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Aspirin could help reduce HIV infections in women

Pilot study indicates Aspirin may make HIV target cells less activated

Colin Graydon * Monika Kowatsch **

With nearly two million new infections and one million associated deaths each year, the HIV (human immunodeficiency virus) pandemic is alive and well. Thirty-seven million people are now living with HIV, more than half of whom are women.

Today, most HIV transmission occurs through sex. Fortunately, you can protect yourself and others by keeping HIV away (abstinence, condom use, circumcision) or by inactivating HIV (microbicide gels or a combination of prophylactic anti-HIV drugs such as PrEP). However, these methods are not always feasible for many and can come with stigma.

Imagine though, if instead of targeting the virus, we could make people less susceptible to HIV and address the needs of communities by using a relatively safe, affordable and globally accessible drug with no associated stigma. This is where Aspirin comes in.

It may sound like a fairy tale, but results from our lab's pilot study published last month suggest it may be true. Plus, there's good science behind the explanation.

Aspirin reduced HIV 'target cells'

The idea comes from a partnership with a community of women in Nairobi, Kenya over more than 30 years. This relationship has led to establishment of a clinic which provides almost 50,000 sex workers with disease prevention and treatment resources, and is often referred to by the WHO and UNAIDS as a model of best practices.

Remarkably, many of these women are naturally resistant to HIV, at least in part because they have very little inflammation in their blood and genital tract. This is important because inflammation can increase HIV infection by 1) recruiting immune cells to the site of inflammation, including the cells that HIV loves to infect — so-called HIV "target cells" and 2) activating these HIV target cells, which increases their susceptibility to viral infection and enhances HIV's ability to replicate within them.

The major question posed by our study was this: as an anti-inflammatory drug, could Aspirin reduce the number of HIV target cells and make them less activated?

To answer this question, our lab quantified HIV target cells in the blood and vagina of 37 Kenyan women before and after taking Aspirin for up to six weeks.

The results, published in the *Journal of the International AIDS Society*, show that aspirin reduced the frequency of vaginal HIV target cells by approximately 35 per cent *and* made them less activated.

As a bonus, Aspirin seemed to increase the structural integrity of the skin in the vagina, which could also prevent HIV infection by further restricting HIV's access to more target cells in the blood.

We also tried another anti-inflammatory drug called hydroxychloroquine (HCQ). HCQ is less well known than Aspirin, but used to be a popular treatment for malaria and is now used to treat autoimmune diseases such as rheumatoid arthritis. HCQ also seemed to reduce inflammation in the vagina, but in a slightly different manner.

First drug to target the host

PrEP (a daily treatment of anti-HIV drugs used for prevention) is often used in the form of a vaginal gel, but does not work for women who have genital inflammation.

The next step will be a clinical trial testing whether Aspirin can reduce inflammation in women using PrEP and thereby reduce the number of HIV infections in women at high risk for HIV, such as female sex workers. This population has been asking about future research plans focusing on using Aspirin to prevent HIV.

If we can demonstrate this, Aspirin would be the first drug that targets the host, rather than the virus, to prevent HIV.

By acting on the host rather than the virus, Aspirin is not prone to generate HIV resistance, since there is no selective pressure for HIV to evolve around.

We are not yet at the stage where Aspirin can be recommended for preventing HIV, but the potential for another tool in our belt against a virus that has killed 35 million people (almost the population of Canada), can only be good news. Especially one as safe, affordable, accessible and non-stigmatizing as Aspirin.

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Disclosure statement

The authors do not work for, consult, own shares in or receive funding from any company or organisation that would benefit from this article, and have disclosed no relevant affiliations beyond their academic appointment.

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Negligible risk of transmitting HIV during sex when viral load is suppressed

Negligible risk of transmitting HIV during sex when a person living with HIV is on antiretroviral therapy and maintains a viral load under a specific threshold

There is a negligible risk of transmitting HIV during sex when a person living with HIV is on antiretroviral therapy and maintains a viral load under a specific threshold, according to a study in *CMAJ (Canadian Medical Association Journal)*.

The systematic review, conducted by the Public Health Agency of Canada, relied on 11 studies and one previously published review to determine the absolute risk of HIV transmission when preventive measures are in place.

"Our findings show that there is a negligible risk of sexually transmitting HIV when an HIV-positive sex partner adheres to antiretroviral therapy and maintains a suppressed viral load of less than 200 copies/mL on consecutive measurements every four to six months. The risk of sexual HIV transmission is low when an HIV-positive sex partner is taking antiretroviral therapy without a suppressed viral load of less than 200 copies/mL, condoms are used or both," writes Rachel Rodin, Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada, with coauthors.

"Based on our findings, relevant case law and other factors, the Department of Justice Canada concluded that the criminal law should not apply to people living with HIV who maintain a suppressed viral load of less than 200 copies/mL." Justice Canada also concluded that the criminal law should generally not apply to those who use condoms, among others.

Previous studies found that antiretroviral therapy and condoms can reduce HIV transmission. This study includes evidence from newer studies that have influenced clinical practice and could affect Canadian criminal law.

"These findings will support individual patient and clinician decision-making, and will have implications for public health case management and contact tracing. The Department of Justice Canada used these findings to inform their 2017 report on the justice system's response to HIV nondisclosure, and they may inform the responses of other justice systems," write the authors.

In a related commentary, Richard Elliott, Canadian HIV/AIDS Legal Network, Toronto, Ontario, also welcomes Justice Canada's conclusions that the criminal law should generally not apply in various circumstances, including cases where condoms are used. However, he cautions that the qualitative descriptions of HIV transmission risk used by the study authors potentially overstate risk as understood in the criminal justice system. "[The study authors'] qualitative assessments of transmission risk apply risk categories originally developed 30 years ago to enable public education about

safer sex and health risk reduction in general," Elliott writes. "These categories reflect the relative riskiness of different activities. But they should not be transposed into a system tasked with determining criminal liability based on risk associated with a single act."

Elliott suggests instead that "consensus statements of expert scientific opinion that specifically address the needs of the criminal justice system should guide that system." These support a more limited use of the criminal law than is currently the case in Canada.

"Risk of sexual transmission of human immunodeficiency virus with antiretroviral therapy, suppressed viral load and condom use: a systematic review" will be published November 19, 2018.

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The 'Swiss Army knife of prehistoric tools' found in Asia, suggests homegrown technology

New analysis of artifacts found at a South China archaeological site shows that sophisticated tool technology emerged in East Asia earlier than previously thought.

A study by an international team of researchers, including from the University of Washington, determines that carved stone tools, also known as Levallois cores, were used in Asia 80,000 to 170,000 years ago. Developed in Africa and Western Europe as far back as 300,000 years ago, the cores are a sign of more-advanced toolmaking -- the "multi-tool" of the prehistoric world -- but, until now, were not believed to have emerged in East Asia until 30,000 to 40,000 years ago.

These artifacts found in China are among the nearly four dozen that reflect the Levallois technique of toolmaking. In a paper published Nov. 19 in Nature, researchers date these artifacts to between 80,000 and 170,000 years ago. **Marwick et al.**

With the find -- and absent human fossils linking the tools to migrating populations -- researchers believe people in Asia developed the technology independently, evidence of similar sets of skills evolving throughout different parts of the ancient world.

The is published online Nov. 19 in *Nature*.

"It used to be thought that Levallois cores came to China relatively recently with modern humans," said Ben Marwick, UW associate professor of anthropology and one of the paper's corresponding authors. "Our work reveals the complexity and adaptability of people there that is equivalent to elsewhere in the world. It shows the diversity of the human experience."

Levallois-shaped cores -- the "Swiss Army knife of prehistoric tools," Marwick said -- were efficient and durable, indispensable to a hunter-gatherer society in which a broken spear point could mean certain death at the claws or jaws of a predator. The cores were named for the Levallois-Perret suburb of Paris, where stone flakes were found in the 1800s.

Featuring a distinctive faceted surface, created through a sequence of steps, Levallois flakes were versatile "blanks," used to spear, slice, scrape or dig. The knapping process represents a more sophisticated approach to tool manufacturing than the simpler, oval-shaped stones of earlier periods.

The Levallois artifacts examined in this study were excavated from Guanyindong Cave in Guizhou Province in the 1960s and 1970s. Previous research using uranium-series dating estimated a wide age range of the archaeological site -- between 50,000 and 240,000 years old -- but that earlier technique focused on fossils found away from the stone artifacts, Marwick said. Analyzing the sediments surrounding the artifacts provides more specific clues as to when the artifacts would have been in use.

Marwick and other members of the team, from universities in China and Australia, used optically stimulated luminescence (OSL) to date

the artifacts. OSL can establish age by determining when a sediment sample, down to a grain of sand, was last exposed to sunlight -- and thus, how long an artifact may have been buried in layers of sediment.

"Dating for this site was challenging because it had been excavated 40 years ago, and the sediment profile was exposed to air and without protection. So trees, plants, animals, insects could disturb the stratigraphy, which may affect the dating results if conventional methods were used for dating," said Bo Li , an associate professor of archaeology at the University of Wollongong in Australia and one of the paper's corresponding authors. "To solve this problem we used a new single-grain dating technique recently developed in our OSL lab at the University of Wollongong to date individual mineral grains in the sediment. Luckily we found residual sediment left over by the previous excavations, so that allowed us to take samples for dating."

The researchers analyzed more than 2,200 artifacts found at Guanyindong Cave, narrowing down the number of Levallois-style stone cores and flakes to 45. Among those believed to be in the older age range, about 130,000 to 180,000 years old, the team also was able to identify the environment in which the tools were used: an open woodland on a rocky landscape, in "a reduced rainforest area compared to today," the authors note.

In Africa and Europe these kinds of stone tools are often found at archaeological sites starting from 300,000 and 200,000 years ago. They are known as Mode III technology, part of a broad evolutionary sequence that was preceded by hand-axe technology (Mode II) and followed by blade tool technology (Mode IV). Archaeologists thought that Mode IV technologies arrived in China by migration from the West, but these new finds suggest they could have been locally invented. At the time people were making tools in Guanyindong Cave, the Denisovans -- ancestors to Homo sapiens and relative contemporaries to Neandertals elsewhere in the world -- roamed East Asia. But while hundreds of fossils of archaic humans and related artifacts, dating as far back as more than 3 million years ago, have been found in Africa and Europe, the archaeological record in East Asia is sparser.

That's partly why a stereotype exists, that ancient peoples in the region were behind in terms of technological development, Marwick said.

"Our work shows that ancient people there were just as capable of innovation as anywhere else. Technological innovations in East Asia can be homegrown, and don't always walk in from the West," he said.

The independent emergence of the Levallois technique at different times and places in the world is not unique in terms of prehistoric innovations. Pyramid construction, for one, appeared in at least three separate societies: the Egyptians, the Aztecs and the Mayans. Boatbuilding began specific to geography and reliant on a community's available materials. And writing, of course, developed in various forms with distinct alphabets and characters.

In the evolution of tools, Levallois cores represent something of a middle stage. Subsequent manufacturing processes yielded more-refined blades made of rocks and minerals that were more resistant to flaking, and composites that, for example, combined a spear point with blades along the edge. The appearance of blades later in time indicates a further increase in the complexity and the number of steps required to make the tools.

"The appearance of the Levallois strategy represents a big increase in the complexity of technology because there are so many steps that have to work in order to get the final product, compared to previous technologies," Marwick said.

The study was funded by the Australian Research Council, the National Science Foundation of China, the University of Wollongong, the China Scholarship Council, the Chinese Academy of Sciences and the State Key Laboratory of Loess and Quaternary Geology.

Other authors on the paper were Yue Hu and Xue Rui of the University of Wollongong; Jia-Fu Zhang of Peking University in China; Ya-Mei Hou, Jian-Ping Yue and Wei-Wen Huang of the Chinese Academy of Sciences; and Wen-Rong Chen of the Bureau of Cultural Relics Protection in Guizhou Province, China.

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Aspirin and omega-3 reduce pre-cancerous bowel polyps

Both aspirin and a purified omega-3, called EPA, reduce the number of pre-cancerous polyps in patients found to be at high risk of developing bowel cancer, according to new research.

A clinical trial, led by the University of Leeds, found that both aspirin and EPA reduced the number of bowel polyps in patients one year on from a screening colonoscopy (large bowel camera test), although they did not reduce the chances of an individual having any polyps present in the bowel.

Patients who took aspirin developed fewer polyps overall, including on the right side of the large bowel, the part which is most difficult to monitor by colonoscopy being furthest from the back-passage.

Patients who took purified omega-3 EPA (eicosapentaenoic acid) also developed fewer polyps, but this effect was seen only on polyps on the left side of the bowel, which is nearest the back-passage.

The seAFOod Trial, the result of a multidisciplinary collaboration between the Universities of Leeds, Nottingham, Bradford and Newcastle, as well as others, is published today in *The Lancet*.

The trial was launched to determine whether aspirin or EPA could reduce the number of people who had any polyps at their one year follow up test, which they did not. However, both compounds had preventative effects by reducing the number of polyps of specific types in patients.

Lead author Mark Hull, Professor of Molecular Gastroenterology at the University of Leeds, said: "The seAFOod Trial demonstrates that both aspirin and EPA have preventative effects, which is particularly exciting given that they are both relatively cheap and safe compounds to give to patients.

"Given this new evidence, clinicians need to consider these agents for patients at elevated risk of bowel cancer, alongside regular colonoscopy surveillance."

Bowel cancer remains the second largest cause of cancer deaths in the UK. Despite a national screening programme, bowel cancer still resulted in over 16,000 deaths in England and Wales in 2014.

People at high risk of the disease are regularly monitored by specialists who use a flexible camera to examine the lining of the large bowel, also called the colon, by a technique called colonoscopy. During a colonoscopy, a specialist looks for polyps, which are fleshy growths on the lining of the colon. The growths are usually benign but they can turn cancerous and so they are removed. However, colonoscopy is not fool-proof and a significant number of people still continue to develop bowel cancer.

The seAFOod Trial, funded by the EME Programme - a Medical Research Council (MRC) and National Institute for Health Research (NIHR) partnership - was conducted to see if aspirin and EPA could provide another layer of prevention, alongside colonoscopy.

Professor Hull is a practising Gastroenterologist at the Leeds Teaching Hospitals Trust and is a member of the NHS Bowel Cancer Screening Programme (BCSP) Research Committee. He said: "With the BCSP in England being extended to cover everyone from the age of 50 in England, there will be even more people found to have bowel polyps, who we know are at increased risk of bowel cancer. We should now evaluate how aspirin and EPA can best provide added benefits to patients given our limited colonoscopy resources."

Just over 700 people took part in the study from 53 hospitals in England, all of whom were identified as being at higher risk of developing bowel cancer after having a colonoscopy in the BCSP. This study is the first drug trial to have taken place in the English BCSP.

People who took part were randomly allocated to one of four treatment groups and, each day over the following year, they took either a 300 milligram aspirin tablet; 2 grams EPA in four capsules; a combination of both aspirin and EPA; or placebos only.

Patients who took aspirin had 22% fewer polyps at the end of the one year study compared to those who took the placebo.

Those who took EPA had 9% fewer polyps at the end of the study compared to those who took the placebo, although this difference was not statistically significant. However, patients who took EPA had 25% fewer polyps in the left side of the bowel compared to those who took the placebo.

The study suggests that a 'precision medicine' approach may be the most appropriate way to use aspirin and omega-3 to prevent bowel polyps, in which patients at risk of particular types of polyps are given treatment specific to that risk.

Professor David Crossman, Interim Director of the NIHR's Efficacy and Mechanism Evaluation (EME) Programme, said: "The seAFOod Trial results are very exciting and I'm particularly pleased that the MRC/NIHR collaboration funded this study.

"Prevention is key in this common disease and it's fascinating that the combination of widely available and relatively cheap drugs seemed to have such an impact."

EPA is naturally present in fish oil, but was given to patients at a higher dose than is present in most omega-3 supplements that are available to the public. Aspirin was provided by Bayer AG and EPA was partly provided by SLA Pharma AG.

Although aspirin and EPA had beneficial effects on polyp number on their own, the combination of aspirin and EPA together appeared to have an even greater effect.

However, the trial was not designed to provide a definitive answer about combination treatment and further research is needed to test aspirin and EPA treatment together for polyp prevention.

Treatment with aspirin and EPA was safe with no increased bleeding risk seen. Individuals who took EPA on its own had a slight increase in stomach-upset symptoms.

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Aspirin Can Help Your Heart. Omega-3s Might. But Together? Maybe Not.

Eating one tuna sandwich might increase the risk of heart disease in people also taking aspirin, but eating three tuna sandwiches and taking aspirin … might not.

By Yasemin Saplakoglu, Staff Writer

At least, that's according to new findings presented Nov. 10 at the American Heart Association (AHA) Scientific Sessions annual meeting. The findings have not yet been published in a peer-reviewed journal.

Senior study author Dr. Robert Block, a cardiologist at the University of Rochester Medical Center, stressed that the new findings should be interpreted with caution and need to be replicated in other studies before recommendations for aspirin intake are changed.

The study found that the levels of omega-3 fatty acids in the blood might change the effects that aspirin can have on heart health, Block told Live Science. (Omega-3's are found in fatty fish, including tuna.)

Doctors often prescribe daily, low-dose aspirin for people at risk of heart attacks. This is because the medicine acts an anti-coagulant and can help prevent blood clots. And omega-3s are thought to help reduce the risk of heart disease, though a major trial called the VITAL study, also presented at the AHA conference, found that omega-3s may have less of an impact on heart health than previously thought.

Block's research, which was unrelated to the VITAL study, set out to see what happened when people took the two compounds together. He noted, however, that taking daily, low-dose aspirin is also considered controversial by some. In particular, doctors are

beginning to question the benefits of giving aspirin to people who have never had a heart attack, partly because it increases the person's risk of internal bleeding, he said.

On the other hand, for someone who has already had a heart attack or stroke or has a diagnosed blood-vessel disease, there's "clear data" that low doses of aspirin can be beneficial, Block said. Those people still have an increased risk for bleeding, but the benefits of aspirin somewhat outweigh the risk, he said.

But that's before omega-3's come into the equation.

The fish-oil factor

Block and his team looked at the effects of omega-3s on heart health, but in their research, they also factored in aspirin use. In 2015, Block published a small study done on 30 participants, which looked at what happens in the blood when people take aspirin and fish oil together. The researchers had found that at moderate levels of omega-3s in the blood, this combination would affect platelets — cells that play an important role in blood clotting but also lead to dangerous blockages in blood vessels.

In this new study, Block and his team turned to a much larger database called the Framingham Heart Study, which dates back to 1948. Here, they looked at the association between the number of people in the study who took aspirin daily and those who had a heart attack, stroke or some other cardiovascular event in the 30-plus follow-up years.

Once the investigators adjusted for factors such as age and heart disease risk, they found that people who took aspirin daily and also consumed a low-dose of omega-3s had around a two-fold increased risk of developing heart disease, compared with those who took neither substance. A low dose of omega-3s meant that of all the fatty acids in the individual's blood, 4.2 to 4.9 percent were omega-3s. This very specific amount translates to around one tuna sandwich a week, Block noted.

The researchers also found that people who didn't take aspirin but consumed that same low amount of omega-3s had a 55 percent lower risk of heart disease, than those who didn't take any omega-3s. But the researchers didn't see a link between aspirin and omega-3 for more or less than that amount of fatty acids, he added.

So, to sum up the findings: Aspirin plus a small amount of omega-3s was associated with a slightly increased risk of heart disease. A small amount of omega-3s plus no aspirin was associated with a lower risk. The odd effects may arise because aspirin and omega-3s work on the same molecular pathway, Block said. So, whether or not people should take aspirin could depend on how much seafood the person eats or how much fish oil they take. But it could also depend on genetic factors that can change the way aspirin and omega-3s are metabolized.

"My overarching statement is that more research needs to be done — we can't say for sure that this means you shouldn't take or should take aspirin," Block said. First, "we need to sort of figure out if [the findings] can be replicated in other studies which is what we're hoping to do."

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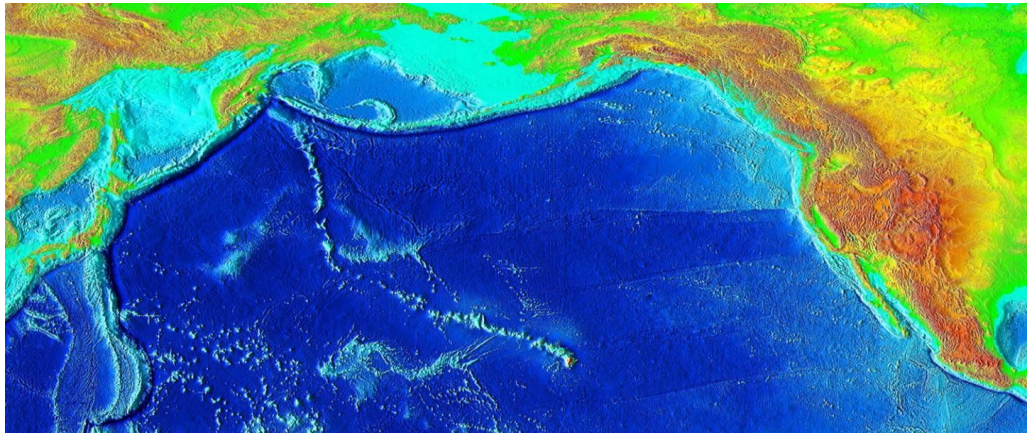
'True polar wander' may have caused ice age

Rice U. scientists use Hawaiian hot spot to study movement of Earth's poles

Earth's latest ice age may have been caused by changes deep inside the planet. Based on evidence from the Pacific Ocean, including the position of the Hawaiian Islands, Rice University geophysicists have determined Earth shifted relative to its spin axis within the past 12 million years, which caused Greenland to move far enough toward the north pole to kick off the ice age that began about 3.2 million years ago.

Their study in the journal *Geophysical Research Letters* is based on an analysis of fossil signatures from deep ocean sediments, the

magnetic signature of oceanic crust and the position of the mantle "hot spot" that created the Hawaiian Islands. Co-authors Richard Gordon and Daniel Woodworth said the evidence suggests Earth spun steadily for millions of years before shifting relative to its spin axis, an effect geophysicists refer to as "true polar wander."



This is the movement of the Pacific plate across a mantle hotspot created the Hawaiian islands over millions of years. **National Geophysical Data Center/USGS/Wikimedia Commons**

"The Hawaiian hot spot was fixed, relative to the spin axis, from about 48 million years ago to about 12 million years ago, but it was fixed at a latitude farther north than we find it today," said Woodworth, a graduate student in Rice's Department of Earth, Environmental and Planetary Sciences. "By comparing the Hawaiian hot spot to the rest of the Earth, we can see that that shift in location was reflected in the rest of the Earth and is superimposed on the motion of tectonic plates. That tells us that the entire Earth moved, relative to the spin axis, which we interpret to be true polar wander."

By volume, Earth is mostly mantle, a thick layer of solid rock that flows under intense pressure and heat. The mantle is covered by an interlocking puzzle of rocky tectonic plates that ride atop it, bumping and slipping against one another at seismically active boundaries. Hot spots, like the one beneath Hawaii, are plumes of hot solid rock that rise from deep within the mantle.

Gordon, the W.M. Keck Professor of Earth, Environmental and Planetary Science, said the new findings build on two 2017 studies: one from his lab that showed how to use hot spots as a global frame of reference for tracking the movement of tectonic plates and another from Harvard University that first tied true polar wander to the onset of the ice age.

"We're taking these hot spots as marked trackers of plumes that come from the deep mantle, and we're using that as our reference frame," he said. "We think the whole global network of hotspots was fixed, relative to the Earth's spin axis, for at least 36 million years before this shift."

Like any spinning object, Earth is subject to centrifugal force, which tugs on the planet's fluid interior. At the equator, where this force is strongest, Earth is more than 26 miles larger in diameter than at the poles. Gordon said true polar wander may occur when dense, highly viscous bumps of mantle build up at latitudes away from the equator.

"Imagine you have really, really cold syrup, and you're putting it on hot pancakes," Gordon said. "As you pour it, you temporarily have a little pile in the center, where it doesn't instantly flatten out because of the viscosity of the cold syrup. We think the dense anomalies in the mantle are like that little temporary pile, only the viscosities are much higher in the lower mantle. Like the syrup, it will eventually deform, but it takes a really, really long time to do so."

If the mantle anomalies are massive enough, they can unbalance the planet, and the equator will gradually shift to bring the excess mass closer to the equator. The planet still spins once every 24 hours and true polar wander does not affect the tilt of the Earth's spin axis relative to the sun. The redistribution of mass to a new equator does change Earth's poles, the points on the planet's surface where the spin axis emerges.

Woodworth said the hot spot data from Hawaii provides some of the best evidence that true polar wander was what caused Earth's poles to start moving 12 million years ago. Islands chains like the Hawaiians are formed when a tectonic plate moves across a hot spot. "True polar wander shouldn't change hot spot tracks because the hot spot track is the record of the motion of the plate relative to the hot spot," Woodworth said.

Gordon said, "It was only about a 3 degree shift, but it had the effect of taking the mantle under the tropical Pacific and moving it to the south, and at the same time, it was shifting Greenland and parts of Europe and North America to the north. That may have triggered what we call the ice age."

Earth is still in an ice age that began about 3.2 million years ago. Earth's poles have been covered with ice throughout the age, and thick ice sheets periodically grow and recede from poles in cycles that have occurred more than 100 times. During these glacial cycles, ice has extended as far south as New York and Yellowstone National Park. Earth today is in an interglacial period in which ice has receded toward the poles.

Gordon said true polar wander is not merely a change in the location of Earth's magnetic poles. As the planet spins, it's iron core produces a magnetic field with "north" and "south" poles near the spin axis. The polarity of this field flips several times every million years, and these changes in polarity are recorded in the magnetic signatures of rocks the world over. The paleomagnetic record, which is often used to study the movement of tectonic plates across Earth's surface, contains many instances of "apparent polar wander," which tracks the motion of the spin axis and which includes the effects of both plate motion and true polar wander, Gordon said.

He said Earth's mantle is ever-changing as new material constantly cycles in and out from tectonic plates. The drawing down and recycling of plates via subduction provides a possible explanation for the highly viscous mantle anomalies that probably cause true polar wander.

"In class, I often demonstrate this with lead fishing weights and pliers," Gordon said. "It's easy to deform the lead with the pliers, and it's not brittle. It doesn't crack or fly apart when it fails. That's a pretty good analogy for mantle flow because that's the way silicate rock deforms under intense heat and pressure."

He and Woodworth are working with colleagues to extend their analysis, both from 12 million years ago to the present as well as further into the past than the 48-million-year start date in the newly published study.

The National Science Foundation supported the research.

The DOI of the Geophysical Research Letters paper is: 10.1029/2018GL080787

A copy of the Geophysical Research Letters paper is available at: https://agupubs.onlinelibrary.wiley.com/doi/full/10.1029/2018GL080787

http://bit.ly/2znKGpz

Shoulder 'brightness' on ultrasound may be a sign of diabetes

A shoulder muscle that appears unusually bright on ultrasound may be a warning sign of diabetes

CHICAGO - A shoulder muscle that appears unusually bright on ultrasound may be a warning sign of diabetes, according to a study being presented next week at the annual meeting of the Radiological Society of North America (RSNA).

Ultrasound is commonly used to diagnose sources of pain in the shoulder. More than 10 years ago, musculoskeletal radiologist Steven B. Soliman, D.O., from Henry Ford Hospital in Detroit, began noticing a pattern when images of the deltoid muscle, the largest muscle of the shoulder, appeared bright on ultrasound.

"Every time we would ask one of these patients if they were diabetic, they would say 'yes' or they would tell us they were borderline and not taking any medications," Dr. Soliman said.

The observations prompted Dr. Soliman and colleagues at Henry Ford to conduct a study to see if the brightness, or echogenicity, of the shoulder muscle could be predictive of diabetes. The results revealed that by using the echogenicity of the muscle, radiologists were able to predict type 2 diabetes, the most common type of diabetes, in almost nine out of 10 patients. Brightness on ultrasound also was an accurate predictor of pre-diabetes, a condition of abnormally high blood sugar that generally progresses to diabetes without changes in lifestyle.

The researchers said the findings could allow for earlier interventions. "If we observe this in patients with pre-diabetes and diabetes, we can get them to exercise, make diet modifications and lose weight," Dr. Soliman said. "If these interventions happen early enough, the patients may be able to avoid going on medications and dealing with all the complications that go with the disease."

For the study, Dr. Soliman and colleagues compiled 137 shoulder ultrasounds from patients with type 2 diabetes, including 13 with pre-diabetes. The researchers also obtained 49 ultrasounds from obese patients without diabetes.

The researchers showed the ultrasounds to two musculoskeletal radiologists who were unaware whether the images came from patients with or without diabetes. The radiologists were asked to classify the patients, based on the brightness of their shoulder muscle, into one of three categories: normal, suspected diabetes and definite diabetes. A third musculoskeletal radiologist acted as an arbitrator in the cases where the other two radiologists disagreed.

The results showed that a consensus diagnosis of "definite diabetes" by the radiologists was a powerful predictor of diabetic status. Using the shoulder ultrasounds, the radiologists correctly predicted diabetes in 70 of 79 patients, or 89 percent.

"We weren't surprised that we had positive results because the shoulder muscle on patients with diabetes looked so bright on ultrasound, but we were surprised at the level of accuracy," Dr. Soliman said.

A hyperechoic, or unusually bright-looking, deltoid muscle was also a strong predictor of pre-diabetes. The musculoskeletal radiologists assigned all 13 pre-diabetic ultrasounds to either the "suspected diabetes" or "definite diabetes" categories.

"A lot of the patients weren't even aware that they were diabetic or pre-diabetic," said Dr. Soliman, who noted that this lack of awareness is a major problem in the U.S.

According to the Centers for Disease Control and Prevention (CDC), nearly one in four Americans with diabetes--about 7.2 million people--are unaware they have the disease and are left undiagnosed.

"Also, the CDC states that pre-diabetes affects an astonishing 84.1 million adults, or nearly 34 percent of the adult U.S. population, and an overwhelming 90 percent of these people are completely unaware of their pre-diabetic status and are at a high risk of developing type 2 diabetes," Dr. Soliman said.

The reasons for the brighter-appearing shoulder muscle on ultrasound among patients with diabetes is not completely understood, according to Dr. Soliman, but the researchers suspect it is due to low levels of glycogen in the muscle, a key source of energy for the body that is stored primarily in the liver and muscles. A study of muscle biopsies in patients with diabetes found that muscle glycogen levels are decreased up to 65 percent. Prior research has also shown that the muscles of athletes appear brighter on ultrasound after exercise, when their glycogen stores are depleted.

"It could be that this appearance in people with diabetes and pre-diabetes is related to the known problems with glycogen synthesis in their muscles because of their insulin abnormalities," Dr. Soliman said.

If they see a bright shoulder muscle on ultrasound, radiologists at Henry Ford now put notes in their reports indicating that this observation has been linked to diabetes.

The researchers plan to continue studying the connection between shoulder muscle echogenicity and diabetes with an eye toward quantifying the phenomenon and seeing if it is reversible.

Co-authors are Paul Williams, M.D., Kelli A. Rosen, D.O., Jessica K. Kim, B.S., D.O., Paul J. Spicer, M.D., and Marnix T. van Holsbeeck, M.D.

https://bbc.in/2Qe2Y6g

Hospital noise levels growing worse, say researchers

Noise levels in hospitals are getting worse, research suggests.

Anyone who has ever stayed overnight in a hospital will know how difficult it can be to sleep, surrounded by staff, machinery, trolleys and telephones.

In the UK, 40% of hospital patients are bothered by noise at night, according to in-patient surveys.

But it's not only the patients' wellbeing that may be affected - high noise levels can also have an impact on staff performance and burnout rates.

Researchers from King's College London say noise levels in intensive care - where the most vulnerable patients are looked after - regularly exceed 100 decibels.

That's the equivalent of loud music being played through headphones.

And it's not just the frustration of being unable to hear each other speak or the fatigue and irritation sparked by poor sleep that are causing concern.

At that level, noise pollution has been implicated in the development of a condition known as intensive care psychosis - a form of delirium where patients experience anxiety, become paranoid, hear voices and see things that are not there.

Increased stress, greater pain sensitivity, high blood pressure, and poor mental health are also possible side-effects.

It means patients often decide to leave hospital before they are completely better - only to be re-admitted at a later stage.

Coronary care patients treated during noisy periods were found to have a higher incidence of rehospitalisation, compared with those treated during quieter periods.

"People leave early, and long after discharge the trauma remains. It puts patients off coming back," Dr Andreas Xyrichis, lead author of the report, told the BBC.

For staff, a noisy working environment is unavoidable - but the consequent stress can affect their performance, while the difficulties of hearing each other and patients speak can compromise the quality and safety of healthcare.

Researchers say progress in combating noise pollution in hospitals has been "unacceptably slow-moving".

So far, they say, attempts to reduce noise have been piecemeal and idiosyncratic. Researchers are calling for a more co-ordinated approach - and solutions that actively involve patients.

The team, from King's and the University of the Arts London (UAL), believe three key areas must be addressed:

- ***The hospital soundscape must be considered as a whole - not just the noisiest elements, such as hospital machinery and alarms, but also low but intrusive sounds, such as the noise of keys in locks and squeaky doors***
- ***Patients' perception and response to a variety of common hospital sounds should be more thoroughly researched. Researchers were surprised to learn some sounds, such as the tea trolley, brought a degree of comfort to patients - as a signal of social interaction***
- ***Patients and families need clear information about probably noise levels during admissions, so they are better prepared in advance, and can consider simple solutions such as bringing their own headphones or earplugs***

Dr Xyrichis questions whether sound "is considered" when creating or redeveloping hospital infrastructure.

But he stresses that modifications can be made to existing environments at a relatively low cost.

Interventions such as sound-absorbing panels and noise-warning systems "have provided some benefit".

Elsewhere, small trials have shown that sound-masking - the use of background sound (such as white noise) in particular environments to reduce noise-induced disturbance - can significantly improve sleep.

Most importantly, says Dr Xyrichis, research should "be more aware of the patients".

He says research made clear that much of patients' agitation over noise was often caused by "not knowing what the noises were".

"It can be very frightening in hospital. We need to do more work with patients to find out about what kinds of noises stress them out."

http://bit.ly/2BvmnHr

DNA vaccine reduces both toxic proteins linked to Alzheimer's

DNA vaccine tested in mice reduces accumulation of both types of toxic proteins associated with Alzheimer's disease

DALLAS - A DNA vaccine tested in mice reduces accumulation of both types of toxic proteins associated with Alzheimer's disease, according to research that scientists say may pave the way to a clinical trial.

A new study by UT Southwestern's Peter O'Donnell Jr. Brain Institute shows that a vaccine delivered to the skin prompts an immune response that reduces buildup of harmful tau and beta-amyloid - without triggering severe brain swelling that earlier antibody treatments caused in some patients.

"This study is the culmination of a decade of research that has repeatedly demonstrated that this vaccine can effectively and safely target in animal models what we think may cause Alzheimer's disease," said Dr. Roger Rosenberg, founding Director of the Alzheimer's Disease Center at UT Southwestern. "I believe we're getting close to testing this therapy in people."

The research published in Alzheimer's Research and Therapy demonstrates how a vaccine containing DNA coding for a segment of beta-amyloid also reduces tau in mice modeled to have Alzheimer's disease. In addition, the vaccine elicits a different immune response that may be safe for humans. Two previous studies from Dr. Rosenberg's lab showed similar immune responses in rabbits and monkeys.

The vaccine is on a shortlist of promising antibody treatments aimed at protecting against both types of proteins that kill brain cells as they spread in deadly plaques and tangles on the brains of Alzheimer's disease patients.

Although earlier research established that antibodies significantly reduce amyloid buildup in the brain, Dr. Rosenberg's team needed to find a safe way to introduce them into the body. A vaccine developed elsewhere showed promise in the early 2000s, but when tested in humans, it caused brain swelling in some patients.

Dr. Rosenberg's idea was to start with DNA coding for amyloid and inject it into the skin rather than the muscle to produce a different kind of immune response. The injected skin cells make a three-molecule chain of beta-amyloid (Aβ42), and the body responds by producing antibodies that inhibit the buildup of amyloid and indirectly also of tau.

The latest study - consisting of four cohorts of between 15 and 24 mice each - shows the vaccine prompted a 40 percent reduction in beta-amyloid and up to a 50 percent reduction in tau, with no adverse immune response. Dr. Rosenberg's team predicts that if amyloid and tau are indeed the cause of Alzheimer's disease, achieving these reductions in humans could have major therapeutic value.

"If the onset of the disease could be delayed by even five years, that would be enormous for the patients and their families," said Dr. Doris

Lambracht-Washington, the study's senior author. "The number of dementia cases could drop by half."

Alzheimer's disease is characterized by progressive deterioration of the brain as neurons are destroyed. About 5.7 million Americans have the fatal disease, with the number expected to more than double by 2050, according to the Centers for Disease Control and Prevention. No effective treatment exists, though several antibody and other therapies are being researched and tested in clinical trials to target amyloid plaques and tau tangles - both hallmarks of the disease. One strategy, still being tested for clinical benefits, involves producing the antibodies in the laboratory and injecting them into the body - a technique referred to as passive immunization.

Dr. Rosenberg said allowing the body to produce its own antibodies through active immunization would be the preferable strategy, if it can be done safely. Among the advantages, the vaccine would be more accessible and less expensive. It also produces a wider variety of antibody types than the preformed antibodies containing only one specific antibody, Dr. Rosenberg said.

The study is the latest contribution to decades of research focusing on clearing toxic proteins in hopes of preventing or slowing the progression of Alzheimer's disease. Scientists have also been trying to develop a method of diagnosing the condition at its earliest stage so that a future breakthrough therapy could be given before the brain deteriorates.

The field advanced significantly earlier this year when UT Southwestern scientists discovered a "Big Bang" of Alzheimer's disease - the precise point at which a healthy tau molecule becomes harmful but has not yet formed tangles in the brain.

The findings offer a new strategy to detect the devastating disease before it takes hold and has spawned an effort to develop treatments that stabilize tau proteins before they shift shape. UT Southwestern scientists are also working to create a spinal fluid test that can detect abnormal tau before symptoms arise.

Dr. Rosenberg said such a test would be an important tool to identify people for vaccine treatment who have not yet shown symptoms but have higher levels of tau and amyloid stored in the brain.

"The longer you wait, the less effect it will probably have," Dr. Rosenberg said. "Once those plaques and tangles have formed, it may be too late."

Dr. Rosenberg is a Professor of Physiology and Neurology & Neurotherapeutics. He holds the Abe (Brunky), Morris and William Zale Distinguished Chair in Neurology.

Dr. Lambracht-Washington is an Assistant Professor of Neurology & Neurotherapeutics. She presented the preliminary findings on tau reduction in mice in 2016 at the Alzheimer's Association International Conference and was awarded a grant by the UT Southwestern Circle of Friends to continue the research. Min Fu, a Research Scientist at UTSW, collaborated on the study.

The research was also supported by the National Institutes of Health; the Zale Foundation; the Rudman Foundation; the Presbyterian Village North Foundation; Freiberger, Losinger, and Denker Family Funds; Triumph Over Alzheimer's; and AWARE.

http://bit.ly/2r23ia3

When storing memories, brain prioritizes those experiences that are most rewarding

A Columbia University study finds that overnight the brain automatically preserves memories for important events and filters out the rest, revealing new insights into the processes that guide decision making and behavior

The brain's ability to preserve memories lies at the heart of our basic human experience. But how does the brain's mechanism for memory make sure we remember the most significant events and not clog our minds with superfluous details?

According to a new study by Columbia University researchers, the brain plays back and prioritizes high-reward events for later retrieval and filters out the neutral, inconsequential events, retaining memories that will be useful to future decisions.

Published today in the journal Nature Communications, the findings offer new insights into the mechanisms of both memory and decision making.

"Our memory is not an accurate snapshot of our experiences. We can't remember everything," said Daphna Shohamy, senior study author and principal investigator at Columbia's Mortimer B. Zuckerman Mind Brain Behavior Institute and a professor in the Department of Psychology. "One way the brain solves this problem is by automatically filtering our experiences, preserving memories of important information and allowing the rest fade away."

The effect, however, takes time to kick in. "The prioritization of rewarding memories requires time for consolidation," said study co-author Erin Kendall Braun, a recent graduate student in the Shohamy lab at the Zuckerman Institute and psychology in Columbia's School of Arts and Sciences.

"Our findings suggest that the window of time immediately following the receipt of the reward -- as well as a longer overnight window including sleep -- work jointly to modulate the sequence of events and shape memory."

To carry out their study, the researchers recruited participants to explore a series of computer-simulated mazes looking for a hidden gold coin, for which they were paid one dollar. The maze was made up of a grid of grey squares and as participants navigated different locations they were shown pictures of everyday objects, such as an umbrella or a mug. The researchers then surprised participants with a test of their memory for these objects.

When the surprise memory test was given 24 hours after exploration, participants remembered the objects closest to the reward (the discovery of the gold coin) but had forgotten the others. This meant that reward had a retroactive effect; memory for objects that had no special significance when they were initially seen were later remembered only because they were close to the reward.

To the researchers' surprise, this pattern of memories was not found when they tested memory immediately. The brain needed time to prioritize memory for the events that led to the reward.

The test was replicated six times in different variations with a total of 174 participants.

"We find the results exciting because they show that experiences considered mundane when they happen are changed in memory due to their association with something meaningful later," Shohamy said. "The experiment demonstrates that what gets remembered isn't random. The brain has mechanisms to automatically preserve memories important for future behavior.

"For memories to be most useful for future decisions, we need them to be shaped by what matters, and it's important that this shaping of memory happen before choices are made."

Though the data provide insight into the structure of memory playback, how this happens in the human brain remains a mystery. The process probably involves dopamine, a chemical known to be important for rewards, and the hippocampus, the brain region that is important to long-term memory, but further research is needed to understand the mechanism by which this happens, Shohamy said.

Additionally, she said, an important follow-up question would be the effect of negative events on memory -- a study "that would be a lot less fun for the participants."

But like the current study, she added, it would help us understand how motivation affects memory and decision making. This understanding would have important implications for education and also for mental health."

This paper is titled "Retroactive and graded prioritization of memory by reward."

This research was supported by the National Institute of Health (5R01DA038891 to D.S.), the McKnight Foundation (MCKNGT CU16-0460 to D.S.) and the National Science Foundation (Career Award BCS-0955494 to D.S. and Graduate Research Fellowship DGE-1144155 to E.K.B.).

http://bit.ly/2Se7zml

Machine learning masters the fingerprint to fool biometric systems

NYU Tandon researchers create synthetic fingerprints capable of spoofing smartphone fingerprint sensors

BROOKLYN, New York - Fingerprint authentication systems are a widely trusted, ubiquitous form of biometric authentication, deployed on billions of smartphones and other devices worldwide. Yet a new study from New York University Tandon School of Engineering reveals a surprising level of vulnerability in these systems. Using a neural network trained to synthesize human fingerprints, the research team evolved a fake fingerprint that could potentially fool a touch-based authentication system for up to one in five people.

Much the way that a master key can unlock every door in a building, these "DeepMasterPrints" use artificial intelligence to match a large number of prints stored in fingerprint databases and could thus theoretically unlock a large number of devices. The research team was headed by NYU Tandon Associate Professor of Computer Science and Engineering Julian Togelius and doctoral student Philip Bontrager, the lead author of the paper, who presented it at the IEEE International Conference of Biometrics: Theory, Applications and Systems, where it won the Best Paper Award.

The work builds on earlier research led by Nasir Memon, professor of computer science and engineering and associate dean for online learning at NYU Tandon. Memon, who coined the term "MasterPrint," described how fingerprint-based systems use partial fingerprints, rather than full ones, to confirm identity. Devices typically allow users to enroll several different finger images, and a match for any saved partial print is enough to confirm identity. Partial fingerprints are less likely to be unique than full prints, and Memon's work demonstrated that enough similarities exist between partial prints to create MasterPrints capable of matching many stored partials in a database. Bontrager and his collaborators, including Memon, took this concept further, training a machine-learning algorithm to generate synthetic fingerprints as MasterPrints. The researchers created complete images of these synthetic fingerprints, a process that has twofold significance. First, it is yet another step toward assessing the viability of MasterPrints against real devices, which the researchers have yet to test; and second, because these images replicate the quality of fingerprint images stored in fingerprint-accessible systems, they could potentially be used to launch a brute force attack against a secure cache of these images.

"Fingerprint-based authentication is still a strong way to protect a device or a system, but at this point, most systems don't verify whether a fingerprint or other biometric is coming from a real person or a replica," said Bontrager. "These experiments demonstrate the need for multi-factor authentication and should be a wake-up call for device manufacturers about the potential for artificial fingerprint attacks." This research has applications in fields beyond security. Togelius noted that their Latent Variable Evolution method used here to generate fingerprints can also be used to make designs in other industries -- notably game development. The technique has already been used to generate new levels in popular video games.

A National Science Foundation grant supported the work. In addition to Bontrager, Togelius, and Memon, the research team includes postdoctoral fellow Aditi Roy and Michigan State University Professor of Computer Science and Engineering Arun Ross. The paper, DeepMasterPrints: Generating MasterPrints for Dictionary Attacks via Latent Variable Evolution, is available at https://arxiv.org/pdf/1705.07386.pdf.

http://bit.ly/2Akcmez

Creutzfeldt-Jakob disease spreads prions throughout the eyes, researchers find

The eyes aren't only a window to the soul; they also offer a new view on rapidly-progressing neurodegenerative disorders called prion diseases.

Washington, DC - Researchers recently studied the eyes of 11 people with sporadic Creutzfeldt-Jakob disease (sCJD), the most common and well-known prion disorder. This week in mBio, they report finding prion seeds -- the infectious proteins that cause the disease -- spread throughout the eyes of all the patients.

"It really suggests we could develop a diagnostic, eye-based assay," says pathologist and senior coauthor Christina Sigurdson at the University of California, San Diego. Future eye-based tests, she adds, may be useful to monitor disease progression and evaluate new treatments.

Prions are misfolded proteins that can emerge spontaneously in the brain; in addition, two case studies suggest they can also be transmitted through a prion-contaminated corneal transplant. About 350 people are diagnosed with CJD every year, with symptoms starting around age 60 on average, according to the National Institutes of Health. There's no treatment for CJD or other prion diseases.

When prions aggregate in the brain, they cause neurons to die. Patients with Parkinson's disease and Alzheimer's disease, similarly, are characterized by cognitive decline and an abnormal accumulation of proteins in the brain. Unlike those diseases, however, prion diseases usually accelerate rapidly, and the majority of patients die within a year of diagnosis.

Roughly 40 percent of patients with CJD develop vision or other eye problems. In some patients, vision problems are the first symptom, suggesting that prions begin accumulating in the eye or in the brain areas associated with vision at an early stage.

"We wanted to know how often prions are deposited in the eye, as well as the distribution and levels of prions in the eye," says Sigurdson.

To find out, the researchers analyzed CJD patients' eyes collected by neurologist and senior coauthor Michael Geschwind and his team at the University of California-San Francisco. Multiple eye components were sent to the laboratory of biochemist and study senior coauthor Byron Caughey, at the National Institutes of Health's Rocky Mountain Laboratory in Hamilton, Montana, for measurements using their highly sensitive prion seeding assay (RT-QuIC).

In all 11 patients, they found the highest levels of prion seeds in the retina, the tissue at the back of the eye that receives light from the lens. The assay also detected prions in other parts of the eye, including the cornea, optic nerve, lens, sclera, and muscles that help control eye movement. Previous studies using immunohistochemistry have previously found prions in patients' retinas and optic nerves, but Caughey's assay is the first to find the proteins elsewhere in the eye.

The findings suggest that surgeons who perform corneal transplants or certain eye procedures should exercise caution with their tools, says Sigurdson. "Surgeons could unknowingly contaminate their instruments with prions," she says, noting that single-use instruments may help prevent accidental spread of the disease.

The study also suggests the assay may have applications in other diseases. "If the RT-QuIC method can be used to amplify other aggregated proteins, this might lead to advances in diagnosis for Alzheimer's, Parkinson's and related diseases," says Geschwind.

Sigurdson is currently working on NIH-funded research to label prions in live mice with fluorescent dyes, with an aim toward developing a new diagnostic test. In the future, she says she wants to test the tears of CJD patients for the presence of prions, as well as further investigate the process by which prions move from cell to cell, and from brain to eye.

"Ultimately we would like to develop new treatment strategies to stop prions from spreading," she says.

http://bit.ly/2DXsarM

Israeli tomb contains a tasty surprise: Vanilla extract

You may call vanilla a boring flavor, but its history just got more interesting.

Kiona N. Smith - 11/21/2018, 5:28 AM

Vanilla may have been used in Israel long before its domestication in Mesoamerica, according to a new find in an ancient tomb. The monumental stone tomb stands near the palace from which ancient kings once ruled the Canaanite city-state of Tel Megiddo, in modern-day northern Israel. Later, the ancient Greeks knew the city by another name: Armageddon. Yes, *that* Armageddon. But Tel Megiddo is a major archaeological site for reasons that have nothing to do with the theological cloud that hangs over it.

Enlarge / Tel Megiddo is a UNESCO World Heritage Site. Liorca / Wikimedia Commons

In 2016, archaeologist Melissa Cradic of the University of California, Berkeley, and her colleagues excavated a 3,000- to 4,000-year-old tomb near the palace. Along with the remains of at least nine people, the tomb contained lavish decorations and funerary goods, including four small jugs. When archaeologist Vanessa Linares of Tel Aviv University analyzed the organic residues left behind on the insides of the jugs, she found something surprising: three of the four contained organic compounds called vanillin and 4-hydroxbenzaldehyde, which are the major compounds found in vanilla extract; they're the chemicals that give vanilla its familiar taste and scent.

After Linares and her colleagues ruled out other possible sources of contamination, they determined that the residue left behind on the offering jugs could only have come from the seed pods of the vanilla orchid.

"This is based on the profuse quantity of vanillin found in the juglets that could have only derived from the abundant amount of vanillin yield from the vanilla orchid pods," wrote Linares in an abstract for her presentation at the American Schools of Oriental Research annual meeting. She pointed out three species as the most likely sources: one native to central East Africa, one from India, and one from Southeast Asia.

Vanilla worldwide

About 110 species of vanilla orchids grow worldwide in a belt of tropical and subtropical environment stretching from the Americas, across Africa and southern Asia, to the islands of the Pacific. It's the most popular—and the second-most expensive—spice in the world, but the three domesticated orchid species that supply today's booming vanilla trade all derive from a single ancestor, first domesticated along the eastern coast of Mexico by the Totonac people. The conquering Aztecs adopted the spice in the 1400s, and Spanish colonizers brought it back to Europe in the early 1500s.

Some archaeological evidence suggests that the Maya used vanilla to flavor their cacao beverages long before Europeans arrived on the scene, but genetic studies suggest that today's commercially grown vanilla is most closely related to that originally cultivated in north-central Veracruz, the heart of former Totonac territory. People domesticated and used vanilla at multiple times and places in Mesoamerica, it seems, but only one of those crops spread around the globe and redefined our taste in desserts.

And the tomb at Tel Megiddo offers the first evidence that people outside Mesoamerica also used vanilla about 2,000 to 3,000 years before the conquistadors carried it home from Mexico. Then, as now, it would likely have been a pricy commodity, because it requires so much work to harvest and produce—and any of the three species

Linares identified would have been imported goods. Megiddo sat perched at a crucial point on an ancient trade route called the Via Maris, which linked Egypt with the Levant, Mesopotamia, and Anatolia. Each of those destinations would have had its own trade networks, easily capable of reaching India or eastern Africa.

But what's it doing in a tomb?

As an expensive imported spice, the small jugs of vanilla extract fit in perfectly with the lavish burial goods in the tomb, which include ceramic vessels and decorated bone inlays. The last three people buried there—a man, woman, and child—wore ornate gold, silver, and bronze jewelry to their final resting place. And the tomb itself is a stonework monument in an elite part of the city, not far from the palace. If the people buried inside weren't royalty, they were certainly wealthy and important, according to Cradic.

"These results shed new light on the first known exploitation of vanilla, local uses, significance in mortuary practice, and possible long-distance trade networks in the ancient Near East during the second millennium BCE," wrote Linares.

The find makes it clear that Megiddo had trade contact, even if it was indirect, with distant locales in East Africa, India, or Southeast Asia and that ancient Canaanites valued vanilla enough to consider it a worthy funeral offering for the city's elites. What's not clear is whether vanilla had a particular role in Megiddo's funerary traditions or whether it was just an expensive luxury to include alongside jewelry and finely crafted ceramics. The presence of vanillin and 4-hydroxbenzaldehyde also isn't enough to reveal exactly where in the world vanilla was being harvested at the time, how it was used, or what eventually happened to the crop.

But there's a final plot twist in vanilla's story. Today, most domesticated vanilla comes from Mesoamerican stock, and although it's still a commercial crop in the Caribbean, Central America, and South America, it's grown mostly on Madagascar and in the islands of the Indian Ocean, including Indonesia.

https://go.nature.com/2KzqT1q

First flight of ion-drive aircraft

A remarkable machine propelled by ionic wind could signal a future with cleaner aeroplanes.

In February 1904, a short news item in *Nature* marked a monumental event. It recorded the achievements of the American brothers Orville and Wilbur Wright and the contraption that they had launched from a hill in North Carolina a couple of months earlier. "They now appear to have succeeded in raising themselves from the ground by a motor-driven machine," *Nature* stated. It was, "the first successful achievement of artificial flight". That first trip lasted barely 12 seconds.

Nearly 115 years later, *Nature* reports on another historic brief flight, which this time lasted 8–9 seconds. Researchers at the Massachusetts Institute of Technology (MIT) in Cambridge describe an aviation breakthrough that will draw inevitable comparisons to that wobbly and fragile first journey by air. The aeroplane is powered by a battery connected to a type of engine called an ion drive that has no moving parts.

There are no passengers, either. The whole device — which has a 5-metre wingspan — weighs just 2.5 kilograms, about one-tenth of a typical commercial flight passenger's baggage allowance. The aeroplane barely gets off the ground, cruising in tests at an altitude of 1.5 feet (0.47 metres). But anyone who watches the machine fly can surely see glimpses of a future with cleaner and quieter aircraft.

A News and Views article delves into the technical details and the challenges that must be addressed to scale up the prototype plane. Is such a goal achievable? Conventional wisdom would say probably not. But then it also said that aircraft with ion-drive, or electroaerodynamic, engines — which create thrust by using

electrical forces to accelerate ions in a fluid to form an ionic wind — would never fly at all. The thrust, after all, is produced only by the wind generated by the movement of ionized air molecules as current passes between two electrodes, one thinner than the other.

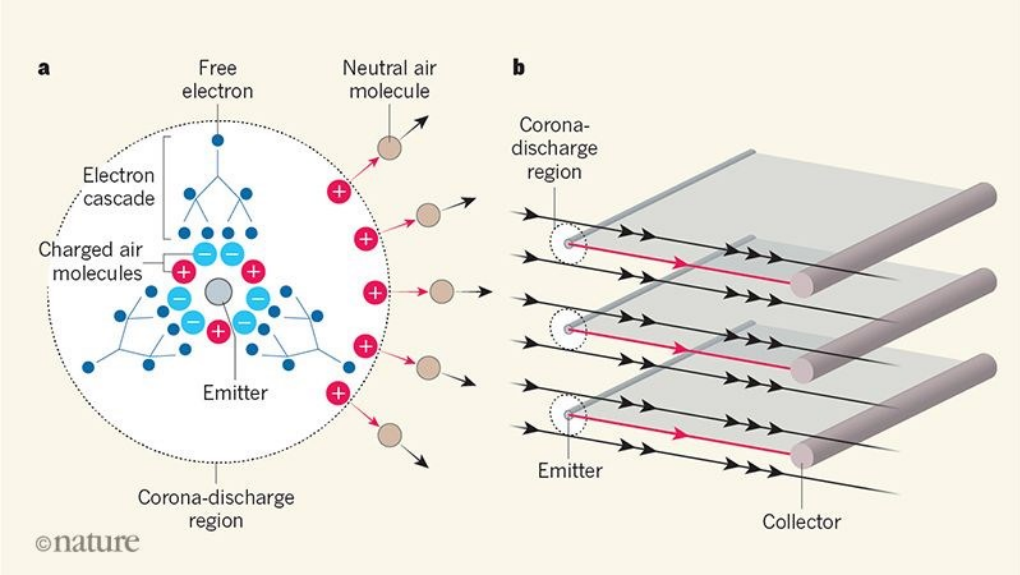


Figure 1 | Ionic-wind propulsion. Xu et al.[2] ***demonstrate that an aeroplane can sustain steady-level flight using air movement known as an ionic wind. a, In the authors' aircraft, an electric field (not shown) is applied to the region surrounding a fine wire called the emitter (shown in cross-section). The field induces electron cascades, whereby free electrons collide with air molecules (not shown in the cascades) and consequently free up more electrons. This process produces charged air molecules in the vicinity of the emitter — a corona discharge. Depending on the electric field, negatively or positively charged molecules drift away (red arrows) from the emitter. These molecules collide with neutral air molecules, generating an ionic wind (black arrows). b, The aircraft uses a series of emitters and devices called collectors, the longitudinal directions of which are perpendicular to the ionic wind. The flow of charged air molecules occurs mainly along the directions (red arrows) joining emitters and collectors. Consequently, the ionic wind is accelerated (black arrows) predominantly in these regions.***

Ionic wind was first identified in the 1960s, but most scientists and aviation professionals since have insisted that the process was never going to be efficient enough to be useful, and left experiments to enthusiasts and hobbyists. Yet, not only do the MIT researchers demonstrate the first flight of an aeroplane propelled in this way, but they also show that the efficiency will increase as the velocity of the aircraft increases, because the electrodes that act as the engine create such little aerodynamic drag.

The scientists' success will surely spur on others to re-explore a technology that was long forgotten. This will no doubt include military research, and some of the possible applications — silent drones and engines with no infrared signal that are thus impossible to detect — will rightly worry many and should be openly discussed.

This first flight will stimulate both awe and anxiety — just as the first powered flight by the Wright brothers did. Will it prove as influential? As you read this, between 6,000 and 12,000 commercial aircraft are airborne, and those are a fraction of the 100,000 or so flights scheduled each day. And every one of these aircraft is sending greenhouse-gas emissions high into Earth's atmosphere.

Predictions about the future of flight are dangerous because work can be overtaken by events or exposed as wishful thinking. (Just four years before the aerial carnage of the Second World War, *Nature* solemnly predicted that the risk of attack from the air was remote. And in the 1970s, it reported claims that a hydrogen-powered aircraft could take to the skies by the end of the twentieth century.)

When the Wright brothers made their historic flight in December 1903, it didn't receive that much attention. In part, that was because their idea was just one of several being explored to achieve flight — with others betting on the success of gliders, airships and even kites. The same is true today. Ion-drive engines are just one much-needed option to improve the efficiency and environmental impact of aircraft

engines, alongside tweaks to fuel and design. Let's hope some of them take off.

Nature ***563***, *443 (2018) doi: 10.1038/d41586-018-07477-9*

https://bbc.in/2TLyQ0N

Sugary supplement mannose could help fight cancer

A nutritional supplement may be able to slow the development of some cancers and enhance the effects of treatment, a study in mice suggests.

By Alex Therrien Health reporter, BBC News

Mice with pancreatic, lung or skin cancer were given mannose, a sugar also found in cranberries and other fruits. It significantly slowed the growth of their tumours, with no obvious side-effects, researchers found. However, patients are being told not to start supplementing with mannose because of the risk of side-effects.

Scientists hope to test the supplement in people soon.

Mannose, which can be bought in health food shops and is sometimes used to treat urinary tract infections, is thought to interfere with the ability of tumours to use glucose to grow.

'Perfect balance'

Scientists also looked at how mannose might affect cancer treatment by giving it to mice that had been treated with two of the most widely used chemotherapy drugs, cisplatin and doxorubicin. They found it enhanced the effects of chemotherapy, slowing the growth of tumours and reducing their size. It also increased the lifespan of some mice.

In further tests, cells from other types of cancer, including leukaemia, osteosarcoma (bone cancer), ovarian and bowel cancer were exposed to mannose in the laboratory. Some cells responded well, while others did not. How well the cells responded appeared to depend on the levels they had of an enzyme that breaks down mannose.

Lead author Prof Kevin Ryan, from the Cancer Research UK Beatson Institute, said his team had found a dosage of mannose that "could block enough glucose to slow tumour growth in mice but not so much that normal tissues were affected".

Bodies require glucose for energy but cancerous tumours also use it to fuel their growth. "This is early research but it is hoped that finding this perfect balance means that, in the future, mannose could be given to cancer patients to enhance chemotherapy without damaging their overall health," he said.

Supplement warning

One advantage of mannose is that it is cheaper than drugs produced by pharmaceutical companies.

And Prof Ryan said he hoped tests in people could begin soon.

However, he and other experts warn that the findings do not mean people with cancer should start supplementing with mannose.

Martin Ledwick, Cancer Research UK's head nurse, said: "Although these results are very promising for the future of some cancer treatments, this is very early research and has not yet been tested in humans.

"Patients should not self-prescribe mannose, as there is a real risk of negative side-effects that haven't been tested for yet.

"It's important to consult with a doctor before drastically changing your diet or taking new supplements."

Prof Ryan said his team would next seek to investigate why mannose worked in some cancer cells and not others, so they could work out which patients might benefit the most.

The research is published in the journal Nature.

http://bit.ly/2DWX6Zs

Study shows skin autofluorescence can predict type 2 diabetes, cardiovascular disease and death

Non-invasive measurement of skin autofluorescence can predict future risk of type 2 diabetes, cardiovascular disease and mortality

New research published in *Diabetologia* (the journal of the European Association for the Study of Diabetes [EASD]) shows that non-

invasive measurement of skin autofluorescence (SAF) can predict future risk of type 2 diabetes, cardiovascular disease (CVD) and mortality, independent of other measures such as measuring blood glucose levels.

This quick, non-invasive technique could be potentially used in non-medical settings or public locations such as supermarkets, pharmacies or drug stores as a first estimate of risk of these conditions, says study lead author Professor Bruce Wolffenbuttel, Department of Endocrinology, University of Groningen, University Medical Center Groningen, Netherlands, and colleagues.

The worldwide prevalence of type 2 diabetes is increasing rapidly; it is predicted to be close to 650 million in 2040. Cardiovascular complications are the main drivers of increased morbidity and premature mortality in diabetes. Several risk factors, such obesity and fasting blood glucose, predict the development of type 2 diabetes and CVD.

More recent research has shown that patients with type 2 diabetes have higher levels of chemicals called advanced glycation end-products (AGEs). Such patients also exhibit higher levels of skin autofluorescence, due to the build-up of some AGEs that fluoresce in the skin. In this study, the authors assess whether SAF was able to predict the development of type 2 diabetes, CVD and mortality in the general population.

For this prospective analysis, the authors included 72880 participants of the Dutch Lifelines Cohort Study, who underwent baseline investigations between 2007 and 2013, had validated baseline skin autofluorescence values available, and were not known to have diabetes or CVD.

Individuals were diagnosed with incident type 2 diabetes by self-report or by a fasting blood glucose ≥ 7.0 mmol/l or HbA_{1c} ≥ 48 mmol/mol (≥6.5%) at follow-up. Participants were diagnosed as having incident CVD by self-report. CVD includes myocardial infarction, coronary interventions, cerebrovascular accident, transient ischaemic attack, intermittent claudication or vascular surgery. Mortality was ascertained using the Dutch Municipal Personal Records Database.

The AGE Reader has a light source which illuminates the tissue of interest. This light excites fluorescent moieties in the tissue, and these will reflect the light with a different wavelength as a result. In the wavelength band used for this study, the major contribution in fluorescence comes from fluorescent AGEs. The emitted light was detected with the use of a spectrometer or photodiodes.

After a median follow-up of 4 years (range 0.5-10 years), 1056 participants (1.4%) had developed type 2 diabetes, 1258 individuals (1.7%) were diagnosed with CVD, while 928 (1.3%) had died. Baseline skin autofluorescence was higher in participants with incident type 2 diabetes and/or CVD and in those who had died compared with individuals who survived and remained free of either disease.

As a single measurement, a 1-unit higher skin autofluorescence was associated with a 3-fold increase in risk of type 2 diabetes or CVD, and a five times increased risk of death. The predictive value of skin autofluorescence for these outcomes was independent of several traditional risk factors, such as obesity, metabolic syndrome, glucose and HbA1c, and, after adjustment for these factors, a 1-unit higher SAF was associated with a 26%, 33% and 96% increased risk for T2D, CVD and mortality, respectively.*

The authors say: "This is the first prospective study to examine SAF as a predictor for type 2 diabetes, CVD and mortality in the general population."

They add: "Our study supports the clinical utility of SAF as a first screening method to predict type 2 diabetes, CVD and mortality. Other risk indicators, such as presence of the metabolic syndrome, require more extensive measurements...The quick, non-invasive

measurement of skin autofluorescence may even allow use in non-medical settings or public locations such as supermarkets, pharmacies or drug stores as a first estimate of risk."

http://bit.ly/2PUn06n

Researchers Develop New Strategy for Detecting Consciousness

The EEG-based method could help clinicians identify patients with severe brain injuries who are actually capable of some cognitive function, despite appearing unresponsive.

Abby Olena

In 2005, a 23-year-old woman in the UK was involved in a traffic accident that left her with a severe brain injury. Five months after the event, she slept and woke and could open her eyes, but she didn't always respond to smells or touch or track things visually. In other words, she fit the clinical criteria for being in a vegetative state.

In a study published in *Science* in 2006, a team of researchers tested her ability to imagine herself playing tennis or walking through her house while they observed activity in her brain using functional magnetic resonance imaging (fMRI). Remarkably, her brain responded with activity in the same areas of the brains of healthy people when asked to do the same, indicating that she was capable of complex cognition, despite her apparent unresponsiveness at the bedside. The findings indicated that this patient and others like her may have hidden cognitive abilities that, if found, could potentially help them communicate or improve their prognosis.

Since then, researchers and clinicians around the world have used task-based neuroimaging to determine that other patients who appear unresponsive or minimally conscious can do challenging cognitive tasks. The problem is that the tests to uncover hidden consciousness can be complex to analyze, expensive to perform, and hard for all patients to access.

"You would like to know if people who look like they're unconscious are actually following what's going on and able to carry out cognitive work, and we don't have an efficient way of sorting those patients," says Nicholas Schiff, a neuroscientist at Weill Cornell Medical College in New York City.

Now, in a study published today (November 21) in *Current Biology*, Schiff and his colleagues have come up with an easier way to test for covert consciousness: measuring electroencephalogram (EEG) responses to human speech. EEG uses a net of electrodes pasted onto the scalp to measure electrical activity in the brain and is cheaper and much more widely available than fMRI. Plus, the EEG can be done at a patient's bedside, which makes it easier to access.

It turns out that the EEG signatures of some patients with brain injuries in response to human speech look similar to those of healthy people. And the same patients whose brains react normally to human speech are also the ones able to do difficult cognitive tasks during fMRI. If this link between EEG results and hidden consciousness is validated in more people with brain injuries, evaluating the response to human speech with EEG could be a more affordable and accessible way to find patients whose cognitive capacity should be further examined.

"It's a groundbreaking study because it shows that there may be a screening test that we can perform that will identify patients who are likely to be covertly conscious," says Brian Edlow, a neurologist at Massachusetts General Hospital who did not participate in the study. He cautions that the strategy "does not prove that the person is covertly conscious because it doesn't show that they're following commands," but adds that if the findings can be replicated, "this is a test that could be generalizable and disseminated to institutions around the world to identify these patients" for further testing and, perhaps eventually, to help them express themselves.

Previous work has shown that the brain keeps track of how sound varies in intensity and it releases corresponding electrical signals that can be measured with EEG. In search of a more straightforward way to detect hidden consciousness, Schiff and his coauthors measured the EEG responses of 13 healthy controls as they listened to another person reading *Alice's Adventures in Wonderland* aloud and compared those readouts to those of 21 patients with brain injuries, who heard family members tell stories about their own lives. The patients ranged in their states of consciousness, from six who were capable of some communication and motor movement to three in a vegetative state.

Then the researchers used fMRI to determine whether any of the patients had the capacity to perform complex cognitive tasks, such as imagining themselves opening and closing a hand, swimming, or playing tennis. They found that the patients whose fMRI results showed activation in the expected brain areas—indicating that they were capable of cognition—also exhibited normal delays in their EEG readouts in response to human speech. In contrast, the patients whose fMRI results didn't correspond to typical brain activity had a much bigger delay in their EEG-measured response to speech.

"fMRI is pretty expensive. It's usually hard to [access] and it takes time and expertise whereas EEG is usually accessible in many clinical settings," says Camille Chatelle, a postdoc at the University of Liège in Belgium who is also affiliated with Edlow's group at Massachusetts General Hospital and was not involved in the work. "We know that these patients sometimes fluctuate and need to be assessed several times within a week to ensure a good diagnosis, so this kind of EEG method could be easier to apply for repetitive assessment and implementation in clinic."

"The problem with severe brain injury is that you have people who all look the same who could have very different trajectories of recovery over time, response to treatment, or already achieved level of recovery," says Schiff. This technique "is a way to sort the variance and also to figure out who we should look at more closely and immediately."

Schiff explains that it will be necessary to examine much larger numbers of patients to determine whether the tight correlation that they found between the brain's response to spoken language and cognitive capacity in this study is preserved in different groups of patients. "There's a pretty good chance that this is going to be a much better way to screen people because it's cheap, it's easy. It takes about five minutes of data that you could record at the bedside anywhere," he says.

C. Braiman et al., "Cortical response to the natural speech envelope correlates with neuroimaging evidence of cognition in severe brain injury," Current Biology, doi:10.1016/j.cub.2018.10.057, 2018.

http://bit.ly/2PW0bPG

Researchers reveal how a deadly fungal infection shape-shifts into an invasive monster

How Candida albicans shape-shifts into a deadly version with hyphae that help it break through human tissues and into the bloodstream

Monash researchers have shed new light on just how the fungal infection, *Candida albicans*, shape-shifts into a deadly version with hyphae or filaments that help it break through human tissues and into the bloodstream. Understanding this process is key to the development of drugs against this fatal infection.

Fungal infections, such as those from *C. albicans*, are a common form of bloodstream infections in hospitals, particularly in very sick or immunocompromised patients. They can also lead to sepsis-like disease. Fungi cause untold harm, largely because they are so similar to mammalian cells that very few antifungal therapies are available.

There is no sure-fire way to treat or prevent *C. albicans* infections. As the population living with weakened immune systems (including

HIV and transplant patients, those undergoing chemotherapy and preterm babies) increases, the threat of this fungus is growing. A review of 750 million hospitalisations in the United States revealed that the rate of fungal bloodstream infections has increased by more than 200 per cent within a couple of decades.

With very high estimated mortality rates of between 10-20 per cent, the human burden is substantial, demanding effective therapeutic strategies.

Although *C. albicans* lives in the gut of about half of all people, it has an ability to transform into a form in which it can invade tissues and also escape from immune cells. In the gut, *C. albicans* sits in a benign state until the right opportunity occurs, when it can overgrow and also start to form hyphae or filaments. These filaments are elongated, stick-shaped cells that the yeast can use to push through the gut wall and get access to the bloodstream and organs, so that it can spread its infection.

Associate Professor Ana Traven, from the Monash Biomedicine Discovery Institute, and her team have shed new light on how *C. albicans* shape-shifts to the deadly hyphal version. Understanding this process is a major breakthrough, building the knowledge base that could lead to development of drugs to treat this infection.

The study, published today in the prestigious journal, *Cell Reports*, focuses on the compound mdivi-1, which is generating global interest in preclinical studies of non-infectious human diseases such as neurodegenerative conditions, stroke, heart attack and cancer. According to Associate Professor Traven, to her knowledge the compound has not been studied extensively in the context of infectious diseases.

In laboratory studies, the Traven team found that adding mdivi-1 to the culture medium inhibits the transition to the hyphal form of the fungus. The researchers used the ability on mdivi-1 to halt this process to study just how this transition happens at a molecular level.

"We revealed a mechanism that operates in *C. albicans* cells to promote hyphal switching via a molecule called nitric oxide—opening a new avenue for understanding this key process and potentially leading to development of new antifungal drugs in the future," Associate Professor Traven said.

"The mortality rate for bloodstream Candida infections are substantial even in countries where the best care is available, so a potential new therapeutic route is very important," she said.

The paper in *Cell Reports* is titled 'A metabolic checkpoint for the yeast to hyphae developmental switch regulated by endogenous nitric oxide signalling.'

More information: *A metabolic checkpoint for the yeast to hyphae developmental switch regulated by endogenous nitric oxide signalling, Cell Reports (2018). DOI: 10.1016/j.celrep.2018.10.08*

http://bit.ly/2zq4YP8

Discovery could neutralize West Nile virus

Human monoclonal antibody could "neutralize" the West Nile virus

Researchers at Vanderbilt University Medical Center and colleagues have isolated a human monoclonal antibody that can "neutralize" the West Nile virus and potentially prevent a leading cause of viral encephalitis (brain inflammation) in the United States.

Their findings, reported this week in the journal *Nature Microbiology*, could lead to the first effective treatment for this mosquito-transmitted infection, which sickens 2,500 and kills more than 100 people throughout the country each year, according to the U.S. Centers for Disease Control and Protection (CDC).

"West Nile virus is still an important cause of brain infections in the U.S., and there is very little we can do to help these patients," said James Crowe Jr., MD, co-corresponding author of the paper and director of the Vanderbilt Vaccine Center.

"It was exciting for us to use our antibody discovery technologies to find naturally occurring human antibodies that can prevent or treat the infection," he said.

Crowe holds the Ann Scott Carell Chair in the Departments of Pediatrics and Pathology, Microbiology & Immunology at Vanderbilt University School of Medicine. He and his colleagues have isolated human monoclonal antibodies for many pathogenic viruses, including Zika, HIV, dengue, influenza, Ebola, norovirus, respiratory syncytial virus (RSV) and rotavirus.

In the current study, the researchers obtained serum and blood cell samples from 13 adults who were infected by the virus during the 2012 outbreak of West Nile encephalitis in Dallas, Texas.

Antibody-producing white blood cells from the subjects were fused to myeloma (cancer) cells to produce fast-growing "factories" of specific, monoclonal antibodies.

One of these antibodies, WNV-86, completely inhibited the virus in laboratory studies. A single dose of WNV-86 completely protected mice from an otherwise lethal West Nile infection.

Further studies are needed before human testing can begin. But these findings are raising hopes for development of the first effective way to counter this potentially dangerous infection.

More information: *A protective human monoclonal antibody targeting the West Nile virus E protein preferentially recognizes mature virions, Nature Microbiology (2018). DOI: 10.1038/s41564-018-0283-7 , https://www.nature.com/articles/s41564-018-0283-7*

http://bit.ly/2Sfo7KI

Your 'Fat-Toothed' Relative May Not Make It for Thanksgiving. He Vanished from Earth 300 Million Years Ago.

Although it may look like a dinosaur, a newly identified sail-backed reptile that lived 300 million years ago is actually more closely related to humans, a new study finds.

By Laura Geggel, Senior Writer

The bizarre 5-foot-long (1.5 meters) reptile is a sail-backed eupelycosaur (yoo-PEL-ee-ko-sore), a group of animals "that were very successful during the Permian," a period that lasted from about 300 million to 251 million years ago, just before the dawn of the dinosaurs, said study lead researcher Spencer Lucas, a curator of paleontology at the New Mexico Museum of Natural History and Science in Albuquerque.

The newfound reptile Gordodon kraineri lived about 300 million years ago in what is now New Mexico. In this illustration, the beast is ready to gobble up the cone-like strobilus of an early cycad. **Matt Celeskey/Lucas, S.G. et al. Palaeontologia Electronica. 2018./CC BY-NC-SA 4.0**

"Eupelycosaurs include the ancestors of mammals, making this new skeleton more closely related to us than to dinosaurs," Lucas told Live Science in an email.

A University of Oklahoma geology class discovered the newfound eupelycosaur fossils peeking out of a roadcut in New Mexico in March 2013. They told Lucas, who then collected the "exquisitely preserved but incomplete skeleton" with his colleagues in 2013 and 2014, he said.

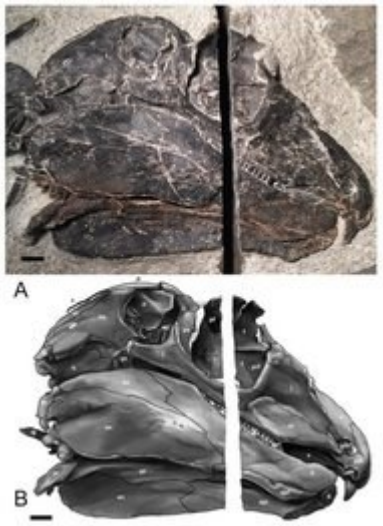
The excellently preserved fossil of the newfound reptile, Gordodon kraineri shows that it sported a large "sail" on its back. **Lucas, S.G. et al. Palaeontologia Electronica. 2018./CC BY-NC-SA 4.0**

After marveling at the reptile's well-preserved, 17-inch-tall (43 centimeters) back sail, the researchers couldn't stop ogling its robust teeth. While the beast has a number of small teeth inside its mouth, it sports larger chompers at the tip of its snout, inspiring the scientific name *Gordodon kraineri*. The genus name is taken from

"gordo," the Spanish word for "fat," and "odon," the Greek word for "tooth." Gordo is also a reference to Alamogordo, the nearby city in southern New Mexico where the fossil was found. The species name honors Karl Krainer, a geologist at the University of Innsbruck in Austria, for his contributions to discoveries about the late Paleozoic geology and paleontology of New Mexico.

The approximately 75-lb. (34 kilograms) reptile had surprisingly advanced structures in its skull, jaws and teeth, indicating that it was a selective feeder that dined on high-nutrient plants, Lucas said.

"Other early herbivorous reptiles were not selective, chomping on any plants they came across," Lucas said. "But *Gordodon* had some of the same specializations found in modern animals, like goats and deer."



The fossilized skull (top) and an illustration of it (bottom). Notice the robust teeth at the front of the skull, which inspired its genus name Gordodon, which translates to "fat tooth." **Lucas, S.G. et al. Palaeontologia Electronica. 2018./CC BY-NC-SA 4.0**

Until now, the oldest animals on record with teeth that were as specialized as *G. kraineri* were found in rocks no older than 205 million years ago, dating to the late Triassic period. "*Gordodon* extends this advanced type of plant eating by 95 million years," Lucas said.

In effect, the discovery of this "fat toothed" reptile rewrites paleontologists' understanding of the early history of reptilian herbivory, he said.

The reason for *G. kraineri's* distinctive sail, however, is still a mystery.

"It has long been thought that the sails on the backs of reptiles like *Gordodon* were used in thermoregulation — the animal pumped blood into the sail, which increased the surface area over which the blood flowed, so that the blood could be more rapidly heated or cooled," Lucas said. "But, this is not certain."

The study was published online in the November issue of the journal Palaeontologia Electronica.

https://wb.md/2BxNqec

FDA Approves New Oral Drug for AML

Glasdegib approved for the treatment of newly diagnosed acute myeloid leukemia

Nick Mulcahy

The US Food and Drug Administration (FDA) approved glasdegib (*Daurismo*, Pfizer) tablets for the treatment of newly diagnosed acute myeloid leukemia (AML) in patients aged 75 years or older or those who have comorbidities that disallow use of intensive chemotherapy, the usual standard of care.

Glasdegib, which belongs to a class of drugs known as *oral smoothened inhibitors,* is for use in combination with low-dose cytarabine (LDAC), a chemotherapy medication.

"Many adults with AML are unable to have intensive chemotherapy because of its toxicities," said Richard Pazdur, MD, of the FDA's Center for Drug Evaluation and Research in a press statement. "Today's approval gives healthcare providers another tool to use in the treatment of AML patients with various, unique needs."

Almost half of the adults diagnosed with AML are not treated with standard, intensive chemotherapy because of comorbidities and chemotherapy-related toxicities, according to the FDA.

The efficacy and safety of glasdegib were evaluated in a clinical trial of 111 patients with newly diagnosed AML. Patients were randomly

assigned to receive either glasdegib plus LDAC or LDAC alone. For those who received glasdebig plus LDAC, median overall survival was 8.3 months; for the patients who received LDAC alone, it was 4.3 months. The difference in overall survival was 4 months and was statistically significant.

Common side effects with glasdegib, reports the FDA, include anemia, fatigue, hemorrhage, febrile neutropenia, muscle pain, nausea, edema, thrombocytopenia, dyspnea, decreased appetite, dysgeusia, mucositis, constipation, and rash.

Healthcare providers should monitor patients for changes in the electrical activity of the heart (ie, QT prolongation).

The FDA granted the glasdegib application a priority review designation. The drug also received an orphan drug designation.

http://bit.ly/2FGXih4

Environmental change, not hominin hunters, drove the demise of African megaherbivores

Decline of megaherbivores began more than a million years before the first evidence of meat-eating hominins

Environmental changes, not the often-blamed ancestors of modern humans, led to the several-million-year decline of east African megaherbivores -- large-bodied mammals like elephants, rhinos and hippos-- a new study finds.

The results suggest that anthropogenic impacts on natural systems are unique to modern Homo sapiens.

Africa is home to many of Earth's modern megaherbivores; however, despite this diversity, the region has witnessed a decline in the diversity of these creatures over time. For decades, research has suggested that the ancient precursors of modern humans, hominins like Homo erectus, drove ecological shifts that led to extinction in large-animal communities in Africa.

While the details differ, most competing hypotheses agree that tool-bearing pre-modern hominin hunters were an important culprit. Despite decades of research is this space, there have been few attempts to test the hypothesis that ancient hominins shaped African ecosystems, or to explore alternatives.

In this study, Tyler Faith and colleagues challenge the traditional "ancient impacts" hypothesis. They analyze megaherbivore diversity in eastern Africa -- which features the longest, most well-documented history of hominin-mammal interaction in the world -- over the last 7 million years using present-day and fossil animal data. Faith et al.'s analysis revealed that the decline of megaherbivores began nearly 4.6 million years ago - more than a million years before the first evidence of meat-eating hominins and about 1.8 million years before the rise of Homo sapiens. What's more, the long-term decline of megaherbivores closely tracks with changes in atmospheric carbon dioxide and with an associated expansion of tropical grasslands, the authors say. The grassland expansion came at the cost of a diminished number of plant types that larger-bodied species depended on, according to the authors.

In a related Perspective, René Bobe and Susana Carvalho critique the results and argue that the role of hominins is still open to question given the limitations of current archaeological and paleontological data.

https://nyti.ms/2DXDvIs

A Memory From Out of the Blue

People sometimes experience random recollections during routine tasks such as housekeeping. Scientists call them “mind-pops.”

By C. Claiborne Ray

Q. Why does a memory come seemingly out of nowhere?

A. This kind of involuntary recall usually involves words, phrases or names, rather than events. Generally, there does not seem to be any immediate trigger or reminder.

The phenomenon was given a name, mind-popping, by one of the few researchers to study it, George Mandler, a pioneer in memory research who died in 2016.

He and his colleagues found that such a memory usually occurred during a task that was relatively automatic, such as routine grooming or housekeeping, which left the mind free to wander.

They speculated that the recall might involve what is called long-term priming, information related to the memory that was acquired days or even weeks earlier than the actual recollection.

Because mind-popping can be perceived as alien or uncontrollable, researchers also have noted its similarity to hallucination.

One study assessed the frequency of mind-pops in small samples of mentally healthy people and in patients with schizophrenia or clinical depression. The results suggested that mind-pops may be more prevalent in individuals with schizophrenia.

http://bit.ly/2RakiGt

Six people swallowed LEGOs and pored through their own poo for science

It takes about two days, or 41 hours, for LEGOs to pass through the body. Science!

Jennifer Ouellette

Here's some good news for worried parents whose small children have ingested a LEGO (or two). A new study by pediatric researchers has concluded that the toy should re-emerge in their poo within a couple of days. They know this because their test subjects voluntarily swallowed LEGO figurine heads and monitored how long it took to retrieve them.

Yes, this is an actual scientific paper, published in the reputable *Journal of Pediatrics and Child Health* with the title, "Everything is Awesome: Don't Forget the LEGOs." It's by the same group of pediatricians behind the popular blog Don't Forget the Bubbles.

"We've finally answered the burning question: how long does it take for an ingested LEGO head to pass?" DFTB co-founder and paper co-author Tessa Davis tweeted. "This is dedication to pediatrics. But it was worth it to advance science and pediatric emergency care."

The horror: it took between 1.14 days to 3.04 days for the swallowed LEGO heads to reappear in subjects' excrement, for an average of 1.71 days.

Warner Bros. Pictures

We jest, but this really is addressing a valid concern. As Bruce Y. Lee, a professor at Johns Hopkins Bloomberg School of Public Health, pointed out at *Forbes*, small children love to swallow things, particularly coins. There have been prior studies examining the passage of coins through the digestive tract, notably a 1971 paper that found most coins passed through harmlessly within three to six days.

But no one had looked closely at the second most commonly swallowed item: small toy parts. And LEGO figurine heads are particularly tempting for the gastronomically curious toddler.

How would you even find six adults (three men and three women) willing to swallow LEGO parts? Davis *et al*. recruited their subjects from the online community of pediatric hospital professionals. They screened out anyone with previous gastrointestinal surgery, problems swallowing objects, or an "aversion to searching through fecal matter."

Each subject kept a "stool diary," recording their bowel movements before and after swallowing the LEGO heads. They evaluated the frequency and looseness of their stool based on the research team's Stool Hardness and Transit (SHAT) score. (Who says pediatricians don't have a sense of humor?) After swallowing the toy, they spent the next three days sifting through their own poo to

determine when the LEGO head reappeared. The number of days it took to pass and retrieve it was dubbed the Found and Retrieved Time (FART) score.

One poor sod never retrieved the LEGO head at all.

Five of the six subjects had FART scores ranging from 1.14 days to 3.04 days, for an average of 1.71 days (about 41 hours). And one poor sod never retrieved the LEGO head at all. We now know that subject is paper co-author and pediatrics consultant Damien Roland, who told the CBC he kept searching through his own poo for two weeks, hoping the toy part would reappear, to no avail. Maybe a bit more roughage in the diet would help?

As Lee points out, this is a small study, focusing on adults rather than toddlers. SHAT and FART scores might vary more widely in the general population. Nor was this a blind study, since the authors felt it would just be asking too much of the study participants' partners or colleagues to sift through poo on their behalf. And other small toy parts of varying shapes might take shorter or longer times to pass through the body.

"A toy object quickly passes through adult subjects with no complications," the authors conclude, adding one important caveat: "parents should be counseled not to search for the object in stools as it is difficult to find." But also maybe don't swallow those LEGO figurine heads in the first place, m'kay?

DOI: *Journal of Paediatrics and Child Health*, 2018. 10.1111/jpc.14309 (About DOIs).

https://bbc.in/2S8fVfc

Patients given unsafe medical implants

Medical devices that are unsafe and have not been adequately tested are ending up inside patients' bodies, an investigation has revealed.

The devices include heart pacemakers, rods to correct spines, and artificial knees and hips.

The investigation found implants that had failed in baboons, or were tested only on pigs and dead bodies, were coming onto the market.

The industry says it has transformed millions of lives for the better.

BBC Panorama has been working with the International Consortium of Investigative Journalists and 58 media organisations around the world including The Guardian newspaper and the British Medical Journal.

The investigation found a lax system of regulation in Europe that allows companies to "shop around" dozens of safety organisations until one of them approves their product.

It also found that doctors can be left in the dark about the true risk of treatments they are recommending to their patients.

Maureen 'the good guinea pig'?

Maureen McCleave, 82 from Essex, was the first person in the UK to be fitted with the "Nanostim" pacemaker because of an irregular heartbeat.

Pacemakers are life-saving implants that deliver electrical pulses to the heart to keep them beating regularly.

Traditional ones have leads from a battery to the heart that deliver the electrical pulse, but the cables can break.

The Nanostim was the first leadless pacemaker that sat inside the heart.

Maureen said she was "over the moon" to be the first and felt like a "good guinea pig" when she was implanted with the device at Bart's hospital in London.

"I was so grateful that I'd been chosen, because it sounded too good to be true."

But three years after it was fitted, the battery in Maureen's Nanostim failed and surgeons could not get it out.

She now has a traditional pacemaker keeping her alive. The Nanostim is still sitting inside her heart.

She says: "I don't like the thought I've got a piece of metal or whatever in my heart that's doing nothing and it's just laying there."

Maureen was not alone - a number of batteries failed and parts fell off inside patients.

The pacemaker was withdrawn for safety reasons. At least two people died and ninety events were recorded in which patients were seriously harmed by the device.

The Nanostim heart pacemaker was turned down by safety bodies in Germany because of a lack of evidence. Yet it was approved by the British Standards Institute in the UK.

How big a problem is this?

Not all medical devices are dangerous. Many save lives or dramatically improve quality of life.

But the investigation has found that some devices are failing patients including:

- ***implants that cracked inside people's backs and had failed in baboon tests***
- ***birth control implants that caused internal damage and bleeding***
- ***misfiring implantable defibrillators***
- ***mesh implants for incontinence that caused abdominal pain***

The BBC also uncovered a treatment for children with a severely curved spine, or scoliosis, which was allowed on to the market following tests only on pigs and dead bodies.

Yet, due to a lack of transparency and data collection, the scale of any problem across the medical device industry remains a mystery to both patients and doctors.

I have an implant, what should I do?

If you are worried, a panel of experts put together by the International Consortium of Investigative Journalists has put together some advice.

It recommends: "Your first point of call should be the medical team that performed the operation.

"If you cannot go back to them for whatever reason, you should consult your primary care doctor.

"The doctor should be able to refer you to a specialist who is familiar with the device and the surgery you had."

Patients in the UK can also report problems to the regulator.

How is all this allowed to happen?

Europe does not have a governmental body that checks medical devices before they are put onto the market.

Instead a series of companies called notified bodies issue CE marks - the same mark of approval given to devices like toasters and kettles.

There are 58 of them in Europe and approval by one means a product can be used anywhere in the European Economic Area (the EU plus Iceland, Liechtenstein, and Norway).

But if one body says no, a company can shop around and ask another.

But surely you need evidence?

Less than patients might think.

And there is so much secrecy that even surgeons implanting these devices do not always see the evidence upon which a device has been approved for its safety and effectiveness.

The British Standards Institution said it could not discuss the evidence for Nanostim due to "confidentiality requirements".

Even the UK's regulator, the Medicines and Healthcare Products Regulatory Agency, says it is "bound by confidentiality when it comes to some of the actions that we've taken around individual devices".

But the investigation discovered there was only one clinical study before Nanostim was approved for use on the public.

It followed just 33 patients for 90 days.

Prof Rita Redberg, one of the world's leading cardiologists and from the University of California, San Francisco, said: "We're talking about a permanently implanted pacemaker, so I think that's a very tiny study.

"They're supposed to last 10, 20 years. A 90-day follow up is not enough to learn much about the pacemaker."

What does the industry say?

MedTech Europe, the body the represents the medical devices industry, said: "Millions of people have safely benefited from medical devices and can now live healthier, more productive and more independent lives.

"Life is unimaginable today without the hundreds of thousands of medical devices in our hospitals and in our homes."

And it defended the system of notified bodies which were "selected for the expertise, impartiality, transparency and independence of their staff".

Abbott, which manufactured Nanostim, says that many patients have been helped by leadless pacemakers and many more will benefit from this technology in the future.

It said: "In accordance with the European CE Mark approval process, the Nanostim leadless pacing system was approved based on strong performance and safety data.

"In addition, upon CE Mark approval Nanostim was further assessed through a European post market clinical follow-up study."

What is the solution?

The UK's Royal College of Surgeons has called for "drastic regulatory changes".

Prof Derek Alderson, president of the Royal College of Surgeons, said: "All implantable devices should be registered and tracked to monitor efficacy and patient safety in the long-term."

But when the European Union suggested tightening the rules, the industry ran a campaign called "Don't lose the 3".

It referred to the fact that manufacturers can get new products to patients three years quicker in Europe then they can in the United States.

New medical device regulation will come into force in Europe in 2020, but campaigners say the new rules do not go far enough.

German MEP Dagmar Roth Behrendt told Panorama that an intensive lobbying campaign by the industry undermined the proposed reforms.

"It's a success for them and a failure for the European parliament and for European patients, I have no doubt about it.

"It is like an open wound for me, that we could not do more for European patients and for the safety of European patients hurts."