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Promiscuity slows down evolution of new species
Researchers found that promiscuous species are less likely to diversify into new species.

April 10, 2017 by Vicky Just

Promiscuity mixes up the gene pool and dilutes genetic differences between populations, slowing down the evolution of new species, says new research by an international team led by the University of Bath's Milner Centre for Evolution.

Darwin's theory of evolution showed that new species evolve when natural selection favours individuals with particular characteristics, allowing them to survive, breed and pass on their genes more successfully than their peers.

Over time, a group of individuals can evolve to adapt to their local environment and form a new species.

Previously it was thought that sexual selection, when one sex prefers to mate with individuals with specific characteristics, was a strong driver of the formation of new species.

One of these processes is the Fisherian runaway selection whereby arbitrary traits such as conspicuous feathers or fancy songs attract female's attention and hence improve the mating success of the bearer. Due to local variations in female preferences, nearby populations can rapidly differentiate and over time evolve into new species.

However new research in birds, published in the leading academic journal *Evolution*, overturns the conventional wisdom and suggests that promiscuity actually slows down the evolution of new species.

A research team led by the University of Bath, Cardiff University and the Max Planck Institute for Ornithology analysed the genetic structure of shorebird populations to track how they had evolved over time.

The team found that polygamous bird species, which breed with several partners during a season, are less diverse genetically within the

species compared to monogamous species that only pair with one mate per season.

This contradicts contemporary theories that predict rapid diversification and thus higher genetic differences between populations of polygamous shorebirds.

First author on the paper, Josie D'Urban Jackson, who is jointly supervised at University of Bath and Cardiff University, analysed the data, she said: "Our findings suggest that because of the pressure to find more than one mate, polygamous shorebirds may search large areas and therefore spread their genes as they go".

"This means they effectively mix up the gene pool by diluting any genetic differences between geographically distant locations, so that populations are less likely to diversify into new species over time".

"In contrast, monogamous species only have to find one partner to pair with each season and tend to come back to the same breeding sites over time. This means they can gradually adapt to their local environment which increases the chance that they will split off and form a new species."

Her supervisor, Professor Tamás Székely from the University of Bath's Milner Centre for Evolution, added: "We're very excited about these findings as this theory completely overturns conventional wisdom.

"You might think that birds choose mates arbitrarily if they are promiscuous, but most individuals prefer a certain type, just as some humans might prefer blonde or dark hair in a partner.

"Our study is consistent with previous findings that polygamous birds sometimes travel hundreds of kilometres to find a suitable partner.

"For example, in Madagascar, we found that the polygamous plovers were similar across the whole island, whereas the monogamous plovers have distinct genetic composition between nearby locations – showing the same pattern that our larger scale study just confirmed."

More information: Josephine D'Urban Jackson et al. Polygamy slows down population divergence in shorebirds, Evolution (2017). DOI: 10.1111/evo.13212

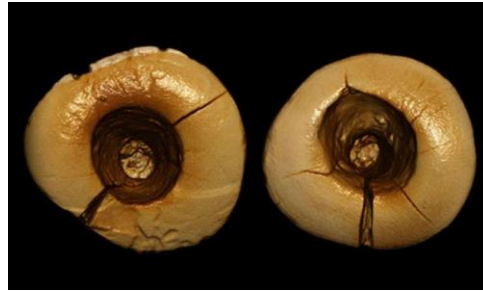
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Ancient teeth offer evidence of Ice Age dentistry

An international team of researchers has found evidence of dental work done during the Ice Age that included using a sharp object to remove diseased cavity tissue and fillings with a tar-like substance.

April 10, 2017 by Bob Yirka [report](#)

(Phys.org) - In their paper published in the *American Journal of Physical Anthropology*, the team describes the condition of the teeth, where they were found, and what they revealed about dental technology during the Ice Age.



A scan of the two teeth with bitumen filling. Credit: American Journal of Physical Anthropology (2017). DOI: 10.1002/ajpa.23216

In studying the [teeth](#) (which were found in a mountainous part of Tuscany, Italy, approximately 20 years ago), two upper incisors (the ones next to the pointy canines), the team found that holes had been "drilled" into them, likely by using a sharp stone, all the way down into the pulp chamber—a procedure that would have almost certainly been very painful. They report scratches and other marks on the inside walls of the teeth, clearly indicating something other than chewing had occurred. Closer examination indicated that the holes had once been filled with bitumen—a tar like substance early people normally used for binding tools together—and bits of straw and what might turn out to be hair. The researchers dated the teeth to a time between 13,000 and 12,740 years ago, placing them in in the Upper Paleolithic. It is not clear what purpose the straw and hair might have served in the procedure, though they note it is possible they were used as an antiseptic or provided some degree of numbness.

The researchers note that it is possible that the holes were drilled for others reasons—to insert jewelry, for example—but the presence of bitumen suggests the purpose was to clean decayed matter from the

teeth and to replace it with something meant to slow tooth loss. They also note that the time period during which the older male lived was prior to the widespread use of agriculture—which meant he lived before the time when people began eating foods high in carbohydrates made from grains. The introduction of such foods to the human diet led to widespread dental problems, most specifically tooth decay.

The researchers acknowledge that two teeth from one person is a small sample size, but due to the evidence of an advance in dental care, it is likely the practice of drilling and filling teeth was widespread.

More information: Gregorio Oxilia et al. *The dawn of dentistry in the late upper Paleolithic: An early case of pathological intervention at Riparo Fredian, American Journal of Physical Anthropology (2017).* [DOI: 10.1002/ajpa.23216](https://doi.org/10.1002/ajpa.23216)

Abstract

Objectives

Early evidence for the treatment of dental pathology is found primarily among food-producing societies associated with high levels of oral pathology. However, some Late Pleistocene hunter-gatherers show extensive oral pathology, suggesting that experimentation with therapeutic dental interventions may have greater antiquity. Here, we report the second earliest probable evidence for dentistry in a Late Upper Paleolithic hunter-gatherer recovered from Riparo Fredian (Tuscany, Italy).

Materials and Methods

The Fredian 5 human consists of an associated maxillary anterior dentition with antemortem exposure of both upper first incisor (I1) pulp chambers. The pulp chambers present probable antemortem modifications that warrant in-depth analyses and direct dating. Scanning electron microscopy, microCT and residue analyses were used to investigate the purported modifications of external and internal surfaces of each I1.

Results

The direct date places Fredian 5 between 13,000 and 12,740 calendar years ago. Both pulp chambers were circumferentially enlarged prior to the death of this individual. Occlusal dentine flaking on the margin of the cavities and striations on their internal aspects suggest anthropic manipulation. Residue analyses revealed a conglomerate of bitumen, vegetal fibers, and probable hairs adherent to the internal walls of the cavities.

Discussion

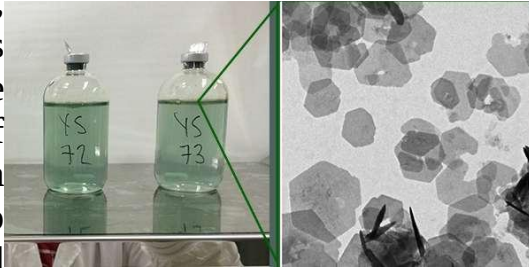
The results are consistent with tool-assisted manipulation to remove necrotic or infected pulp in vivo and the subsequent use of a composite, organic filling. Fredian 5 confirms the practice of dentistry—specifically, a pathology-induced intervention—among Late Pleistocene hunter-gatherers. As such, it appears that fundamental perceptions of biomedical knowledge and practice were in place long before the socioeconomic changes associated with the transition to food production in the Neolithic.

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A rusty green early ocean? Lab recreates one mechanism by which today's ore deposits originally formed

How iron went from a dissolved state to banded iron formations

Though they may seem rock solid, the ancient sedimentary rocks called iron formations - the world's chief economic source of iron ore - were once dissolved in seawater. How did that iron go from a dissolved state to banded iron formations?



Green rust (l) forming in Halevy's lab in conditions similar to those in the Precambrian ocean. (r) Electron microscope images reveal the thin, hexagonal plates typical of green rust. Credit: Weizmann Institute of Science

Dr. Itay Halevy and his group in the Weizmann Institute of Science's Earth and Planetary Sciences Department suggest that billions of years ago, the "rust" that formed in the seawater and sank to the ocean bed was green - an iron-based mineral that is rare on Earth today but might once have been relatively common.

We know there was dissolved iron in the early oceans, and this is a strong indication that Earth's free oxygen (O₂) concentrations were exceedingly low. Otherwise, the iron would have reacted with oxygen to form iron oxides, which are the rusty red deposits familiar to anyone who's left a bike out in the rain. Today, says Halevy, iron is delivered from the land to the oceans as small insoluble oxide particles in rivers. But this mode of sedimentation only came about as free oxygen accumulated in Earth's atmosphere, about 2.5 billion years ago. With almost no oxygen, the oceans were iron-rich, but that did not mean that iron remained dissolved in seawater indefinitely: It ultimately formed insoluble compounds with other elements and settled to the seabed to give rise to banded iron formations.

The idea that one of those insoluble compounds could be a rusty green [mineral](#), says Halevy, occurred to him during his doctoral research, when he was trying to recreate the conditions on early Mars, including its rusty-red iron sediments. "I got some green stuff I didn't recognize at first, which quickly turned orange when I exposed it to air. With a little more careful experimentation, I found that this was a mineral called [green rust](#), which is extremely rare on Earth today, owing to its affinity for oxygen."

Today green [rust](#) quickly transforms into the familiar red rust, but with not much free oxygen around, Halevy reasoned, it could have been an important way for dissolved iron to form solid compounds and settle to the seafloor.



In Lake Matano, Indonesia, (l) low oxygen and high iron concentrations enable the formation of green rust; this may have been the original source of the banded iron formations (r) that are a major source of iron ore today Credit:

Weizmann Institute of Science

Support for these ideas comes from Sulawesi, Indonesia, where green rust forms today in iron-rich, oxygen-poor Lake Matano, thought to be similar to the seawater that existed during extended periods of Earth's early history. To test his ideas in detail and explore their significance, Halevy set up experiments in which he and his team recreated, as closely as possible, the conditions of the ancient, [oxygen](#)-free, Precambrian ocean. They found that green rust not only forms under these conditions, but that when left to age, it transforms into the minerals found in Precambrian [iron formations](#) - a combination of iron-bearing oxides, carbonates and silicates.

Could green rust have been a main vehicle for settling iron out of seawater? Halevy and his team developed models to depict the iron

cycle in Earth's early oceans, including the possibility of green rust formation and competition with other mineral shuttles of iron to the seafloor. Their findings suggest that green rust was probably a major player in the iron cycle. The iron in the green rust later transformed into the minerals we can now observe in the geologic record. "Of course, it would have been one of several means of iron deposition, just as a number of different processes are involved in chemical sedimentation in the oceans today," says Halevy. "But as far as we can tell, green rust should have delivered a substantial proportion of [iron](#) to the very early [ocean](#) sediments."

More information: I. Halevy et al. A key role for green rust in the Precambrian oceans and the genesis of iron formations, *Nature Geoscience* (2017). DOI: [10.1038/ngeo2878](https://doi.org/10.1038/ngeo2878)

<http://bit.ly/2p47FCn>

Mysterious outbreak of disfiguring tropical disease in western Uganda linked to decades of walking barefoot in volcanic soils

Surprising finding highlights less known cause of debilitating elephantiasis

Oakbrook Terrace, Ill. - A puzzling surge in western Uganda patients diagnosed with a painful, disfiguring skin condition known as elephantiasis was caused not by the parasitic worms typically associated with the affliction, but by long-term exposure to irritating soil minerals absorbed while walking barefoot, according to a new study published today in the *American Journal of Tropical Medicine and Hygiene*.

The investigation by a team of experts from the Uganda Ministry of Health, the World Health Organization (WHO) and U.S. Centers for Disease Control and Prevention (CDC) was prompted by what appeared to be a relatively recent and intense outbreak of elephantiasis in 2014 and 2015 in the Kamwenge District of Western Uganda, an area not previously known to harbor the inflammatory disease.

While the people affected had painful swelling and ulcerating sores associated with the condition, they lacked evidence of the microscopic

filarial worms that cause the most common form of elephantiasis, a condition known as lymphatic filariasis. After reviewing the medical history of 52 of the victims, scientists concluded they were suffering from a form of elephantiasis podoconiosis--which also meant this was no sudden outbreak.

"People can be suffering from podoconiosis, a non-infectious disease, for decades before it becomes obvious that they are developing elephantiasis," said Christine Kihembo, MD, a senior field epidemiologist with the Ugandan Ministry of Health and the lead author of the study. "Many of the people affected in Western Uganda probably had been suffering silently without help for more than 30 years."

Podoconiosis is caused by repeatedly walking barefoot in volcanic soils, which contain tiny, sharp mineral crystals that can penetrate the soles of the feet. For some people, once these crystals are under the skin, they provoke repeated cycles of inflammation. Over time, the inflammation produces a build-up of scar tissue that eventually blocks lymphatic vessels and produces dramatic and disabling swelling and open sores in the lower legs.

According to the WHO, this type of elephantiasis is typically associated with farming and years of working barefoot in freshly turned soil. But Kihembo said that until about 50 years ago, the area of Uganda where the patients she studied live was completely covered with forest and grasslands.

According to the report, in the 1960s, a large migration of people swept into the area in search of farmland "and subsequently, the soils were laid bare." But early signs of the disease went undetected because neither the settlers nor healthcare workers in the region had any experience with podoconiosis, which is known to occur in some parts of Eastern Uganda, but is more commonly described in Ethiopia. The WHO estimates at least 1 million people in Ethiopia are estimated to be affected by podoconiosis, but it affects other parts of Africa

along with volcanic regions of Southeast Asia and Central and South America as well.

Investigations by the researchers revealed patients who for many years had suffered routine bouts of itching, foot pain and swelling that were dismissed as minor problems.

The scientists ultimately concluded that "contrary to the perception that an outbreak of elephantiasis had occurred in the area, we have uncovered a chronic neglected tropical disease with a relatively stable annual incidence over the last 30 years."

According to the study, the mean age of those diagnosed with elephantiasis in the region is 48 years old. However, the scientists believe the disease process itself likely began when the victims were much younger.

Evidence shows that the easiest way to prevent podoconiosis is for people to wear shoes and regularly wash their feet. Indeed, many of the patients in the study reported frequently digging in the soil to grow crops and never wearing shoes or washing their feet after being barefoot in the soil. There is now an effort underway in the region to conduct a public health education campaign to focus on the importance of better foot hygiene.

Kihembo noted there have been some misperceptions in the community about the cause of the disease. For example, she said that when word got out that people were suffering from a condition called elephantiasis, a rumor spread that it was caused by dung from elephants that live in surrounding forests and occasionally stroll through local farms. And even when people understand the real cause, the solution is not as simple as it may sound, Kihembo said.

"It can be a challenge to get people to focus on foot hygiene in a poor, rural community where there are many hardships, and going barefoot is not generally viewed as one of them," she said.

Kihembo said flagging early signs of the disease is crucial because proper foot care can prevent it from progressing any further.

Eventually, podoconiosis reaches a "point of no return" where the swelling cannot be reversed, she said.

"People end up being isolated and stigmatized by the disease and they can develop secondary infections due to the ulcers on the skin, all of which cause a further decline in their health and their ability to be productive members of the community," Kihembo said.

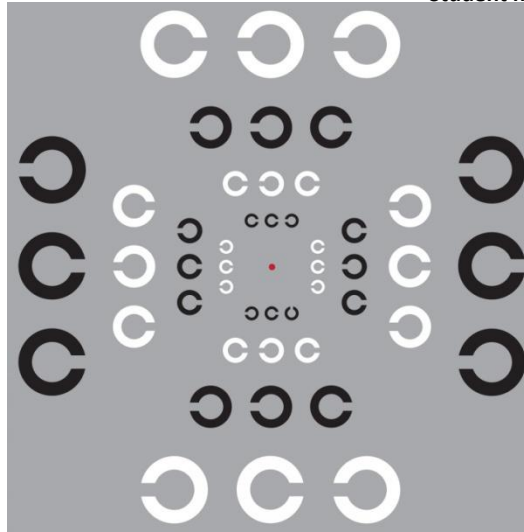
The podoconiosis investigation was undertaken as part of the Uganda Field Epidemiology Training Program (FETP), a collaborative effort between the Uganda Ministry of Health and Makerere University School of Public Health, with support from CDC. Since the program's inauguration in January 2015, the Uganda fellows have successfully investigated more than 60 disease outbreaks and conducted dozens of other applied epidemiologic investigations on emerging public health threats across the country.

This is a perfect illustration of why there is often no substitute for getting out into the field and interviewing patients to determine why they are getting sick and what can be done to help them," said ASTMH President Patricia F. Walker, MD, DTM&H, FASTMH. "These findings can help inform the decisions of health authorities in planning education campaigns to stop further suffering from this terrible, but entirely preventable, form of elephantiasis."

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

Everyone has different 'bad spots' in their vision
The ability to distinguish objects in peripheral vision varies significantly between individuals, for example some people are better at spotting things above their centre of vision while others are better at spotting things off to the right

The ability to distinguish objects in peripheral vision varies significantly between individuals, finds new research from UCL, Paris Descartes University and Dartmouth College, USA. For example, some people are better at spotting things above their centre of vision while others are better at spotting things off to the right.



The research, published in Proceedings of the National Academy of Sciences and funded by the Medical Research Council (MRC), the European Research Council and Dartmouth College, shows that on average we are worse at spotting objects in crowded environments when they are above or below eye level, although the extent to which this happens varies between individuals.

This is an image to demonstrate visual 'crowding' and test peripheral vision.

Ensure that the red dot in the centre of the image is at eye level and focus on it.

While holding your focus on the red dot, try to read the middle 'C' in every triplet. Is the gap facing left or right? You may find it easier to read in some directions than others. People usually find it easier to read below the dot than above, and easier still to the left or right. John Greenwood, UCL

"If you're driving a truck with a high cabin and looking straight ahead, you're less likely to notice pedestrians or cyclists at street level in your peripheral vision than if you were lower down with those same pedestrians on the left and right," explains lead author Dr John Greenwood (UCL Experimental Psychology). "A visually cluttered environment like a busy city road makes it even more difficult. As well as the physical blind spots on vehicles, people behind the wheel will also have different areas where their peripheral vision is better or worse."

The study involved 12 volunteers who took part in a series of perception tests over several years. The key experiment involved focusing on a point in the centre of the screen while images of clocks were shown in different parts of the visual field, either a clock alone or with two other clocks next to it. It is more difficult to tell the time on the central clock when the surrounding clocks are closer to it, as

the scene is more visually 'cluttered'. This is known as 'visual crowding'.

Participants' ability to successfully identify the central clock in a cluttered scene varied significantly, with different people better at spotting it in different positions. On average, most participants were weakest with their upper peripheral vision, followed by the lower peripheral vision. There was no significant difference between left and right on average, with some volunteers better on the left and others on the right.

In the same task, participants were also asked to move their eyes to where the centre of the middle clock had been once it disappeared. There was a strong correlation between the amount of disruption from clutter and the ability of individuals to make precise eye movements to those same locations.

"Everyone has their own pattern of sensitivity, with islands of poor vision and other regions of good vision," explains Dr Greenwood. "If you're looking for your keys, then this profile will affect your ability to find them. For example, if your keys are on a table to the left of where you're focusing, the presence of books and papers on the table may stop you spotting the keys. Someone with strong left-sided vision could spot the keys even if they're right next to the book, whereas someone else might not notice the keys unless they're a foot away from the book. There is substantial variation between different people."

These 'islands' of poor vision were apparent across several tasks tested by the researchers, despite each relying on different processes in the brain. The implication is that these differences in peripheral vision could occur very early in the visual system, possibly beginning as early as the retina. It is unclear whether these differences are due to genetics or environment, but they are observed consistently over time.

"What is striking is the consistency of the pattern from the first levels of vision up to the highest levels, processing that involves very different areas of the brain," explains senior author Professor Patrick

Cavanagh (Dartmouth College). "We propose that these variations originate at the first levels of vision very early in our development where simple features like edges and colours are registered, and then are inherited by higher levels as the rest of the brain wires itself up to deal with the information being sent from the eyes. The higher levels deal with recognizing objects, faces, and actions, and directing our eyes toward areas of interest."

Most people do not experience visual crowding in the centre of their vision, unlike the periphery, however in some conditions central vision is also affected. In amblyopia, also known as 'lazy eye', the brain does not interpret visual signals from one eye properly, leading to an increase in visual crowding. In dyslexia, some research has shown that people with the condition find it easier to read words when the letter spacing is increased to reduce visual crowding. Similarly, visual crowding effects may be one of the early symptoms of Posterior Cortical Atrophy, a form of dementia that predominantly affects vision. Crowding is also a factor in macular degeneration, the most common form of blindness, where the centre of the eye is affected first and so patients must rely on their peripheral vision to see.

"Our new paper helps us to better understand the mechanisms that cause visual crowding and where these occur in the visual system," says Professor Cavanagh. "In the long term, we hope that this will help with the development of better treatment strategies for a wide range of conditions that limits the usefulness of vision for millions of people worldwide."

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

Dry needling offers alternative to cortisone injection for hip pain

Dry needling may be a viable treatment alternative to cortisone injection for patients with chronic, intermittent pain and tenderness on the outside of the hip, thus avoiding the potentially harmful effects of steroids

Dry needling may be a viable treatment alternative to cortisone injection for patients with chronic, intermittent pain and tenderness on the outside of the hip, thus avoiding the potentially harmful effects of steroids, according to a new study published in the April 2017 issue of the Journal of Orthopaedic & Sports Physical Therapy® (JOSPT®). Researchers at Baylor Scott & White Health in Temple, Texas, found that dry needling, which uses filament needles to stimulate sensitive loci, or trigger points, in the muscles, is as effective as cortisone injection in reducing pain and improving movement problems caused by greater trochanteric pain syndrome (GTPS). GTPS is the current term for what used to be called greater trochanteric or subgluteal bursitis. This study is the first to directly compare these two treatments for the syndrome.

The medical community once thought that a swollen hip bursa--a fluid-filled sac that acts as a gliding surface to reduce friction between moving tissues in this joint--was the source of this hip pain. This conclusion led to the use of steroid injections to the bursa to help decrease swelling and pain. However, evidence now indicates that injuries to the muscles and tendons around the hip are the actual cause of this pain, and that inflammation is often not involved, calling injecting the bursa with a steroid into question.

GTPS is estimated to affect 10% to 25% of the general population. This kind of hip pain has been reported to be more common in women and in patients with coexisting low back pain, osteoarthritis, Iliotibial band tenderness, and obesity. The study demonstrates that patients with GTPS can get similar results from dry needling as from a steroid injection.

"Evidence for dry needling of the hip in lieu of steroid injection is in its infancy," acknowledges lead author Kindyle L. Brennan, PT, PhD, with Baylor Scott & White Health. However, "this study suggests dry needling as an effective alternative to cortisone injection."

Dr. Brennan adds that, "The potential detrimental side effects of steroid injection, particularly repeated injections, are of concern for

patients and providers alike." As a result, "the identification of a comparable treatment alternative with minimal side effects, such as dry needling, offers valuable clinical advantages," she says.

Dr. Brennan and her fellow researchers treated 43 patients with GPTS and a total of 50 painful hips. The patients were randomly assigned to one of two groups: one group receiving cortisone injection and the other group, dry needling. Treatments were administered over six weeks, and clinical outcomes were collected at the start of the trial and at one, three, and six weeks. The researchers measured pain and function. They also collected information about medication intake for pain in the involved hip, as well as the sex, age, and body mass index of study participants.

The baseline characteristics were similar between the two groups. The results showed that cortisone injection did not provide better outcomes than dry needling for either pain or function in patients with GTPS. Both groups experienced a decrease in pain and an improved ability to move and complete daily activities.

Dr. Brennan cautions that while this study uses a larger sample than most, further studies are warranted. In particular, participants were only followed for six weeks; additional studies over longer time periods will be important.

The study is titled "Dry Needling Versus Cortisone Injection in the Treatment of Greater Trochanteric Pain Syndrome: A Noninferiority Randomized Clinical Trial." Co-authors on the paper are Bryce C. Allen, MD, and Yolanda Munoz Maldonado, PhD, also with Baylor Scott & White Health. The research report's full citation is: J Orthop Sports Phys Ther 2017;47(4):232-239. Epub March 3, 2017. doi:10.2519/jospt.2017.6994

The study was approved through the Baylor Scott & White Health Institutional Review Board. Internal grant support was provided by Baylor Scott & White Health. The trial was registered at <http://www.clinicaltrials.gov> (NCT02639039).

<http://bit.ly/2oxP6Dr>

Cold temperatures perceived in a photo increase cognitive control

Ben-Gurion University of the Negev (BGU) researchers have demonstrated that the perception of cold temperatures elicits greater cognitive control, even from a photo.

BEER-SHEVA, Israel - "Metaphorical phrases like 'coldly calculating,' 'heated response,' and 'cool-headed' actually have some scientific validity, which we demonstrate in our study," says lead researcher Dr. Idit Shalev of the BGU Department of Education.

Dr. Shalev conducted the research with Prof. Nachshon Meiran of the BGU Department of Psychology and their Ph.D. student, Eliran Halali, now of the Department of Psychology at Bar-Ilan University.

"Previous research focused on the actual effect of temperature on the psychological phenomenon known as 'cognitive control,'" says Dr. Shalev. "But this is the first time we were able to measure the effects of perceived temperature." The study, "Keep it Cool: Temperature Priming Effect on Cognitive Control," was published in Psychological Research.

Cognitive control is the ability to deliberately inhibit responses or make choices that maximize the long-term best interests of the individual. For example, when a person is very hungry and sees a sandwich but does not eat it, he is exhibiting cognitive control.

The researchers conducted two experiments for the study. In the first, 87 students performed an "anti-saccade task," which requires looking in the opposite direction an object is moving and measures cognitive control.

In the second experiment, 28 students were shown images of winter scenery, a temperature-neutral concrete street and a sunny landscape, and told to picture themselves in those settings.

"The result indicated that those viewing the cold landscape did better and that even without a physical trigger, cognitive control can be activated through conceptual processes alone," says Dr. Shalev.

The researchers state there is a possible explanation for the relation of temperature and cognitive control with social proximity. "While signals of warmth induce a relaxed attitude, cool signals trigger alertness and a possible need for greater cognitive control."

<http://bit.ly/2p66sus>

Dengue fever often goes unrecognised by Australian doctors, study finds

New research shows that Australian doctors often fail to give dengue patients appropriate treatment. Jana Howden reports.

Infecting 50 to 100 million people each year and causing symptoms ranging from a rash to haemorrhaging, dengue virus is categorised by the World Health Organization (WHO) as both a major international public health problem, and a neglected one.

A new study published in the Medical Journal of Australia has revealed that the mosquito-borne virus is indeed flying under the radar. It revealed that a significant number of Australian travellers bringing home the unwanted souvenir – predominately those returning from Indonesia and Thailand – presented warning signs that were not recognised by clinicians, with more than 20% of patients prescribed medication that could in fact increase their risk of haemorrhage.

In a collaborative project conducted by researchers from Austin Health, Monash Health, Monash University, the University of Melbourne, the Victorian Infectious Diseases Services in Melbourne, and the Royal Darwin Hospital, 208 hospitalised patients from January 2012 to May 2015 were included in the study.

Analysing the archives of four health care networks in Australia, the researchers searched the hospitals' databases to see what symptoms dengue sufferers were presenting with, where they had travelled, and what the response of their health care facility was.

They found that WHO guidelines for the classifications of dengue – designed to make classification of the condition simpler to better determine a patient's treatment plan – were followed in only 10 of the 208 cases.

They also found that only 14% of the patients had a complete fluid balance chart for at least one day. The authors write that “managing the patient's fluid balance is vital when treating dengue,” calling this lack of fluid monitoring “concerning”.

Yet “even more worrying,” according to the researchers, was the discovery that 22% of patients were prescribed NSAIDs – a family of common anti-inflammatory drugs, including aspirin – which can worsen the impact of dengue on patients through risk of bleeding complications.

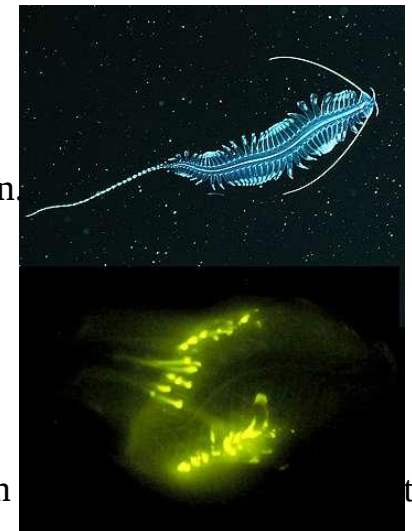
As Australian travel to Asia continues to increase, the researchers urge Australian GPs and clinicians to increase their familiarity with the variety of clinical manifestations of the disease to ensure treatment errors, including the prescription of NSAIDs, are avoided.

<http://bit.ly/2oz3P11>

New study shows that three quarters of deep-sea animals make their own light

Three quarters of the animals in Monterey Bay waters between the surface and 4,000 meters deep can produce their own light

Ever since explorer William Beebe descended into the depths in a metal sphere in the 1930s, marine biologists have been astounded by the number and diversity of glowing animals in the ocean. Yet few studies have actually documented the numbers of glowing animals at different depths. In a new study in *Scientific Reports*, MBARI researchers Séverine Martini and Steve Haddock show that three quarters of the animals in Monterey Bay waters between the surface and 4,000 meters deep can produce their own light.



This image shows a deep-sea tomoptorid worm lit by lights on a remotely operated vehicle (top) and emitting bioluminescence in the lab (bottom). Tomoptorids are one of the few deep sea animals that emit yellow light. Credit: Top image: © 2002 MBARI. Bottom image: Steve Haddock © 2017 MBARI.

You would think it would be easy to count the number of glowing (bioluminescent) [animals](#) in the ocean, just by looking at videos or photographs taken at different depths. Unfortunately, very few cameras are sensitive enough to show the pale glow of many marine animals. Below 300 meters (1,000 feet) the ocean is essentially pitch black, so animals don't need to glow very brightly. Also most animals don't glow continuously because making light takes extra energy and can attract predators.

Because of the difficulty in counting glowing animals at depth, most previous estimates of the proportion of glowing animals were based on qualitative observations made by researchers peering out the windows of submersibles. Martini and Haddock's study is the first ever quantitative analysis of the numbers and types of individual glowing animals at different depths.

The researchers compiled data on every animal larger than one centimeter that appeared in video from 240 dives by MBARI's remotely operated vehicles (ROVs) in and around Monterey Canyon. They counted over 350,000 individual animals, each of which had been identified by MBARI video technicians using a vast database known as the Video Annotation and Reference System (VARS). The VARS database contains over five million observations of deep-sea animals, and has been used as a source of data for more than 360 research papers.

Martini, the lead author of the recent study, compared the list of animals seen during the 240 ROV dives with a list of animals and animal groups that were known to be bioluminescent. This list was based on a review of previous scientific papers, as well as firsthand observations by Haddock and others. As an indication of the lack of research in this area, the most complete source of bioluminescence information for [marine animals](#) was a paper published in 1987, 30 years ago.

Martini divided the observed animals into five categories:

- ***Definitely bioluminescent***
- ***Highly likely to be bioluminescent***
- ***Very unlikely to be bioluminescent***
- ***Definitely not bioluminescent, and,***
- ***Undefined (not enough information was available to determine if an animal is bioluminescent or not).***

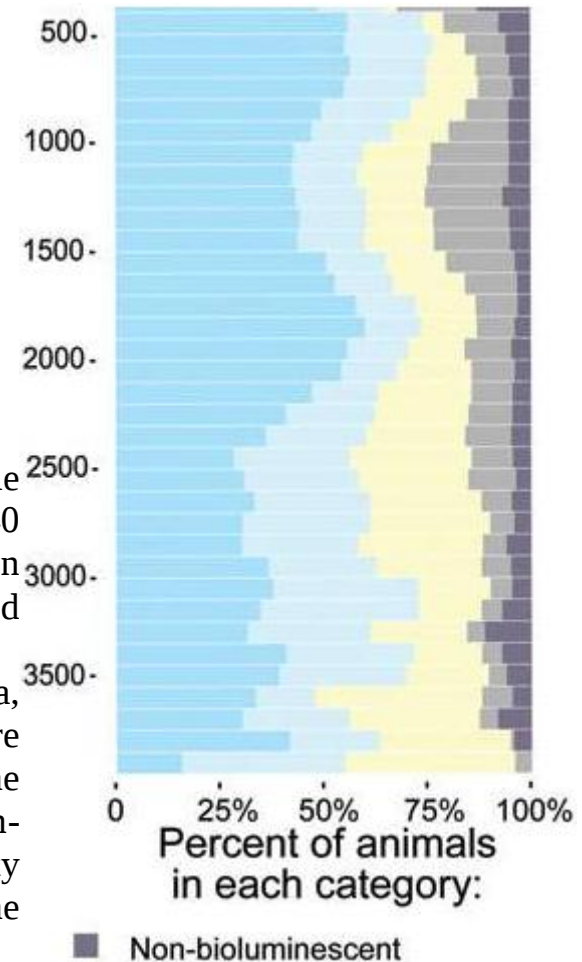
Because scientists know so little about deep-sea animals, 20 to 40 percent of the animals seen below 2,000 meters were classed as "Undefined."

Looking through the data, Martini and Haddock were surprised to find that the proportion of glowing to non-glowing animals was pretty similar from the surface all the way down to 4,000 meters.

This graph shows the proportion of midwater animals that glow at different depths in Monterey Bay. Although there are more "undefined" animals in deeper water, the proportion of glowing to non-glowing animals is relatively similar at all depths. Credit: Severine Martini © 2017 MBARI.

Although the total number of glowing animals decreased with depth (something that had been previously observed), this was apparently due to the fact that there are simply fewer animals of any kind in deeper water.

Even though the proportion of glowing to non-glowing animals was similar at all depths, the researchers found that different groups of animals were responsible for the light produced at different depths.



For example, from the sea surface down to 1,500 meters, most of the glowing animals were jellyfish (medusae) or comb jellies (ctenophores). From 1,500 meters to 2,250 meters down, worms were the most abundant glowing animals. Below that, small tadpole-like animals known as larvaceans accounted for about half of the glowing animals observed.

The analysis also showed that some groups of animals were much more likely to glow than others. For example, 97 to 99.7 percent of the cnidarians (jellyfish and siphonophores) in the videos are able to produce their own light. In contrast, only about half of the fishes and cephalopods (squids and octopuses) are bioluminescent.

The finding that the proportion of glowing to non-glowing animals is relatively constant at all depths suggests that scientists may be able to estimate the total numbers of animals at specific depths "just" by measuring the amount of light produced by animals at each depth. Unfortunately, researchers do not yet have instruments that can reliably measure the total bioluminescence from all animals at a given depth. But Martini is working on instruments that may be able to do this, and plans to publish her findings in a future paper.

Commenting on the significance of her research, Martini said, "I'm not sure people realize how common bioluminescence is. It's not just a few deep-sea fishes, like the angler fish. It's jellies, worms, squids...all sort of things." In fact, she and Haddock concluded their paper by writing, "Given that the deep ocean is the largest habitat on Earth by volume, bioluminescence can certainly be said to be a major ecological trait on Earth."

More information: Séverine Martini et al, Quantification of bioluminescence from the surface to the deep sea demonstrates its predominance as an ecological trait, *Scientific Reports* (2017). [DOI: 10.1038/srep45750](https://doi.org/10.1038/srep45750)

<http://bbc.in/2nQgK1z>

Brain cell therapy 'promising' for Parkinson's disease
Scientists believe they have found a way to treat and perhaps reverse Parkinson's disease, by making replacement cells to mend the damaged brain.

They say human brain cells can be coaxed to take over the job of the ones that are destroyed in Parkinson's. Tests in mice with Parkinson-like symptoms showed that the therapy appeared to ease the condition. Many more studies are needed before similar tests can begin in people. Experts say the research published in [Nature Biotechnology](#) is hugely promising, although at a very early stage. The scientists still have to check if the treatment is safe, and whether the converted cells, which started out in life as astrocytes, can truly function like the dopamine-producing neurons lost in Parkinson's.

Parkinson's disease

People with Parkinson's lack enough dopamine because some of the brain cells that make it have died. It is not known what kills the cells, but this loss causes debilitating symptoms, such as tremor and difficulty in walking and moving. Doctors can prescribe drugs to help manage the symptoms, but cannot treat the cause.

Scientists have been looking for ways to replace the damaged dopamine neurons by injecting new ones into the brain.

The international team of researchers who carried out the latest work, however, used a different approach that does not require a cell transplant. They used a cocktail of small molecules to reprogramme cells already present in the brain.

When they mixed a sample of human astrocytes with the cocktail in their laboratory, they produced cells that closely resembled dopamine neurons, although not a perfect match. Next, they gave the same cocktail to sick mice. The treatment appeared to work, reprogramming their brain cells and lessening their Parkinson's symptoms.

Viable therapy?

Dr Patrick Lewis, an expert in neuroscience at the University of Reading, said work like this could potentially offer a game-changing therapy for Parkinson's. But he added: "Moving from this study to doing the same in humans will be a huge challenge."

Prof David Dexter of Parkinson's UK said: "Further development of this technique is now needed."

"If successful, it would turn this approach into a viable therapy that could improve the lives of people with Parkinson's and, ultimately, lead to the cure that millions are waiting for."

<http://bit.ly/2pEx2Xz>

Is this the magic ingredient that makes olive oil so healthy?

A new study in mice may shed light on the often-claimed health benefits of olive oil

Andrew Masterson.

A compound found in extra virgin olive oil reduces symptoms of insulin resistance and non-alcoholic fatty liver disease – at least in mice. The finding – published in the journal *Lipids in Health and Disease* – provides a tantalizing insight into why olive oil has been consistently identified as a valuable part of healthy eating regimes.

The mouse study, conducted by researchers led by Rodrigo Valenzuela of the University of Chile, focused on hydroxytyrosol, a polyphenol found in extra virgin olive oil.

In an elegant experiment, Valenzuela's team set up four small cohorts of mice. Over a 12-week period, two groups were put on a diet comprising 60% fat, with the others enjoying a "normal" 10% fat regime. One group from each pair was also given daily oral doses of hydroxytyrosol. The high-fat cohort without the supplement was found to have decreased levels of enzymes in the liver, which, in turn, negatively affected the production of long-chain polyunsaturated fatty acids – critical for vascular health.

The cohort enjoying the added hydroxytyrosol, however, showed enzyme production on a par with the mice on the lower-fat diets.

The results illustrate at least a partial mechanism to explain why olive oil appears to have a positive and protective effect on health. They also suggest that it might also ameliorate the adverse health consequences of high fat diets. "However, caution should be taken when extrapolating these findings to human consumption of

hydroxytyrosol as our experiments have been conducted with mice in a controlled environment," warns Valenzuela.

<http://bit.ly/2nQH8bq>

Experts walk back on prostate screening; men 55-69 should consider it

New data tipped the scales just a bit, showing some benefit to screening.

Beth Mole

Men aged 55 to 69 should talk with their doctors about the possibility of taking a blood-based prostate cancer test. The test comes with many potential problems but brings the benefit of ever so slightly reducing the chance of dying from the cancer. That's according to a new draft guidance out Tuesday from the US Preventive Services Task Force, an independent panel of experts appointed by the government to make evidence-based medical recommendations.

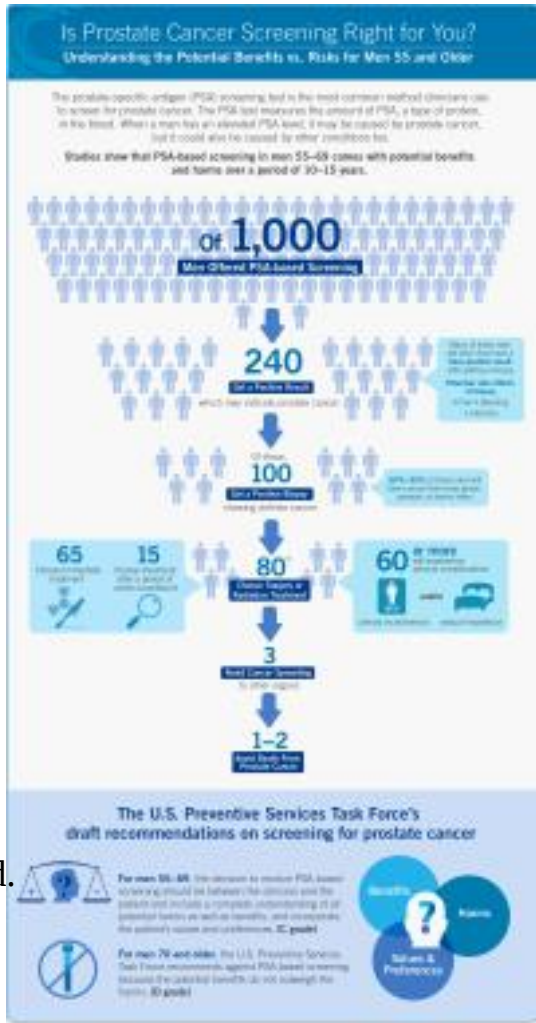
The new guidance is a bit of a walk-back from the USPSTF's 2012 recommendation that all men take a hard pass on the blood screening, called a PSA test. Men 70 or older are still advised to skip. While the USPSTF doesn't address men younger than 55, that group is generally considered at low risk and not in need screening either. But, the new guidance opens the door to screening on a case-by-case basis for the 55 to 69 age group.

For that group, the task force writes in its draft guidance: "the USPSTF recommends individualized decision-making about screening for prostate cancer after discussion with a clinician, so that each man has an opportunity to understand the potential benefits and harms of screening and to incorporate his values and preferences into his decision."

Those potential harms include over-diagnosis—getting a positive test result back that is later found to be false, causing stress and/or unnecessary treatments in between. There are also over-treatments, as well as complications that arise from normal treatments. For many men with prostate cancer, their disease will progress so slowly that

they would not die from it if it were left untreated. However, doctors can't tell the sluggish cancers from the killer ones. This spurs many men to opt for radiation and surgery right off the bat, which can cause urinary incontinence and impotence. The upside, of course, is the potential to not die from cancer. The calculations to weigh those risks and benefits are tricky and inevitably controversial.

In crunching the latest numbers on the matter, the USPSTF came up with this statistical run-down: Let's say 1,000 men get a blood test for prostate cancer, which runs about \$40 and measures the prostate-specific antigen (PSA), a protein made by the prostate gland. PSA levels become elevated in cases of cancer—but also benign prostate problems. Of the 1,000 getting a PSA test, 240 will get a positive result back (meaning their PSA levels appear elevated). Of those 240, biopsies would find that only 100 have prostate cancer. The other 140 were false-positives.



Of the 100 with prostate cancer, 80 would typically choose surgery or radiation—either right away or after a period of “active surveillance” or mild treatment options. In those 80, at least 60 would have to suffer

from the complications of urinary incontinence and/or impotence. Of those 80, three men would be spared from having their cancer spread. And one or two would be kept from dying of prostate cancer over a 10- to 15-year period.

The new calculation of the one to two lives spared tipped the scales for the USPSTF to recommend that men 55 to 69 talk with their doctor and think about it.

“The balance of benefits and harms is still close,” Kirsten Bibbins-Domingo, an internist at the University of California at San Francisco and task force chair, told The Washington Post. “This is not a recommendation that says men should go get screened. This is a complex decision. Some men will want to avoid the chance of dying of prostate cancer no matter what, while others, given the side effects, will not think the benefits are worth it.”

The American Cancer Society and the American Urological Association are also on board with the "informed" or "shared" decision-making plan for screening. The new guidance from the USPSTF is just a draft. The task force is taking public comments on it until May 8.

Editor's Note: The post has been updated to clarify the age groups that USPSTF examined.

<http://bit.ly/2pEIp1I>

Precision chronology sheds new light on the origins of Mongolia's nomadic horse culture

Domestic horse's roots traced back more than 3,000 years in the eastern Eurasian Steppes

According to new research, nomadic horse culture—famously associated with Genghis Khan and his Mongol hordes—can trace its roots back more than 3,000 years in the eastern Eurasian Steppes, in the territory of modern Mongolia.

The study, published online March 31 in Journal of Archaeological Science, produces scientific estimates of the age of horse bones found from archaeological sites belonging to a culture known as the Deer Stone-Khirgisuur Complex. This culture, named for the beautiful

carved standing stones ("deer stones") and burial mounds (khirigsuurs) it built across the Mongolian Steppe (Figure 2), is linked with some of the oldest evidence for nomadic herding and domestic livestock use in eastern Eurasia. At both deer stones and khirigsuurs, stone mounds containing ritual burials of domestic horses - sometimes numbering the hundreds or thousands - are found buried around the edge of each monument (Figure 3).

A team of researchers from several academic institutions - including the Max Planck Institute for the Science of Human History, Yale University, University of Chicago, the American Center for Mongolian Studies, and the National Museum of Mongolia - used a scientific dating technique known as radiocarbon dating to estimate the spread of domestic horse ritual at deer stones and khirigsuurs.



"Deer stone" stela in Bayankhongor province, central Mongolia, surrounded by small stone mounds containing domestic horse remains. William Taylor

When an organism dies, an unstable radioactive molecule present in living tissues, known as radiocarbon, begins to decay at a known rate. By measuring the remaining concentration of radiocarbon in organic materials, such as horse bone, archaeologists can estimate how many years ago an animal took its final step. Many previous archaeological projects in Mongolia produced radiocarbon date estimates from horse remains found at these Bronze Age archaeological sites. However, because each of these measurements must be calibrated to account for natural variation in the environment over time, individual dates have large amounts of error and uncertainty, making them difficult to aggregate or interpret in groups.

By using a statistical technique known as Bayesian analysis - which combines probability with archaeological information to improve

precision for groups of radiocarbon dates - the study authors were able to produce a high-precision chronology model for early domestic horse use in Mongolia. Lead author William Taylor, a postdoctoral research fellow at the Max Planck Institute for the Science of Human History, says that this model "enables us for the first time to link horse use with other important cultural developments in ancient Mongolia and eastern Eurasia, and evaluate the role of climate and environmental change in the local origins of horse riding."

According to the study, domestic horse ritual spread rapidly across the Mongol Steppe at around 1200 BC - several hundred years before mounted horsemen are clearly documented historical records. When considered alongside other evidence for horse transport in the Deer Stone-Khirigsuur Complex these results suggest that Mongolia was an epicenter for early horse culture - and probably early mounted horseback riding.

The study has important consequences for our understanding of human responses to climate change. For example, one particularly influential hypothesis argues that horse riding and nomadic herding societies developed during the late second millennium BCE, as a response to drought and a worsening climate. Taylor and colleagues' results indicate instead that early horsemanship took place during a wetter, more productive climate period - which may have given herders more room to experiment with horse breeding and transport.

In recent years, scholars have become increasingly aware of the role played by Inner Asian nomads in early waves of globalization. A key article published this month in Nature argues that nomadic movement patterns shaped the early trans-Eurasian trade networks that would eventually move goods, people, and information across the continent. The development of horsemanship by Mongolian cultures might have been one of the most influential changes in Eurasian prehistory - laying the groundwork for the economic and ecological exchange networks that defined the Old World for centuries to come.

<http://bit.ly/2ofv53L>

Trans Fat Ban Tied to Fewer Heart Attacks and Strokes *Rates of heart attack and stroke have dropped in New York counties with trans fat bans*

By Cari Nierenberg, Live Science Contributor

New York residents have benefited from rules that ban trans fat in restaurants: Rates of heart attack and stroke have dropped in New York counties where such bans have been enacted, a new study suggests.

Researchers found that starting three years after the effort to restrict the use of trans fats in eating establishments was introduced, the New York counties with these restrictions experienced a 6.2 percent reduction in hospital admissions for heart attacks and strokes, compared with New York counties without similar restrictions.

This translates to 43 fewer heart attacks and strokes per 100,000 adult residents (ages 25 and older) in the New York counties with trans fat restrictions, according to the study published online today (April 12) in the journal JAMA Cardiology.

The 6.2 percent decline in cardiovascular events found in the new study fell within the bounds of what other researchers have found in their estimates, said the study's lead author, Dr. Eric Brandt, a cardiovascular disease fellow at the Yale University School of Medicine in New Haven, Connecticut.

One previous estimate, from 2009, predicted that nearly eliminating trans fat from people's diets could prevent between 6 and 19 percent of heart disease hospitalizations.

However, the limitations on trans fat that the researchers looked at in this new study are not entirely comprehensive, Brandt told Live Science. The restrictions apply to trans fat in New York restaurants, bakeries, cafeterias, caterers, senior-meal programs and other food-service locations, but they do not apply to food sold in grocery stores, he said.

The decline in cardiovascular events observed in this study is promising, and suggests that similar if not greater decreases in heart attack and stroke rates could be seen when the Food and Drug Administration's nationwide restriction on trans fat goes into effect in 2018, Brandt said.

The FDA restrictions on trans fat will prevent manufacturers and food preparers from using partially hydrogenated oils, which contain these unhealthy fats, in foods. These measures will nearly eliminate trans fat in grocery stores and will ban them from eateries across the country.

Although food companies have been gradually eliminating trans fat from their products in preparation for the FDA's ban, partially hydrogenated oils are still a part of people's diets. The oils are found in baked goods, fried foods, yeast breads, chips, crackers and margarine, the study authors wrote.

Studies have suggested that people with higher levels of trans fat in their diets are at greater risk for stroke and cardiovascular disease.

Heart health benefits

New York City first introduced restrictions on trans fat in eating establishments in July 2007, and similar actions were initiated in 11 counties in New York state between 2007 and 2011.

In the study, the researchers analyzed data on hospital admission rates for heart attacks and stroke over an 11-year period, from 2002 to 2013. The study period covered about five years before and after the restrictions took effect. The researchers compared the hospitalization rates for heart attacks and stroke in adults ages 25 and older in the 11 New York counties with restrictions on trans fat, with the hospitalization rates for these cardiovascular problems in 25 New York counties without restrictions.

Rates of heart attack and stroke were already declining in New York state before the trans fat restrictions, the study authors noted. However, after 2006, the analysis found that populations in counties with the ban experienced additional declines beyond what would have been expected based on the existing downward trends.

The study found that declines in heart attacks and strokes within the areas of the ban became apparent three or more years after trans fat was restricted in the county's eateries.

It usually takes a few years for this kind of dietary modification to reduce cardiovascular disease risk enough to be measurable, Brandt said.

He expects that when the FDA restrictions on trans fat get implemented next year on all foods, a continued decline in heart attacks and strokes will be seen in the New York counties that had already limited the use of these fats in restaurants.

There are likely to be further measurable differences in heart attack and stroke rates, especially among younger age groups, who may benefit by spending an even longer portion of their lives without trans fat in their diets, Brandt said.

Although it may be costly for food companies to reformulate their products to eliminate trans fat, this data suggests that by restricting trans fat in foods, there is a potential to improve the health of Americans and lessen the burden of cardiovascular disease, Brandt said.

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

Why Scientists Must Share Their Failures

We don't ask people in other professions to do it, but it's vital for speeding up progress in crucial areas of research from climate to medicine and public health

By Ijad Madisch

Ask any budding director if they would like to see the first iterations of Francis Ford Coppola's Godfather. I don't think many would pass up the opportunity to see Coppola's process from filming, to editing, to deciding what makes the final cut.

Indeed, people in nearly any occupation, from painters to journalists to architects could learn from failed iterations of the respective masters of their crafts. Yet in all these fields, we don't expect—nor do we get—any of this. We generally only see the final, perfected product.

In the sciences, however, I want to shift this thinking. I want researchers to share everything from start to finish. Why?

Because we need them to. Their failures, if seen, could stop another researcher from making the same mistakes. What's more, knowing what doesn't work will help researchers—or computers, in the future—deduce what might work, and in turn, speed up scientific progress.

This scientific progress is critical if we are going to tackle global challenges; preventing pandemics and finding sustainable energy sources that will fuel growing societies. However, if other fields are any indication, getting to a point where sharing failed scientific results is commonplace will be hard and take time. It will be worth it though, because the benefits are immense.

From my experience, 99 percent of work in research never makes it into the final, published article. Yet, in the past, that article was all we'd see. Not only does this give the public a distorted view of the scientific process, but it also slows progress for other researchers.

Take my own research, for example. I started my medical research in 2002, and ended it in 2010. What I've got to show for these eight years are my thesis, 18 articles, 17 conference papers and 69 datasets. What isn't seen is the thousands of hours I spent working on things that yielded results that I didn't expect or simply didn't work.

For people like me who left academia, the hard drives full of negative results may already be lost. To prevent this from happening to others, [ResearchGate](#), the professional network for scientists I founded with two friends nine years ago, encourages researchers to document their entire research process step-by-step, publishing everything. Along the way, we hope that they will also share things that didn't work out.

However, I understand the barriers to achieving this. Perhaps the biggest barrier is simply putting your hand up and saying, "Hey, I thought this would work but it didn't."

This, in itself, is just another finding. But maybe you're afraid of someone else interpreting it as failure. What's more, writing up and

publishing a negative result is to do something that largely benefits others. *You* know it didn't work and have already learned from it. Most people wouldn't blame you from wanting to move on and get started on the next thing. But despite, or maybe because of this, ResearchGate members have started sharing their negative results.

Take [Wiebke Kämper](#). She wanted to find a faster way to work out which flowers bumblebees were visiting. Rather than using a traditional and time-consuming observational method, she decided to try using the chemical footprints that bumblebees leave behind when they visit a flower.

Early experiments were positive, but tests in the field were not successful. By publishing her [negative results](#), she insured that others could save time and work on other methods to get behind bumblebees' floral preferences.

Or consider surgeon [Anees Chagpar](#) from Yale University, who takes the business school mantra "fail early, fail often" to heart in her research. She [hypothesized](#) that surgeons conducting breast conserving surgery for breast cancer patients could benefit from a three-dimensional model.

However, she conducted a study and found the model made no difference. [Publishing](#) these results means other researchers can invest their time in other options, increasing the chance that they will discover results that improve outcomes for patients.

I deeply respect researchers like Kämper and Chagpar who have the courage to share these valuable findings with their peers, advancing their own, and their peers' work. Science is inherently collaborative. Reporting negative results is scary, but it means our colleagues won't waste their time and resources repeating our mistakes. In this spirit, feel free to check out my ResearchGate profile for the failed iterations of this article.

<http://bit.ly/2oMGH1q>

Potential Energy Source for Life Spotted on Saturn Moon Enceladus

Saturn's icy moon Enceladus is looking more and more like a habitable world.

By Mike Wall, Space.com Senior Writer

The same sorts of chemical reactions that sustain life near deep-sea hydrothermal vents here on Earth could potentially be occurring within [Enceladus' subsurface ocean](#), a new study published today (April 13) in the journal *Science* suggests.

These reactions depend on the presence of molecular hydrogen (H₂), which, the new study reports, is likely being produced continuously by reactions between hot water and rock deep down in Enceladus' sea.

"The abundance of H₂, along with previously observed carbonate species, suggests a state of chemical disequilibria in the Enceladus ocean that represents a chemical energy source capable of supporting life," Jeffrey Seewald of the Marine Chemistry and Geochemistry Department at the Woods Hole Oceanographic Institution in Massachusetts wrote in an accompanying "Perspectives" piece in the same issue of *Science*.

(Seewald was not involved in the new Enceladus study.)

This enhanced-color image of Enceladus by NASA's Cassini spacecraft features the "tiger stripe" fractures, from which geysers blast water ice and other material from the Saturn moon's subsurface ocean out into space.

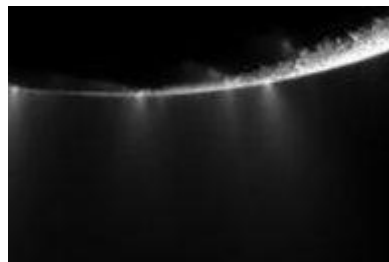
NASA/JPL/Space Science Institute



A geyser-blasting ocean world

The 313-mile-wide (504 kilometers) [Enceladus](#) is just Saturn's sixth-largest moon, but the object has loomed large in the minds of astrobiologists since 2005.

In that year, NASA's Saturn-orbiting [Cassini spacecraft](#) first spotted geysers of water ice erupting from "tiger stripe" fissures near Enceladus' south pole. Scientists think these geysers are blasting material from a sizeable ocean buried beneath the satellite's ice shell.



More than 100 individual geysers blast water ice, organic molecules and other material into space from the south polar region of Saturn's moon Enceladus, as seen here by NASA's Cassini spacecraft. NASA/JPL/SSI

So, Enceladus has liquid water, one of the key ingredients required for life as we know it. (This ocean stays liquid because Saturn's immense gravitational pull twists and stretches the moon, generating internal "tidal" heat.) And the new study suggests that the satellite possesses another key ingredient as well: an energy source.

A team of researchers led by Hunter Waite, of the Southwest Research Institute (SwRI) in San Antonio, analyzed observations made by Cassini during an [October 2015 dive](#) through Enceladus' geyser plume. This plunge was special in several ways. For one thing, it was Cassini's deepest-ever dive through the plume; the probe got within a mere 30 miles (49 km) of Enceladus' surface. In addition, Cassini's Ion and Neutral Mass Spectrometer (INMS) instrument alternated between "open-source" and "closed-source" modes during the encounter, rather than sticking to closed source (the usual routine).

INMS is just 0.25 percent as sensitive in open-source mode as it is in closed-source mode, Waite and his colleagues wrote in the [new Science paper](#). But open source has a key advantage: It minimizes artifacts that have complicated previous attempts to measure H₂ levels in the plume.

With this analytical hurdle cleared, Waite and his team were able to calculate that H₂ makes up between 0.4 percent and 1.4 percent of the volume of Enceladus' geyser plume. Further calculations revealed that carbon dioxide (CO₂) makes up an additional 0.3 percent to 0.8 percent of the plume's volume.

The molecular hydrogen is most likely being produced continuously by reactions between hot water and rock in and around Enceladus' core, Waite and his colleagues concluded. They considered other possible explanations and found them wanting. For example, neither Enceladus' ocean nor its ice shell are viable long-term reservoirs for volatile H₂, the authors wrote, and processes that disassociate H₂ from water ice in the shell don't seem capable of generating the volume measured in the plume.

The hydrothermal explanation is also consistent with a 2016 study by another research group, which concluded that tiny silica grains detected by Cassini could have been produced [only in hot water at significant depths](#).

"The story seems to be fitting together," Chris Glein of SwRI, a co-author of the new Science paper, told Space.com.

Deep-sea chemical reactions

Earth's deep-sea [hydrothermal vents](#) support rich communities of life, ecosystems powered by chemical energy rather than sunlight.

"Some of the most primitive metabolic pathways utilized by microbes in these environments involve the reduction of carbon dioxide (CO₂) with H₂ to form methane (CH₄) by a process known as methanogenesis," Seewald wrote.

The inferred presence of H₂ and CO₂ in Enceladus' ocean therefore suggests that similar reactions could well be occurring deep beneath the moon's icy shell. Indeed, the observed H₂ levels indicate that a lot of chemical energy is potentially available in the ocean, Glein said.

"It's quite a bit larger than the minimum energy required to support methanogenesis," he said.

Glein stressed, however, that nobody knows whether such reactions are actually occurring on Enceladus.

"This is not a detection of life," Glein said. "It increases the habitability, but I would never suggest that this makes Enceladus more or less likely to have life itself. I think the only way to answer that question is, we need data."

Seewald also counseled caution on astrobiological interpretations. He noted, for example, that molecular hydrogen is rare in Earth's seawater, because hungry microbes quickly gobble it up.

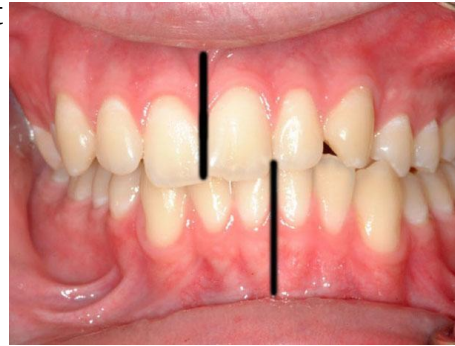
"Is the presence of H₂ in the Enceladus ocean an indicator for the absence of life, or is it a reflection of the very different geochemical environment and associated ecosystems on Enceladus?" Seewald wrote. "We still have a long way to go in our understanding of processes regulating the exchange of mass and heat across geological interfaces that define the internal structure of Enceladus and other ice-covered planetary bodies."

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

Crooked bite may indicate early life stress

University of Washington Dentistry researchers ID novel marker for developmental instability

Research has repeatedly confirmed that the first 1,000 days after conception strongly influence a person's life expectancy and susceptibility to chronic diseases. The primary marker used to identify early life stress is low birth weight, which can, for instance, indicate poor nutrition of the mother during pregnancy.



This is an example of a crooked bite which led to a large shift between the midlines (black lines added to image) of the upper and lower incisors. Courtesy of Philippe Hujuel

But low birth weight is a marker only until birth, about 280 days -- far short of a measurement useful for the first thousand days.

New research from University of Washington investigators suggests that an asymmetric lower face is a novel marker that also captures early life stresses that occur after birth.

"Asymmetries in the skull and teeth have been used for decades by anthropologists to mark environmental stress, but they have only

rarely been used in living populations," said Philippe Hujuel, the corresponding author. "Such lower-face asymmetries can be assessed by looking at the dental bite in the permanent teeth -- an exam that can be completed in seconds and with more certainty than a mother's recall of birth weight and more ease than a search for a birth certificate."

Hujuel, a professor in the UW School of Dentistry, described a crooked, or asymmetric, bite as the teeth biting backward or forward on one side of the face and normally on the other side.

Backward-biting asymmetries, the most common lower-face asymmetry in the U.S. population, were found to fluctuate randomly between the left and right sides of the face. Such randomness is evidence for early life stress, he said.

Hujuel emphasized that crooked teeth, overbites and underbites are different than an asymmetric bite. Those conditions can be associated with asymmetric and symmetric bites, the latter of which is largely a reflection of genetics, not environmental stress, he said.

Hujuel, Erin Masterson and Anne-Marie Bollen researched data gathered from 1966 to 1970, a sample of 6,654 12- to 17-year-olds involved in a National Health Examination Survey. The study found that one in four of the U.S. adolescents had lower-face asymmetries.

"Lower-face asymmetries were common in a generation that became typified by an epidemic of diabetes and obesity in adulthood," noted Hujuel, an adjunct professor of epidemiology in the School of Public Health.

The team had to look back four decades for data because in the 1970's, he said, dental researchers in charge of designing U.S. surveys began to disregard the value of diagnosing facial asymmetry, and stopped taking those measurements.

"From a biological perspective, this decision resulted in an inability to reliably track trends in the U.S.," Hujuel said. "We don't have current information on the prevalence of lower-face asymmetries in the U.S. population."

Further research is needed to identify whether lower-face asymmetries are predictive of chronic diseases in living populations in the same way that skull asymmetries have been associated with degenerative diseases in long-deceased populations.

<http://bit.ly/2ojyUE3>

Here's What Happens During a Fentanyl Overdose
Deaths due to opioid overdoses have risen sharply in the past few years, partly due to a particularly potent drug called fentanyl.

By Sara G. Miller, Staff Writer

Fentanyl is between 50 and 100 times more powerful than another opioid, morphine, and its use seems to be on the rise in the U.S.

In Massachusetts, for example, from 2013 to 2014, 32 percent of opioid overdose deaths involved fentanyl. During the first half of 2016, the percentage of fentanyl-related opioid deaths had more than doubled, jumping to 74 percent, according to a new report.

In an effort to better understand the effects of this powerful drug, as well as educate first responders and bystanders on how to best identify and treat people who have overdosed on fentanyl, researchers at the Centers for Disease Control and Prevention interviewed more than 60 people from southeastern Massachusetts, who were recruited from harm-reduction programs.

All of the people in the study had either used the drug in the previous year and survived an overdose in past six months, or had witnessed an overdose between October 2014 and March 2015. The researchers asked them about their experiences, knowledge, attitudes and beliefs about opioid overdoses. In addition, the researchers gathered information from death records to track fatalities that occurred during the same time period.

The interviews shed light on the fast-acting and sometimes gruesome nature of fentanyl overdoses - as well as how widespread the drug has become - according to the report, which the CDC published April 13.

When the researchers asked the participants why there had been an increase in opioid overdose deaths in recent years, 88 percent of the

respondents placed the blame on fentanyl. (In fact, when the CDC researchers reviewed death records for nearly 200 people who overdosed on opioids during the study period, they found that two-thirds tested positive for fentanyl.)

From pain patch to deadly powder

Fentanyl can be used legally — doctors prescribe the drug for people with chronic pain. The drug comes as a transdermal patch, which slowly releases the drug into the person's body at a rate that is considered safe.

But the drug can also be found in an illegal, powdered form.

In the interviews, the participants said that fentanyl powder can be purchased on its own or mixed with heroin. They also said that sometimes, people didn't know if the heroin they had purchased also contained fentanyl.

The death records revealed that 82 percent of the fatalities involved the illegal powdered form of the drug, and just 4 percent involved the prescription patch. In 14 percent of the cases, the form of the drug that the person had used was not known.

The researchers noted that some of the people interviewed said that they specifically sought out fentanyl. Others said they had tried to avoid the drug, but they also said that the possibility that they might wind up with fentanyl, or fentanyl-laced heroin, didn't stop them from seeking opioids, the researchers found.

One of the major characteristics that the respondents described was the speed of a fentanyl overdose: Seventy-five percent of the respondents said that the symptoms occurred within seconds to minutes.

When a person overdoses on heroin, he or she may take the drug and then proceed to carry on a conversation for a few moments, one respondent said. Then suddenly, that person stops talking and "you look over and realize that they're overdosing," the respondent said.

But with fentanyl, the same respondent said that the effect is immediate: "I would say you notice it [a fentanyl overdose] as soon as

they are done [injecting the fentanyl]. They don't even have time to pull the needle out [of their body] and they're on the ground."

Injecting fentanyl was the most common way that a person overdosed on the drug, accounting for 75 percent of the overdoses witnessed, according to the respondents. The remaining 25 percent of the overdoses resulted from people snorting the drug, the researchers said.

Anatomy of an overdose

The researchers asked the respondents to describe what happened during a suspected fentanyl overdose. The most common characteristic, described in 20 percent of the cases, was that the person's lips immediately turned blue, followed by gurgling sounds with breathing (16 percent of the cases), stiffening of the body or seizure-like activity (13 percent), foaming at the mouth (6 percent) and confusion or strange behavior before the person became unresponsive (6 percent), according to the report.

Fentanyl overdoses can be reversed with the same antidote that is used to treat other opioid overdoses — a drug called naloxone, which is sold under the brand name Narcan.

In the report, in 83 percent of the cases when naloxone was used, one dose was not sufficient. Instead, the respondents said that two or more doses of the antidote were needed to revive the person who had overdosed, according to the report.

Indeed, some opioid users are aware of the dangers of both fentanyl and heroin: According to the report, 30 percent of the respondents said that, in order to help protect themselves against a deadly overdose, they don't use the drugs when they are alone.

<http://bit.ly/2ojC0Ix>

France, Japan aim to land probe on Mars moon

France and Japan want to recover pieces of a Martian Moon and bring them back to Earth, the head of France's National Centre for Space Studies (CNES) said Thursday.

The Martian Moons Exploration project would launch a probe in 2024 destined for Phobos, the largest and closest of two moons circling the

Red Planet. Paris and Tokyo signed a preliminary agreement on Monday, and will make a final decision before the end of the year, CNES president Jean-Yves Le Gall told AFP.

"It's a very important mission because—besides the Moon—it would be the first time samples from the satellite of a planet would be brought back to Earth," he said by phone.

Slightly egg-shaped, Phobos is 27 kilometres (17 miles) in diameter from end-to-end. Analysing its composition would solve a long-standing question as to its origins.

One theory holds that the oblong moon is an asteroid captured by the gravitational pull of Mars. Another says that it is left-over matter from the Red Planet's creation event.

Landing on Phobos will also provide another vantage point for observing Mars, only 6,000 kilometres (3,700 miles) distant.

Getting there poses fewer challenges than landing on Mars, a graveyard for several failed missions. "It should be twice as easy because the probe will not have to go through the Martian atmosphere," Le Gall said. The Japanese partner for the project is the Japan Aerospace Exploration Agency.

Phobos—closer to its planet than any other moon in the solar system—is approaching Mars by about 2 metres (6.5 feet) every century. Scientists expect the moon to be pulled apart in 30 to 50 million years.

In 2011, a Phobos-bound probe launched by Russia—it's first interplanetary mission in 15 years—failed, with pieces falling into the Pacific two months later.

In 2020, the joint Europe-Russia ExoMars mission will launch a rover tasked with finding traces of Martian life, past or present. NASA's Curiosity rover has been criss-crossing the planet for more than three years. The American agency has plans for a manned trip in the next 10-15 years, with a similar project also being pursued by US billionaire Elon Musk.

<http://bit.ly/2p7j3qL>

'I'm just too busy'—is being overworked the new status symbol?

Workaholism, it seems, is the new black.

by Alan Mozes, Healthday Reporter

People who complain endlessly about being overworked and overwhelmed may be sending others a less-than-subtle message: "I'm more important than you."

So finds new research suggesting that some Americans are eschewing old tipoffs to status—weekday rounds of golf and months-long vacations. Instead, higher status is now transmitted by at least claiming to be oh so busy. "In the past, living a leisurely life and not working was the most powerful way to signal one's status," explained study lead author Silvia Bellezza.

"Fast-forward to America today, and complaining about being busy and working all the time—rather than being on holiday—has become increasingly common," said Bellezza. She's an assistant professor of marketing at Columbia University in New York City.

Bellezza's team conducted a series of experiments focused on what psychologists call "status attribution"—characteristics that help establish an individual's position in society.

These status-markers can change with time. So to examine current "status attributions," the researchers first reviewed 1,100 examples of online "humble-bragging."

"Humble-brags" are a form of showing off by feigning self-deprecation. For example, "I'm just so swamped by all my charity work."

Most of the social media humble-brags in the study were placed on Twitter by well-known celebrities, Bellezza's team said. The posts had one thing in common: a tendency to complain about 'having no life' or 'being in desperate need for a vacation.' "

Another experiment asked participants to indicate whether they thought "being busy" meant spending a lot of time at work, spending a

lot of time performing house-related chores, or spending a lot of time engaged with hobbies or leisure activities.

A third study recruited about 300 men and women who were asked to guess the social status and wealth of a series of Facebook users who had posted updates on leisure activities or workplace busyness.

The take-home message from the experiments: Americans viewed relentless work in a more favorable light than they did leisure-seeking. Brand and product use tended to reinforce this view, with services such as dog-walkers or online grocery purchasing designed with the busy worker in mind. Use of these services connotes higher status, the researchers said, in the same way that owning an expensive watch or purse might have in the past.

However, one other experiment suggested that America's glorification of the "busy-bee" lifestyle might not be shared by people in other countries. Comparing people from the United States and Italy, Bellezza and her colleagues found that Italians still placed a higher value on a more leisurely life versus the career "rat race."

Why would Americans be enamored of working too hard? It might be due to being "heavily influenced by our own beliefs in social mobility," according to Bellezza.

"The more we believe that one has the opportunity for social affirmation based on hard work," she noted, "the more we tend to think that people who skip leisure, and work all the time, are of higher standing."

Bellezza added that the move to a more service-oriented economy has also likely encouraged the shift. She theorized that people with busy jobs involving information processing may be perceived as more talented and skillful compared with, say, someone on a factory floor.

The study appeared in a recent issue of the Journal of Consumer Research.

Seth Kaplan is an associate professor of industrial/organizational psychology at George Mason University in Fairfax, Va. Reviewing the new findings, he said they "are consistent with other research

indicating that reporting being busy and even 'stressed' is socially desirable."

In fact, not projecting such stress could prove problematic, given the "potential inference is that that person is lazy and/or incompetent," Kaplan said.

"[But] what is perhaps especially interesting about this effect," Kaplan added, "is that the evidence does not conclusively show that leisure time is actually decreasing," he noted.

"Although there is some debate in this area, most time-use data suggest that American leisure time has not decreased—at least not significantly so—in recent years," Kaplan said. "We tend to just perceive and/or report that it has."

More information: Silvia Bellezza, Ph.D., assistant professor, marketing, Columbia Business School, Columbia University, New York City; Seth Kaplan, Ph.D., associate professor, Industrial/Organizational Psychology, and director, Industrial/Organizational Psychology Ph.D. Program, George Mason University, Fairfax, Va.; March 22, 2017, Journal of Consumer Research

<http://nyti.ms/2oDnQ8p>

St. Jude Medical Played Down Defibrillator Failures for Years, F.D.A. Says

Manufacturer shipped them for years before recalling the devices last fall

By KATIE THOMAS APRIL 13, 2017

The medical device maker St. Jude Medical played down the failure of some batteries in its defibrillators, shipping them for years before recalling the devices last fall, according to a warning letter the Food and Drug Administration issued this week.

The company, acquired by Abbott Laboratories in January, also failed to tell its own management and a medical advisory board that the battery problems had led to the death of a patient, the agency found.

The F.D.A. said St. Jude Medical had not shown it was taking sufficient action to fix the problems that led to the slow recall and ordered the company to provide a new reporting plan within 15 days.

Faulty defibrillators and other implanted devices are particularly problematic because removing them requires surgery that can be more risky than keeping them in. When the company announced the recall in October, the F.D.A. recommended that doctors closely monitor their patients' devices for problems. Saying the malfunction did not appear to be widespread, the agency warned that "patients could be at greater risk of complications from the surgical procedure required to replace the device."

One of the nearly 400,000 defibrillators recalled by the F.D.A last fall. St. Jude Medical was ordered by the agency to provide a plan for correcting its reporting on the device problems within 15 days. St. Jude Medical

In October, the F.D.A. said that of the nearly 400,000 devices sold worldwide that were affected by the recall, 841 were returned to the company for analysis because the battery had died unexpectedly. As of January, two people had died because their defibrillators failed to work, the agency said, and dozens of others had suffered adverse effects. Defibrillators deliver an electric shock to return the heart to a normal pace when it is not beating properly.

An F.D.A. spokeswoman, Angela Stark, said Thursday that nearly 200,000 people in the United States have a defibrillator included in the recall. The recalled devices include models in the company's Fortify, Unify and Assura defibrillator lines.

Physicians at Duke University reported two cases of battery problems with the devices in 2014, and another team at the University of Illinois did so in 2015, concluding that lithium in the battery was forming clusters and causing it to short-circuit. That same year, St. Jude fixed the problem in new defibrillators it manufactured, but it did not recall the older devices or alert doctors or patients about the potential problem until October. As a result, doctors continued implanting the old devices in patients.



“What bothers me most about this is that the doctors and the patients weren’t told about the potential” for failure, said Dr. Robert G. Hauser, a retired cardiologist who campaigns for improved safety of medical devices. “And clearly this is for St. Jude’s benefit. They can sell products rather than scrapping it.”

He also faulted the F.D.A. for not having investigated St. Jude earlier. “They should have been in there years ago, looking at all the raw data in order to determine if the incidence was low enough to allow these devices to be shipped and implanted,” he said.

Defibrillators accounted for nearly a third of St. Jude’s sales in 2015, or about \$1.6 billion, according to The Minneapolis Star Tribune, which reported on the defibrillator issue last fall. In January, the company was acquired by Abbott for \$25 billion.

Abbott said that it was reviewing the warning letter and that it was committed to addressing the issues raised by the agency. “We have a strong history and commitment to product safety and quality,” the company said.

Ms. Stark, the F.D.A. spokeswoman, said the agency did not insist on an earlier recall because it was relying on information the company had provided at the time. But while the agency now says the company misrepresented the risk, Ms. Stark said, “I don’t think we can speculate on how that might have changed the decision almost two years ago.”

According to the letter, St. Jude understated the problem by concluding that reports about failing batteries were “unconfirmed” even though the battery manufacturer, Greatbatch (now known as Integer Holdings), concluded that the lithium clusters were the culprit. The company did not include these “unconfirmed” cases when it calculated the likelihood that the devices would malfunction, making it appear that the problem was less serious than it was, the agency said. The agency also found that the company knew of a patient’s death in 2014 but did not disclose it to St. Jude Medical management or a medical advisory board. “Both presentations stated there were no

serious injury or death directly related to lithium cluster formations,” the letter said.

In addition, the F.D.A. said that St. Jude still had not fully addressed concerns raised in January, when the agency warned that hackers could gain access to St. Jude’s defibrillators and remote monitoring system and could cause the devices to deliver unnecessary shocks.

This is not the first time a device maker has been accused of being slow to warn the public about a faulty defibrillator. In 2011, Guidant pleaded guilty to federal criminal charges and paid nearly \$300 million in fines after it was revealed, in part because of Dr. Hauser’s efforts, that it had allowed some of its defibrillators to be implanted in patients even though the company knew the devices might short-circuit.

And that year, St. Jude came under scrutiny after it was accused of being too slow to recall faulty wires that connect the defibrillator to the heart.

Correction: April 15, 2017

An article on Friday about problems with defibrillators made by St. Jude Medical referred incorrectly to one aspect of a warning letter the Food and Drug Administration sent to St. Jude. The battery manufacturer was identified in the letter as Greatbatch, now known as Integer Holdings; it is not the case that the agency’s letter did not identify the battery manufacturer.

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

Psychedelic drug ayahuasca improves hard-to-treat depression

It tastes foul and makes people vomit. But [ayahuasca](#), a hallucinogenic concoction that has been drunk in South America for centuries in religious rituals, may help people with [depression](#) that is resistant to antidepressants.

By Andy Coghlan

Tourists are increasingly trying ayahuasca during holidays to countries such as Brazil and Peru, where the psychedelic drug is legal. Now the world’s first randomised clinical trial of ayahuasca for treating depression has found that it can rapidly improve mood.

The trial, which took place in Brazil, involved administering a single dose to 14 people with treatment-resistant depression, while 15 people with the same condition received a placebo drink.

A week later, those given ayahuasca showed dramatic improvements, with their mood shifting from severe to mild on a standard scale of depression. “The main evidence is that the antidepressant effect of ayahuasca is superior to the placebo effect,” says [Dráulio de Araújo](#) of the Brain Institute at the Federal University of Rio Grande do Norte in Natal, who led the trial.

Bitter brew

Shamans traditionally prepare the bitter, deep-brown brew of ayahuasca using two plants native to South America. The first, *Psychotria viridis*, is packed with the mind-altering compound dimethyltryptamine (DMT). The second, the ayahuasca vine (*Banisteriopsis caapi*), contains substances that stop DMT from being broken down before it crosses the gut and reaches the brain.

To fool placebo recipients into thinking they were getting the real thing, de Araújo and his team concocted an equally foul tasting brown-coloured drink. They also carefully selected participants who had never tried ayahuasca or other psychedelic drugs before.

A day before their dose, the participants filled in standard questionnaires to rate their depression. The next day, they spent 8 hours in a quiet, supervised environment, where they received either the placebo or the potion, which produces hallucinogenic effects for around 4 hours. They then repeated filling in the questionnaires one, two and seven days later.

Both groups reported substantial improvements one and two days after the treatment, with placebo scores often as high as those of people who had taken the drug. In trials of new antidepressant drugs, it is common for as many as 40 per cent of participants to respond positively to placebos, says de Araújo.

But a week into this trial, 64 per cent of people who had taken ayahuasca felt the severity of their depression reduce by 50 per cent or

more. This was true for only 27 per cent of those who drank the placebo.

Psychedelic treatments

“The findings suggest a rapid antidepressant benefit for ayahuasca, at least for the short term,” says [David Mischoulon](#) of Massachusetts General Hospital in Boston. “But we need studies that follow patients for longer periods to see whether these effects are sustained.”

“There is clearly potential to explore further how this most ancient of plant medicines may have a salutary effect in modern treatment settings, particularly in patients who haven’t responded well to conventional treatments,” says [Charles Grob](#) at the University of California, Los Angeles.

If the finding holds up in longer studies, it could provide a valuable new tool for helping people with treatment-resistant depression. An estimated 350 million people worldwide experience depression, and between a third to a half of them don’t improve when given standard antidepressants.

[Ayahuasca](#) isn’t the only psychedelic drug being investigated as a potential treatment for depression. Researchers have also seen some benefits with [ketamine](#) and [psilocybin](#), extracted from magic mushrooms, although psilocybin is yet to be tested against a placebo.

Journal reference: *bioRxiv*, DOI: [10.1101/103531](https://doi.org/10.1101/103531)

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

New method for tapping vast plant pharmacopeia to make more effective drugs

Effective and powerful new way for identifying the elusive gene networks that plants use to make bioactive compounds

April 14, 2017 by David Salisbury

Cocaine, nicotine, capsaicin. These are just three familiar examples of the hundreds of thousands of small molecules (also called specialized or secondary metabolites) that plants use as chemical ammunition to protect themselves from predation.

Unfortunately, identifying the networks of [genes](#) that plants use to make these biologically active compounds, which are the source of many of the drugs that people use and abuse daily, has vexed scientists for years, hindering efforts to tap this vast pharmacopeia to produce new and improved therapeutics.

Now, Vanderbilt University geneticists think they have come up with an effective and powerful new way for identifying these elusive gene networks, which typically consist of a handful to dozens of different genes, that may overcome this road block.

"Plants synthesize massive numbers of bioproducts that are of benefit to society. This team has revolutionized the potential to uncover these natural bioproducts and understand how they are synthesized," said Anne Sylvester, program director in the National Science Foundation's Biological Sciences Directorate, which funded the research.

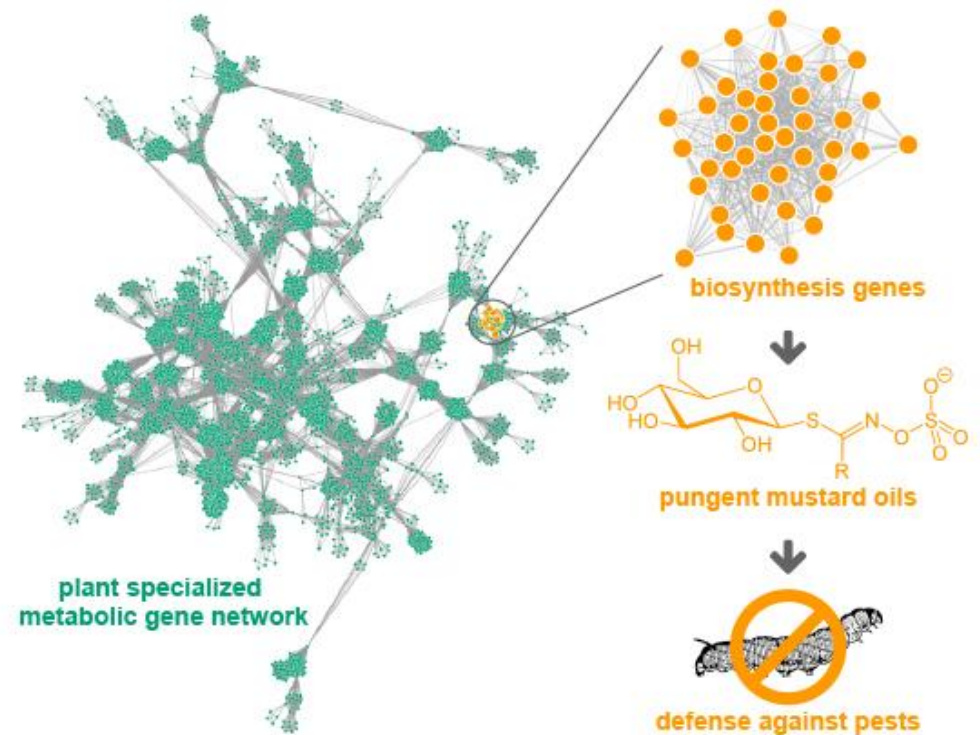
The revolutionary new approach is based on the well-established observation that plants produce these compounds in response to specific environmental conditions.

"We hypothesized that the genes within a network that work together to make a specific compound would all respond similarly to the same environmental conditions," explained Jennifer Wisecaver, the post-doctoral fellow who conducted the study.

To test this hypothesis, Wisecaver - working with Cornelius Vanderbilt Professor of Biological Sciences Antonis Rokas and undergraduate researcher Alexander Borowsky - turned to Vanderbilt's in-house supercomputer at the Advanced Computing Center for Research & Education in order to crunch data from more than 22,000 gene expression studies performed on eight different model plant species.

"These studies use advanced genomic technologies that can detect all the genes that plants turn on or off under specific conditions, such as high salinity, drought or the presence of a specific predator or pathogen," said Wisecaver.

But identifying the networks of genes responsible for producing these [small molecules](#) from thousands of experiments measuring the activity of thousands of genes is no trivial matter. That's where the Vanderbilt scientists stepped in; They devised a powerful algorithm capable of identifying the networks of genes that show the same behavior (for



One of the gene networks created in this study is shown on the left. Each green dot is a gene, and genes that likely work together are connected by a line. Dense regions in the network show genes that work together to make a specialized product. For example, the genes in orange make glucosinolates (the pungent mustard oils found in broccoli, cauliflower, and other vegetables), which plants produce to fight off pests. Investigating the unknown regions of the gene network has the potential to uncover new plant products to harness for medicine and agriculture.

example, all turning on) across these expression studies.

The result of all this number crunching - described in the paper titled "A global co-expression network approach for connecting genes to specialized metabolic pathways in plants" published online Apr. 13 by *The Plant Cell* journal - was the identification of dozens, possibly

even hundreds of gene pathways that produce small metabolites, including several that previous experiments had identified.

Vanderbilt geneticists have developed an effective method for identifying the plant genes that produce the chemical ammunition plants use to protect themselves from predation and is a natural source of many important drugs. Credit: Jennifer Wisecaver, Rokas Lab, Vanderbilt University

Vered Tzin from Ben-Gurion University's Jacob Blaustein Institutes for Desert Research in Israel and Georg Jander from Cornell University's Boyce Thompson Institute for Plant Research in Ithaca, NY, helped verify the predictions the analysis made in corn, and Daniel Kliebenstein from the Department of Plant Sciences at the University of California, Davis helped verify the predictions in the model plant system *Arabidopsis*.

The results of their analysis go against the prevailing theory that the genes that make up these pathways are clustered together on the plant genome. "This idea comes from the observation in fungi and bacteria that the genes that make up these specialized metabolite pathways are clustered together," said Rokas. "In plants, however, these genes appear to be mostly scattered across the genome. Consequently, the strategies for discovering plant gene pathways will need to be different from those developed in the other organisms."

The researchers argue that the results of their study show that this approach "is a novel, rich and largely untapped means for high-throughput discovery of the genetic basis and architecture of plant natural products."

If that proves to be true, then it could help open the tap on new plant-based therapeutics for treating a broad range of conditions and diseases.