort and the models were applied to a validation cohort. The derivation cohort included 493 patients with OPSCC, a known tumor p16 status, and a smoking history measured in pack-years, who were randomized into two clinical trials: NRG Oncology/RTOG 0129, a phase 3 trial that evaluated standard fractionated (SFX) vs. accelerated fractionated (AFX) radiotherapy with cisplatin; and, NRG Oncology/RTOG 0522, a phase 3 trial that

evaluated the addition of cisplatin to AFX radiotherapy and concurrent cisplatin. The validation cohort included 153 patients with OSPCC, a known tumor p16 status, and a smoking history who were randomized into NRG Oncology/RTOG 9003, a phase 3 study that evaluated SFX vs. concomitant boost vs. split-course accelerated vs. hyperfractionated radiotherapy. The Cox model was used to determine if the survival distributions differed among the three risk groups.

Both models included age, Zubrod performance status, pack-years, education, p16 status, tumor and nodal stage; however, the OS model also included anemia and age to-pack-year interaction, while the PFS model included marital status, weight loss, and p16 to Zubrod interaction. Predictions correlated well with observed 2-year and 5-year outcomes.

"These nomograms will help in providing patient-specific estimates of survival that can be used for risk-stratification and discussions of prognosis with patients," added Dr. Fakhry.

*NRG Oncology/RTOG 0129 and 0522 were funded by grants from the National Cancer Institute and Eli Lilly.*

*Citation:*

*Fakhry C, Zhang Q, Nguyen-Tân PF, Rosenthal DI, Weber RS, Lambert L, Trotti AM, Barrett WL, Thorstad WL, Jones CU, Yom SS, Wong SJ, Ridge JA, Rao SSD, Bonner JA, Vigneault E, Raben D, Kudrimoti MR, Harris J, Le QT, Gillison ML. Development and validation of nomograms predictive of overall and progression-free survival in patients with oropharyngeal cancer. *Journal of Clinical Oncology*. August 4, 2017. [DOI: 10.1200/JCO.2016.72.0748](https://doi.org/10.1200/JCO.2016.72.0748).*

<http://bit.ly/2xftK1y>

## 80 percent of Ebola survivors suffer disabilities one year after discharge

### *Almost 80% of those interviewed were found to have major limitations*

New research, conducted by the University of Liverpool and Liverpool School of Tropical Medicine, highlights the need for long-term rehabilitation of Ebola survivors after almost 80% of those interviewed were found to have major limitations in mobility, cognition and vision.

The scale of the 2014-2016 West African Ebola outbreak has resulted in an unprecedented number of survivors and the opportunity to vastly improve the understanding of the health challenges they face.

Researchers, led by Soushieta Jagadesh, assessed disability amongst a cohort of Ebola Virus Disease (EVD) survivors 12 months following their discharge from the Ebola Survivors Clinic, 34 Military Hospital (MH34) in Freetown, Sierra Leone and compared with their close contacts. Twenty-seven EVD survivors and 54 unaffected contacts were recruited.

### **Physical and mental impairments**

Disability was measured using the Washington Group-Disability Extended Questionnaire (WG ES-F) for both the EVD survivors and their non-affected contacts. The questionnaire measured self-reported physical and mental impairments present at the time of the interview.

The questionnaire assessed six domains: vision, hearing, mobility, self-care, communication and cognition. Functionality scores were calculated from the severity and frequency of anxiety, depression, pain and fatigability. Disability in at least one of the six domains was reported by significantly more EVD survivors than controls.

### **Mobility**

Disability was reported by 78% of EVD survivors compared to 11% of non survivors. Differences in physical disability were most marked with the EVD survivors' cohort being between up to 206 times more likely to experience difficulty in walking 100m, 500m, climbing 12 stairs or overall moderate difficulty with mobility.

Pain, fatigue, anxiety and depression all influence disability in mobility. Relative to controls the EVD survivors had very significantly increased mean pain scores, fatigue scores, anxiety scores and depression scores.

The study also showed that EVD survivors had significantly higher subjective difficulties remembering or concentrating and were eight times more likely than controls to suffer from blurred vision.

### **Future care**

Dr Soushieta Jagadesh, said: "We have demonstrated that a year following acute disease, survivors of the West African EVD outbreak continue to have a higher chance of disability in mobility, cognition and vision than their close-contacts. Issues such as anxiety and depression persist in EVD survivors and must not be neglected."

Dr Janet Scott, Clinical Lecturer, University of Liverpool, said: "This study highlights that EVD results in long term substantial disability. Understanding post Ebola syndrome could improve our future care of EVD patients and patients suffering the sequelae of other severe viral infections."

### **Rehabilitation**

Dr Ralf Weigel, Senior Clinical Lecturer, Liverpool School of Tropical Medicine, said: "Further evaluation of the scale of disability in larger survivor cohorts would be useful, as is a new focus on sustainable long-term rehabilitation in EVD survivors."

Dr Sesay, Clinical Lead EVD Survivors Clinic, MH34, commented: "We continue to care for over 500 Ebola Survivors, as part of the country wide integrated network of EVD Survivors Care. This study highlights the continuing need for focused care for EVD survivors."

*The full study, entitled 'Disability among Ebola survivors and their close contacts in Sierra Leone: a retrospective case-controlled cohort study', can be found here <https://academic.oup.com/cid/article/doi/10.1093/cid/cix705/4085646/Disability-among-Ebola-survivors-and-their-close>*

*This study was carried out as a MSc at the Liverpool School of Tropical Medicine supervised by Dr Ralf Weigel and was hosted by the project "Characterizing Post Ebola Syndrome, Sierra Leone" lead by Dr Foday Sesay, Military Hospital 34, Freetown (MH34) , and Drs Janet Scott and Calum Semple, University of Liverpool with a grant from Wellcome Trust Enhancing Research Activity in Epidemic Situation (ERAES)*

<http://bit.ly/2xvaf4C>

## **Study: Clear link between heavy vitamin B intake and lung cancer**

### **Long-term use of high-dose supplements more than triple risk in male smokers**

New research suggests long-term, high-dose supplementation with vitamins B6 and B12 -- long touted by the vitamin industry for

increasing energy and improving metabolism -- is associated with a two- to four-fold increased lung cancer risk in men relative to non-users.

Risk was further elevated in male smokers taking more than 20 mg of B6 or 55 micrograms of B12 a day for 10 years. Male smokers taking B6 at this dose were three times more likely to develop lung cancer. Male smokers taking B12 at such doses were approximately four times more likely to develop the disease compared to non-users.

Epidemiologists from The Ohio State University Comprehensive Cancer Center - Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James), Fred Hutchinson Cancer Research Center and National Taiwan University report their findings in the Aug. 22, 2017 issue of the Journal of Clinical Oncology.

This is the first prospective, observational study to look at the effects of long-term high-dose B6/B12 supplement use and lung cancer risk. These supplements have been broadly thought to reduce cancer risk.

For this study, Theodore Brasky, PhD, of the OSUCCC - James, and colleagues analyzed data from more than 77,000 patients participants in the VITamins And Lifestyle (VITAL) cohort study, a long-term prospective observational study designed to evaluate vitamin and other mineral supplements in relation to cancer risk. All participants were aged between 50 and 76 were recruited in the state of Washington between the years 2000 and 2002. Upon enrolling in the study, participants reported information to researchers about B-vitamin usage over the past 10 years. This included dosage information -- a critical but often missing detail needed for strong risk assessment and association research.

For this new analysis, researchers used statistical techniques to adjust for numerous factors including: personal smoking history, age, race, education, body size, alcohol consumption, personal history of cancer or chronic lung disease, family history of lung cancer and use of anti-inflammatory drugs.

"This sets all of these other influencing factors as equal, so we are left with a less confounded effect of long-term B6 and B12 supplementation," explains Brasky. "Our data shows that taking high doses of B6 and B12 over a very long period of time could contribute to lung cancer incidence rates in male smokers. This is certainly a concern worthy of further evaluation."

Brasky notes these findings relate to doses that are well above those from taking a multivitamin every day for 10 years.

"These are doses that can only be obtained from taking high-dose B vitamin supplements, and these supplements are many times the U.S. Recommended Dietary Allowance," he said.

Two additional studies are underway at The OSUCCC - James to further evaluate high dose, long-term B6 and B12 supplementation and lung cancer risk. One study will examine associations in post-menopausal women in order to confirm the current finding of no elevated risk in women. The second will examine B6/B12 high dose, long-term supplementation in a second large prospective study of men in an effort to determine whether the increases risk observed in the current study can be replicated.

*This study was supported by the National Institutes of Health, the National Cancer Institute and the Office of Dietary Supplements. Collaborators include last author Chi-Ling Chen, PhD, of National Taiwan University, and Emily White, PhD, of Fred Hutchinson Cancer Research Center.*

<http://bit.ly/2vjgdES>

### **A potential breeding site of a Miocene era baleen whale Researcher identifies evidence of a calf whale from the Miocene of Hiroshima, Japan suggesting the earliest known site for baleen whale breeding in the northern hemisphere**

Baleen whales are amongst the largest animals to have ever lived and yet very little is known about their breeding habits.

One researcher's second look at previously found baleen whale fossils from Japan provides new evidence of a now long-gone breeding ground of the extinct baleen whale *Parietobalaena yamaokai* dating back over 15 million years.

The research published in the open-access journal PeerJ elaborates on the evidence of the presence of a very young individual of an extinct baleen whale, along with the occurrence of several fossil specimens of the same whale species.

This study claims to have discovered a very uncommon case -- a breeding ground for a long extinct large whale.

Researcher Cheng-Hsiu Tsai noticed the open suture in the skull of one fossil specimen, which indicates the preservation of a very young whale -- under six months old, perhaps even close to a new-born calf. The fossil specimens investigated were originally found in the 20th century and are currently held at the Hiwa Museum for Natural History, Shobara, Hiroshima, Japan.

Identifying breeding grounds of living species of whales are incredibly rare, let alone for extinct Miocene species.

For example, scientists are not certain where the endangered western gray whales reproduce, in turn leading to no concrete strategies to recover this critically endangered population of around 100 individuals.

The discovery of an ancient paleo-breeding site, which dates back to 15 million years ago, could provide new insights into the future of baleen whale survival.

In a rapidly changing world, locating breeding sites and understanding why a breeding site disappeared may subsequently lead to information on how best to respond in order to conserve these living endangered populations.

Full Media Pack including image:

<https://drive.google.com/open?id=0BzGrFBtalE6wV3d6RmUtM0xsT2ZvY1d0SVR6bjJGY18tQIRj>

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Link to the Published Version of the article (quote this link in your story - the link will ONLY work after the embargo lifts): <https://peerj.com/articles/3711> your readers will be able to freely access this article at this URL.

Citation to the article: Tsai (2017), A Miocene breeding ground of an extinct baleen whale (Cetacea: Mysticeti). *PeerJ* 5:e3711; DOI 10.7717/peerj.3711

<http://bit.ly/2q9m90r>

## **Dogma overturned: New studies into inflammation in the infarcted heart could lead to changes in therapy**

*The results are published in 2 independent articles in the leading journals **Circulation and Circulation Research***

Scientists at the Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC) and the Fundación Jiménez Díaz (FJD) and Salamanca University Hospitals have demonstrated that the response of the human heart to an infarction is very different to what was previously thought. The study, led by cardiologist Borja Ibáñez and published in 2 independent articles in the leading journals *Circulation* and *Circulation Research*, overturns the established view that an infarction is followed by progressive repair of the myocardium.

For many years, scientists have assumed that a heart attack is followed immediately by an inflammatory response featuring increases in water content and cellular infiltration and that this response remains stable for at least 1 week and then progressively dissipates. Two years ago, the research team behind the new studies published a series of animal studies that challenged this view, but the most important challenge remained: to validate the new findings in human patients. The new studies used the most advanced magnetic resonance imaging (MRI) technology to demonstrate that the human heart produces 2 well-differentiated edematous reactions occurring at distinct times after an infarction. These results have immediate clinical implications for ongoing clinical trials and could form the basis of future studies focused on the specific modulation of each of these independent edematous phases.

The project came out of research started more than 10 years ago at the Mount Sinai Hospital in New York, directed by renowned cardiologist Valentín Fuster, who is an author on both of the new CNIC-led studies. Two years ago, the CNIC and the FJD University Hospital signed a collaboration agreement to coordinate their studies of cardiac muscle after an acute myocardial infarction. The collaboration is directed by

Borja Ibáñez, who is both Director of Clinical Research at the CNIC and a cardiologist at FJD University Hospital, and has led to a prolific scientific production. Rodrigo Fernández-Jiménez, first author on both studies, explained that "surprisingly, we still know very little about how the myocardium reacts to an infarction, and it is only through the use of MRI, which allows noninvasive, millimeter-resolution mapping of tissue composition, that we are beginning to understand many of its mysteries."

The bimodal postinfarction inflammatory reaction was first demonstrated in animals in 2015, but this left the much more difficult challenge of demonstrating that the same phenomenon occurs in patients. Undertaking such a study required a special set up that would allow detailed MRI studies to be carried out immediately after the re-establishment of blood flow through the blocked coronary artery in heart attack patients. This requires highly complex technology and is therefore possible in only a handful of centers. One center with the technology and expertise to carry out this type of study is the university hospital in Salamanca. As chief cardiologist Pedro Luis Sánchez explained "we've been able to carry out this work thanks to the enthusiasm and commitment of everyone in the service. Heart attacks can happen at any time of day or night or at weekends, and for this study we needed to do the first MRI scan within 3 hours of fitting a stent in the blocked artery to re-establish blood flow. Patients are particularly vulnerable during this period, so in addition to the expert MRI specialists, we also needed a full clinical support team on hand to provide continuous care during the examination period."

#### Pioneering study

The study is the first in the world to study heart attack patients by MRI so soon after the re-establishment of blood flow. In addition to studies in patients, the team have also extended their investigation of infarction in pigs, the experimental model most similar to humans. The unique translational research infrastructure at the CNIC includes identical imaging equipment for human and animal studies, allowing

the team to demonstrate that treatments during an infarction can change the composition of the cardiac muscle during the first hours after reperfusion, resulting in a much more rapid recovery of the heart. In the words of Dr. Fernández-Jiménez, "MRI provides an extraordinary ability to noninvasively visualize events occurring after an infarction in real time, including inflammation, tissue volume expansion, hemorrhage, and obstruction of the microcirculation."

According to Dr. Ibáñez, who recently won the Fundación Banco Sabadell Biomedical Research Prize, the discovery of the bimodal inflammatory response in the human heart "forces us to think about the best timing for MRI scans used in clinical trials to quantify irreversible injury and to monitor the effectiveness of interventions to reduce this injury. Until now this question was not considered important, and cardiac imaging studies have been conducted on any day in the postinfarction period. The new findings show that the optimal time for these scans is between postinfarction days 4 and 7, when the second inflammatory/edematous wave is prominent and affects the entire region that was shut off from the blood supply during the infarction."

This research project was possible thanks to the unique research infrastructure at the CNIC, which boasts imaging analysis equipment unrivalled anywhere in Europe, all at the service of leading international research groups. CNIC General Director Dr. Fuster commented "We invested in the best imaging technology in order to study biological and clinical processes from a totally new perspective." This unique technology is allowing translational researchers to address clinically relevant questions in a way that greatly accelerates the pace of research.

Another essential element of this research endeavor is the scientific collaboration between the CNIC and technology partner Philips Iberia. Physicist Javier Sánchez-González, a Philips researcher embedded at the CNIC, leads the technological development of these cardiac imaging projects, and his input is essential for transferring the initial



findings from the CNIC to collaborating hospitals, so that the new algorithms can be tested in a clinical environment. Recently, the consortium formed by the CNIC, the FJD and Salamanca university hospitals, and Philips was awarded funding under the Carlos III Institute of Health's technology development program for the development of new three-dimensional cardiac resonance sequences.

<http://bit.ly/2xfr11H>

**Leaping Lizards! Live Gecko Found Inside a Man's Ear**  
*Talk about an earache: When a man in China went to the hospital because of severe ear pain, doctors found a live gecko curled up in his ear canal, according to news reports.*

By Sara G. Miller, Staff Writer | August 22, 2017 01:26pm ET

The man woke up in the morning complaining of severe pain in his ear, as well as the feeling of something squirming around in there, according to the Deccan Chronicle, a South Indian newspaper. When doctors peered inside, they spotted a live lizard.

Initially, the doctors tried to remove the gecko with tweezers, but the lizard squirmed when it was touched, the Deccan Chronicle reported.

To prevent the gecko from wiggling further into the ear canal, the doctors anesthetized the reptile, and then safely removed it from the man's ear using long pliers, UPI reported on Aug. 18. The procedure took about 5 minutes.

But not all of the gecko was removed during the procedure: The Deccan Chronicle noted that the gecko appeared to be missing its tail, which the doctors could not find in the man's ear. It's possible that the lizard lost its tail before getting stuck in the man's ear canal. Some species of geckos can shed their tails as a means of self-defense, and a recently discovered species can even shed all of its scales to protect itself if a predator catches hold of it.

Geckos aren't the only unwanted visitors that have made their way into human ears; people have found spiders, fruit-fly larvae and flesh-eating worms residing in their ear canals.

<http://bit.ly/2wLlLvs>

**Shedding old cells rejuvenates the brittle bones of ageing mice**

*New osteoporosis drugs that kill off senescent cells and rebuild bone may be a few years away. Ella Finkel reports.*

The last few years have seen a novel idea emerge in anti-ageing science. [Several studies](#) have shown that pruning away old, inactive senescent cells [can do wonders for aged mice](#), restoring their bald patches, strengthening their aged muscles, improving their cardiovascular function and repairing their damaged kidneys. “Oh, to be a mouse,” as Christopher Reeve once wistfully mused.

Now researchers at the Mayo Clinic in Rochester, Minnesota, have shown for the first time that the same approach can restore the strength of brittle bones. Their work [appears in Nature Medicine](#).

Unlike current treatments for osteoporosis, which muzzle bone-destroying cells, this approach doesn't just halt the destruction of bone, it actually rebuilds it, according to the researchers. Treatments of this kind would also have the appealing side-effect of rejuvenating other tissues. “We targeted a fundamental aging process that has the potential to improve not only bone mass, but also alleviate other age-related conditions as a group,” says Sundeep Khosla, director of the Aging Bone and Muscle program at the Mayo Clinic.

For years Khosla, whose specialty is bone biology, had been watching the work of his colleague across the hall with great interest. Jim Kirkland focuses on the mechanism of ageing. The director of the Kogod Center on Aging, his research had identified factors that killed aged cells in the test tube, and when given to rapidly ageing mice, slowed the onset of their decline. For instance, ageing mice start losing muscle strength and the ability to clear glucose from their bloodstream, a harbinger of diabetes. Treatment with compounds that culled senescent cells, so-called *senolytics*, delayed these effects.

Encouraged by Kirkland's results, Khosla checked to see if naturally aging mice also accumulate senescent cells in their bone. Last year he

found [that was the case](#). Some of the worn-out hangers-on were identified as osteocytes. These were of particular interest. Bone may appear inert but it is constantly being remodelled – chipped away here, filled out there – to cope with the changing physical stresses on our bodies. It is the osteocytes that orchestrate the sculpting process. Once they senesce, they may lose their touch and start pumping out an excess of inflammatory factors, as other senescent cells have been shown to do. The age-related tipping of the balance toward bone destruction may be the result.

Khosla, Kirkland and colleagues tested their hunch by treating 20-month-old mice (the equivalent of 70-year-old humans) with two senolytic compounds previously identified by Kirkland's screens: quercetin and dasatinib. Quercetin is a plant-based natural product. Dasatinib is a drug used to treat leukaemia, though the doses used here were much smaller.

Mice received their senolytic cocktail once a month for four months. Those treated showed a 30% increase in their bone volume. Scans showed that not only had their bone mass increased – a finding that could be due to increased mineralization – but the structure of their bone revealed new deposition of bone tissue, increasing its strength. This ability to stimulate new bone growth is not seen with current osteoporosis drugs, says Khosla.

The bone-building effects seen with elderly mice were not evident in younger mice, supporting the interpretation that the compounds were acting on aged cells. "This is another piece of the mounting evidence that senolytic drugs are targeting basic aging processes and could have widespread application in treating multiple chronic diseases," says Kirkland.

"With the aging of the population in the U.S. and around the world, age-related bone loss is going to continue to be an enormous public health problem, and patients with osteoporosis have a higher risk for other age-related comorbidities," says Khosla. He says preliminary

clinical trials with the bone-strengthening agents have already begun in people.

<http://bit.ly/2xhiUsb>

## **Mosquitoes fatally attracted to deadly, sweet-smelling potion**

***Mosquitoes aren't just blood thirsty. They also have a sweet tooth, relying on plant nectar to get the sugar they need to survive.***

WASHINGTON, Aug. - Exploiting this weakness, scientists have developed an environmentally friendly eradication method. The new, inexpensive technique tricks these annoying pests into gorging themselves on insecticides laced with a concoction that mimics the sweet-smelling scents and aromas that they find irresistible. It could bolster efforts to suppress malaria, Zika and other mosquito-borne diseases worldwide.

The researchers are presenting their work today at the 254th National Meeting & Exposition of the American Chemical Society (ACS). ACS, the world's largest scientific society, is holding the meeting here through Thursday. It features nearly 9,400 presentations on a wide range of science topics.

"The blend of chemicals that we use to attract mosquitoes is so powerful that they will ignore natural plant odors and attractants in order to get to our formulation," says Agenor Mafra-Neto, Ph.D. "From a mosquito's point of view, it's like having an irresistible chocolate shop on every corner. The product is so seductive that they will feed on it almost exclusively, even when it contains lethal doses of insecticide."

Conventional chemical insecticides used to control mosquitoes are used as cover sprays, frequently dispersed over wide areas. But this blanket spray approach exposes people and animals to potentially harmful compounds and can kill bees and other beneficial insects. In addition, residues of these sprays can contaminate soils and streams, as well as promote increased pesticide resistance. To overcome these issues, Mafra-Neto of ISCA Technologies and colleagues at several

universities sought to create a more targeted approach using an insecticide potion spiked with a blend of semiochemicals, or chemical signals, that mosquitoes can't resist.

They collected the scent of flowers and other plants that produce nectar. Then, they used gas chromatography-electroantennographic detection (GC-EAD) to separate and identify the odorous compounds within them. They exposed mosquito antennae to thousands of these compounds to determine which ones might have a biological effect. They also carefully eliminated any scents or aromas that also might attract bees. Ultimately, they used a semiochemical blend in a matrix containing sugars and proteins to mimic 20 common chemical signals that attract mosquitoes to nectar-producing flowers and induce them to feed. Combining these compounds with insecticides such as pyrethroids or spinosad led to highly effective formulations.

The resulting product, which is called Vectrax®, is a slow-release formula for use indoors or outdoors. It can be applied as a spray, which produces 1- to 5-millimeter dollops on vegetation or building eaves, or as a semi-solid, caulk-like gel on cracks or holes in outdoor structures. Because the mosquitoes visit and manipulate the dollops, they receive precise doses of the insecticide, and thus are more effectively controlled. Unlike with traditional blanket sprays, nearby surfaces can remain insecticide free.

The researchers are conducting field tests in Tanzania, an African nation where 93 percent of the population is at risk for malaria. In preliminary results, they found that mosquito populations plunged by two-thirds in just two weeks in Vectrax-treated communities compared to untreated ones.

"If the trend continues like this, we expect that the Anopheles malaria mosquito population will soon be collapsing down to nearly zero in the treated villages," Mafra-Neto says. He hopes to have more data available from these trials soon.

While Mafra-Neto acknowledges that mosquitoes play a small role in the food chain, helping sustain small animals like fish and spiders, he

would like to see fewer of them around, particularly in disease-ravaged countries. The same goes for ticks, which like mosquitoes, transmit deadly diseases. He also hopes to corral them using a similar attract-and-kill technique.

"I truly hate mosquitoes and ticks," he says. "Imagine: Maybe one day we will be able to go into our backyards or parks and not have to worry about being bothered by either of them."

*Mafra-Neto acknowledges funding from the U.S. Department of Agriculture, U.S. Department of Defense, the National Science Foundation and the National Institutes of Health.*

<http://bit.ly/2vu2tXo>

## **More than 99 percent of the microbes inside us are unknown to science**

### ***New survey suggests our bodies contain vastly more diverse microbes than previously understood***

A new survey of DNA fragments circulating in human blood suggests our bodies contain vastly more diverse microbes than anyone previously understood. What's more, the overwhelming majority of those microbes have never been seen before, let alone classified and named, Stanford researchers report August 22 in the Proceedings of the National Academy of Sciences.

"We found the gamut," said Stephen Quake, a professor of bioengineering and applied physics, a member of Stanford Bio-X and the paper's senior author. "We found things that are related to things people have seen before, we found things that are divergent, and we found things that are completely novel."

### **Searching for rejection**

The survey was inspired by a curious observation Quake's lab made while searching for non-invasive ways to predict whether an organ transplant patient's immune system would recognize the new organ as foreign and attack it, an event known as rejection. Ordinarily, it takes a tissue biopsy -- meaning a large needle jabbed into one's side and at least an afternoon in a hospital bed for observation -- to detect rejection.

The lab members figured there was a better way. In theory, they might be able to detect rejection by taking blood samples and looking at the cell-free DNA -- bits and pieces of DNA circulating freely in blood plasma - contained therein. Apart from fragments of a patient's DNA, those samples would contain fragments of the organ donor's DNA as well as a comprehensive view of the collection of bacteria, viruses and other microbes that make up a person's microbiome.

Over the course of several studies, the first of which was published in 2013, Quake, postdoctoral fellow Iwijn De Vlaminc, and others collected samples from 156 heart, lung and bone marrow transplant recipients, along with 32 pregnant women. (Pregnancy, like immunosuppressant drugs taken by transplant patients, also changes the immune system, albeit in ways both more complicated and less well understood.)

The results of those earlier studies suggested there were identifiable changes to the microbiomes of people with compromised immune systems and that positive tests for the organ donor's DNA were a good sign of rejection.

### **Something weirder**

But there was something else, too -- something weirder. Of all the non-human DNA fragments the team gathered, 99 percent of them failed to match anything in existing genetic databases the researchers examined.

With that in mind, Mark Kowarsky, a graduate student in Quake's lab and the paper's first author, set about characterizing all of that mystery DNA.

The "vast majority" of it belonged to a phylum called proteobacteria, which includes, among many other species, pathogens such as E. coli and Salmonella. Previously unidentified viruses in the torque teno family, generally not associated with disease but often found in immunocompromised patients, made up the largest group of viruses.

"We've doubled the number of known viruses in that family through this work," Quake said. Perhaps more important, they've found an

entirely new group of torque teno viruses. Among the known torque teno viruses, one group infects humans and another infects animals, but many of the ones the researchers found didn't fit in either group. "We've now found a whole new class of human-infecting ones that are closer to the animal class than to the previously known human ones, so quite divergent on the evolutionary scale," he said.

### **An unsurprising surprise?**

"I'd say it's not that baffling in some respects because the lens that people examined the microbial universe was one that was very biased," Quake said, in the sense that narrow studies often miss the bigger picture. For one thing, researchers tend to go deep in the microbiome in only one part of the body, such as the gut or skin, at a time. Blood samples, in contrast, "go deeply everywhere at the same time."

For another, researchers often focus their attention on just a few interesting microbes, "and people just don't look at what the remaining things are," Kowarsky said. "There probably are some interesting, novel things there, but it's not relevant to the experiment people want to do at that time."

It was by looking at blood samples in an unbiased way, Quake said, that led to the new results and a new appreciation of just how diverse the human microbiome is.

Going forward, Quake said, the lab hopes to study the microbiomes of other organisms to see what's there. "There's all kinds of viruses that jump from other species into humans, a sort of spillover effect, and one of the dreams here is to discover new viruses that might ultimately become human pandemics." Understanding what those viruses are could help doctors manage and track outbreaks, he said.

"What this does is it arms infectious disease doctors with a whole set of new bugs to track and see if they're associated with disease," Quake said. "That's going to be a whole other chapter of work for people to do."

<http://bit.ly/2w9Pb46>

## Less REM sleep tied to greater risk of dementia

*People who get less rapid eye movement (REM) sleep may have a greater risk of developing dementia*

MINNEAPOLIS - People who get less rapid eye movement (REM) sleep may have a greater risk of developing dementia, according to a new study published in the August 23, 2017, online issue of *Neurology*®, the medical journal of the American Academy of Neurology. REM sleep is the sleep stage when dreaming occurs.

There are five stages of sleep. Stage one is light sleep. Stage two is when the body begins to prepare for deeper sleep, including stages three and four. Stage five is REM sleep. During this dream stage, the eyes move rapidly and there is increased brain activity as well as higher body temperature, quicker pulse and faster breathing. The first REM stage occurs about an hour to an hour-and-a-half into sleep and then recurs multiple times throughout the night as the cycles repeat.

"Sleep disturbances are common in dementia but little is known about the various stages of sleep and whether they play a role in dementia risk," said study author Matthew P. Pase, PhD, of Swinburne University of Technology in Australia. "We set out to discover which stages of sleep may be linked to dementia and while we did not find a link with deep sleep, we did with REM sleep."

For the study, researchers looked at 321 people with an average age of 67 from Massachusetts who participated in The Framingham Heart Study. During that study, sleep cycles were measured for each participant. Researchers collected the sleep data and then followed participants for an average of 12 years. During that time, 32 people were diagnosed with some form of dementia and of those, 24 were determined to have Alzheimer's disease.

The people who developed dementia spent an average of 17 percent of their sleep time in REM sleep, compared to 20 percent for those who did not develop dementia. After adjusting for age and sex, researchers found links between both a lower percentage of REM sleep and a

longer time to get to the REM sleep stage and a greater risk of dementia. In fact, for every percent reduction in REM sleep there was a 9 percent increase in the risk of dementia. The results were similar after researchers adjusted for other factors that could affect dementia risk or sleep, such as heart disease factors, depression symptoms and medication use. Other stages of sleep were not associated with an increased dementia risk.

"Our findings point to REM sleep as a predictor of dementia," said Pase. "The next step will be to determine why lower REM sleep predicts a greater risk of dementia. By clarifying the role of sleep in the onset of dementia, the hope is to eventually identify possible ways to intervene so that dementia can be delayed or even prevented."

Limitations of the study include a small sample size. Studies on larger groups of people need to be done to confirm findings. There was also no data available on shift work among study participants, which can cause unusual sleep patterns and possibly lead to sleep disorders.

*The study was supported by the National Heart, Lung and Blood Institute, the National Institute on Aging and the National Institute for Neurological Disorders and Stroke.*

<http://bit.ly/2w9QUGs>

## Death rates from rheumatic heart disease falling since 1990

*But persistent disease remains in the world's poorest regions*

The risk of dying from rheumatic heart disease, a condition of damaged heart valves caused by bacterial infection that leads to rheumatic fever, has dropped around the world over the last 25 years, according to a new scientific study published today in *The New England Journal of Medicine*. However, progress on rheumatic heart disease remains uneven. In several regions that include some of the world's poorest countries, mortality from rheumatic heart disease has not appreciably declined since 1990. The number of individuals who were living with rheumatic heart disease had not declined, either.

"The persistence of rheumatic fever and rheumatic heart disease reflects the challenges many countries face in improving the social,

environmental, and economic conditions that lead to the disease." said Dr. Gregory A. Roth, senior author on the study, and Assistant Professor at the Institute for Health Metrics and Evaluation (IHME) at the University of Washington, and in the Division of Cardiology at the University of Washington School of Medicine. "It is a tragedy that, in 2016, rheumatic fever remains a serious health concern for so many people."

Rheumatic heart disease is a long-term consequence of untreated strep throat, which can be highly contagious, especially for children living in overcrowded and unsanitary settings. In susceptible individuals, untreated strep throat leads to rheumatic fever that damages heart valves over time. The symptoms of the heart condition can appear up to 10 or 20 years after the original infection and can disable or kill individuals during their prime working years. Pregnant women are also at very high risk. In most countries, progress - or lack of progress - in addressing social factors such as education, income, and access to health care has tracked closely with rheumatic heart disease.

The study, "Global, Regional, and National Burden of Rheumatic Heart Disease, 1990-2015," estimates 347,500 deaths from rheumatic heart disease in 1990 and 319,400 deaths in 2015, an 8% decrease.

The global age-standardized death rate for rheumatic heart disease decreased from 9.2 per 100,000 in 1990 to 4.8 per 100,000 in 2015, a reduction of 48%. Countries with the highest estimated numbers of deaths in 2015 were Indonesia (1.18 million), the Democratic Republic of the Congo (805,000), India, (119,100), China (72,600), and Pakistan (18,900). These five nations account for 73% of rheumatic heart disease deaths globally.

The highest estimated death rates - more than 10 per 100,000 - occurred in: the Central African Republic, Federated States of Micronesia, Fiji, India, Kiribati, Lesotho, Marshall Islands, Pakistan, Papua New Guinea, the Solomon Islands, and Vanuatu.

About 1% of school age children in these endemic countries have evidence of rheumatic heart disease, said Dr. David Watkins, lead

author on the study and an instructor of medicine in the Division of General Internal Medicine at the University of Washington School of Medicine.

"We have very cost-effective interventions that treat strep throat and prevent rheumatic fever and rheumatic heart disease from getting worse, but these children often don't have access to the care they need," Dr. Watkins said. As a result, their heart conditions usually get worse with age and lead to premature death. Many of these individuals could be saved by open-heart surgery to repair or replace damaged valves, but unfortunately in these countries access to advanced cardiac surgery care is very low."

"We also need better data on rheumatic heart disease prevalence and mortality," he said. "In order to track progress and devote adequate resources to prevention and early treatment, countries where rheumatic heart disease is endemic need stronger national surveillance systems and more studies on the prevalence of rheumatic heart disease, especially among adults."

The paper is based on the annual Global Burden of Disease Study (GBD), the world's largest health science enterprise, examining 400 diseases, injuries, and risk factors among all age groups in 195 countries. The GBD is convened by IHME and includes more than 2,500 scientists in 130 countries.

<http://bit.ly/2wDmv6D>

### **Antioxidant/zinc supplement cost saving and effective for degenerative eye disease**

***NHS should fund this for people with 'wet' age-related macular degeneration, say researchers***

A supplement that combines antioxidants with zinc and copper is a relatively inexpensive and effective means of halting the progression of a certain type of degenerative eye disease, concludes research published online in the British Journal of Ophthalmology.

Given the costs and side effects of the current range of drugs used to treat the 'wet' form of age related macular degeneration (nAMD), the

NHS should fund this treatment in people who already have the condition in one eye, say the researchers.

In 'wet' AMD, abnormal blood vessels grow underneath the retina. These vessels can leak fluid and blood, which can damage the macula—the part of the retina responsible for central vision.

But the drugs (anti-VEGF therapies) currently used to 'wet' AMD are expensive and have been linked to heightened risk of inflammation of the inside of the eye (endophthalmitis) and possibly stroke as well.

The researchers base their findings on data from the Age Related Eye Disease Study (AREDS) as well as UK treatment costs and AMD prevalence figures for people over the age of 55.

AREDS concluded that a daily supplement combining high dose antioxidants and zinc lowered the risk of developing 'wet' AMD after assessing the effectiveness of two types of supplement for treating people with early stage disease in one (category 4) or both (category 3) eyes.

Formulation 1 contained high doses of vitamins C and E, beta carotene, zinc and copper; in formulation 2, beta carotene was replaced with lutein and zeaxanthin, but the other constituents remained the same. Both formulations are commercially available.

The researchers applied a statistical approach (Markov Model) to all the data to predict outcomes in those given one or other supplement compared with those not given them.

Their analysis showed that both formulations are cost effective for treating patients with early stage 'wet' AMD, but they were more cost effective for those with the condition in just one eye.

Over the course of a lifetime, the researchers calculated that these patients would need nearly eight fewer injections of anti-VEGF therapies into their eye. This represents a cost saving to the NHS of nearly £3000 per patient, adding up to around £131 million a year.

And these patients would gain additional time lived without impaired vision, known as QALYs (10.59 compared with 10.43 for those not given the supplements).

"Given the burden and cost of treatment, prevention of nAMD seems, therefore, an attractive strategy to avoid the chronic and costly anti-VEG therapies and preserve visual function," write the researchers.

The beneficial costs and outcomes do assume that people with wet AMD in one eye would be highly motivated to keep on taking the supplements to stave off vision loss in the second eye, acknowledge the researchers.

While there would still be savings to be made by giving supplements to people with intermediate stage wet AMD in both eyes, the argument for funding them for people with the condition in one eye is extremely strong, they say.

"AREDS supplements are a dominant cost-effective intervention for category 4 AREDS patients, as they are both less expensive than standard care and more effective, and therefore should be considered for public funding," they conclude.

<http://bit.ly/2w9UWyZ>

## **Researchers link high levels of 'good' cholesterol with excessive mortality**

### ***The good cholesterol might not be as good as we think***

It has been accepted wisdom for many years that the more good cholesterol people have in their blood, the better. But the good cholesterol, also known as HDL, might not be as good as we think.

In any case, the results of a [new study from the University of Copenhagen](#) seriously contradict the assumption that high levels of HDL in the blood are only a good thing. The researchers have shown that people with extremely high levels of good cholesterol have a higher mortality rate than people with normal levels. For men with extremely high levels, the mortality rate was 106 per cent higher than for the normal group. For women with extremely high levels, the mortality rate was 68 per cent higher.

"These results radically change the way we understand 'good' cholesterol. Doctors like myself have been used to congratulating patients who had a very high level of HDL in their blood. But we

should no longer do so, as this study shows a dramatically higher mortality rate," says Børge Nordestgaard, Professor at the Department of Clinical Medicine and one of the authors of the study.

The researchers analysed data for 116,000 subjects from the Copenhagen City Heart Study and the Copenhagen General Population Study, in combination with mortality data from the Danish Civil Registration System. They have followed the subjects for an average of 6 years, and based the study on just over 10,500 deaths.

The researchers were able to calculate the mortality rate based on these deaths and medical information on the subjects. The results showed that men with extremely high HDL levels in the blood had a 106 per cent higher mortality rate than men with a normal HDL level. Among women, those with extremely high levels of HDL had a 68 per cent higher mortality rate than the normal group. Men in the next group, with very high levels, also had a 36 per cent higher mortality rate.

0.4 per cent of the men and 0.3 per cent of the women covered by the study had an extremely high level of HDL in their blood, and a further 1.9 per cent of the men had a very high level.

The study also found excessive mortality for people with extremely low levels of HDL in the blood. The people with medium levels of HDL in the blood had the lowest mortality. For men, this level was 1.9 mmol/L. For women, it was 2.4 mmol/L.

Earlier US studies have shown similar correlations between good cholesterol and excessive mortality among specific population groups, but this is the first time excessive mortality has been shown in the general population.

Professor Børge Nordestgaard, who also works as a consultant doctor at the Department of Clinical Biochemistry at Herlev and Gentofte Hospital, hopes the results can change our perception of HDL.

"It appears that we need to remove the focus from HDL as an important health indicator in research, at hospitals and at the general practitioner. These are the smallest lipoproteins in the blood, and

perhaps we ought to examine some of the larger ones instead. For example, looking at blood levels of triglyceride and LDL, the 'bad' cholesterol, are probably better health indicators," he notes.

The new study examines the statistical correlation between mortality and HDL levels. It therefore cannot explain why people with extremely high or low HDL levels have higher mortality.

*The study was conducted jointly by Dr Christian Medom Madsen and Dr Anette Varbo, and was funded by the Novo Nordisk Foundation and Chief Physician Johan Boserup and Lise Boserup's Fund. The study in the European Heart Journal is published in print on 23 August 2017.*

<http://bit.ly/2qcyGQL>

## **Exercise in a Pill? Scientists Move One Step Closer What if you could reap the benefits of exercise without moving a muscle?**

**By Sara G. Miller, Staff Writer | August 24, 2017 07:43am ET**

A new study from England has taken an important step toward understanding how the human body senses when it's exercising and developing a potential way to flip this "switch" without breaking a sweat.

But don't cancel your gym membership just yet: The new study was done in mice, and much more research is needed to explore the effects in humans.

During exercise, a person's heart rate increases, pumping more blood throughout the body. But this increased blood flow doesn't reach all parts of a person's body equally; more blood goes to a person's skeletal muscles and brain, and less goes to internal organs such as the stomach and intestines.

What wasn't clear, however, was how the body knew to divert blood from one part of the body to another during exercise, said senior study author David Beech, a professor of cardiovascular science at the University of Leeds in England.

In the new study, the researchers identified a protein in mice that appears to do just that: detect when exercise is happening and divert blood flow accordingly, Beech told Live Science.



The protein, called Piezo1, acts as an "exercise sensor," Beech said. It's found in the cells that line the inner parts of the blood vessels near the stomach and intestines. During exercise, the blood flows faster, and Piezo1 can sense this change in speed. In turn, the protein triggers the blood vessels near the digestive organs to constrict, so that less blood flows to this part of the body and more goes to the skeletal muscles and the brain, according to the study.

In the study, published today (Aug. 24) in the journal Nature Communications, the researchers compared the blood flow in normal mice with the blood flow of mice without the Piezo1 protein. During physical activity (in this case, running on a wheel), the blood vessels near the digestive organs didn't constrict in the mice without the protein. In addition, the mice that had the protein performed better physically than the mice without the protein.

### Use the force

Exercise plays an important role in a person's health, and a big question is whether this protein could contribute to these health benefits, Beech said. And, if that's the case, could scientists [develop a drug](#) that could activate the protein?

Beech and his team have already taken a step in that direction. In another part of the study, the researchers did experiments with a compound called "Yoda1" that interacted with the Piezo1 protein. (Yoda1 was given this name by a different group of scientists because it was known that the protein it interacted with had something to do with force, Beech added.)

In the experiments, which were conducted in lab dishes, Yoda1 appeared to turn on Piezo1, similar to the way increased blood flow would, the researchers found.

Now, they're working on making a form of the Yoda1 compound that they could give to mice, to see if it would have the same effects inside the animals' bodies, Beech said. In other words, the research could be an early step toward developing a drug that could mimic the [effects of exercise](#).

Although the new study was done in animals, Beech noted that human cells also have the Piezo1 protein.

"We know the mechanism is present in human" blood vessel cells, Beech said. And "we know that blood flow is restricted to the intestines in humans during exercise just like it is in mice," he said. The researchers would expect similar findings in humans, Beech said, but of course, that still needs to be studied in great detail.

<http://bit.ly/2wMyM7W>

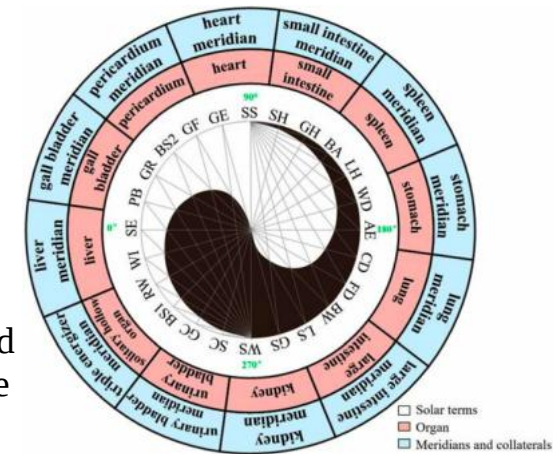
## Scientists develop modern Medical Terms to enhance precise Chinese Medicine

### *Applications of the Twenty-four Solar Terms lie in TCM and agriculture*

Besides agriculture, another important area for the applications of the Twenty-four Solar Terms (24-STs) lies in the traditional Chinese Medicine (TCM). In fact, along with the theories of the Vigourism, the Meridian Circuits, and the Yin-Yang, Five Primary Elements and Six Key Factors, the annual cycle of the 24-STs is considered as one of the principal foundations of the TCM.

*This is the interrelationships of the 24-STs, the human organs and the meridians.* ©Science China Press

Figure 1 illustrates the interrelationships of the STs, human organs and meridians. Within the inner circle is the so-called map of Yin and Yang, referring to two kinds of opposing states or vital energies, a concept used to explain the theory of unity of opposites relationship between things. While Yin would be lunar, dark, passive, cold, downward, contracting, and weak, Yang would be solar, bright, active,



hot, upward, expanding and strong. The changes between Yin and Yang cause everything to happen: Just as temperature changes from cold to hot, for example from Great Cold (GC) to Great Heat (GH) in terms of STs, forming a yearly variation of the seasonality.

A general philosophy of the TCM is the so-called "adaption of the human body to the universe", a crucial aspect of which is that the prevention and treatment of deceases should be performed in accordance with the evolution of natural environment including the 24-STs. In the clinical practice of the TCM, the occurrences of many deceases are found to be coincident with the timings of specific STs. The timing of performing the treatment during the year is therefore an important issue for maximizing its effectiveness.

In a companion work published in *SCIENCE CHINA Earth Sciences* by Chen and Shi (2017), based on over half a century of observational and reanalysis data, a modified calendric system, named the Twenty-four Medical Terms (24-MTs), has been established for mainland China following a systematic calibration and geographical adjustment of the classic 24-STs.

"A profound implication of the refined 24-MTs calendar is its potential contribution to reviving the traditional Chinese Medicine towards a precise modern medicine by emphasizing its core philosophy of viewing the human body itself and the nature as a whole", said the corresponding author of this article, Dr. Jie Shi, a senior pharmacologist at the Municipal Hospital of Qingdao.

An important aspect of precise Chinese Medicine is to find the best geographically dependent timing for performing a given treatment. As a common practice in TCM, curing a winter decease in summer requires a localized precise timing for the action.

"We have developed two maps of localized timings for the so-called Triple-Fu (TF) and Triple-Jiu (TJ) defined using a joint heat index of air temperature and relative humidity are created as an alternative to the two nationwide unified timings representing the warmest and

coldest periods of the year", said Prof. Ge Chen, a senior scientist at Ocean University of China.

As a result, TCM treatment like the TF-stick may have a location-specific time window to follow so as to achieve its optimal effectiveness in the framework of human-nature integration. Such a geographical adjustment is likely to make significant practical sense given that a TF time shift of one week is common in different regions of mainland China.

The two scholars also point out that, another unique contribution of the present study is the proposed concept and timing of peak spring and peak autumn, so as to provide a helpful guidance for practicing season related and geographically dependent precise health care in the context of "born in spring, grow in summer, harvest in autumn, and preserve in winter", which is a key ideology in the traditional Chinese Medicine.

*This research was funded by National Natural Science Foundation of China (No. 61361136001).*

Shi J, Chen G. 2017. From solar terms to medical terms (Part II): Some implications for traditional Chinese Medicine. *Science China Earth Sciences*, 60, doi: 10.1007/s11430-016-9060-5 <http://engine.scichina.com/doi/10.1007/s11430-016-9060-5>

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<http://bit.ly/2xiTII9>

## **Leprosy turns the immune system against itself, study finds**

### ***Leprosy turns a repair mechanism into one causing irreparable damage to nerve cells***

Leprosy hijacks our immune system, turning an important repair mechanism into one that causes potentially irreparable damage to our nerve cells, according to new research that uses zebrafish to study the disease. As such, the disease may share common characteristics with conditions such as multiple sclerosis.

Leprosy is an infectious disease that affects the skin and peripheral nerves and is caused by *Mycobacterium leprae* and, less commonly,

Mycobacterium lepromatosis. According to the World Health Organization, there has been a dramatic decrease in the global disease burden in the past few decades: from 5.2 million people with leprosy in 1985 to 176,176 at the end of 2015.

Despite the disease having been known about for thousands of years - many people will have first heard about it through references in the Bible -- very little is understood about its biology. This is in part because the bacteria are difficult to grow in culture and there are no good animal models: *M. leprae* can grow in the footpads of mice, but do not cause nerve damage; the disease causes nerve damage in armadillos, but these animals are rarely used in research.

Now, an international team led by researchers at the University of Cambridge, UK, and the University of Washington, the University of California Los Angeles and Harvard University, USA, have used a new animal model, the zebrafish, to show for the first time how *M. leprae* damage nerves by infiltrating the very cells that are meant to protect us. Zebrafish are already used to study another species of mycobacteria, to help understand tuberculosis (TB).

Scientists have previously shown that the nerve damage in leprosy is caused by a stripping away of the protective insulation, the myelin sheath, that protects nerve fibres, but it was thought that this process occurred because the bacteria got inside Schwann cells, specialist cells that produce myelin.

In new research published today in the journal *Cell*, researchers used zebrafish that had been genetically modified so that their myelin is fluorescent green; young zebrafish are themselves transparent, and so the researchers could more easily observe what was happening to the nerve cells. When they injected bacteria close to the nerve cells of the zebrafish, they observed that the bacteria settled on the nerve, developing donut-like 'bubbles' of myelin that had dissociated from the myelin sheath.

When they examined these bubbles more closely, they found that they were caused by *M. leprae* bacteria inside of macrophages - literally

'big eaters', immune cells that consume and destroy foreign bodies and unwanted material within the body. But, as is also often the case with TB, the *M. leprae* was consumed by the macrophages but not destroyed.

"These 'Pac-Man'-like immune cells swallow the leprosy bacteria, but are not always able to destroy them," explains Professor Lalita Ramakrishnan from the Department of Medicine at the University of Cambridge, whose lab is within the Medical Research Council's Laboratory of Molecular Biology. "Instead, the macrophages -- which should be moving up and down the nerve fibre repairing damage -- slow down and settle in place, destroying the myelin sheath."

Professor Ramakrishnan working with Dr Cressida Madigan, Professor Alvaro Sagasti, and other colleagues confirmed that this was the case by knocking out the macrophages and showing that when the bacteria sit directly on the nerves, they do not damage the myelin sheath.

The team further demonstrated how this damage occurs. A molecule known as PGL-1 that sits on the surface of *M. leprae* 'reprograms' the macrophage, causing it to overproduce a potentially destructive form of the chemical nitric oxide that damages mitochondria, the 'batteries' that power nerves.

"The leprosy bacteria are, essentially, hijacking an important repair mechanism and causing it to go awry," says Professor Ramakrishnan.

"It then starts spewing out toxic chemicals. Not only does it stop repairing damage, but it creates more damage itself."

"We know that the immune system can lead to nerve damage - and in particular to the myelin sheath - in other diseases, such as multiple sclerosis and Guillain-Barré syndrome," says Dr Cressida Madigan from the University of California, Los Angeles. "Our study appears to place leprosy in the same category of these diseases."

The researchers say it is too early to say whether this study will lead to new treatments. There are several drugs being tested that inhibit the production of nitric oxide, but, says Professor Ramakrishnan, the key

may be to catch the disease at an early enough stage to prevent damage to the nerve cells.

"We need to be thinking about degeneration versus regeneration," she says. "At the moment, leprosy can be treated by a combination of drugs. While these succeed in killing the bacteria, once the nerve damage has been done, it is currently irreversible. We would like to understand how to change that. In other words, are we able to prevent damage to nerve cells in the first place and can we additionally focus on repairing damaged nerve cells?"

*The research was funded by the National Institutes of Health, the Wellcome Trust, and the AP Giannini Foundation.*

*Madigan, CA et al. A Macrophage Response To Mycobacterium leprae Phenolic Glycolipid Initiates Nerve Damage In Leprosy. Cell; 24 Aug 2017; DOI: 10.1016/j.cell.2017.07.030*

*A video illustrating the research is available at:*

<https://www.youtube.com/watch?v=oXxWvHCdx7E&feature=youtu.be>

<http://bit.ly/2wuRiSM>

## **New dinosaur discovery suggests new species roosted together like modern birds**

### ***New remains suggest an entirely unknown behavior for bird-like dinosaurs about 70 million years ago***

CALGARY, ALBERTA - The Mongolian Desert has been known for decades for its amazing array of dinosaurs, immaculately preserved in incredible detail and in associations that give exceedingly rare glimpses at behavior in the fossil record. New remains from this region suggest an entirely unknown behavior for bird-like dinosaurs about 70 million years ago. At least some dinosaurs likely roosted together to sleep, quite possibly as a family, much like many modern birds do today. Gregory Funston, Ph.D. Candidate at the University of Alberta, will present the team's research findings at the annual meeting of the Society of Vertebrate Paleontology, held this year in Calgary, Alberta (Canada) on Friday, Aug. 25th at 2:30pm.

This new evidence for dinosaur roosting stems from a confiscated fossil block that was illegally exported from Mongolia, which preserved the amazing remains of three juvenile dinosaurs known as

oviraptorids (part of the bird line of dinosaur evolution). These three dinosaurs represent the same species that were roughly the same age, preserved in a sleeping posture, so close to each other that they would have been touching in life. Known as "communal roosting", this behavior is seen in many birds today including chickens and pigeons. The specimen luckily made its way into the hands of researchers currently led by Gregory Funston of the University of Alberta, along with his advisor Dr. Philip Currie (also of the University of Alberta) and the Institute of Paleontology and Geology of Mongolia (based in Ulaanbaatar). Regarding the finding, Funston said, "It's a fantastic specimen. It's rare to find a skeleton preserved in life position, so having two complete individuals and parts of a third is really incredible".

The three juvenile oviraptors had several features that indicated they belonged to a whole new species. Other fossils found in Mongolia also seem to belong to this new species, and further flesh out the life history of these animals. The notable head crest is present even at a young age, but the dinosaurs would have had gradually shorter tails as they aged, and some of their bones fused across their lifetime. Their head crests and tails have been argued to represent sexual display features used in mating, somewhat similar to modern peacocks or turkeys. Funston added "The origins of communal roosting in birds are still debated, so this specimen will provide valuable information on roosting habits in bird-line theropods".

<http://bit.ly/2wzOVxZ>

## **HKBU clinical observation finds efficacy rate of over 70 percent in Chinese medicine treatment of chronic renal failure**

### ***Type of Chinese medicine treatment is effective in improving the clinical symptoms of CRF patients and helps postpone the deterioration of renal function***

The School of Chinese Medicine (SCM) of Hong Kong Baptist University (HKBU) recently conducted a clinical observation on

Chinese medicine treatment of chronic renal failure (CRF). The results indicates that a particular type of Chinese medicine treatment which nourishes kidney, removes blood stasis and turbidity is effective in improving the clinical symptoms of CRF patients and helps postpone the deterioration of renal function. The overall efficacy rate of such treatment is 72.7%.

CRF is caused by multiple chronic kidney diseases or systemic diseases that affect the kidneys, leading to chronic progressive damage to the kidneys. CRF patients will have decreased renal function, in which the kidneys cannot maintain the metabolism of waste and resulting in disorders of electrolyte and acid-base balance. In addition, the kidneys lose the secretion and regulation of hormonal metabolism and other basic functions, and may lead to azotemia, metabolic disorders and other clinical symptoms due to the damage of different systems. When the glomerular filtration rate of CRF patients is less than 60 ml/min and serum creatinine is higher than the upper limit of normal range, the functional unit of kidney has been damaged more than 50%, suggesting that there is the presence of kidney damage.

Mr Cai Xunyu, a visiting scholar of the SCM Clinical Division at HKBU, conducted a clinical observation of 33 patients attending HKBU's Chinese medicine clinics for treatment of CRF from March 2013 to August 2017. The study aimed to find the impact of this particular Chinese medicine treatment on the patients' serum creatinine, glomerular filtration rate and their clinical symptoms before and after the treatment.

Of the 33 patients, 19 were male and 14 were female with ages ranging from 18 to 70. All the patients were in the CRF diagnosis stage of three to four with serum creatinine less than 707umol/l. The observation indicated that the overall efficacy rate of the treatment for CRF was 72.7%, with seven patients showing obvious improvement, 17 having general improvement while nine showed no improvement. A better therapeutic effect was observed in patients who were in the diagnosis stage of 3a (serum creatinine <200umol/l). During the

observation, 16 out of 20 patients in this group recorded a decrease in their serum creatinine with an efficacy rate of 80%, and five of them had an upturn from stage 3a to 2, meaning that renal function was recovering from a decompensatory stage to a compensatory stage.

This particular treatment is a prescription of Chinese herbs such as *Herba Epimedii*, *Isaria Cicadae*, *Radix Salviae Miltiorrhizae*, *Rhizoma Ligustici Chuanxiong*, and *Radix et Rhizoma Rhei*. They work well in supplementing yang and warming the kidney, protecting the patients' kidneys and liver, promoting regeneration of blood, and removing blood stasis, turbidity and detoxification.

Mr Cai explained that the Chinese medicine treatment, with the application of specific kinds of Chinese herbs to tonify kidney and remove blood stasis and turbidity, coheres with the traditional Chinese medicine principle of combining enhancement of physical fitness, eliminating pathogenic factors and tackling both the principal and subordinate symptoms. Through invigorating the spleen and kidneys, such treatment helps to lower a patient's serum creatinine and urea, eliminate the factors promoting the progression of CRF, prevent further damage of the body from the toxins, increase the glomerular filtration rate, stabilise kidney function and reduce the urine protein and red blood cells. As a result, the patient's daily life quality is enhanced by having a better appetite and healthier body with an improvement in clinical symptoms. This also helps to delay the progression of CRF and the time for patient undergo dialysis.

Mr Cai said that chronic glomerulonephritis was the primary cause of CRF, with 13 cases. He therefore reminded people to have regular urine tests, especially after recovery from a cold, fever, tonsillitis and boils. If the urine appears with protein or red blood cells, patients should seek Chinese medicine treatment as early as possible to avoid progression of disease and damage of kidneys. For patients already with renal dysfunction, they should urge to seek professional diagnosis and treatment from registered Chinese medicine practitioners. The treatment of early CRF with traditional Chinese

medicine has an irreplaceable advantage. Once the condition changes into renal failure and even stage of uremia, the vast majority of patient's kidney units have been damaged, and it is more difficult to reverse.

<http://bit.ly/2wJqChy>

### **Physical activity in midlife not linked to cognitive fitness in later years, long-term study shows**

#### ***Activity in later life improved short-term cognitive fitness***

Johns Hopkins University Bloomberg School of Public Health

A study led by Johns Hopkins Bloomberg School of Public Health researchers that tracked activity levels of 646 adults over 30 years found that, contrary to previous research, exercise in mid-life was not linked to cognitive fitness in later years.

The finding suggests that physical activity may not help maintain cognitive function, or help avoid or delay the onset of the debilitating conditions like dementia and Alzheimer's. Alzheimer's affects as many as 30 million, mostly older people throughout the world. With no known treatment or cure, researchers are trying to identify measures that might help delay Alzheimer's onset or limit its reach.

The study, which appears online in the Journal of Alzheimer's Disease, did find that activity levels among study participants in the later years were associated with high cognitive function two years later. This supports earlier research findings that exercise may help to maintain cognitive fitness in the short term.

"This study reminds us that physical activity has all sorts of benefits for people, including promoting cardiovascular health, managing optimal weight levels and maintaining bone and muscle mass," says Alden L. Gross, assistant professor in the Bloomberg School's Department of Epidemiology. "Unfortunately it is too early for us to say the same about exercise and Alzheimer's, especially as a possible long-term preventive measure."

There is no known treatment or cure for Alzheimer's or dementia, syndromes that involves declining memory, confusion and eventually

limited ability to perform daily tasks. To date, there are no preventive measures, such as physical exercise, brain games or a diet regimen, that have been proven to help delay or altogether prevent its onset. In the US, an estimated five million adults are currently living with Alzheimer's, according to the Centers for Disease Control and Prevention (CDC), and the CDC predicts that this number will rise to 14 million by 2050.

The researchers undertook the study because of a growing consensus that physical activity levels helps prevent Alzheimer's, however much of the evidence for this thinking is based on cross-sectional studies that compare responses from one group of participants with another at a given point in time or within a very short duration, typically several years. Such studies can be valuable for confirming associations, or links, but not at establishing actual causation because of what is known as reverse causation: it is possible that people who eventually develop dementia may reduce their physical activity and exercise as dementia advances. That's where longitudinal studies, which look at the same group of participants over a long time, are more helpful.

The researchers used data from the Johns Hopkins Precursors study, which registered students studying at Johns Hopkins School of Medicine between 1948 and 1964 and tracked them with annual questionnaires about their overall health. The researchers note that the cohort's homogeneity - students at a selective medical school - meant that any differences in physical activity and later cognitive function could not be explained by other differences among participants.

The median age for study participants was 46 years in 1978 and 77 years in 2008. Every several years, the questionnaire asked about exercise, physical activity and physical limitations. The researchers used responses from 1978 through 2008 from 646 participants (598 men, 48 women) to calculate so-called metabolic equivalents, which quantify physical activity levels. Participants were also asked whether they regularly exercise to a sweat.

The team administered cognitive tests in 2008, and, using participants' medical records, scored for dementia through 2011. The researchers identified 28, or 4.5 percent of the cohort, to have Alzheimer's.

No physical activity measure in mid-life was associated with late-life cognitive fitness or onset of dementia. The study confirmed findings of other cross-sectional studies, that higher levels of physical activity and exercise measured close in time to the cognitive testing were associated with better cognitive functioning. The authors also looked at whether patterns of change in physical activity levels over the life span were associated with cognitive health and found no relationships. The idea that exercise might play a role in preventing or limiting Alzheimer's makes sense, the researchers say, because physical activity, at least in mouse models, has shown less accumulation of B-amyloid plaques, which are thought to play a role in dementia, including Alzheimer's. In addition, physical activity improves blood flow to the brain, which is linked to better cognitive performance. This may explain why studies find that exercise may contribute to cognitive fitness in the short term.

"These findings have implications for intervention work moving forward," says Gross. "We still need to focus on causes and mechanisms of Alzheimer's and dementia, since we don't yet know which preventive measures may or may not work. For now, when I speak in the community about Alzheimer's, I find that people take some relief in understanding that there wasn't anything that anyone might have done to avoid a loved one developing Alzheimer's. Of course, the goal for researchers is to identify factors that may help older people maintain their cognitive function into their later years. More long-term studies like the Precursors study are needed."

*"Physical Activity in Midlife is not Associated with Cognitive Health in Later Life Among Cognitively Normal Older Adults was written by Alden L. Gross, Haidong Lu, Lucy Meoni, Joseph J. Gallo, Jennifer A. Schrack and A. Richey Sharrett. The research was supported by from the National Institutes of Health (grants AG01760, DK02856 and DK07732) and the National Institute on Aging (grants K01-AG050699 and K01-AG048765).*

<http://bit.ly/2iydZzu>

## Sine o' the Times: Babylonian Tablet Holds Oldest Evidence of Trigonometry

***Scientists recently decoded a clay tablet from ancient Babylonia that dates to around 3,700 years ago, and found that it contains the oldest trigonometric table in the world.***

**By Mindy Weisberger, Senior Writer | August 24, 2017 03:59pm ET**

The tablet, discovered in the early 1900s and first interpreted in 1945, has long fascinated mathematics scholars, but they were puzzled by its description of triangles, which researchers recently linked to a type of trigonometry.

These ancient mathematical inscriptions predate the earliest known evidence of trigonometry - thought to have originated around 120 B.C. with Greek astronomer Hipparchus - by approximately 1,000 years, the researchers reported in a new study.



***Researchers offer a new angle on interpreting mathematical inscriptions on a very old tablet.*** UNSW

This finding suggests that the Babylonians, not the ancient Greeks, were the first to study trigonometry — the mathematics of triangles — perhaps using it in architectural calculations for constructing pyramids, temples and palaces, the study authors wrote.

The tablet, which measures 5 inches (12.7 centimeters) long and 3.5 inches (8.8 cm) wide, is known as Plimpton 322, named for its owner, American philanthropist George Arthur Plimpton, who purchased the artifact in 1922 from archaeologist and antiquities dealer Edgar Banks. Banks — the real-life inspiration for the adventure-seeking archaeologist movie character Indiana Jones — discovered the clay object in Iraq. Similarities in its writing style to that on other Babylonian tablets enabled experts to date it to between 1822 B.C.

and 1726 B.C., around the time that King Hammurabi ruled [the Babylonian Empire](#).

Experts interpreted the 15 rows of characters written in four columns on the tablet as descriptions of 15 triangles forming right angles, with their angles of inclination decreasing incrementally, the study authors wrote.

About 70 years ago, researchers determined that the notations on the tablet represented a special numerical pattern known as Pythagorean triples, a grouping of three positive integers, study co-author David Mansfield, a researcher with the School of Mathematics and Statistics at the University of New South Wales in Sydney, said in a statement.

"The huge mystery, until now, was its purpose — why the ancient scribes carried out the complex task of generating and sorting the numbers on the tablet," Mansfield said.

### A new angle

[Trigonometry](#) analyzes the relationships between the sides and angles of triangles; it is intrinsic to geometry and plays an important role in other branches of mathematics. The study authors expanded on prior research suggesting that Plimpton 322 was broken and incomplete, and they determined that there were originally six columns of figures on the tablet. Relationships between numbers in the completed table would have represented a novel type of trigonometry — one that relied on ratios instead of angles and circles, according to the study.

Thousands of years ago, [mathematicians in Babylonia](#) used a base 60 numerical system rather than the base 10 system that forms the foundation of modern arithmetic. In the study, the authors used the ancient base 60 system to demonstrate how scribes would have arrived at the numbers that were chiseled on Plimpton 322.

"The tablet not only contains the world's oldest trigonometric table; it is also the only completely accurate trigonometric table, because of the very different Babylonian approach to [arithmetic and geometry](#)," Mansfield said.

The simplicity and accuracy of this once-lost form of Babylonian trigonometry "has clear advantages" over modern trigonometry, study co-author Norman Wildberger, an associate professor in the School of Mathematics and Statistics at the University of New South Wales in Sydney, said in the statement.

Archaeologists have uncovered numerous tablets produced during the time of the Babylonian Empire, but very few of them have been examined in detail. This study's findings hint that these understudied artifacts from a long-dead empire could hold exciting discoveries, not only for understanding the [history of mathematics](#) but also for enhancing how math is studied today, Wildberger explained.

"It opens up new possibilities not just for modern mathematics research, but also for mathematics education," he said. "The mathematical world is only waking up to the fact that this ancient but very sophisticated mathematical culture has much to teach us."

The findings were published online today (Aug. 24) in the journal *Historia Mathematica*.

<http://wb.md/2vAaej>

## Seizures, Vomiting, Fear of Dying: The Threat of Hypoglycemia

### Patients With Diabetes Explain How They Experience Hypoglycemia

Anne L. Peters, MD August 24, 2017

As a physician without diabetes, I often fail to understand the experience my patients have of living with diabetes. A real part of the experience of giving insulin is the fear of hypoglycemia.

As a physician, I'm judged on how my patients do with their A1c targets. I always want people to be at less than 7% so that they do not get horrible complications. But day in and day out, patients have to live with the overarching concern of being too low. That can happen anytime, day or night. A patient can go too low if they misjudge insulin by maybe a unit or two, eat too little, or exercise too much.



Increasingly, hypoglycemia is becoming an endpoint. I'm part of a group that consists of the [Endocrine Society](#), the [JDRF](#), and others that is considering including hypoglycemia in clinical trials outcomes and in the ways we monitor our patients.

I asked one of my patients to make a video of four other patients discussing what they feel like when experiencing hypoglycemia. I think their voices are much stronger than anything I can say about hypoglycemia, because it shows you how much they worry about it and how much it impacts their life in real time.

### **'The Deal With Lows'**

**Patient 1:** I hate feeling low. Feeling low is one of the worst feelings in the world for me. It's scary.

**Patient 2:** It feels awful. It just feels like the worst thing.

**Patient 3:** I feel like I'm empty inside. I just want to lie down, curl into a ball, and go to sleep. And I hope that when I wake up, everything is fine and I'll feel better.

**Patient 4:** I don't feel like myself. I almost feel like I'm having an out-of-body experience.

**Patient 2:** I don't think clearly. I can't always make good judgments for myself. I get sidetracked. I get confused. I start panicking.

**If I die tomorrow from a low blood sugar, who cares what my A1c is?**

**Patient 1:** I get angry when I'm low. When I was younger, I'd be in denial. Close friends would tell me I was low based on my symptoms. A couple of times I threw glucose tablets at them, saying that I wasn't.

**Patient 3:** My brain starts to panic. I shake a lot, and I feel like I'm in the desert trying to crawl to the fridge to get something to survive, I guess.

**Patient 4:** You don't know what's going to happen once you're going low, and I think that's the scariest part.

**Patient 1:** I go low during work pretty often, because I'm always on my feet. I can't just go in the back, have sugar, and get right back out on the floor and start serving again. It's embarrassing. No, I need

longer. I know I just had three sugar tablets, but I need about 20 minutes before I can get back to work. You almost feel like a liability.

**Patient 3:** I'll wait the 15 minutes and my blood sugar recuperates, but my body does not at all. That feeling of still not caring and not wanting to do anything can last up to an hour after being low.

**Patient 4:** Sometimes after you get low and fix yourself, you go high. You correct from going high and then you go low again. I feel like when I go low, I tend to go up and down for the rest of the day.

**Patient 2:** It's tough for me to say how often I think about how scary and how bad a low can be—how life-threatening it can be.

**Patient 3:** I got out of the show and almost keeled over. I thought I was going to pass out. I sat on the ground in the middle of the queue and people just walked by me. My friend ran to the concessions and bought like five bottles of orange juice and just kept feeding them to me. It was a panic moment—like, "Oh, my God. I didn't know that this was actually a thing."

**Patient 1:** I've probably had five seizures in my sleep. I somehow wake up from them. I'll wake up and be able to tell that I just had a seizure. It's so hard. I know what's happening. I know I need juice, but my head is telling me how much easier it would be to close my eyes and just relax.

**Patient 4:** I had three juice boxes. That's the last thing that I remember. I must have passed out because right when I woke up, I immediately ran to the bathroom and threw up.

**Patient 2:** I would purposely keep my blood sugar at a higher level before going to bed, even though I knew having those higher blood sugars put me at greater risk for a higher A1c and complications down the road. I didn't care. If I die tomorrow from a low blood sugar, who cares what my A1c is? Having a blood sugar of 200 at bed rather than 100 gave me the peace of mind to think, "Okay, at least I know I'll wake up tomorrow."

*Any views expressed above are the author's own and do not necessarily reflect the views of WebMD or Medscape.*

<http://bit.ly/2wSK3DP>

## Monkeys can see faces in inanimate things, just like us

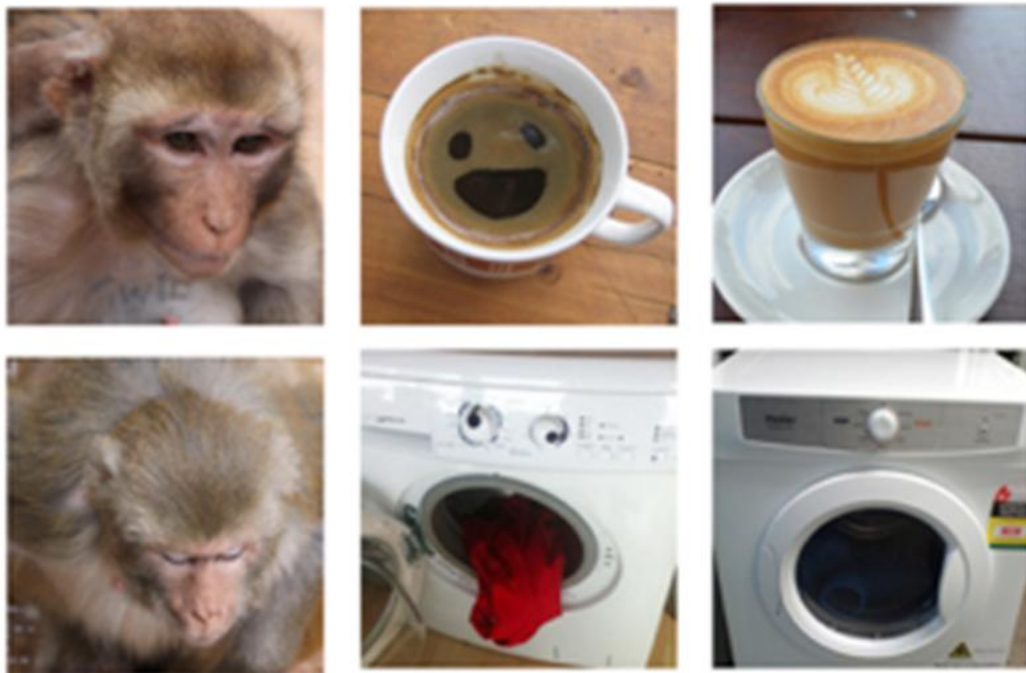
Have you ever seen the [Virgin Mary in your grilled cheese](#)? Or a screaming face inside a bell pepper?

By Helen Thomson

Seeing faces in inanimate objects is a common phenomenon. Now it seems that we're not alone in experiencing it – monkeys do too.

Pareidolia is the scientific term for erroneously perceiving faces where none exist. Other examples including [seeing “ghosts” in blurry photos](#) and the [man in the moon](#).

To investigate whether pareidolia was a uniquely human experience, [Jessica Taubert](#) at the US National Institute of Mental Health in Maryland and her colleagues trained five rhesus macaques to stare at pairs of photos. Each photo showed either an inanimate object that prompts pareidolia in humans, an equivalent object that doesn't, or the face of a monkey (below).



We already knew that both people and monkeys will look longer at images of faces than other things. So the team presented each of the photos in every possible pairing – 1980 in all – and measured the time the monkeys spent looking at each.

The monkeys did indeed seem to succumb to pareidolia – they spent more time looking at illusory faces than the non-illusory photos they were paired with.

Interestingly, they also spent more time looking at the illusory faces than the monkey faces, perhaps because they spent longer studying these more unusual “faces”, or because they tend to dislike holding the gaze of another monkey.

Examining the eye gaze patterns of the monkeys, the team found that they frequently fixated on the “eye” and “mouth” regions of the false faces, which is also how people behave when viewing real faces.

[Vincent Reid](#), a psychologist at Lancaster University, UK, says he is not surprised by the finding because rhesus monkeys are very social animals. “Just like humans, they rely on facial information for communicative purposes.”

But why do we – and monkeys – so often perceive faces where there are none?

Our brain is primed to see faces from an early age. Babies can recognise a face while still in the womb – scans show that when dots of light are shone through the skin, [fetuses preferentially turn to look at patterns that resemble faces](#), but ignore random shapes.

Being able to quickly spot and interpret a face can give vital information about whether a social group is friendly or hostile. But sometimes we are too good at spotting faces, seeing [Jesus in a jar of Marmite](#).

The fact that monkeys also easily perceive false faces underscores the biological advantage for social animals to preferentially detect faces in the environment. “It shows how deeply ingrained it is in humans,” says Reid.

Journal reference: *Current Biology*, [DOI: 10.1016/j.cub.2017.06.075](https://doi.org/10.1016/j.cub.2017.06.075)

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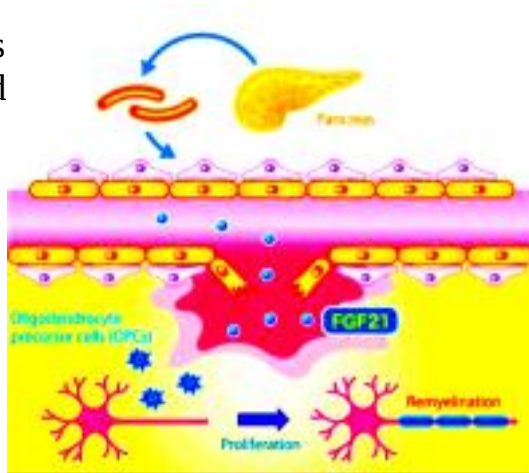
## The pancreas provides a potential drug candidate for brain disease

### *Fibroblast growth factor 21 promotes remyelination in mice and may be a promising key molecule for treating demyelinating diseases*

Osaka, Japan - Brain functions are maintained by the neural network.

Neural network is formed by the connection between the neurite, and this connection is supported by the wrapping of myelin.

Demyelination is detected in the patients of several diseases, such as multiple sclerosis, and is associated with neurological dysfunctions. A new study in The Journal of Clinical Investigation by scientists at Osaka University shows that fibroblast growth factor (FGF) 21 promotes remyelination in mice and may be a promising key molecule for treating demyelinating diseases.



**Remyelination is promoted by peripheral FGF21.** Osaka University

In normal development, oligodendrocyte precursor cells (OPCs) differentiate into oligodendrocytes, which are required for myelination. OPCs will proliferate around the lesions of demyelination after injury and contribute to spontaneous remyelination, but the molecular mechanism of OPCs proliferation is not fully clarified. Osaka University Associate Professor Rieko Muramatsu focused on the blood leakage around demyelinating lesion. "Factors in the blood cannot reach the normal brain because central nervous system has blood-brain barrier. In demyelination diseases like multiple sclerosis, the blood-brain barrier around the lesion is disrupted," she said.

Muramatsu suspected that with the breach, factors from peripheral organs secreted into the blood could now reach the brain.

To test her hypothesis, "We disrupted the vascular barrier and myelin structures in mice by injecting Lysophosphatidylcholine (LPC). We looked for circulating factors that promote OPCs proliferation and found FGF21 as a candidate," she said.

FGF21 is secreted by the pancreas.

Mice treated with LPC showed high levels of FGF21 around demyelinated lesions leading to remyelination. This was not the case in mutant mice that could not express FGF21. Other mice that received direct administration of FGF21 to demyelinated lesions caused by LPC injection also showed increased remyelination and better recovery of neurological function.

In addition, the researchers found OPCs expressed higher levels of  $\beta$ -klotho, co-receptor for FGF21, following LPC injection. Without this expression, FGF21 could not promote remyelination.

"FGF21 is known to regulates metabolism, but its effects on OPC proliferation were unexpected," said Muramatsu.

The results suggest that FGF21 has therapeutic potential for demyelinating diseases. FGF21 analogs are already being used for clinical studies on diabetes, which means its development for remyelination could go faster than had it been an untested compound.

"There are many drugs that inhibit demyelination, but none that promote remyelination. FGF21 is a new candidate that deserves more testing. The most important finding is that we show the peripheral milieu promotes central nervous system remyelination."

<http://bit.ly/2viZEgq>

## Dancing can reverse the signs of aging in the brain

### *A comparison of 2 different fitness routines shows that both can have an anti-aging effect on the brain in the elderly, but only dancing gives rise to a measurable difference in behavior*

As we grow older we suffer a decline in mental and physical fitness, which can be made worse by conditions like Alzheimer's disease. A new study, [published in the open-access journal Frontiers in Human Neuroscience](#), shows that older people who routinely partake in

physical exercise can reverse the signs of aging in the brain, and dancing has the most profound effect.

"Exercise has the beneficial effect of slowing down or even counteracting age-related decline in mental and physical capacity," says Dr Kathrin Rehfeld, lead author of the study, based at the German center for [Neurodegenerative](#) Diseases, Magdeburg, Germany. "In this study, we show that two different types of physical exercise (dancing and endurance training) both increase the area of the brain that declines with age. In comparison, it was only dancing that led to noticeable behavioral changes in terms of improved balance."

Elderly volunteers, with an average age of 68, were recruited to the study and assigned either an eighteen-month weekly course of learning dance routines, or endurance and flexibility training. Both groups showed an increase in the hippocampus region of the brain. This is important because this area can be prone to age-related decline and is affected by diseases like Alzheimer's. It also plays a key role in memory and learning, as well as keeping one's balance.

While previous research has shown that physical exercise can combat age-related brain decline, it is not known if one type of exercise can be better than another. To assess this, the exercise routines given to the volunteers differed. The traditional fitness training program conducted mainly repetitive exercises, such as cycling or Nordic walking, but the dance group were challenged with something new each week.

Dr Rehfeld explains, "We tried to provide our seniors in the dance group with constantly changing dance routines of different genres (Jazz, Square, Latin-American and Line Dance). Steps, arm-patterns, formations, speed and rhythms were changed every second week to keep them in a constant learning process. The most challenging aspect for them was to recall the routines under the pressure of time and without any cues from the instructor."

These extra challenges are thought to account for the noticeable difference in balance displayed by those participants in dancing group. Dr Rehfeld and her colleagues are building on this research to trial

new fitness programs that have the potential of maximizing anti-aging effects on the brain.

"Right now, we are evaluating a new system called "Jymmin" (jamming and gymnastic). This is a sensor-based system which generates sounds (melodies, rhythm) based on physical activity. We know that dementia patients react strongly when listening to music. We want to combine the promising aspects of physical activity and active music making in a feasibility study with dementia patients."

Dr Rehfeld concludes with advice that could get us up out of our seats and dancing to our favorite beat.

"I believe that everybody would like to live an independent and healthy life, for as long as possible. Physical activity is one of the lifestyle factors that can contribute to this, counteracting several risk factors and slowing down age-related decline. I think dancing is a powerful tool to set new challenges for body and mind, especially in older age."

This study falls into a broader collection of research investigating the [cognitive and neural effects of physical and cognitive activity across the lifespan](#).

<http://bit.ly/2whj9Da>

### **Stem cell treatment for children with spina bifida helps dogs first**

***English bulldog puppies are first patients successfully treated with a combination of surgery and stem cells to help preserve lower-limb function in children with spina bifida***

August 25, 2017 by Karen Finney

A pair of English bulldog puppies are the first patients to be successfully treated with a unique therapy—a combination of surgery and stem cells—developed at the University of California, Davis, to help preserve lower-limb function in children with spina bifida.

Because dogs with the birth defect frequently have little control of their hindquarters, they also have little hope for a future. They are typically euthanized as puppies.

At their postsurgery re-check at 4 months old, however, the siblings, named Darla and Spanky, showed off their abilities to walk, run and play to their doctor, veterinary neurosurgeon Beverly Sturges.

"The initial results of the surgery are promising, as far as hind limb control," said Sturges. "Both dogs seemed to have improved range of motion and control of their limbs." The dogs have since been adopted, and continue to do well at their home in New Mexico.

### **A major step toward curing spina bifida**

Spina bifida occurs when spinal tissue improperly fuses in utero, causing a range of cognitive, mobility, urinary and bowel disabilities in about 1,500 to 2,000 children born in the U.S. each year. The dogs' procedure, which involved surgical techniques developed by fetal surgeon Diana Farmer of UC Davis Health together with a cellular treatment developed by stem cell scientists Aijun Wang and Dori Borjesson, director of the university's Veterinary Institute for Regenerative Cures, represents a major step toward curing [spina bifida](#) for both humans and dogs.

Farmer pioneered the use of surgery prior to birth to improve brain development in children with spina bifida. She later showed that prenatal surgery combined with human placenta-derived mesenchymal stromal cells (PMSCs), held in place with a cellular scaffold, helped research lambs born with the disorder walk without noticeable disability.

Sturges wanted to find out if the surgery-plus-stem-cell approach could give dogs closer-to-normal lives along with better chances of survival and adoption. At 10-weeks old, Darla and Spanky were transported from Southern California Bulldog Rescue to the UC Davis veterinary hospital, where they were the first dogs to receive the treatment, this time using canine instead of human PMSCs.

Another distinction for Darla and Spanky is that their treatment occurred after birth, since prenatal diagnosis of spina bifida is not performed on dogs, Sturges explained. The disorder becomes apparent

between 1 and 2 weeks of age, when puppies show hind-end weakness, poor muscle tone, incoordination and abnormal use of their tails.

### **A unique environment for collaborative research**

UC Davis is the only place where this type of cross-disciplinary, transformational medicine could happen, according to Farmer.

"It's rare to have a combination of excellent medical and veterinary schools and strong commitment to advancing stem cell science at one institution," she said.

UC Davis is also home to the One Health initiative aimed at finding novel treatments like these for diseases that affect both humans and animals. "I've often said that I have the greatest job on the planet, because I get to help kids," Farmer said. "Now my job is even better, because I get to help puppies too."

### **Hopes for clinical trials in humans and dogs**

With additional evaluation and U.S. Food and Drug Administration approval, Farmer and Wang hope to test the therapy in human clinical trials. Sturges and Borjesson hope to do the same with a canine clinical trial. They hope the outcomes of their work help eradicate spina bifida in [dogs](#) and humans.

In the meantime, the team wants dog breeders to send more puppies with spina bifida to UC Davis for treatment and refinements that help the researchers fix an additional hallmark of spina bifida— incontinence. While Darla and Spanky are very mobile and doing well on their feet, they still require diapers.

"Further analysis of their progress will determine if the surgery improves their incontinence conditions," Sturges said.

<http://bit.ly/2wapXnT>

### **Underweight associated with highest mortality and costs after cardiac catheterisation**

*Being underweight, and not overweight, has highest mortality, cost for those undergoing cardiac catheterisation*

Barcelona, Spain - Being underweight, and not overweight, has the highest mortality, cost, length of stay, and readmission rate for those

undergoing cardiac catheterisation, according to an analysis of more than one million patients presented at ESC Congress today.

"Elevated body mass index (BMI) is a risk factor for coronary artery disease, yet studies have shown that overweight and obese patients actually have fewer complications and better clinical outcomes after revascularisation using percutaneous coronary intervention (PCI) - a phenomenon dubbed the obesity paradox," said lead author Dr Afnan Tariq, an interventional cardiology fellow, Lenox Hill Hospital, New York, USA.

This study examined the association of BMI with in-hospital mortality, cost of care, length of stay, and rate of readmission within 30 days in patients undergoing cardiac catheterisation (coronary angiography) in 2013 in a nationally representative cohort.

Researchers used the National Readmission Database and Nationwide Inpatient Sample Database to retrospectively analyse discharge and readmission data. These are the largest all payer USA inpatient databases and include more than 35 million hospitalisations annually.

In 2013, 1 035 727 patients underwent cardiac catheterisation, of which 42% also received PCI with a stent or balloon. When categorised by BMI, 0.4% of patients were underweight (BMI<19 kg/m<sup>2</sup>), while 11.4% were obese (BMI 30.1-40 kg/m<sup>2</sup>) and 8.0% were morbidly obese (BMI over 40 kg/m<sup>2</sup>). Of those undergoing cardiac catheterisation, only 25.8% of the underweight patients went on to receive PCI, while 32.5% of the morbidly obese, 41% of the overweight, 41% of the obese, and 43.2% of the normal weight categories went on to have a balloon or stent (PCI) placed for coronary blockages (adjusted for comorbidities: all values p<0.001).

Despite the low percentage of cardiac catheterisations and lower rate of PCI compared to normal and overweight BMI groups, underweight patients were over three times more likely to die after cardiac catheterisation than morbidly obese patients and five times more likely to die than obese patients (6.0% mortality for underweight patients, 2.3% normal weight, 1.7% overweight, 1.2% obese, 1.9%

morbidly obese, all values adjusted for comorbidities: p<0.001). Interestingly, despite the extreme BMI, morbidly obese patients had a lower mortality rate than normal weight patients and obese patients had the lowest mortality of all groups undergoing cardiac catheterisation.

Length of stay for underweight patients was more than double that of normal weight patients (10.5 days versus 5.1 days) resulting in nearly 50% higher costs for underweight patients (\$USD 33 540 versus \$USD 22 581). Morbidly obese patients had a slightly longer length of stay and higher costs compared to normal weight patients (6.2 days, p<0.01 and \$USD 23 889, p<0.01).

After adjustment for comorbidities, underweight patients were 18% more likely than normal weight patients to be readmitted within 30 days (p<0.007), while morbidly obese patients were 8.2% less likely to be readmitted within 30 days (p<0.001). Overweight and obese patients had the lowest readmission rates, and were over 10% less likely to be readmitted than normal weight patients within 30 days.

Dr Tariq said: "The obesity paradox has flummoxed researchers for some time, and our research also flips the conventional wisdom that a higher BMI should portend a worse outcome. We found that the lower BMI group had worse outcomes across the board, including readmission, length of stay, cost, and mortality."

"Furthermore, using the largest all payer publicly available database in the USA, we observe that obese and morbidly obese patients receive stents or balloons at a lower rate than normal weight patients, are less likely to be readmitted within 30 days, and have lower mortality than normal weight patients undergoing cardiac catheterisation," he continued.

Dr Tariq concluded: "Further research will certainly add to the growing body of evidence, but the scales seem to be tipping in favour of higher BMI patients having better outcomes than normal weight patients. This study also reinforces the notion that the frail, those with the lowest BMI, have the worst outcomes - suggesting that when it

comes to cardiac catheterisation, the smaller they are, the harder they fall."

<http://bit.ly/2xpI9Zq>

## 90-million-year-old tooth unearthed in Kyushu, may provide clues on mammal evolution in Asia

***Fossilized tooth of an extinct mammal unearthed in central Kyushu dates back about 90 million years***

KUMAMOTO – A fossilized tooth of an extinct mammal thought to be a close relative of marsupials has been unearthed in central Kyushu, a find that dates back about 90 million years and may provide clues to how mammals evolved in Asia, the Mifune Dinosaur Museum said Thursday.



*This image shows a Deltatheridium, an ancient relative of marsupials which include kangaroos and koalas. The Mifune Dinosaur Museum in Kumamoto Prefecture said a fossil tooth of a marsupial relative has been unearthed in the town of Mifune. Akio Ito & Yasuko Okamoto Via Kyodo*

The tooth, the first of its kind excavated in Japan, was uncovered from sandstone in the Tashiro district in Mifune, Kumamoto Prefecture. The stone was found in March 2014 from a geological layer formed in the late Cretaceous period, according to the museum.

The uncovered tooth measures about 2 mm in length and 3 mm in width. Based on the shape and size, it is assumed to be a back tooth from the upper left jaw of a carnivore that was about 10 to 15 cm tall.

The fossil is believed to be of an animal similar to a Deltatheridium, an ancient relative of marsupials that lived in Mongolia in the Cretaceous period about 145 million to 66 million years ago.

Marsupials — a subclass of mammals that today include kangaroos and koalas — and Deltatheridiums are classified in the metatheria group. In Asia, some metatheria fossils have been discovered in a geological layer of the late Cretaceous period in inland areas of Mongolia and China.

Kazunori Miyata, an associate professor at the Dinosaur Research Institute of Fukui Prefectural University, said the fossil's discovery is "significant."

"It suggests the possibility that primitive marsupial ancestors were thriving on the east bank of Asia including Japan in the late Cretaceous period when dinosaurs were still dominant."

The fossilized tooth will be displayed at the museum from Friday to Nov. 26.

<http://bit.ly/2xFf4s3>

## Studies reveal how shingles vaccine should be used in arthritis patients

***Live vaccine elicits robust immune responses in patients when administered several weeks prior to treatment with tofacitinib***

New research indicates that the live varicella-zoster vaccine--which is given to protect against shingles--elicits robust immune responses in patients when administered several weeks prior to the start of treatment with the arthritis drug tofacitinib. The *Arthritis & Rheumatology* findings are encouraging because patients with rheumatoid arthritis have a higher risk of developing shingles than other adults, and tofacitinib and certain other disease-modifying antirheumatic drugs are thought to further increase this risk. Importantly, however, the virus should not be given to patients who have not had the chicken pox in the past.

Kevin Winthrop MD, MPH of the Oregon Health and Science University and his colleagues conducted the research, which consisted of two studies. In one study, 112 patients with active rheumatoid arthritis were vaccinated and then randomized to receive either tofacitinib (a Janus kinase inhibitor) or placebo, initiated 2-3 weeks post-vaccination.

Patients developed robust immune responses to the vaccine, and the start of tofacitinib after vaccination had no negative impact on the established immune response. In fact, patients treated with tofacitinib had similar or even higher immune responses to the vaccine compared

with placebo-treated patients, perhaps because they had better control of their rheumatoid arthritis.

"We showed that the vaccine was adequately immunogenic in patients whether they were starting tofacitinib or placebo in a few weeks, and the immunogenicity and the response to the vaccine were similar to what we've seen outside the rheumatoid arthritis setting in general population studies," said Dr. Winthrop.

One patient experienced disseminated varicella infection after starting tofacitinib. The investigators discovered that this patient was the sole participant who did not have chicken pox in the past. The finding emphasizes the importance of only giving the vaccine to patients who have had chicken pox because shingles arises when the chicken pox virus that remains dormant in the body is reactivated. Arthritis drugs that suppress the immune system put patients at an elevated risk of disseminated varicella infection following vaccination.

The second study by the group looked to see if concomitant use of what are called conventional synthetic disease-modifying antirheumatic drugs (csDMARDs, such as methotrexate and chloroquine) or corticosteroids contribute to the increased risk of shingles linked to tofacitinib. The study involved an analysis of 19 clinical trials involving a total of 6192 patients with rheumatoid arthritis.

Shingles rates were lowest for patients taking tofacitinib without csDMARDs or corticosteroids and highest for those taking tofacitinib with csDMARDs and corticosteroids. The investigators noted that similar efficacy has been observed with tofacitinib in phase III clinical studies regardless of whether it is administered as monotherapy or in combination with csDMARDs and/or corticosteroids. Therefore, the use of tofacitinib alone for the treatment of rheumatoid arthritis should be considered to help reduce the risk of shingles in vaccinated patients, provided that the patient's arthritis remains controlled on the drug.

"If you want to lower shingles risk for rheumatoid arthritis patients, there are two strategies: one is vaccinating them and the other is

getting them off steroids and methotrexate if you can," said Dr. Winthrop.

#### **Full Citations**

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URL Upon Publication: <http://doi.wiley.com/10.1002/art.40187>

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URL Upon Publication: <http://doi.wiley.com/10.1002/art.40188>

<http://bit.ly/2whjdD0>

## **Vaccine for Meningitis Shows Some Protection Against Gonorrhea**

***Scientists have not been able to develop a vaccine against the sexually transmitted disease gonorrhea, despite working toward one for more than 100 years.***

***Carol Pearson***

However, they may have stumbled onto something that could provide clues to advance the development of such a vaccine.

Decades ago, in the late 1990s, a strain of meningitis B was reaching epidemic proportions in New Zealand. A vaccine, MeNZB, was developed to protect young people who were at the highest risk of getting this particular type. It did not provide protection against any other strain.

Between 2004 and 2006, MeNZB was given to anyone under the age of 20. Babies and preschoolers were routinely immunized until 2008. People with a high medical risk continued to get the vaccine until 2011. Once the epidemic was over, the vaccination program was stopped.



However, scientists noticed that the meningitis vaccine also seemed to offer some protection against gonorrhea. A study published in the Lancet last month showed that one-third of the people who had received MeNZB did not get gonorrhea, compared to a control group who was not inoculated. The lead author noted that the bacteria causing both diseases share between 80 and 90 percent of their primary genetic sequences.

Dr. Steven Black, an infectious disease expert at Cincinnati Children's Hospital, noted, "This is the first time it's been shown that you could have a vaccine that would protect against gonorrhea. And if these results are confirmed in another setting, that would mean that it would be very reasonable ... to go forward with developing perhaps a more targeted vaccine." Black's comments were published in the current issue of JAMA, the Journal of the American Medical Association.

The World Health Organization reports that gonorrhea is becoming harder, and sometimes impossible, to treat, warning that it could become incurable in the not-too-distant future. At the moment, there no new antibiotics being developed to treat this disease.

"The bacteria that cause gonorrhea are particularly smart. Every time we use a new class of antibiotics to treat the infection, the bacteria evolve to resist them," according to Dr. Teodora Wi, a medical officer involved in human reproduction at the WHO, quoted in a news release from the UN agency.

The U.S. Centers for Disease Control and Prevention (CDC) reports that gonorrhea is the second most commonly reported notifiable disease in the United States. All known cases must be reported to the CDC, but officials there estimate that they are notified of fewer than half of the 800,000 new cases each year.

Women may not have any symptoms, but untreated gonorrhea can cause serious health problems. It can lead to pelvic inflammatory disease. It can cause life-threatening ectopic pregnancies, and pregnant women can pass the disease to their babies. Gonorrhea can

lead to infertility for both men and women, and can make those who have it more likely to get HIV.

The study about the New Zealand epidemic may change the approach toward developing a vaccine against gonorrhea.

The JAMA article concludes that ultimately, a preventive vaccine could be the only sustainable solution to a fast-changing bug that has proven adept at developing resistance.