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Blow out your knee? Hope your surgeon's got a VR headset

VR gets much-needed validation as a surgical training tool.

Peter Rubin, wired.com

With all due respect to games, porn, and lion kings, virtual reality's killer app might just be saving lives.

At a Stanford-affiliated children's hospital, pediatric cardiologists use an interactive virtual heart to help young patients and their families better understand congenital defects. Researchers in Maryland put on headsets to study viruses in the pursuit of a universal flu vaccine. In Minnesota, surgeons stood inside a VR model of the circulatory systems of conjoined twins—which proved integral to the ensuing separation surgery.

Great uses, certainly, but all variations on *The Fantastic Voyage* (or *Innerspace*, if you prefer). Now, building on a pile of evidence stretching back more than a decade, VR is finally getting clinical validation for actual surgical *training*. In a pilot study conducted at UCLA and presented recently at a meeting of orthopedic surgeons, medical students who practiced a common procedure in VR significantly outperformed those who used conventional preparation methods.

This wasn't a highly specialized procedure, but the bread and butter of orthopedic surgeons everywhere: fixing a bone fracture. Specifically, a break in the tibia, the larger of the two bones in your lower leg. The tibia isn't the most commonly broken bone, but it certainly figures prominently in Most Gruesome Sports Injuries lists. Joe Theisman? Tibia. Gordon Hayward? Tibia. Paul George? Sweet lord, tibia. (If you didn't see them when they happened, there's video, but you probably don't want to watch.) As with most long bones, the preferred method to fix a fractured tibia is by inserting a nail into the cavity—an intramedullary nail, or IMN, as it's known clinically.

It's not exactly easy. You've got to make the incision, insert a guide wire at the correct angle, ream out the incision with a drill, build the nail assembly, insert the nail, then place a proximal interlocking screw to help keep the nail static. That's a lot of steps and a lot of tools—and not a lot of opportunity to practice. "It's complicated if you don't know the anatomy that well," says Kevin Varner, chair of orthopedics and sports medicine at Houston Methodist.

You could use bone models or cadavers, but with the power tools involved, those are expensive, single-use propositions. The best training typically comes during a medical residency: you watch senior residents, then you assist in a procedure, then maybe you perform some—but always under the direct supervision of your attending physician. As a result, says Michael P. Ast, an assistant professor of orthopedic surgery at the Hospital for Special Surgery in New York City, flying truly solo might not happen until you're out of school entirely: "When you went into practice, your first intramedullary nail was probably the first one where you had your own hands doing every step of the procedure, with no one else watching."

In the UCLA study, 20 first- and second-year med students got a five-minute hands-on tutorial with the drill used in the IMN procedure, then got split into two groups of 10—one that received a printed technique guide with photographs and step-by-step instructions, the other that received similar instructions by way of a virtual-reality training module from Osso VR, a Palo Alto, California-based surgical-training company. All students could take as much time as they wanted with their training materials, then each was taken to a room to perform a simulated IMN procedure on a commonly used bone model system. Two weeks later, they all came back and repeated the procedure.

Each time, the students' test procedures were evaluated on two different scales—one noting whether they had completed each step of the surgery correctly, the other grading them on their instrument handling, the time and elegance with which they performed the procedure, and other subjective measures. On nearly every measure, the VR-trained group outperformed the standard trained group, with significant improvement in inserting the nail and the most complex steps. (In fact, *only* VR-trained students successfully put together the nail assembly.) There was even more difference in the subjective proficiency grading: VR-trained students outperformed the others significantly in all five areas. And when they came back two weeks later, the VR-trained students improved over their previous performance on every single count—while the standard-trained students declined in two areas.

A couple of caveats should probably enter the discussion at this point. For one, Osso VR's CEO did his medical residency at UCLA, and one of the company's advisers works there currently. For another, this was a presentation rather than a publication, meaning the study hasn't been peer-reviewed to fully vet its methodology. Still, there's a lot of promise here—something that doesn't surprise Ast, whose hospital has offered Osso's training platforms to its 50 residents over the last year. "The beauty of the people we've seen train in VR is that they're way more prepared when they actually get in the operating room," he says. "As opposed to spending all their time thinking what's the next step, they're able to talk and listen and observe the unique surgical considerations of that patient, because they're already completely comfortable with the procedure."

Even surgeons who haven't used VR see its promise as a training tool. "There's a lot of benefit in trying to do things in a VR environment," Varner says, "whether it's improving hand-eye coordination or just understanding the steps of the procedure. I learned by doing more than 100 tibial nails when I was in my residency, but I think there's a lot to learn from these kinds of things."

A lot, of course, doesn't mean everything. "I've known people that play a lot of racing computer games," Varner adds. "That doesn't make them a better race car driver."

https://go.nature.com/2H7PJyd

Did the mysterious Denisovans make these prehistoric etchings?

Archaeologists have turned up inscribed bones from a site in northern China previously linked to the ancient hominins.

Two decorated bones might have been crafted by the enigmatic ancient humans known as Denisovans, who interbred with early modern humans tens of thousands of years ago.

Francesco d'Errico at the University of Bordeaux in France and his colleagues studied two fragments of animal rib found at a site in China known to have been used by ancient hominins. The ribs came from unknown large mammals and are 105,000–125,000 years old.

The lines on this animal bone, which dates to more than 100,000 years ago, might have been inscribed by one of the ancient humans called Denisovans.

F. d'Errico & L. Doyon

After the bones had aged, a sharp tool was used to carve them with roughly parallel lines. One bone is flecked with ochre, a coloured mineral often used by early modern humans.

According to the authors, neither butchery nor modern handling could account for the lines. The researchers also say that Denisovans — who are known mainly from their DNA — were probably the hominins using the site when the bones were marked.

The team argues that the deliberately incised bones suggest that Denisovans were capable of using symbols.

Antiquity (2019)

http://bit.ly/31LA93j

Osteoporosis drugs linked to reduced risk of premature death

New advice of the significant benefits of taking approved osteoporosis medicine for those at risk of osteoporosis

Two studies led by the Garvan Institute of Medical Research have revealed that nitrogen-bisphosphonates, drugs commonly prescribed for osteoporosis, reduced the risk of premature mortality by 34% in a cohort of over 6,000 individuals. This reduction in early mortality risk was significantly associated with a reduction in bone loss compared with no treatment.

The findings present new advice of the significant benefits of taking approved osteoporosis medicine for those at risk of osteoporosis, and their health care professional.

After the age of 50, 40% of women and 25% of men will sustain an osteoporotic fragility fracture in their life, an injury that puts them at risk of further fractures. However, currently fewer than 30% of women and 20% of men with fragility fractures are taking approved treatments for osteoporosis.

"It's a common misconception that osteoporosis affects only women, and many people choose to not take recommended treatments," says Professor Jacqueline Center, who heads the Clinical Studies and Epidemiology laboratory at the Garvan Institute and is an Endocrinologist at St Vincent's Hospital, who led the studies. "But osteoporotic fractures are not benign. Osteoporosis medication not only decreases the risk of further fractures - but it appears that this same medication also decreases mortality rates over the subsequent 15 years."

Reduction in mortality risk

Osteoporosis affects around 200 million people worldwide, and is a progressive disease in which bones become more porous and fragile, often without symptoms until the first fracture occurs.

A Garvan-led team of international researchers analysed data from a cohort of 6,120 participants aged over 50, who took part in the observational Canadian Multicentre Osteoporosis Study.

The analysis showed that individuals treated with nitrogen-bisphosphonates (alendronate or risedronate) had a 34% reduction in mortality risk over the subsequent 15 years, compared to non-treated individuals. The study was published in the April issue of the journal *Osteoporosis International*(1).

In a second follow-up study, published in the Journal of Bone and Mineral Research, the team analysed data from a cohort of 1,735 women, from the same study. The analysis revealed that 39% of the reduction in premature mortality risk was mediated through a reduction in the rate of bone loss.

The researchers also directly compared the nitrogen-bisphosphonates (alendronate or risedronate) with a weaker, non-nitrogen bisphosphonate and found a similar reduction in mortality risk benefit with the nitrogen-bisphosphonates.

The study provides additional evidence that nitrogen-bisphosphonate treatment can provide significant benefits for those with osteoporosis and is the first to examine potential mechanisms.

"For many individuals with osteoporosis, bone health isn't front-of-mind," says first author of both studies, Garvan's Dr Dana Bliuc, Research Officer in the Clinical Studies and Epidemiology laboratory. "We hope our study results will encourage people with osteoporosis or at risk of a fracture to seek treatment - and commit to taking it."

(1) Bliuc, D., Tran, T., van Geel, T. et al. Osteoporos Int *(2019) 30: 817.* https://doi.org/10.1007/s00198-018-4806-0

http://bit.ly/2yXHH6u

Ancient Sea Life May Have Hitched Across Oceans on Giant Living Rafts

Enormous crinoids of the Jurassic era, related to sea stars and sea urchins, could have carried whole ecosystems around the world

Today's oceans are jammed with plastic, which not only pollutes the water and poisons its inhabitants but also carries some animals to distant destinations. As researchers rush to discern the imminent repercussions of these virtually indestructible plastic rafts on global ecosystems, others are turning to the past to explore whether this buoyant lifestyle is actually new. The subject of their study? A giant of the Jurassic era: the crinoid.

Scientists think gigantic crinoids would cling to logs with anchor-like stems, creating a floating raft that likely supported a host of other species and enabled their long-distance transport across Jurassic seas. **(Julius Csotonyi / Smithsonian Institution)**

Crinoids look more like plants than animals, but they are invertebrates related to sea stars and sea urchins. With floweresque crowns atop stems reaching 26 meters in length, crinoids living in the Jurassic were one of the world's largest known invertebrates. In warm prehistoric seas, a subset of these behemoths used their anchor-like stems to grip floating logs and surf in colonies hundreds strong. And with them, life may have spread far and wide.

For marine and terrestrial organisms alike, rafting may be a key dispersal mechanism. In fact, rafting may have been one way islands like New Zealand were initially colonized by some organisms. But drifting crinoid communities represent the earliest example of rafters in the fossil record, says Aaron Hunter, an evolutionary paleoecologist at the University of Cambridge in England.

According to Hunter's newest statistical analyses, logs carrying rafting crinoids could float on even the most hostile oceans for a decade or more. Rafting crinoids and their driftwood vessels, Hunter says, "would have created a little island of activity" in an otherwise nutrient-poor ocean.

Though the rugged mussels that accompanied the crinoids remain as relics of this early mode of marine transport, no other passengers were preserved. Hunter speculates that crinoid rafts could have ferried additional stowaways including plants, bryozoans and crustaceans. Animals such as fish might have also trailed in their wake, feasting on the travelers.

Michael Simms, a paleontologist at National Museums NI in Northern Ireland who was not involved in Hunter's research, theorizes that these buoyed communities could have traveled thousands of kilometers, provided they could make it to the open ocean without getting caught in currents or sinking. They might have even traversed entire oceans, he speculates, although the exact routes they took can't be extrapolated from the fossil record.

Although this rafting lifestyle was once the subject of intense debate among crinoid researchers, most now agree that at least two crinoid lineages spent tens of millions of years rafting. Scientists initially estimated that crinoids floated for a few years. More recently, Hunter, Simms and others have extended these estimates to at least a decade, maybe two. Depending on factors like ocean currents, rafting longer could mean rafting farther for the crinoids and their passengers.

Simms based his calculations on observations of modern driftwood to surmise how long ancient logs could have stayed afloat, even encrusted by crinoids. Hunter, meanwhile, is using statistical

approaches to analyze crinoid fossils and reverse-engineer their time of death. These methods, he hopes, will add credence to the rafting hypothesis and derive more accurate estimates of floatation duration.

Rafting crinoids flourished until roughly 180 million years ago, when, some scientists think, the appearance of wood-boring organisms like shipworms drastically curtailed their drifting ways. Once their vessels collapsed, the crinoids would plummet to the bottom of the ocean, in many cases becoming frozen in time by the oxygen-starved seabed.

By analyzing fossilized crinoids, scientists are trying to determine how long and far they could have rafted. Some fossils even contain mussels, suggesting the crinoids supported a small ecosystem. **(Scott Camazine / Alamy Stock Photo)**

Modern crinoids no longer raft attached to logs—instead, some species get around by crawling along the seafloor or swimming with feathered arms. But that hasn't stopped the rafting process for other species. Now, creatures looking to hitch a ride enjoy a fleet of vessels even more durable than Jurassic driftwood: plastic.

"Every day we throw plastic in the ocean, so there is a continuous supply of tickets for these travelers," says Martin Thiel, a marine biologist at the Catholic University of the North in Chile.

In 2015, Thiel and his colleagues reported that nearly 400 different types of organisms have been found rafting on floating litter, a figure that has only grown. Compared to Jurassic logs, most plastics are highly resistant to decay. Forget decades, these plastic rafts could theoretically drift for centuries.

Figures like these raise concerns about the threat of invasive species, which now have a new way to surpass their natural distributions. According to Lars Gutow, an ecologist at the Alfred Wegener Institute in Germany, invaders riding on plastic rafts are a major threat to biodiversity that could lead to the homogenization of species on a global scale.

But for Hunter and Simms, Jurassic crinoids are a good reminder that rafting is not new. While some in the scientific community were shaken by recent reports of organisms rafting on plastic and other debris for upwards of five years after the 2011 Japanese tsunami, Hunter's reaction was, "Wow, that's too short."

Just like the ancient crinoids, he says, these tsunami-born travelers could have floated for decades but ultimately bumped into land. Many of these travelers, he thinks, may still be out there.

What makes today's plastic rafters different from Jurassic crinoids, though, is that no wood-boring organism will expedite their demise. The durability of plastic means that the full impact of these impervious rafting communities on native species has yet to be seen. As Simms says, it's a great time to be a rafting organism, "but a terrible time to be almost anything else."

http://bit.ly/2N5XgkO

Tested: Idea that sea ice steadies jet stream, blocking cold winters

Analysis shows why correlation is not causation, in this case.

Scott K. Johnson

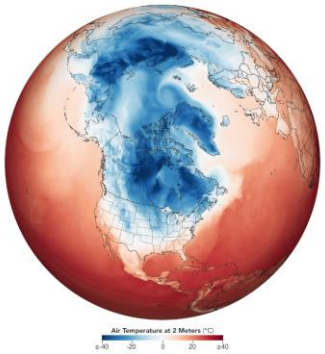
A lot has been made of the possibility that the loss of Arctic sea ice could make mid-latitude weather weirder by causing wriggling meanders in the jet stream. One possible manifestation of that is bitter cold snaps in winter, as Arctic air slides south along with the jet stream boundary. There is a correlation between cold mid-latitude winters and low sea ice cover in the Arctic. But does the one really cause the other?

The possible relationship between a warming Arctic and changing behavior of the jet stream is still a matter of real scientific debate. For a number of reasons, it's a difficult question to resolve. In this

case, a team led by the University of Exeter's Russell Blackport tried to disentangle the chain of events with a clever analysis.

Checking causality

Ultimately, the question is whether shrinking sea ice allows the ocean to warm the atmosphere, or whether the warm air forms separately and then melts the sea ice. The researchers used a pair of climate models and global maps of observed weather; the measurement gaps were filled in by simulated physics. First, the team categorized each winter in North America and Asia based on two measures: cooler or warmer mid-latitude temperatures and lower or higher Arctic sea ice. As in other studies, they found a correlation between the two.



***Enlarge** / Cold weather for the Midwest on January 29, 2019.* NASA Earth Observatory

They then turned to calculating the flow of heat between the Arctic atmosphere and ocean, categorizing winters dominated by heat moving into the atmosphere or heat moving into the ocean. If lower sea ice coverage was responsible for the cold mid-latitude winters, you'd expect to see heat moving from the ocean into the atmosphere (and bullying the jet stream) in those years. But instead, they saw the opposite—low sea ice winters were associated with heat coming in the atmosphere that would cause the sea ice to melt.

The researchers did the same thing on shorter timescales, looking to see what came first. They found that the mid-latitude cold weather—and movement of heat from the atmosphere into the ocean—was present about a month before drops in sea ice extent. One month after, they could see heat moving from the newly exposed ocean into the atmosphere, but the cold weather in the mid-latitudes had already ended.

A single cause

In other words, unusual atmospheric circulation patterns would start the wiggle in the jet stream, which both brings cold air south to the mid-latitudes and warm air north to melt sea ice. So the correlation between low sea ice coverage and cold mid-latitude winters is actually because they are both being caused by the same thing.

For a third way of checking this, the researchers ran climate model simulations where Arctic sea ice coverage was set to be smaller than it is today, just without any further greenhouse gas increases and global warming. The idea was to isolate the effect of the sea ice itself. In the simulation, there was still a correlation between low sea ice winters and cold in the mid-latitudes, but the mid-latitudes didn't get any colder than they were with modern, greater sea ice coverage—supporting the overall conclusion.

This doesn't mean there's no connection between global warming and a wriggly jet stream. That research will continue. It does, however, mean that suggestions of a link between shrinking Arctic sea ice and wilder mid-latitude winters were off the mark.

Nature Climate Change, 2019. DOI: 10.1038/s41558-019-0551-4 (About DOIs).

http://bit.ly/2Z85Qlm

A New Clue to How Life Originated

A long-standing mystery about early cells has a solution—and it's a rather magical one.

Ed Yong

When Caitlin Cornell looked down her microscope, she saw large bright spots against a black background. They resembled miniature suns, blazing against the backdrop of space. And when Cornell showed the spots to her supervisor, Sarah Keller, a chemist at the University of Washington, "we got really excited," she recalls. "It was a bit of an 'Aha!' moment." Those spots, she realized, might help address a long-standing puzzle about the origin of life itself.

The cells that make up all living things, despite their endless variations, contain three fundamental elements. There are molecules that encode information and can be copied—DNA and its simpler relative, RNA. There are proteins—workhorse molecules that perform important tasks. And encapsulating them all, there's a membrane made from fatty acids. Go back far enough in time, before animals and plants and even bacteria existed, and you'd find that the precursor of all life—what scientists call a "protocell"—likely had this same trinity of parts: RNA and proteins, in a membrane. As the physicist Freeman Dyson once said, "Life began with little bags of garbage."

The bags—the membranes—were crucial. Without something to corral the other molecules, they would all just float away, diffusing into the world and achieving nothing. By concentrating them, membranes transformed an inanimate world of disordered chemicals into one teeming with redwoods and redstarts, elephants and *E. coli*, humans and hagfish. Life, at its core, is about creating compartments. And that's much easier *and* much harder than it might seem.

First, the easy bit. Early cell membranes were built from fatty acids—molecules that look like lollipops, with round heads and long tails. The heads enjoy the company of water; the tails despise it. So, when placed in water, fatty acids self-assemble into hollow spheres, with the water-hating tails pointing inward and the water-loving heads on the surface. These spheres can enclose RNA and proteins, making protocells. Fatty acids, then, can *automatically* create the compartments that were necessary for life to emerge. It almost seems too good to be true.

And it is, for two reasons. Life first arose in salty oceans, and salt catastrophically destabilizes the fatty-acid spheres. Also, certain ions, including magnesium and iron, cause the spheres to collapse, which is problematic since RNA—another key component of early protocells—requires these ions. How, then, could life possibly have arisen, when the compartments it needs are destroyed by the conditions in which it first emerged, and by the very ingredients it needs to thrive?

Caitlin Cornell and Sarah Keller have an answer to this paradox. They've shown that the spheres can withstand both salt and magnesium ions, as long as they're in the presence of amino acids—the simple molecules that are the building blocks of proteins. The little suns that Cornell saw under her microscope were mixtures of amino acids and fatty acids, holding their spherical shape in the presence of salt.

I find that utterly magical. It means that two of the essential components of life, a protocell's membrane and its proteins, *provided the conditions for each other to exist.* By sticking to the fatty acids, the amino acids gave them stability. In turn, the fatty acids concentrated the amino acids, perhaps encouraging them to coalesce into proteins. From the very beginning, these partners were locked in a two-step dance that continued for 3.5 billion years, and helped create all the richness of biology from a starting place of mere chemistry. "I agree completely," Keller tells me. "It's completely magical. You need those two parts together."

"It's fantastic work," says Neal Devaraj, of UC San Diego. "Their suggestion that membranes could promote the synthesis of [proteins] is really fascinating."

This discovery happened almost by accident. Originally, Keller set out to address a different problem, posed to her by her colleague Roy Black. He noted that no one had good ideas about how exactly the protocell trinity—RNA, proteins, and membranes—actually assembled in the first place. It seemed that people were just waving their hands and attributing this crucial convergence to some random event. Black, instead, suggested that the membranes themselves were key. If fatty acids can stick to the constituents of both proteins

and RNA, they could have gathered these building blocks together as they themselves assembled.

Cornell tested that idea by incubating a fatty acid with three different amino acids, all of which are thought to have existed on the primordial Earth. Sure enough, as Black had suspected, the molecules interacted with one another. But when she looked under the microscope, Cornell realized something special was happening.

On their own, the fatty acids predictably self-assembled into hollow spheres. "They looked like jellyfish: clear insides with opaque edges, floating around," she says. If she added salt or magnesium ions, these jellyfish disintegrated. But if she did that after adding amino acids, they held their shape. What's more, they transformed into shapes that Cornell likens to glowing onions. Their once-hollow centers were filled with another layer of fatty acids—spheres within spheres. Not coincidentally, that's what our actual cells are like, with membranes that comprise two fatty layers instead of one.

So, the presence of amino acids not only protects the fatty-acid spheres, but also turns them into something more obviously biological. Why? "We have no idea, and we wouldn't have predicted it," Keller says, laughing. "We're in a lovely place that opens the field up to future theory."

"This is great work," says Kate Adamala of the University of Minnesota. Other studies, she notes, have found interactions between any two of amino acids, fatty-acid membranes, and RNA, but Cornell and Keller's study effectively ties all three together. Amino acids allow membranes to exist in the presence of magnesium, which RNA needs to function.

The study of life's origins is always contentious. Scientists often disagree furiously about things that are happening right now, let alone events that occurred more than 3.5 *billion years ago*. Some researchers, for example, think that life began in shallow volcanic pools, while others argue that it must have arisen in underwater vents. Keller's ideas, mercifully, work in both environments. "I'm agnostic," she says. "I'm excited that [our study] makes the idea of protocells more plausible independent of the location."

She's now looking into what happens *after* the protocells assemble. Sure, there's a compartment that contains the building blocks for making proteins and RNA. "But how do those individual building blocks bond to form the larger molecules?" she says. "It's a very hard question."

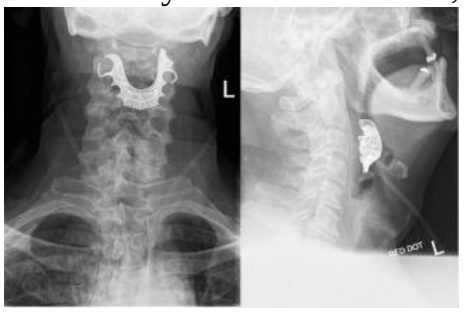
http://bit.ly/2Mj0i5G

A Man's Dentures Were Stuck in His Throat for More Than a Week

The case highlights the dangers of leaving dentures in a patient's mouth during surgery.

By Rachael Rettner Health

A U.K. man's dentures fell down his throat during surgery and were stuck there for more than a week before they were discovered, according to a new report.



(Image: © BMJ Case Reports 2019)

The case highlights the dangers of leaving dentures in a patient's mouth during any surgery that requires general anesthesia, according to the report, published today (Aug. 12) in the journal BMJ Case Reports.

The 72-year-old man had undergone surgery to remove a harmless lump in his abdominal wall tissue, the report said. Six days after the surgery, he went to the emergency room (ER) with symptoms including pain in his throat, difficulty swallowing and a cough that produced blood. He told doctors that he hadn't been able to swallow any solid foods since his surgery

At first, based on results from a chest X-ray, doctors thought the man had a respiratory infection. They didn't find any problems with his throat on an initial examination, and they suspected his pain was a side effect of having a tube down his throat during surgery. Doctors prescribed the man antibiotics and sent him home.

But two days later, the man was back in the ER. His throat pain was worse, and he was still coughing up blood. His voice was hoarse, and he told doctors he hadn't been able to swallow any of the medications they had given him. The man was also feeling short of breath, particularly when lying down.

He was admitted to the hospital, and doctors suspected he had a severe chest infection. But when they performed a procedure to look at his throat and voice box, they saw a metal, "semicircular object" lying across his vocal cords that had caused swelling and blistering.

When doctors told the man what they saw, he mentioned that his dentures had been lost during his surgery. This prompted doctors to perform an X-ray of the patient's neck, which revealed the missing dentures — consisting of three false teeth attached to a metal roof plate — stuck in his throat. The man had apparently inhaled, or aspirated, his dentures during the surgery.

He underwent emergency surgery to remove the dentures and was released from the hospital six days later.

But that wasn't the end of the man's medical saga. Over the next several weeks, he returned to the hospital four times with bouts of bleeding in his throat and coughing that produced blood. Doctors eventually discovered that the man had a torn artery in his neck near the area where the dentures had caused tissue damage. He needed another emergency surgery, along with several blood transfusions. Six weeks later, the man appeared to be healing well and didn't need to return to the hospital.

This isn't the first case of it's kind. Earlier this year, a report in the journal Case Reports in Surgery described a 50-year-old man in Turkey who apparently swallowed his dentures during sedation before surgery. And a 1976 report in the journal Anesthesia & Analgesia described the case of a patient in Austria who died after inhaling dentures when a breathing tube was placed down the individual's throat.

There are no national guidelines on how dentures should be managed when a patient undergoes anaesthesia for surgery, according to Dr. Harriet Cunniffe, an otolaryngologist at James Paget University Hospitals NHS Foundation Trust in Great Yarmouth, United Kingdom, and author of the new report.

Some hospitals allow dentures to remain in place while the anaesthetic is being infused but remove them before placing a tube in the patient's mouth. In general, the "presence of any dental prosthetics should be clearly documented before and after any [surgical] procedure," Cunniffe wrote in the report.

Cunniffe also stressed that doctors should "listen to the story the patient is telling you." In the current case, the man's initial test results suggested a respiratory infection, but such an infection would not typically explain the man's throat pain and difficulty swallowing. In other words, doctors should have continued to consider other diagnoses that would explain more of the man's symptoms. The results of the chest X-ray ended up acting "as a distraction" from the real diagnosis, Cunniffe said.

https://bbc.in/2N5BT39

Chlamydia sex infection vaccine passes safety test

A vaccine to protect people against the common sexually transmitted infection chlamydia has passed initial safety tests.

It is the first of its kind to enter human trials. Experts say immunisation may be the best way to tackle the disease that accounts for nearly half of all sex infections diagnosed in the UK.

More trials must check how well it works and what dose to give, The Lancet Infectious Diseases journal says. Those tests will take years and in the meantime the best way to avoid getting chlamydia during sex is by using a condom.

What is chlamydia?

It is a bacterial infection that is passed on through unprotected sex (even if there is no penetration).

Chlamydia bacteria reside in semen and vaginal fluid. Often, the infected person will have no symptoms, which is why people sometimes refer to it as a "silent" disease. If it is not treated with antibiotics, it can cause serious complications and affect fertility.

People under 25 who are sexually active are advised to get tested for chlamydia every year. The NHS offers a free screening service. People can also buy self-testing kits from pharmacies to do at home with a swab or urine sample.

Why do we need a vaccine?

Although antibiotics can treat chlamydia, people can catch the infection again if they come into contact with it. Chlamydia remains the most common STI despite screening and effective treatment being available. Vaccination could offer long-lasting protection, experts hope.

In the trial, researchers from Imperial College London compared two different formulations of the vaccine alongside a dummy or placebo jab in 35 women. Both formulations appeared to be safe, but one stood out as a front runner. The researchers now want to move this vaccine into the next phase of testing.

Investigator Prof Robin Shattock said: "The findings are encouraging as they show the vaccine is safe and produces the type of immune response that could potentially protect against chlamydia.

"The next step is to take the vaccine forward to further trials, but until that's done, we won't know whether it is truly protective or not. "We hope to start the next phase of testing in the next year to two. If those trials go well we might have a vaccine that can be rolled out in around five years."

He suggested it could potentially be offered alongside the HPV jab that is currently used to protect against cervical cancer.

A spokeswoman from the young people's sexual health and wellbeing charity Brook, said: "Whilst these initial results are promising, it's still very early days and a widely available vaccine could be years in development.

"We would be thrilled to see a vaccine for chlamydia in the future and we are hopeful that this will become a reality.

"As diagnoses of STIs continue to increase nationally and globally, including antibiotic-resistant gonorrhoea, it remains essential that people use condoms to protect themselves."

http://bit.ly/2N6cYMI

Preclinical research suggests anti-cancer effect of keto diet

Suggestion that restricting blood glucose levels might also keep certain cancers at bay.

It's well known that keeping blood glucose levels in check can help individuals avoid or manage diabetes, but new research led by biologists at The University of Texas at Dallas suggests that restricting blood glucose levels might also keep certain cancers at bay.

In a study published online Aug. 13 in the journal Cell Reports, researchers restricted circulating glucose in mice with lung cancer. Circulating glucose restriction was achieved by feeding the mice a ketogenic diet, which is very low in sugar, and by giving them a diabetes drug that prevents glucose in the blood from being reabsorbed by the kidneys.

"Both the ketogenic diet and the pharmacological restriction of blood glucose by themselves inhibited the further growth of

squamous cell carcinoma tumors in mice with lung cancer," said Dr. Jung-Whan "Jay" Kim, corresponding author of the multinational study and an assistant professor of biological sciences at UT Dallas. "While these interventions did not shrink the tumors, they did keep them from progressing, which suggests this type of cancer might be vulnerable to glucose restriction."

While many types of cancer cells are suspected to be heavily dependent on glucose -- or sugar -- as their energy supply, Kim and his colleagues have shown in previous laboratory studies that one specific type -- squamous cell carcinoma -- is remarkably more dependent than other cancer types, such as adenocarcinoma.

"The key finding of our new study in mice is that a ketogenic diet alone does have some tumor-growth inhibitory effect in squamous cell cancer," Kim said. "When we combined this with the diabetes drug and chemotherapy, it was even more effective."

Kim noted that glucose restriction did not have any effect on non-squamous-cell cancer types.

"Our results suggest that this approach is cancer-cell-type specific. We cannot generalize to all types of cancer," he said.

The researchers also examined glucose levels in blood samples from 192 patients who had either lung or esophageal squamous cell cancer, as well as 120 patients with lung adenocarcinoma. The blood samples were taken at random parts of the day and classified into those containing glucose concentrations higher or lower than 120 mg/dL, which is one clinical measure of diabetes. None of the patients had been diagnosed with diabetes.

"Surprisingly, we found a robust correlation between higher blood-glucose concentration and worse survival among patients with squamous cell carcinoma," Kim said. "We found no such correlation among the lung adenocarcinoma patients. This is an important observation that further implicates the potential efficacy of glucose restriction in attenuating squamous-cell cancer growth."

Kim emphasized that more comprehensive and detailed clinical studies are needed, but the results indicate a potentially novel approach to enhancing cancer treatment.

"Manipulating host glucose levels would be a new strategy that is different from just trying to kill cancer cells directly," Kim said. "I believe this is part of a paradigm shift from targeting cancer cells themselves. Immunotherapy is a good example of this, where the human immune system is activated to go after cancer cells.

"Maybe we can manipulate our own biological system a little bit or activate something we already have in place in order to more effectively combat cancer."

Lead author of the study was Kim's former graduate student Meng-Hsiung Hsieh MS'18. Other UT Dallas authors included molecular and cell biology graduate students Jashkaran Gadhvi, Haleigh Gerold, Chance Nowak, Hung Do and Simbarashe Mazambani; former research scientist Dr. Yoon Jung Kim, now at UT Southwestern Medical Center's Children's Medical Center Research Institute; undergraduates Marcus Arguez, Jordan Knighton and Matthew Cha; Madison Palmer BS'19; Dr. Zhenyu Xuan, associate professor of biological sciences; Dr. Tae Hoon Kim, head of biological sciences; and Dr. Leonidas Bleris and Dr. Kenneth Hoyt, both associate professors of bioengineering.

Researchers from the University of North Texas and UT Southwestern's Harold C. Simmons Comprehensive Cancer Center and Children's Medical Center Research Institute also participated in the work. Other contributors included researchers at Columbia University, Yale School of Medicine, Carver College of Medicine at the University of Iowa, David Geffen School of Medicine at UCLA, University of Nebraska Medical Center, Kyungpook National University School of Medicine in South Korea and Kyota University Graduate School of Medicine in Japan.

The research was funded by the National Institutes of Health, the Department of Defense, the American Lung Association, the Cancer Prevention and Research Institute of Texas, the American Cancer Society, the Tobacco-Related Disease Research Program, the Japan Agency for Medical Research and Development, and the National Research Foundation of Korea.

http://bit.ly/2z3CMkB

‘Stature gene’ may reveal why these hunter-gatherers are among the world’s smallest humans

Largest ever genetic analysis of rainforest hunter-gatherers may have fingered the gene responsible

By Michael Price

African rainforest hunter-gatherers are among the smallest humans on the planet. Adult men rarely exceed 1.5 meters tall, about a quarter-meter shorter than the global average. Now, the largest ever genetic analysis of this group may have fingered the gene responsible—and settled a mystery that has vexed scientists for decades.

Once called “Pygmies” by outsiders, African rainforest hunter-gatherers live in densely forested environments across Central Africa. Their way of life includes gathering wild fruits and vegetables, fishing, and hunting monkeys and antelope. Their most striking physical characteristic is their relatively short stature (The name “pygmy” is derived from the ancient Greek word for “dwarf.”)

Some anthropologists have speculated that the group’s small body size gave them an advantage in Africa’s spectacularly hot, humid rainforests. Put simply, there’s less body to cool down, be it by sweating or other means. But other scientists say their stature may be just an accident. People in African rainforests have long battled numerous infectious diseases—including hepatitis B and C—and the genes this group evolved to help protect them have been linked to reduced levels of growth hormones.

To settle the debate, researchers at the Pasteur Institute in Paris consulted existing DNA databases built from blood or saliva samples given by nearly 300 African rainforest hunter-gatherers from Cameroon, Gabon, and Uganda, as well as nearly 300 people from neighboring agriculturalist groups who live outside the rainforests.

The researchers report that the donors gave their informed consent to use their DNA in these studies.

They ran the data through a computer algorithm that calculates whether it’s more likely that particular snippets of DNA arose by pure chance or through natural selection.

What they found surpassed their expectations: All the hunter-gatherer populations showed a strong signal of selection within a short stretch of DNA on chromosome 8, and all the agriculturalists lacked this signal. This genetic region helps regulate a gene called *TRPS1*, which plays an important role in skeletal development. That suggests natural selection specifically favored short stature in this group, the authors say.

Further analysis revealed additional strong signals of natural selection in genes unrelated to height that code for proteins thought to protect against various types of viruses. As with *TRPS1*, this signal was pronounced in the hunter-gatherers but not in the agriculturalists, the scientists report this month in *Current Biology*.

The finding further confirms that short stature and enhanced protection against viruses were both critical adaptations to rainforest living for African rainforest hunter-gatherers, says Pasteur Institute geneticist and study author Lluís Quintana-Murci. He hopes the work could one day help researchers develop more effective medicine for this population.

The study presents a solid argument that height and viral disease resistance were separate, independent targets of evolution, says Thomas Kraft, an anthropologist at the University of California, Santa Barbara, who studies hunter-gatherers. He says he’d like future studies to delve into whether these evolutionary pressures are still at work in modern hunter-gatherer societies.

Pontus Skoglund, a population geneticist at the Francis Crick Institute in London, adds that the results make him want to know more about when and where these unique genetic adaptations first arose.

“There’s not so many people with a hunter-gatherer lifestyle in the world today,” he says, “and this can perhaps tell us about important processes that happened in the past.”

http://bit.ly/2Typl5s

Memory and attention difficulties are often part of a normal life

Can't remember what you came for? Don't worry – you probably have a lot going on.

Jacqueline Anderson *

From young adults to people in their 60s, everyday functioning in today's world can place high demands on our attention and memory skills. Memory lapses such as forgetting an appointment, losing our keys, forgetting a distant relative's name or not remembering why you opened the fridge can leave us believing our thinking skills are impaired.

But you might be too hard on yourself. Tiredness, stress and worry, and feeling down or depressed are all common reasons adults experience attention and memory difficulties.

Attention and memory systems

Attention and memory skills are closely connected. Whether we can learn and remember something partly depends on our ability to concentrate on the information at the time.

It also depends on our ability to focus our attention on retrieving that information when it's being recalled at a later time.

This attention system, which is so important for successful memory function, has a limited capacity – we can only make sense of, and learn, a limited amount of information in any given moment.

Being able to learn, and later successfully remember something, also depends on our memory system, which stores the information.

Changes in attention and memory skills

In people who are ageing normally, both attention and memory systems gradually decline. This decline starts in our early 20s and continues slowly until our 60s, when it tends to speed up.

During normal ageing, the number of connections between brain cells slowly reduce and some areas of the brain progressively work less efficiently. These changes particularly occur in the areas of the brain that are important for memory and attention systems.

This normal ageing decline is different from dementia and Alzheimer's disease, which cause progressive changes in thinking skills, emotions and behaviour that are not typical of the normal ageing process. Dementia comes from a group of diseases that affect brain tissue and cause abnormal changes in the way the brain works.

If you're concerned your memory difficulties may be a symptom of dementia, talk to your GP, who can refer you to a specialist, if needed, to determine whether these changes are due to normal ageing, dementia or some other cause.

If you experience persistent changes in your thinking skills, which are clearly greater than your friends and acquaintances who are of a similar age and in similar life circumstances, see your GP.

Normal attention and memory difficulties

Broadly, there are two main reasons healthy adults experience difficulties with their memory and/or attention: highly demanding lives and normal age-related changes.

A person can be consistently using their attention and memory skills at high levels without sufficient mental relaxation time and/or sleep to keep their brain working at its best.

Young adults who are working, studying and then consistently using attention-demanding devices as "relaxation" techniques, such as computer games and social media interaction, fall into this group.

Adults juggling the demands of work or study, family and social requirements also fall into this group. Most adults need around seven to nine hours of sleep per night for their brain to work at its best, with older adults needing seven to eight hours.

The second common reason is a combination of ageing-related brain changes and highly demanding work requirements.

For people in jobs that place a high load on thinking skills, the thinking changes that occur with normal ageing can become noticeable at some point around 55 to 70 years of age. It's around this time age-related changes in the ability to carry out complex thinking tasks become large enough to be noticeable. People who are retired or don't have the same mentally demanding jobs generally experience the same changes, but may not notice them as much.

This is also the age many people become more aware of the potential risk of dementia. Consequently, these normal changes can result in high levels of stress and concern, which can result in a person experiencing even greater difficulties day to day.

Emotional distress can take its toll

Feeling down and sad can affect memory and concentration. When a person is feeling worried and/or down regularly, they may become consumed by their thoughts. It's important to recognise how you're feeling, to make changes or seek help if needed. But thinking a lot about how you're feeling can also take a person's attention away from the task at hand and make it difficult for them to concentrate on what is happening, or remember it clearly in the future. So feeling worried or down can make it seem there is something wrong with their memory and concentration.

Boosting your attention and memory skills

There are a number of things that can be done to help your day-to-day memory and attention skills.

First, it's important to properly rest your mind on a regular basis. This involves routinely doing something you enjoy that doesn't demand high levels of attention or memory, such as exercising, reading for pleasure, walking the dog, listening to music, relaxed socialising with friends, and so on.

Playing computer games, or having a lengthy and focused session on social media, requires high levels of attention and other thinking skills, so these are not good mental relaxation techniques when you are already mentally tired.

It's also important to get enough sleep, so you are not consistently tired – undertaking exercise on a regular basis often helps with getting good quality sleep, as does keeping alcohol consumption within recommended limits.

Looking after your mental health is also important. Noticing how you are feeling and getting support (social and/or professional) during longer periods of high stress or lowered mood will help ensure these things are not affecting your memory or concentration.

Finally, be fair to yourself if you notice difficulties with your thinking. Are the changes you notice any different to those of other people your own age and in similar circumstances, or are you comparing yourself to someone younger or with less demands in their life?

If you have ongoing concerns about your attention and memory, speak with your GP, who can refer you to a specialist, such as a clinical neuropsychologist, if needed.

Senior Lecturer in Clinical Neuropsychology, University of Melbourne

Disclosure statement

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Partners

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https://go.nature.com/2H6pCHQ

Nationality shapes views of a global war's burdens

People in many countries generally think their homeland did the most in the Second World War.

Which country put the most effort into the Second World War? It depends on who you ask.

Henry Roediger III at Washington University in St. Louis, Missouri, and his colleagues surveyed 1,338 people from 11 countries that

participated in the Second World War about their homeland's contribution. The team found that individuals from many nations tended to overestimate their countries' efforts, though the researchers also note that precise measurements of a nation's contribution to the war are impossible.

People from Russia, the United Kingdom and the United States assigned more than 50% of the victory to their own country. Participants from Germany — one of the defeated powers — assigned their country 64% of the effort in the losing cause.

Although far more Soviet soldiers died than those from any other country, participants outside of Russia tended to minimize Soviet efforts. Few respondents listed the Battle of Stalingrad as one of the war's most important events, although most historians consider it a turning point.

These skewed perceptions reveal an example of what the researchers call 'national narcissism' — a tendency to believe that one's own country is exceptional compared with other countries.

Proc. Natl. Acad. Sci. USA (2019)

http://bit.ly/2Mj2Rou

New Form of Biofluorescence Discovered

Previously undescribed metabolites responsible for biofluorescence in two species of sharks

by News Staff / Source

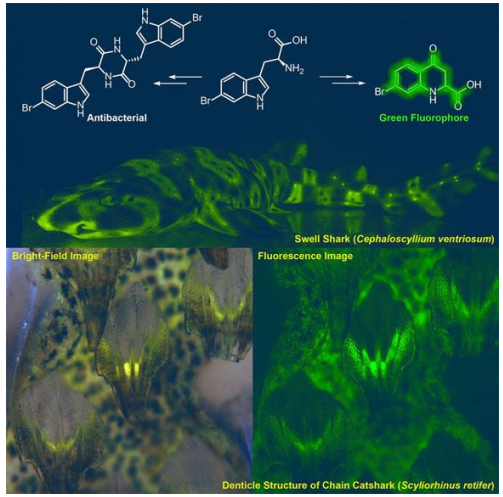
A team of U.S. researchers has discovered a previously undescribed group of small molecule metabolites responsible for the green biofluorescence in two species of sharks.

Not only is the newly-discovered chemical mechanism different from how most marine creatures glow, but it may also play other useful roles for the sharks, including helping them identify each other in the ocean and fight against microbial infections.

Biofluorescence is a widespread phenomenon in the marine environment, which results from the absorbance of the ambient blue ocean light and its re-emittance at longer, lower-energy wavelengths, visually resulting in green, orange, and red fluorescence.

"Studying biofluorescence in the ocean is like a constantly evolving mystery novel, with new clues being provided as we move the research forward," said City University of New York's Professor David Gruber.

"After we first reported that swell sharks were biofluorescent, my collaborators and I decided to dive deeper into this topic. We wanted to learn more about what their biofluorescence might mean to them."



***Green biofluorescence in swell sharks (*Cephaloscyllium ventriosum*) and chain catsharks (*Scyliorhinus retifer*).* Image credit: Park *et al*, doi: 10.1016/j.isci.2019.07.019.**

Professor Gruber and colleagues focused on two species of sharks, both in the family Scyliorhinidae: the swell shark (*Cephaloscyllium ventriosum*) from the eastern Pacific and the chain catshark (*Scyliorhinus retifer*) from the western Atlantic.

The scientists noticed that the sharks' skin had two tones — light and dark — and extracted chemicals from the two skin types.

What they found was a type of fluorescent molecule that was only present in the light skin.

"The exciting part of this study is the description of an entirely new form of marine biofluorescence from sharks — one that is based on brominated tryptophan-kynurenine small-molecule metabolites," Professor Gruber said.

These types of small-molecule metabolites are known to be fluorescent and activate pathways similar to those that, in other vertebrates, play a role in the central nervous system and immune system.

But in the sharks, the novel small-molecule fluorescent variants account for the biophysical and spectral properties of their lighter skin.

"This mechanism is different from animals in the upper ocean, such as jellyfish, that commonly use green fluorescent proteins as mechanisms to transform blue light into other colors," Professor Gruber said.

"It's a completely different system for them to see each other that other animals cannot necessarily tap into," said Yale University's Professor Jason Crawford.

"They have a completely different view of the world that they're in because of these biofluorescent properties that their skin exhibits and that their eyes can detect."

"Imagine if I were bright green, but only you could see me as being bright green, but others could not."

"The molecules also serve multiple other purposes, including to help the sharks identify each other in the ocean and potentially provide protection against microbial infections," he added.

"It is also interesting that these biofluorescent molecules display antimicrobial properties. These catsharks live on the ocean bottom, yet we don't see any biofouling or growth, so this could help explain yet another amazing feature of shark skin."

"This study opens new questions related to potential function of biofluorescence in central nervous system signaling, resilience to microbial infections, and photoprotection."

The findings were published in the journal *iScience*.

Hyun Bong Park et al. *Bright Green Biofluorescence in Sharks Derives from Bromo-Kynurenine Metabolism.* iScience, *published online August 8, 2019; doi: 10.1016/j.isci.2019.07.019*

http://bit.ly/2THq7Nv

The sex gene SRY and Parkinson's disease: how genes act differently in male and female brains

Parkinson's disease, a debilitating neurodegenerative disease common in elderly people, is twice as prevalent in men than in women.

Jenny Graves *

A new study published this month suggests the sex gene (SRY on the male-specific Y chromosome) plays a role in the loss of dopamine-making neurons that underlies this disease.

As well as providing a spectacular example of how genes act differently in male and female brains, this discovery may lead to a new treatment option for men suffering from Parkinson's disease.

Sex and disease

Many diseases are more common in one sex than the other. For example, multiple sclerosis and other immune disorders are more common in women than men. Parkinson's disease, and several mental health conditions such as schizophrenia and autism, are more common in men than women.

Treatments, too, may be differently effective in men and women because of differences in expression of genes important for drug metabolism.

The bases of these sex differences are often unclear. Is it a hormonal difference that makes men and women differently susceptible to diseases, and differently amenable to treatment? For instance, the sex difference in Parkinson's disease was previously attributed solely to the protective effect of the hormone oestrogen in female brains.

But as well as hormonal differences, we now have reason to believe genes on sex chromosomes may directly affect the brain.

Parkinson's disease

Parkinson's disease is a growing problem, particularly with an ageing population. Nearly one in 300 Australians live with Parkinson's disease. It usually appears in later life as problems in starting and maintaining voluntary movements, and may be accompanied by severe tremor.

Parkinson's disease is caused by a loss of neurons responsible for making dopamine, a hormone and neurotransmitter that sends messages to other nerve cells. Symptoms appear when 70% of these dopamine-synthesising cells have been depleted. We don't understand how these neurons are lost, but expect the effect of loss on motor function is due to the curtailed dopamine production.

Parkinson's disease is progressive and incurable, but the symptoms may be ameliorated and delayed by medications that boost dopamine or substitute for it.

SRY and Parkinson's disease

In humans and other mammals, females have two X chromosomes (XX), and males a single X and a male-specific Y chromosome (XY). SRY is the master gene on the Y chromosome that determines the male sex of a baby in the embryo.

But research has found SRY seems to be active in other parts of the body, too. In mice and rats, SRY is active in the brain, and in humans it's expressed in several tissues and organs, including the brain.

SRY has been found to be expressed at abnormally high levels in the brains of mice and rats mutated to have symptoms of Parkinson's disease, and in animals where the disease was induced by chemical treatment.

Previous work showed overactivity of the SRY gene destroys neurons that synthesise dopamine. We're not entirely sure how this happens, but given the link between dopamine production and Parkinson's disease, it might partly explain why Parkinson's disease affects males more commonly than females.

This new study now shows that interfering with SRY expression in the brains of rodents with Parkinson's disease ameliorates the severity of symptoms. Vince Harley and Joohyung Lee from the Hudson Institute in Melbourne found that quashing SRY action prevented or mitigated the reduced mobility of male animals with Parkinson's disease.

So, suppressing the activity of SRY in neurons of Parkinson's disease patients could ameliorate their symptoms.

This sort of a cure may be many years away, but it would have a huge impact on the quality of life of thousands of men in Australia living with Parkinson's disease.

Sex and the brain

Male and female brains really are different at every level; molecular, cellular, and behavioural. For 60 years this has been attributed to sex hormones. But we're beginning to find that genes may also have direct effects.

A recent analysis of the activity of most of the 20,000-odd genes in the bodies of hundreds of men and women showed that more than one-third were expressed much more highly in one sex than the other. This sex bias was not limited to sex organs, but was obvious at many other sites, including the brain.

The effect of SRY in the brain is a strong demonstration that male and female brains are genetically different in health and disease, and a reminder we must take account of sex differences in diagnosing and treating disease in men and women.

* *Distinguished Professor of Genetics, La Trobe University*

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Partners

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Ebola drugs show '90% survival rate' in breakthrough trial

Ebola may soon be a "preventable and treatable" disease after a trial of two drugs showed significantly improved survival rates, scientists have said.

Four drugs were trialled on patients in the Democratic Republic of Congo, where there is a major outbreak of the virus.

More than 90% of infected people can survive if treated early with the most effective drugs, the research showed.

The drugs will now be used to treat all patients with the disease in DR Congo, according to health officials.

On Tuesday, two people cured of Ebola using the experimental drugs were released from a treatment centre in Goma, eastern DR Congo, and reunited with their families.

The US National Institute of Allergy and Infectious Diseases (NIAID), which co-sponsored the trial, said the results are "very good news" for the fight against Ebola.

The drugs, named REGN-EB3 and mAb114, work by attacking the Ebola virus with antibodies, neutralising its impact on human cells.

They are the "first drugs that, in a scientifically sound study, have clearly shown a significant diminution in mortality" for Ebola patients, said Dr Anthony Fauci, director of NIAID.

The drug mAb114 was developed using antibodies harvested from survivors of Ebola while REGN-EB3 comes from antibodies generated within mice infected with the disease.

Ebola has killed more than 1,800 people in DR Congo in the past year.

Two other treatments, called ZMapp and Remdesivir, have been dropped from trials as they were found to be less effective.

What were the results of the trial?

The trial, conducted by an international research group co-ordinated by the World Health Organization (WHO), began in November last year.

Since then, four experimental drugs have been tested on around 700 patients, with the preliminary results from the first 499 now known.

Of the patients given the two more effective drugs, 29% on REGN-EB3 and 34% on mAb114 died, NIAID said.

In contrast, 49% on ZMapp and 53% on Remdesivir died in the study, the agency said.

The survival rate among patients with low levels of the virus in their blood was as high as 94% when they were given REGN-EB3, and 89% when on mAb114, the agency said.

The findings mean health authorities can "stress to people that more than 90% of people survive" if they are treated early, said Sabue Mulangu, an infectious-disease researcher who worked on the trial.

What impact could the drugs have?

Hailing the success of the study, Jeremy Farrar, director of the Wellcome Trust global health charity, said the treatments would "undoubtedly save lives".

The findings, Mr Farrar said, indicate scientists are getting closer to turning Ebola into a "preventable and treatable" disease. "We won't ever get rid of Ebola but we should be able to stop these outbreaks from turning into major national and regional epidemics," he added.

A sense that Ebola is incurable, paired with widespread mistrust of medical workers in the DR Congo, has hampered efforts to stop the spread of the disease.

It is hoped that the effectiveness of the drugs, made by US-based pharmaceutical firms, will make patients feel "more comfortable about seeking care early", said Dr Fauci.

But the best way to end the outbreak, he added, is "with a good vaccine". A vaccine is a type of medicine that improves immunity to a particular disease, as a preventative measure.

The World Health Organization (WHO) say vaccines developed to protect against Ebola, which are allowed for "compassionate use" before official licensing, have proven highly effective.

How serious is the DR Congo outbreak?

The current outbreak in eastern DR Congo began in August last year and is the biggest of the 10 to hit the country since 1976, when the virus was first discovered.

In July, the WHO declared the Ebola crisis in the country a "public health emergency of international concern".

But it is dwarfed by the West African epidemic of 2014-16, which affected 28,616 people, mainly in Guinea, Liberia and Sierra Leone. About 11,310 people died in what was the largest outbreak of the virus ever recorded. However, attempts to contain the latest outbreak are proving difficult. In particular, militia group violence and suspicion towards foreign medical assistance have hindered efforts. Earlier this month, three Congolese doctors were arrested in DR Congo over the killing of a WHO medic.

About 200 health facilities have been attacked in the country this year, causing disruption to vaccinations and treatments. In one incident, family members assaulted health workers who were overseeing the burial of their relative.

A 2018 study published in the Lancet medical journal says "belief in misinformation was widespread" concerning the Ebola outbreak.

What is Ebola?

- ***Ebola is a virus that initially causes sudden fever, intense weakness, muscle pain and a sore throat***
- ***It progresses to vomiting, diarrhoea and both internal and external bleeding***
- ***People are infected when they have direct contact through broken skin, or the mouth and nose, with the blood, vomit, faeces or bodily fluids of someone with Ebola***
- ***Patients tend to die from dehydration and multiple organ failure***

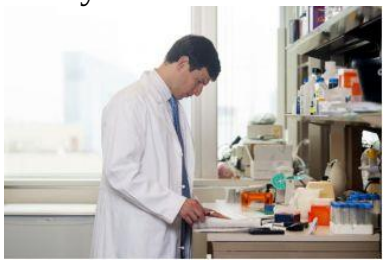
http://bit.ly/2Z5f6qA

A Doctor Tested a New Treatment on Himself. Now, It May Help Others with This Rare Disease.

A doctor's quest to understand his own rare disease led him to test an experimental treatment on himself.

By Rachael Rettner

A doctor's quest to understand his own rare disease led him to test an experimental treatment on himself, and it may have worked. The physician, Dr. David Fajgenbaum, an assistant professor at the University of Pennsylvania's Perelman School of Medicine, has been in remission ever since he first used himself as a "test subject" five years ago.



Dr. David Fajgenbaum, above, has a rare disease known as Castleman disease. He identified a treatment for himself that may work for others. **© Penn Medicine)**

Now, a new study suggests Fajgenbaum's treatment may help others with this rare inflammatory disorder known as Castleman disease.

The new research shows that patients with severe forms of the condition, who haven't responded to previous therapies, may benefit from a treatment that targets a specific signaling pathway inside cells called the PI3K/Akt/mTOR pathway.

The work, published today (Aug. 13) in the Journal of Clinical Investigation, is one of the few occasions when the lead author of the report (Fajgenbaum) is also a patient in the study.

The doctor's quest began in 2010, when Fajgenbaum, who was then an athletic 25-year-old in medical school, suddenly fell ill. He developed swollen lymph nodes, abdominal pain, fatigue and an eruption of small red spots on his body, according to the report. Fajgenbaum's condition soon worsened and became life-threatening.

Fajgenbaum was eventually diagnosed with Castleman disease, which is actually a group of inflammatory disorders that affect the lymph nodes. About 5,000 people in the U.S. are diagnosed with some form of Castleman disease each year. Patients with Castleman disease may have a mild form of the disease with a single affected lymph node, while others have abnormal lymph nodes throughout their body and develop life-threatening symptoms, including organ failure.

Fajgenbaum has this more severe form, known as idiopathic multicentric Castleman disease (iMCD), which is diagnosed in only about 1,500 to 1,800 Americans each year, according to the report. The severe form of the disease is similar to several autoimmune conditions, but like cancer, it also causes an overgrowth of cells, in this case in the lymph nodes. About 35% of people with iMCD die within five years of the diagnosis. Although there is one approved treatment for Castleman disease, a drug called siltuximab, not all patients respond to the therapy.

Fajgenbaum fell into this group. No existing therapies helped him and his symptoms kept coming back — during the 3.5 years after his diagnosis, he was hospitalized eight times, the report said. But by studying his own blood samples, Fajgenbaum identified a possible clue to his illness. Right before a flare-up, he saw a spike in the number of immune cells called activated T cells, as well as an increase in levels of a protein called VEGF-A. Both of these factors are regulated by the PI3K/Akt/mTOR pathway.

Fajgenbaum hypothesized that a drug that inhibited this pathway may help with his condition. He turned to a drug called sirolimus, which inhibits this pathway and is already used to prevent organ rejection in kidney transplant patients. Fajgenbaum hasn't had a flare-up of symptoms since he started taking the drug in 2014.

In the new study, Fajgenbaum and colleagues report that two other patients with iMCD also showed increased levels of activated T cells and VEGF-A before their symptoms flared up. After treatment with sirolimus, both patients also showed sustained remission. So far, both patients have gone 19 months without a relapse.

"Our findings are the first to link T cells, VEGF-A, and the PI3K/Akt/mTOR pathway to iMCD," Fajgenbaum said in a statement. "Most importantly, these patients improved when we inhibited mTOR. This is crucial because it gives us a therapeutic target for patients who don't respond to siltuximab."

Although the new findings are promising, the study involved only three patients, and larger trials will be needed to show that this drug is an effective treatment for iMCD. Soon, Fajgenbaum and colleagues plan to start a clinical trial to test sirolimus in up to 24 patients with iMCD.

http://bit.ly/2NcKalQ

Turbo-charged Crispr gene-editor can make 25 alterations in one go

An enhanced Crispr gene-editing technique has been developed that can introduce as many as 25 different regulatory changes or alteration to a gene simultaneously.

By Frances Addison

Originally identified as a primitive immune response in bacteria, the Crispr system is now a popular tool for targeted gene-editing in mammalian cells. The technique involves introducing plasmids that code for the different Crispr components into a target cell, including sequences for Cas proteins and gRNAs, which direct the proteins to the correct genes. By doing so, researchers have been able to perform highly targeted gene knockout, gene activation and gene repression with minimal off-target effects.

Previously, however, Cas proteins and gRNAs have needed to be encoded on separate transcripts before being introduced to the target cells, limiting our ability to target multiple genes simultaneously. Now, a team of researchers have shown that by

employing a tertiary structural motif, it is possible to stabilise an RNA transcript encoding both a Cas12a protein and up to 25 individual gRNA sequences in a single plasmid. The novel structure also encouraged Cas12a production and improved gRNA processing.

As mammalian transcripts have an average length of 13.5kb, the team has theorised that it may be possible to employ hundreds or even thousands of gRNAs in parallel using single plasmids. They do acknowledge, however, that as the transcripts increase in length, the challenges involved in synthesising and cloning them would become more significant.

This new approach to encoding Crispr components has both advantages and disadvantages when compared with more traditional techniques. One of the most important distinctions is that when Cas proteins and gRNAs are introduced separately, they are expressed by different promoters. Contrastingly, when they are both part of the same plasmid, both components are expressed by a single promoter and therefore have a fixed ratio to one another. This enables much tighter control of expression, but may also result in a fixed ratio that isn't optimised for the situation in question, resulting in poorer activity.

Such issues may be overcome by increasing plasmid concentration or by encoding multiple gRNAs per target gene, but this has not been confirmed.

References ***C C Campa* et al, Nat. Methods, *2019, DOI: 10.1038/s41592-019-0508-6***

http://bit.ly/30bLIQB

Up to half of patients withhold life-threatening issues from doctors

47.5 percent of patients who feel they face these four threats do not disclose this critical information to care providers

Facing the threat of domestic violence, being a survivor of sexual assault, struggling with depression or thoughts of suicide are four topics that are difficult to broach with anyone. Including those who can help you.

A new study reveals up to 47.5 percent of patients who feel they face one or more of these four threats do not disclose this critical information to care providers out of embarrassment, fear of judgement or the possible long-term implications of sharing such information.

Scientists at University of Utah Health, Middlesex Community College, University of Michigan and University of Iowa collaborated on the study, which was published online in *JAMA Network Open* on August 14.

Understanding how to make patients feel more comfortable with clinicians is key to helping patients address such life-threatening risks, says the study's senior author Angela Fagerlin, Ph.D.

"For primary care providers to help patients to achieve their best health, they need to know what the patient is struggling with," says Fagerlin. Patients who withhold they have been sexually assaulted are potentially at risk for post-traumatic stress disorder and sexually-transmitted diseases, she explains. "These are numerous ways providers can help patients with such as getting resources, therapy and treatment." She is chair of the department of Population Health Sciences at U of U Health and an investigator with the VA Salt Lake City Health System's Informatics Decision-Enhancement and Analytic Sciences (IDEAS) Center for innovation.

The study reflects responses from over 4,500 people in two national online surveys from 2015. Participants in one survey averaged 36 years old, while participants from the second had a median age of 61. They reviewed a list of types of medically relevant information and asked to indicate whether they had ever withheld this information from a clinician. They were also asked to recall why.

The surveys show that 40 to 47.5 percent of participants chose not to tell their provider that they had experienced at least one of the

four threats. Over 70 percent said the reason why was embarrassment or fear of being judged or lectured.

If the patient was female or younger then the odds were higher they would keep this information to themselves. What compounds this issue is that multiple studies in recent years have highlighted how health care providers downplay or fail to take seriously women's medical complaints.

One limitation noted by the study's first author Andrea Gurmankin Levy, Ph.D., MBe, a professor in social sciences at Middlesex Community College in Middletown, Connecticut, is that study participants may have not shared in their survey responses all the information they withheld, meaning that this phenomenon may be even more prevalent than the study reveals.

Levy says the survey reinforces the point that there is discomfort and a lack of trust between patients and providers. If patients filled out a questionnaire about sensitive information when they arrive at the provider's office, might that improve the information flow? She wonders, "Is it easier to tell a piece of paper something sensitive than to look into your clinician's eyes and say it?"

The next step in Fagerlin and Levy's research may be contacting patients as they leave an appointment with their provider. Person-to-person interviews would permit the research team to get patients to respond while their memories are still clear.

"If we are there, we can ask them right in the moment so they can more easily put their finger on exactly what was at issue - why they didn't share such crucial information," Levy says.

This is the second article by this team to draw upon the 2015 surveys. The first, published in November 2018 revealed that 60 to 80 percent of those surveyed did not share pertinent information with their provider regarding daily issues like diet and exercise. One third did not speak up when they disagreed with their provider's recommendations.

Both surveys raise concerns about communication and trust between patients and their care givers. Improving rapport falls both on providers' and patients' shoulders, the authors say. Providers need to establish an atmosphere where the patient feels neither judged nor rushed but rather are able to share concerns fundamental to their well-being. In addition, patients will benefit by sharing sensitive information with their providers.

http://bit.ly/33FHtPD

Joint lubricating fluid plays key role in osteoarthritic pain, study finds

Lubricant that allows our joints to move smoothly triggers a pain response from nerves similar to that caused by chili peppers

A team at the University of Cambridge has shown how, in osteoarthritis patients, the viscous lubricant that ordinarily allows our joints to move smoothly triggers a pain response from nerve cells similar to that caused by chili peppers.

Osteoarthritis is the most common form of arthritis. It causes joint pain and stiffness, and in some people swelling and tenderness of the joints. The condition affects an individual's quality of life and costs millions to the global economy, both directly in terms of healthcare costs and indirectly due to impact on the individual's working life.

Osteoarthritis tends to occur later in life and has been largely considered as a degenerative disorder in which pain is produced by damage and wear and tear to bone and cartilage. However, in recent years it has become clear that osteoarthritis is not restricted to cartilage damage, but is a failure of the entire joint, with inflammation - the body's response to stress and injury - being a major contributor to the pain experienced by patients. A recent collaboration between the two pharmaceutical companies Pfizer and Eli Lilly has found that their anti-inflammatory drug, tanezumab,

produced pain relief for osteoarthritic patients in a phase 3 clinical trial.

When inflammation occurs during osteoarthritis, the body produces an increased number of cells within and around the joint. These cells release inflammatory substances into the synovial fluid, the lubricant that allows joints to move smoothly. During osteoarthritis, synovial fluid becomes less viscous and these inflammatory substances come into direct contact with sensory nerve cells in the joint, producing the sensation of pain.

In a study published in the journal *Rheumatology* on 13 August 2019, researchers at the University of Cambridge and Addenbrooke's Hospital, part of Cambridge University Hospitals, examined whether synovial fluid produced during osteoarthritis is capable of directly exciting sensory nerves supplying knee joints - those nerves responsible for transmitting pain signals.

"Osteoarthritis can be a very painful condition, but we only know a little about what causes this pain," says Sam Chakrabarti, a Gates Cambridge Scholar. "We wanted to investigate what was happening in the joint and to see whether it was the lubricant that ordinarily keeps these joints moving that was contributing to the pain. Studies such as these are important in helping us develop better treatments."

The researchers obtained synovial fluid from consenting osteoarthritis patients at Addenbrooke's Hospital and from post-mortem donors with no known joint disease. They then incubated knee sensory nerves isolated from mice in either healthy or osteoarthritis synovial fluid and recorded the activity of these nerves.

The team found that when incubated with osteoarthritic synovial fluid, the knee nerves were more excitable. The nerves also showed an increase in the function of TRPV1, a molecule that detects the hotness of chili peppers (TRPV1 is also activated by heat, which is why chilis tastes hot). Although the presence of inflammatory chemicals in osteoarthritis synovial fluid has been known since 1959, this is the first evidence that synovial fluid can directly excite sensory nerves and hence is an important contributor to an individual's experience of pain.

"This is the first time we have been able to use synovial fluid from human osteoarthritis patients to excite sensory nerve cells, making it more clinically-relevant than mouse studies alone, and so will hopefully help translating treatments from bench to bedside," says Dr Ewan St John Smith from the Department of Pharmacology at the University of Cambridge.

"In the future, this set up can be used to identify the specific components of synovial fluid that cause pain and then to test if and how a drug will be useful in arthritic pain. Since synovial fluid is regularly collected from arthritic patients as part of their treatment regime, our technique can be easily set up in laboratories throughout the world to understand and help to identify a cure for arthritic pain."

Dr Deepak Jadon, Director of the Rheumatology Research Unit at Cambridge University Hospitals, adds: "This study highlights how much we can learn with the help of our patients, as well as the importance of collaboration between clinicians and basic scientists."

The research was funded by Versus Arthritis and the Gates Cambridge Trust.

Reference *Chakrabarti, S et al. Human osteoarthritic synovial fluid increases excitability of mouse dorsal root ganglion sensory neurons: an in-vitro translational model to study arthritic pain.* Rheumatology*; 13 August 2019; DOI: 10.1093/rheumatology/kez331*
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http://bit.ly/2KCOcCr

Paralytic Shellfish Poisoning Meets Its Match

As climate change brings more red tides, a protein from the American bullfrog might provide protection from paralytic shellfish poisoning.

by Casey Rentz

Every summer, warm waters bathe the west coast of the United States, Canada, and other parts of the world in toxic algae. Particularly frightening are dinoflagellates in the genus *Gonyaulax*, *Alexandrium*, *Gymnodinium*, and *Pyrodinium*, which secrete saxitoxin, one of the world's most lethal neurotoxins. Shellfish swallow saxitoxin and concentrate it in their bodies so readily that eating just one saxitoxin-laden mussel can cause paralysis and even death. Despite government warnings, people are poisoned every year by mussels they've gathered and eaten—as are birds, whales, and seals. But algae eaters—including shellfish, pufferfish, and freshwater frogs—remain blissfully unaffected.

Since the 1990s, scientists have known that these animals are naturally resistant to saxitoxin: they make proteins that sequester saxitoxin so it can't affect their nervous systems. Recently, a team led by Daniel Minor, a biophysicist at the University of California, San Francisco, has taken on a molecular investigation of the novel phenomenon.

Minor and his colleagues used X-ray crystallography—the same technique used to first identify the structure of DNA—to create an atomic-resolution picture of saxiphilin, an antitoxin protein collected from American bullfrogs. They could see, in intricate detail, how saxiphilin binds with saxitoxin to render it harmless. This sophisticated image could bring researchers one step closer to detecting saxitoxin and dozens of other similar marine toxins, and even developing an antitoxin.

Detection may prove ever more essential in coming years. As climate change begets rising ocean temperatures and the deoxygenation of coastal waters, algal blooms worldwide are becoming bigger and lasting longer. More algal blooms mean more toxin-laden seafood and more sick humans, birds, and seals. If the trend continues, a better toxin detector will be a vital part of public health efforts.

"This is a case where we perhaps have an opportunity to do something that has a real public health impact," says Minor.

Minor's curiosity about marine toxins was sparked in 2011 by a surprise email. At the time, he had been researching sodium channels, the passages by which cells communicate, in bacteria. Sodium channels are also the site at which saxitoxin and other neurotoxins attack human nerve cells. One day, James Hungerford, a toxin research chemist at the US Food and Drug Administration, cold-emailed Minor with a question: could he use bacteria to make saxitoxin detectors for state agencies like the California Department of Public Health?

To protect the public, the department routinely tests for saxitoxin and other marine toxins at hundreds of spots along the coast every week. But the saxitoxin test used at the time—and still in use today—was developed in the 1930s and involves dosing mice with toxic seawater and seeing how long it takes them to die. Some people think the test is inhumane, considering how many mice must die to confirm the quality of the water. But the test remains the quickest and cheapest approach available.

Hungerford wondered if Minor could develop a bacteria-based detector instead*. If the bacteria would stick to the saxitoxin, he thought, testers could quickly visualize if there were dangerously high concentrations of the toxin in the water.

Sadly, Minor knew from previous research that the approach wouldn't work. But the seed was planted. "It got me thinking about the problem—it was kicking around in my head for a long time," Minor says.

In his new study, Minor focused on identifying the physical structure of saxiphilin and found that it is shaped somewhat like a butterfly. Saxitoxin binds at an indented spot on one of the wings. The pocket fits saxitoxin snugly and is negatively charged, attracting the toxin electrostatically. To Minor's surprise, the

binding site looks almost exactly the same as when saxitoxin binds to sodium channels in human nerve cells, which means that saxiphilin might work to mitigate the effects of saxitoxin in people, too.

Coincidentally, Lauren O'Connell, an ecologist at Princeton University in New Jersey, also became interested in saxiphilin last year when she discovered that it is abundant in the blood of poison dart frogs, and may be involved in their own toxin resistance. Neither Minor nor O'Connell knew of the other's work, but they both think saxiphilin is an exciting, up-and-coming topic of research. "Dr. Minor's work represents a resurgence in the importance of saxiphilin and has opened up a new field of study on toxin binding and sequestration," says O'Connell.

It will take more research and development to make a functioning saxitoxin detector, but knowing the structure of the binding pair helps. In the future, scientists may use saxiphilin or a similar synthetic molecule to produce an antitoxin that could bind just enough saxitoxin so that the liver can flush it out before it accumulates and makes someone sick. But until funding materializes for such an imaginative solution, detection is still the front line of the effort.

**Correction: This section of the story has been updated to clarify the relationship between Hungerford and Minor.*

http://bit.ly/2NhuoX7

Study: many of the "oldest" people in the world may not be as old as we think

A new paper explores what "supercentenarians" have in common. Turns out it's bad record-keeping.

By Kelsey Piper Aug 8, 2019, 12:00pm EDT

We've long been obsessed with the super-elderly. How do some people make it to 100 or even 110 years old? Why do some regions — say, Sardinia, Italy, or Okinawa, Japan —produce dozens of these "supercentenarians" while other regions produce none? Is it genetics? Diet? Environmental factors? Long walks at dawn?

A new working paper released on bioRxiv, the open access site for prepublication biology papers, appears to have cleared up the mystery once and for all: It's none of the above.

A village mural in Sardinia, Italy. Sardinia is one of the few regions in the world with high concentration of people who live past 110. Massimiliano Maddanu/REDA&CO/Universal Images Group via Getty Images

Instead, it looks like the majority of the supercentenarians (people who've reached the age of 110) in the United States are engaged in — intentional or unintentional — exaggeration.

The paper, by Saul Justin Newman of the Biological Data Science Institute at Australian National University, looked at something we often don't give a second thought to: the state of official record-keeping.

Across the United States, the state recording of vital information — that is, reliable, accurate state record-keeping surrounding new births — was introduced in different states at different times. A century ago, many states didn't have very good record-keeping in place. But that changed gradually over time in different places.

Newman looks at the introduction of birth certificates in various states and finds that "the state-specific introduction of birth certificates is associated with a 69-82% fall in the number of supercentenarian records."

In other words, as soon as a state starts keeping good records of when people are born, there's a 69 to 82 percent fall in the number of people who live to the age of 110. That suggests that of every 10 supposed supercentenarians, seven or eight of them are actually

younger than that, but we just don't know it because of poor record-keeping.

This doesn't mean that any of these false supercentenarians are lying. It could be that they lost track of their age a long time ago, accidentally double-counted some years, or were told the wrong birth year. But it does mean that the majority of people claiming to be supercentenarians, born in areas that didn't keep reliable, accurate birth records, are probably not quite as old as they say they are.

As a result, most of the studies we've conducted on them — trying to divine the secrets of old age from genetic tests and diet surveys — may be no good. But this isn't just a funny little accident of old-age science: It actually illustrates a serious challenge in science.

Why we may have to question what we know about supercentenarians

The paper also looks at the phenomenon in Italy and Japan, where something different seems to be happening.

Italy keeps better vital statistics than the United States does, and has had reliable vital statistics across the country for hundreds of years — yet in Italy, too, there are clusters of the country where lots of supercentenarians pop up. Maybe the Italian supercentenarians are for real?

Newman's analysis suggests not. He starts out by noticing something fishy: The parts of Italy that claim the most supercentenarians overall have high crime rates and low life expectancy. Isn't that weird? Why would an area generally have low life expectancy but also produce an extremely disproportionate share of the world's oldest people?

The same pattern repeats itself in Japan: Okinawa has the greatest density of super-old people, despite having one of the lowest life expectancies in the country and generally poor health outcomes.

The paper puts forward a controversial proposal. It seems unlikely that living in high-crime, low-life-expectancy areas is the thing that makes it likeliest to reach age 110. It seems likelier, the paper concludes, that many — perhaps even most — of the people claiming to reach age 110 are engaged in fraud or at least exaggeration. The paper gives a couple of examples of how this might come about; some of it might be reporting error, and some of the supercentenarians might be produced by pension fraud (someone might be claiming a dead person is still alive for pension benefits, or claiming the identity of a parent or older sibling).

Newman's overall conclusion: "Remarkable age attainment is predicted by indicators of error and fraud," and isn't correlated with things like a healthy population of 80-year-olds or high-quality access to medical care. "As a result, these findings raise serious questions about the validity of an extensive body of research based on the remarkable reported ages of populations and individuals."

In other words, all of our research into the biomarkers, habits, and diets that predict extreme old age? Probably worthless, because a significant share of the sample was not actually as old as we thought.

The paper still needs to undergo peer review, but if its findings hold, it does illustrate an interesting statistical phenomenon: When you're looking for something exceptionally rare, your data set will be dominated by errors and false positives. For example, if you're looking for a disease that affects only one in a million people, and your test for the disease is 99.99 percent accurate, then it'll turn up 100 false positives for every true positive. Even though you used a highly accurate test, most of your "positives" don't have the disease!

Similarly, supercentenarians are extremely rare. Only about one in 1,000 people who live to the age of 100 make it to 110. The vast majority of people would never impersonate their parent or older

sibling for benefits, or forge a birth certificate, or participate in identity theft, or get confused about how old they even are. But if one in 1,000 people would do that, then fraudulent supercentenarians will be more common than bona fide supercentenarians. When you're looking at an exceptionally rare phenomenon, you have to be exceptionally careful — or you'll mostly find yourself studying something else entirely.

https://wb.md/2Zbr1mP

FDA OKs 'Game Changer' Pretomanid for Highly Resistant TB

FDA approves 3-drug combination in a major breakthrough treatment for the most drug-resistant tuberculosis

Marcia Frellick

The US Food and Drug Administration (FDA) approved pretomanid today, a "major" breakthrough treatment for the most drug-resistant tuberculosis (TB) when used in combination with bedaquiline and linezolid.

It is only the third TB drug approved by the FDA in more than 40 years, according to a news release from RTI International, one of the collaborators in the drug's development.

The pretomanid combination treats extensively drug-resistant tuberculosis (XDR-TB), a type of multidrug-resistant tuberculosis (MDR-TB) of the lungs that is resistant to the two strongest TB drugs, isoniazid and rifampin, as well as to any fluoroquinolone and at least one of three injectable second-line drugs (amikacin, kanamycin, or capreomycin).

The FDA said in a news release that the safety and effectiveness of the pretomanid combination, taken orally, was primarily demonstrated in a study of 109 patients with extensively drug-resistant, treatment-intolerant, or nonresponsive MDR-TB. Of the 107 patients who were evaluated 6 months after the end of therapy, 95 (89%) had successful treatment, far exceeding success rates of available treatments.

Amita Gupta, MD, professor of medicine and deputy director of the Johns Hopkins University Center for Clinical Global Health Education in Baltimore, Maryland, told *Medscape Medical News* there was much anticipation of this announcement.

"This is a very exciting development," she said. "It will be a game changer for these highly resistant patients."

There are very few treatments for people with XDR-TB, she noted, cure rates are very low (a trial in South Africa showed 2%-22% cure rates), treatment duration is typically 2 years, mortality rates are as high as 80%, and treatments have had severe toxicities.

The New Drug Application (NDA) for pretomanid said previous treatments have typically involved taking at least five drugs, some intramuscular, some intravenous, with no defined regimen and with side effects that can include deafness, renal failure, and psychosis.

The pretomanid regimen, on the other hand, is all-oral, well tolerated, has a treatment duration of 6 months, and cure rate of 89%, she noted.

The most common adverse reactions observed from the pretomanid combination "included damage to the nerves (peripheral neuropathy), acne, anemia, nausea, vomiting, headache, increased liver enzymes (transaminases and gamma-glutamyltransferase), indigestion (dyspepsia), rash, increased pancreatic enzymes (hyperamylasemia), visual impairment, low blood sugar (hypoglycemia), and diarrhea," the FDA said.

The FDA also warned that the combination should not be used in patients with hypersensitivity to bedaquiline or linezolid.

Now the question, Gupta said, is whether the population that needs the drug combination will have affordable access to it. She said the less traditional path of development will help in that regard.

The FDA said pretomanid is the second drug to be approved under the Limited Population Pathway for Antibacterial and Antifungal Drugs, or LPAD pathway, established under the 21st Century Cures Act to advance development and approval of antibacterial and antifungal drugs to treat serious infections in a limited population with unmet need.

Collaboration on Development

RTI International, an independent, nonprofit research institute, collaborated with the nonprofit public-private partnership called the TB Alliance, the developer of pretomanid. The initial commercial partner is Mylan. The FDA granted the approval of pretomanid tablets to the TB Alliance.

The TB Alliance has negotiated license agreements enabling an affordable price for pretomanid in low-resource countries.

Doris Rouse, PhD, vice president of global health technologies at RTI International told *Medscape Medical News*, "The current treatment is many hundreds of times more in cost than the proposed regimen."

"This is a growing and very successful model for addressing pressing global health needs that may not have the commercial attractiveness for a company to invest in," she said. "But when you have the resources of governments and industry and nonprofits and foundations, you can bring together the expertise and the resources to take these new drugs to market."

XDR-TB is extremely rare in the United States: There were two cases of XDR-TB in the US in 2017, according to the Centers for Disease Control and Prevention. However, it's not rare in Europe and can be "just a plane ride away to get tuberculosis," Rouse said.

She added, "It is a major and growing problem around the world as 127 countries have reported cases of XDR-TB and there are half a million cases of drug-resistant TB annually."

A "Major Breakthrough"

Rouse called today's announcement "a major breakthrough."

She said patients needing this drug may have coughing, weakness, lack of appetite, loss of weight, and night sweats.

"I've seen these patients in the wards and it's really a horrible thing to see," Rouse said.

The World Health Organization (WHO) reports that about 6.2% of the MDR-TB cases worldwide have XDR-TB. Detection of XDR-TB is difficult because some countries lack the resources to test for resistance to second-line drugs.

In June, the FDA's Antimicrobial Drugs Advisory Committee voted 14-4 that there was "substantial evidence of the effectiveness and sufficient evidence of the safety of pretomanid as part of a combination regimen with bedaquiline and linezolid, in adults for the treatment of pulmonary extensively drug-resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis."

Pretomanid is a member of a class of compounds known as nitroimidazooxazines. "It has been studied in 20 clinical trials alone or in combination with other anti-TB drugs. Since TB Alliance began development of pretomanid in 2002, it has been administered in a clinical trial setting to more than 1,200 people in 14 countries," the alliance said in a news release.

TB kills more than 1.6 million people a year globally, according to WHO, more than any other infectious disease.

http://bit.ly/2N8FQ7f

New pain organ discovered in the skin

Researchers at Karolinska Institutet in Sweden have discovered a new sensory organ that is able to detect painful mechanical damage, such as pricks and impacts.

The discovery is being published in the journal 'Science'.

Pain causes suffering and results in substantial costs for society. Almost one person in every five experiences constant pain and there is a considerable need to find new painkilling drugs. However, sensitivity to pain is also required for survival and it has a protective function. It prompts reflex reactions that prevent damage to tissue, such as pulling your hand away when you feel a jab from a sharp object or when you burn yourself.

Researchers at Karolinska Institutet have now discovered a new sensory organ in the skin that is sensitive to hazardous environmental irritation. It is comprised of glia cells with multiple long protrusions and which collectively go to make up a mesh-like organ within the skin. This organ is sensitive to painful mechanical damage such as pricks and pressure.

The study describes what the new pain-sensitive organ looks like, how it is organised together with pain-sensitive nerves in the skin and how activation of the organ results in electrical impulses in the nervous system that result in reflex reactions and an experience of pain. The cells that make up the organ are highly sensitive to mechanical stimuli, which explain how they can participate in the detection of painful pinpricks and pressure. In experiments, the researchers also blocked the organ and saw a resultant decreased ability to feel mechanical pain.

"Our study shows that sensitivity to pain does not occur only in the skin's nerve fibres, but also in this recently-discovered pain-sensitive organ. The discovery changes our understanding of the cellular mechanisms of physical sensation and it may be of significance in the understanding of chronic pain," says Patrik Ernfors, professor at Karolinska Institutet's Department of Medical Biochemistry and Biophysics and chief investigator for the study.

The research was carried out with financial assistance from ERC, the Swedish Research Council, the Knut and Alice Wallenberg Foundation and Welcome Trust.

Publication: 'Specialized cutaneous Schwann cells initiate pain sensation'. Abdo H, Calvo-Enrique L, Martinez Lopez J, Song J, Zhang MD, Usoskin D, El Manira A, Adameyko I, Hjerling-Leffler J, Ernfors P. Science, 16 August 2019.

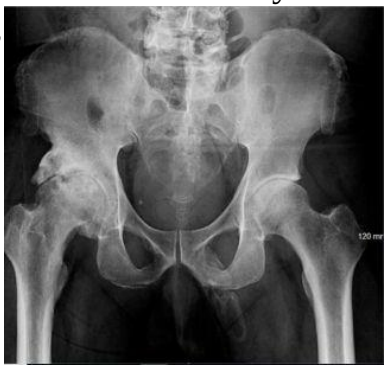
http://bit.ly/2YXBqXW

Man's X-Ray Reveals His Penis Is Turning to Bone

Sometimes, the body grows bone in places it shouldn't.

By Rachael Rettner 2 days ago Health

Sometimes, the body grows bone in places it shouldn't. That was the case for a man who was diagnosed with an extremely rare condition — his penis was turning to bone, according to a new report.



The 63-year-old man went to the emergency room after he fell on the sidewalk onto his buttocks, according to the report, published in the September issue of the journal Urology Case Reports. He was able to walk, but he told doctors he was experiencing knee pain.

A man was diagnosed with penile ossification, a rare condition in which bone forms inside the penis. Above, the man's X-ray showing calcified tissue in the expected area of the penis. **(Image: © Georges El Hasbani, et al./Urology Case Reports/CC BY NC-ND 4.0)**

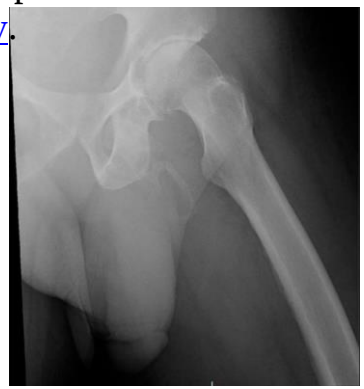
When doctors performed a physical exam, the man also reported penile pain, the report said.

Given that the man had fallen on his butt, doctors decided to first X-ray his pelvis to check for bone fractures. That's when they noticed something very strange: The man appeared to have "ossification" along the entire shaft of his penis, according to the report. In other words, bone had formed inside the penis.

The man was diagnosed with "penile ossification." The condition is very rare, with fewer than 40 cases reported in the medical literature, according to the report authors, from Lincoln Medical

and Mental Health Center in the Bronx, New York; and the American University of Beirut in Lebanon.

Ossification happens when calcium salts build up in soft tissues, "leading to bone formation in areas of the body where there is connective tissue," according to a 2017 report of a similar case published in the journal Reviews in Urology.



Exactly why this happens isn't always clear. But doctors know that penile ossification, though rare, is often linked with another condition called Peyronie's disease, which occurs when scar tissue builds up in the penis, causing the organ to bend or curve. This condition can also cause penile pain with or without erections, according to the Mayo Clinic.

An X-ray showing "plaque-like calcification" in the expected area of the penis. (Georges El Hasbani, et al./Urology Case Reports/ CC BY NC-ND 4.0)

In the current case, the man left the hospital against medical advice, and doctors couldn't perform the tests needed to pinpoint the cause of his condition. But they suspect the man may have had Peyronie's disease, given his report of penile pain and the known link between the two conditions.

Other possible causes can include metabolic diseases, end stage kidney disease or trauma, the authors said.

Treatment for penile ossification depends on the extent of bone formation and the patient's symptoms, the report said. Men who don't have any symptoms typically don't need treatment right away. But those with bothersome symptoms, such as pain, may be prescribed painkillers or receive injections in the penis with certain drugs to reduce pain or curvature. In severe cases, men may need surgical treatment, the report said.

In the 2017 case, a 43-year-old man in Texas went to the doctor because he felt a "firmness" in his penis, and he reported difficulty having erections. The man was diagnosed with Peyronie's disease, and he elected to have an inflatable penile prosthesis, also known as a penile implant, to treat his erectile dysfunction (ED). But while doctors were performing the surgery, they found "calcified tissue" (i.e., bone) in the penis, which was removed with surgery. The man later experienced some complications with his implant, but the device was ultimately successful in treating the man's ED, the report said.

http://bit.ly/2z18qI7

Swearing: attempts to ban it are a waste of time – wherever there is language, people cuss

Attempts to ban swearing in public places, in the workplace and even in the home appear to be on the rise.

Monika Schmid *

The common thinking seems to be that people swear more and swear worse than they used to – and that this is a recent phenomenon.

The apparent rise of profanity is easily ascribed to our language, interactions and society deteriorating under the bad influence of social media. This has to be stopped, the appalled guardians of “polite” behaviour argue, and the way to stop it is to impose bans, fines, sackings – or send us to bed without our dinner.

In response, those of us who find relief in using the occasional expletive will tirelessly cite studies suggesting that swearing is a sign not only of being more honest, healthier and better adjusted, but also that regular swearers are more intelligent and have a larger vocabulary than non-swearers.

All well and good, you might say. Go ahead and swear if you think it’ll reduce your blood pressure, increase your IQ and make you more eloquent – but don’t do it around me, in public or at work.

The problem is that attempts to legislate against any kind of verbal behaviour are doomed from the start.

If a linguistic phenomenon becomes widespread and noticeable enough for someone to perceive the need to stop it, it has already caught on to such a degree that it will never be stamped out. Especially if it is a phenomenon that is eminently useful, which swearing is.

Why swearing works

Some of the reasons why that should be the case are obvious. Using swearwords is similar to highlighting a written phrase in flashing neon red. It grabs the attention and signals that you are not only absolutely serious about something, but that it is also emotionally important to you.

When you use a word that the people you are talking to aren't expecting, it causes them to sit up and listen, and that can often bring your message home more effectively than if you had phrased it in a clear but neutral way. This noticeable effect is enhanced by the fact that swearing often consists of short words (they aren't called "four-letter words" for nothing). They stand out from the context not only because of their content but also in terms of their intonation.

Swearing can also function as a safety valve, relieving emotional or even physical pressure. Research has found that people subjected to mild levels of pain (by putting their hands into a container of hot water) were able to withstand the discomfort longer and judged it to be less severe while uttering swearwords than while using neutral words.

These and many other studies on swearing show its beneficial aspects. But swearing is fascinating on a completely different level, too.

Trauma to the brain as a result of accident or injury, neurodegenerative illnesses or strokes often affect our ability to formulate messages. Needless to say, this loss of linguistic function is incredibly frustrating to the people experiencing it. They may have become unable to formulate even the simplest sentences, or retrieve basic words, but their intellectual abilities are often completely unaffected.

One of the oldest reported studies, conducted by Paul Broca in 1861, reports the case of a patient who, as a result of epilepsy, had almost entirely lost his ability to speak. While he was able to understand most of what was said to him, he only ever produced the nonsense monosyllable "tan", except when he became so exasperated at his inability to communicate that he would exclaim "Sacré nom de Dieu!" ("Holy name of God" – or "For God's sake!").

Part of the foundation of language

The fact that someone who may no longer be able to put a name to an apple or a house can produce a fairly complex phrase such as "Holy name of God" suggests that swearing occurs at a more automatised level than general speech production, and in a different part of the brain – and that it can therefore not satisfactorily be replaced by a non-expletive sentence.

Nowadays, the expletive of choice would probably no longer be the name of God. The expressions that were spared by aphasia would probably get you in trouble in Cheshire, Dartford, Canterbury or any of the 15 British councils that have banned swearing. They would, however, allow such patients to vent their frustration at having lost all other linguistic function.

Swearing plays an important role in maintaining mental hygiene and sanity because it is associated with relieving unpleasant emotions, feelings and sensations. What's more, people who became fluent in a foreign language later in life experience even the strongest swearwords as less taboo than the equivalent in their mother tongue.

This suggests that the swearwords we acquired early, while we learned to speak, fundamentally connect us to our deepest emotions. Small children often delight in the shock they can produce by using simple words – even though they may have no idea what the word means or why it is so inappropriate – and these impressions stay with us.

Historical linguistics tells us that this has always been the case. The things we swore by have changed over the centuries from religious taboos to physical ones, and vary from country to country. In Dutch, if you want to insult someone badly you will tell them to contract a horrible disease, while in Chinese, if you are calling someone a show-off, you might say that they are blowing steam into the private parts of a cow.

Whatever the expletive of choice, the fact that people swear – and that others object to it – is probably as old as language itself. Wherever there is a substantial enough record of an ancient language, there is a record of swearing. Indeed, swearing is one of the most fundamental functions of language, which is why the Fry and Laurie sketch about made-up swearwords is so funny: we have no idea what the words ("Prunk", "Cucking", "Pempslider") mean, but we know they are bad.

So when that policeman in Cheshire or Dartford or Canterbury tries to fine you, just tell them that you were swearing for purely medicinal reasons – and that they are fighting a battle that was lost thousands of years ago. Just don't use any four-letter words while you do so.

* *Professor of Linguistics, University of Essex*

Disclosure statement

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https://cnet.co/2PhPI1l

Scientists want to mass-produce seaweed that stops cows burping methane

Finding a way to farm seaweed on a global scale could dramatically lessen greenhouse gas emissions worldwide.

By Bonnie Burton

In 2014, Australia's national science agency CSIRO discovered that by adding the pink seaweed Asparagopsis to a cow's diet, it reduces the amount of the gas produced by the cow up to 99 per cent. Now scientists want to farm Asparagopsis on a large scale to reduce Australia's greenhouse gas emissions -- and the world's.

University of the Sunshine Coast (USC) Associate Professor Nicholas Paul said if enough pink seaweed was grown it could help to reduce greenhouse gas emissions in Australia by an impressive 10 percent, according to ABC news on Wednesday.

"When added to cow feed at less than two percent of the dry matter, this particular seaweed completely knocks out methane production," Paul said in a statement on Wednesday. "It contains chemicals that reduce the microbes in the cows' stomachs that cause them to burp when they eat grass."

The USC team headed by Paul is currently working at the Bribie Island Research Centre in Moreton Bay, Australia to learn more about how to grow the pink seaweed species to better figure out a solution to scale-up of production of the seaweed.

The best way to increase the pink seaweed supply is to find the fastest way to grow it outside of a lab.

"We know the chemical composition of Asparagopsis and we know the chemical compounds, so now we want to maximize the concentration of that chemical so we can use less seaweed for the same effect," USC Seaweed Research Group project scientist Ana Wegner said in a video about the discovery.

"If we're able to work out how to scale up the seaweed to become at a level that can feed all of the cows and the sheep and the goats around the world then it's going to have a huge impact on the climate," Paul said in the video.

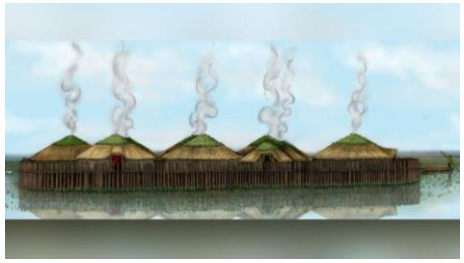
https://bbc.in/2Mn3NrN

Early fish tapeworms found at 'Britain's Pompeii' Must Farm

The earliest evidence of fish tapeworm in Britain has been discovered preserved in human faeces, according to experts at Cambridge University.

The finds were unearthed at a site dubbed "Britain's Pompeii", a burnt-out 3,000-year-old village at Must Farm in Cambridgeshire.

Fish tapeworm can grow up to 10m (32ft) long and live coiled in the intestines.



Archaeologists were astonished by the "fabulous artefacts" found at the site **V Herring/Cambridge Archaeological Unit**

The university said the research offered the first clear understanding of prehistoric Fen people's diseases.

Cambridge University's Dr Marissa Ledger said it also appeared they shared food with their dogs, because both were infected by similar parasitic worms from eating the raw fish, amphibians and molluscs.

Archaeologists uncovered at least five roundhouses at the Must Farm quarry site, with many ancillary finds **D Webb/Cambridge Archaeological Unit**

Experts from the Cambridge Archaeological Unit at the university said they believed the "exceptionally well-preserved" village was just a few months old when it burnt down.

Circular wooden houses built on stilts, pots with food still inside, jewellery and evidence of fine fabric-making were just some of the finds unearthed during the 10-month long dig in 2016.

In addition waterlogged "coprolites" - pieces of human faeces - were discovered preserved in the surrounding mud, according to a study published in the journal Parasitology.

Teams from Cambridge and Bristol universities used microscopy techniques to detect ancient parasite eggs within the faeces and determined whether it was from a human or dog.

Evidence for Echinostoma and giant kidney worms was also discovered, during months of analysis since the dig was completed.

The researchers said little was known about the intestinal diseases of Bronze Age Britain.

A previous study of a farming village in Somerset found evidence of parasites spread through the contamination of food by human faeces.

This was less evident at Must Farm, possibly because waste was disposed of into the water around the marshy settlement.

Dr Ledger said the research "enables us for the first time to clearly understand the infectious diseases experienced by prehistoric people living in the Fens".

http://bit.ly/2P0JToM

Metal tree cleans polluted air

Artificial tree sucks up as much air pollution as 368 real trees

PUEBLA, MEXICO – Trees are one of the best things we have to clean the Earth’s air, but they have drawbacks: They need time and space to grow. Enter the BioUrban, an artificial tree that sucks up as much air pollution as 368 real trees.

A BioUrban 2.0 air purification system, pictured in Puebla, Mexico **| AFP-JIJ**

Designed by a Mexican startup, the towering metal structure uses algae to clean carbon dioxide and other contaminants from the air, returning pure oxygen to the environment.

Measuring 4.2 meters tall and nearly 3 meters wide, the device looks something like a cross between a tree and a postmodernist high-rise, with a steel trunk that radiates rising bands of concentric metal.

"What this system does, through technology, is inhale air pollution and use biology to carry out the natural process (of photosynthesis), just like a tree," said Jaime Ferrer, a founding partner in BiomiTech, the company behind the invention.

Photosynthesis is the process by which green plants manufacture organic compounds. They take in water and carbon dioxide and, using energy from sun light, create glucose and oxygen.

Mexicans know a thing or two about air pollution.

Mexico City, a sprawling urban area of more than 20 million people, regularly grinds to a halt under air pollution alerts, triggered by emissions from the capital's more than 5 million cars, its polluting industries and even the nearby Popocatepetl volcano.

Ferrer says the company's goal is to help such cities achieve cleaner air in targeted areas — those used by pedestrians, cyclists or the elderly, for example — when planting large numbers of trees is not an option.

Worldwide, an estimated 7 million people die from exposure to air pollution each year, according to the World Health Organization.

"We decided our job was to not just stand by and let people keep dying," Ferrer said.

Launched in 2016, BiomiTech has so far planted three of the trees: one in the city of Puebla, in central Mexico, where it is headquartered; one in Colombia; and one in Panama.

It has a contract for two more in Turkey, and projects in the works to install them in Mexico City and Monterrey, in northern Mexico.

A BioUrban typically costs about $50,000, though the final price varies depending on the site.

The company has mainly sold them to local governments so far, though private donors are providing the funding in Monterrey, an industrial hub that is also no stranger to air pollution.

Each tree weighs about one ton, and cleans as much air as a hectare of forest — the equivalent of what 2,890 people breathe in a day.

The project is reminiscent of another launched by a German firm in 2015, the City Tree — a giant, vertical square of moss that also uses photosynthesis to clean the surrounding air.

Ferrer insists the idea of the BioUrban is not to replace real trees, but complement them in areas where planting a forest would not be viable. "They can be used in high-traffic areas, transportation terminals, where you can't just plant a hectare of trees," he said. "The system isn't going to end air pollution in Mexico City. But it can alleviate the problem in high-traffic areas."

Maria Jose Negrete, 21, who goes to university near the spot where the first tree was installed, is a fan. "It uses technology to help the environment. That's what we need right now," she said.

https://go.nature.com/31FZPhw

The 'net' that leads to excruciating stones in the belly

Immune cell extrudes a webbing that can encourage the growth of gallstones, a common and painful malady.

The hard lumps called gallstones can be as large as golf balls and cause intense pain, but new insights suggest a way to stop their growth.

Gallstones are pebble-like deposits of digestive fluid that form in the gallbladder. To understand how they form, Martin Herrmann at University Hospital Erlangen in Germany and his colleagues studied human gallstones that had been removed during surgery.

The team found that the stones' surfaces were riddled with crystals of calcium and cholesterol — the basic ingredients of gallstones —

mixed with DNA. Experiments on the gallstones showed that neutrophils, a type of white blood cell activated by infection, can produce net-like structures that are made mostly of genetic material and trap calcium and cholesterol.

The researchers gave one group of mice an existing drug that reduces neutrophil activity and another group a compound that blocks the cells' formation of the net-like structures. In both groups, gallstone growth was slower than it was in untreated mice.

The authors' findings suggest that a drug against gallstones could be just around the corner. *Immunity (2019)*

https://nyti.ms/2NebD6L

For 'Diagnosis' Show, Dr. Lisa Sanders Lets Times Readers Around the World Join in the Detective Work

A Times Magazine columnist credits Sherlock Holmes and global crowdsourcing with helping her solve patients' mysterious ailments.

By Aidan Gardiner

When Dr. Lisa Sanders saw an early version of the forthcoming Netflix documentary series about her efforts to help diagnose the mysterious ailments of eight patients, she delivered what she now readily admits was "badly designed feedback."

"Stop! Stop! This is awful!" Dr. Sanders recalls saying. "Oh, my God, this is terrible! You can't do it like that! You can't say things like that!"

Granted, the producers were trying to create an innovative show, for the first time asking the global audience of the popular column Dr. Sanders has written for The New York Times Magazine since 2002 to help diagnose seemingly impossible medical cases.

But Dr. Sanders, an internist, felt that subtle and important things were off in the way that early cut portrayed the stakes of a diagnosis, the overwhelming doubt patients can feel, doctors' talks with patients and, in short, her life's work.

The final cut of the show — like her column, called "Diagnosis" — which Netflix released today, fixed all that, capturing her beliefs about diagnosis and the lessons she's learned over the course of her career.

Years ago, for example, she used a then-common phrase of hers with a patient.

"You know, diagnosis is just a word," Dr. Sanders said.

"No!" the patient sharply corrected. "It's everything."

In the show, a diagnosis means parents don't have to let doctors cleave their music-loving daughter's brain, possibly making her mute. It means a nearly bankrupt young woman can stop paying for stumped doctors and know she can have a child without fear of passing on crippling muscle pain.

In one of her earliest pieces for The Times, Dr. Sanders wrote about her own grief-filled efforts to diagnose her alcoholic sister's cause of death, to get an answer.

"It's *not* 'just a word.' It's actually a word that carries a lot of meaning — social meaning and medical meaning," she now says.

Dr. Sanders, who'd grown up in South Carolina loving Arthur Conan Doyle's works and the satisfying "clunk" of the once disconnected pieces of a mystery story coming together, started her professional life as a journalist. She won an Emmy Award for her 1989 CBS News coverage of Hurricane Hugo's impact on Charleston.

But she decided to switch careers after an assignment about white-water rafting in North Carolina, during which a fellow reporter, who was also a doctor, leapt into a fast-moving river to pull out a woman who had been floating face down.

"I watched him change from a journalist who watches things to a doctor who does things," Dr. Sanders told The Times in a 1992 article about people's unusual paths to medical school. "It made me realize I'm not a person who wants to just sit around and watch."

She still vividly remembers the reporter doing chest compressions on the woman, who then turned her head and coughed up "a ton of water" and vomited.

At Yale University, where Dr. Sanders got her medical degree and did her residency, she was quickly captivated by the Sherlock Holmesian nature of diagnostic work.

Shortly afterward, a longtime friend who had just started as an editor at The Times Magazine called her and asked, "What can doctors write?" Dr. Sanders thought about the reports she did for all new patients.

"I write little mysteries every single day," she said.

For the column that sprang from that conversation, Dr. Sanders pulled from unusual and already solved cases that had brought up unexpected questions for the doctors who told her about them around the proverbial water cooler.

She also began to look out for unique cases among her own patients at Yale New Haven Hospital.

"This column helps me remember that most people have what other people have had, but not everybody," she says. "It opens me up to the possibility of 'weird.'"

In 2010, she introduced the idea of crowdsourcing in her column by sharing the case of a feverish academic who had let the readers of a popular medical website help diagnose his illness.

Then, the following year, she let her own readers get in on the detective work with a Well column, Think Like a Doctor, that invited them to speculate about symptoms of an ailment she would reveal the following day.

"Because I saw how good they were with these solved cases, I knew for sure that they would be good with unsolved cases," Dr. Sanders recalls.

She didn't build on that idea until the Academy Award-winning producer Scott Rudin approached The Times about making a documentary series with the production company Lightbox.

Last April, the magazine published the first in a series of unsolved cases that Dr. Sanders and producers had spent months collecting. For the first time, they invited readers to share their best guesses about what the patients were suffering from.

Thousands of readers from around the globe responded. Many were members of the medical community.

But others were just people who recognized their own suffering in someone else a world away and wanted to help, like a California mother who saw one young "Diagnosis" patient's behavior as a symptom of the same untreatable genetic condition her son has.

"I feel like it's a diagnosis," she said through tears. "But it's a diagnosis to nowhere. I think that our kids are going to help future kids, and future parents, not go through what we went through."

This is what Dr. Sanders hoped to capture. Where many medical dramas use odd cases to show a doctor's deductive brilliance in the third act, she wanted to show something else.

"It's so much more than that," she counters. "The patients are not the backdrop. They are the show."

http://bit.ly/2KEjd8Z

Here's what Earth might look like to aliens

Transforming images of the nearest habitable planet into something alien astronomers light-years away would see

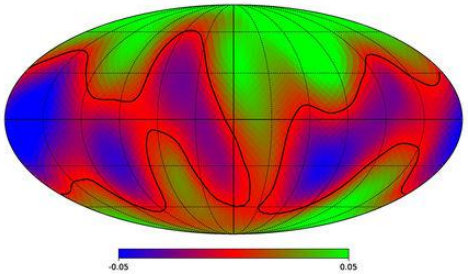
By Daniel Clery

When Earthly astronomers train their telescopes on exoplanets beyond our solar system, they're lucky to see even a single dot of light. How can they figure out whether it might have suitable conditions for life?

To find out how they might know more, a team of scientists turned the problem on its head: They took images of a habitable planet—

Earth—and transformed them into something alien astronomers light-years away would see.

The team started with about 10,000 images of our planet taken by NASA's Deep Space Climate Observatory (DSCOVR) satellite, which sits at a gravitational balance point between Earth and the sun, allowing it to see only the daytime side of the planet. The images were taken at 10 specific wavelengths every 1 to 2 hours during 2016 and 2017.



S. Fan *et. al.*, arXiv (2019) arXiv:1908.04350

To simulate an alien point of view, the researchers reduced the images into a single brightness reading for each wavelength—10 "dots" that, when plotted over time, produce 10 light curves that represent what a distant observer might see if they steadily watched exoplanet Earth over 2 years.

When researchers analyzed the curves and compared them with the original images, they figured out which parameters of the curves corresponded to land and cloud cover in the images.

Once they knew those relationships, they picked out the parameter most closely related to land area, adjusted it for the 24-hour rotation of the Earth, and constructed the above contour map, soon to be published in *The Astrophysical Journal Letters*.

The black lines, which mark the median values for the land parameter, serves as an approximate coastline. Rough outlines of Africa (center), Asia (upper right), and the Americas (left) are clearly visible. While this is obviously no substitute for an actual image of an alien world, it may allow future astronomers to assess whether an exoplanet has oceans, clouds, and icecaps—key requirements for a habitable world.

doi:10.1126/science.aaz1608

http://bit.ly/31Fu1JM

The Moon rock that turned out to be from Earth

All is not what it seems in the world of lunar samples.

Michelle Wheeler Freelance science journalist

If you put a Moon rock alongside one from Earth, they usually don't have a lot in common. So when Curtin University planetary scientist Professor Alexander Nemchin looked closely at a Moon rock in his laboratory, he realised something wasn't right. The rock's composition was similar to granite, which is extremely rare on the Moon but fairly common on Earth.

Stranger still, the 1.8 gram rock also contained quartz. And the zircon in the sample was very different to every other rock analysed from the Moon. "This particular piece – there is nothing similar to it in the rest of the 400 kilograms of samples, not at least that we've found so far," Alexander says. Chemically, it looked less like a typical Moon rock and more like some of the oldest rocks on Earth.

Lost in space

The rock in question is on loan to Curtin University from NASA.

And it definitely came from the Moon – the Apollo 14 astronauts collected it in 1971. But Alexander's team discovered something no one else had picked up on for almost half a century. This rock was probably flung to the Moon from Earth roughly 4 billion years ago.

"We find lunar meteorites on Earth, so there is an exchange of rocks. It certainly happens," Alexander says. "Especially considering that, 4 billion years ago, the Moon was much closer to the Earth, so this exchange would be much more efficient."

Planetary rock tossing

Alexander says this particular rock likely landed on the Moon after an asteroid hit the Earth and launched it into space.

So why were Alexander and his team the first to work it out?

"Usually these things happen out of nowhere," he says. "You just look at the sample or set of data and suddenly realise that there is

the possibility of a certain interpretation." "Even though, sometimes 50 people looked at the same dataset or the same sample before."

Alexander was able to access the Apollo 14 sample due to a NASA decree dating back to the 1970s – the returned rocks belonged to the whole world.

Scientists can access the lunar samples by applying to NASA with a detailed proposal of the research they want to conduct on the rocks.

Curtin has been lucky to access several Apollo samples over a decade of research on Moon rocks, Alexander says.

Chinese mission to the Moon

Alexander is currently in China, laying the groundwork for any lunar samples returned from the Chang'e 5 mission to the Moon.

He says there's a lot of preparation to be done before any rocks arrive. "It's a complicated procedure," he says. "Before you even start doing research, you need to open the samples and it takes quite [a long time]. "You need to follow specific protocols so you don't contaminate your samples."

For Alexander, lunar research is one area where human beings can work together to solve problems, regardless of borders. "It has this profound impact on people in creating an ability to collaborate, at least on something."

http://bit.ly/31Q8XAu

Wind power prices now lower than the cost of natural gas

In the US, it's cheaper to build and operate wind farms than buy fossil fuels.

John Timmer

This week, the US Department of Energy released a report that looks back on the state of wind power in the US by running the numbers on 2018. The analysis shows that wind hardware prices are dropping, even as new turbine designs are increasing the typical power generated by each turbine. As a result, recent wind farms have gotten so cheap that you can build and operate them for less than the expected cost of buying fuel for an equivalent natural gas plant.

Wind is even cheaper at the moment because of a tax credit given to renewable energy generation. But that credit is in the process of fading out, leading to long term uncertainty in a power market where demand is generally stable or dropping.

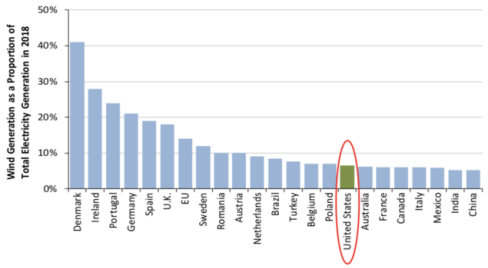
A lot of GigaWatts

2018 saw about 7.6 GigaWatts of new wind capacity added to the grid, accounting for just over 20 percent of the US' capacity additions. This puts it in third place behind natural gas and solar power. That's less impressive than it might sound, however, given that things like coal and nuclear are essentially at a standstill. Because the best winds aren't evenly distributed in the US, there are areas, like parts of the Great Plains, where wind installations were more than half of the new power capacity installed.

Overall, that brings the US' installed capacity up to nearly 100GW. That leaves only China ahead of the US, although the gap is substantial with China having more than double the US' installed capacity. It still leaves wind supplying only 6.5 percent of the US' total electricity in 2018, though, which places it behind a dozen other countries. Four of them—Denmark, Germany, Ireland, and Portugal—get over 20 percent of their total electric needs supplied by wind, with Denmark at over 40 percent.

That figure is notable, as having over 30 percent of your power supplied by an intermittent source is a challenge for many existing grids. But there are a number of states that have now cleared the 30 percent threshold: Kansas, Iowa, and Oklahoma, with the two Dakotas not far behind. The Southwest Power Pool, which serves two of those states plus wind giant Texas, is currently getting a quarter of its electricity from wind. (Texas leads the US with 25GW of installed wind capacity.)

So while wind remains a small factor in the total electricity market in the US, there are parts of the country where it's a major factor in the generating mix. And, given the prices, those parts are likely to expand.

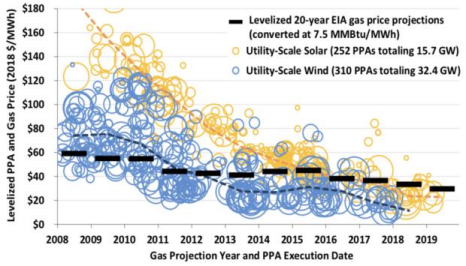


***Enlarge** / Despite having a lot of wind installed, the US uses far more power from other sources.* **US DOE**

Plummeting prices

In the US, the prices for wind power had risen up until 2009, when power purchase agreements for wind-generated electricity peaked at about $70 per MegaWatt-hour. Since then, there's been a very steady decline, and 2018 saw the national average fall below $20/MW-hr for the first time. Again, there's regional variation with the Great Plains seeing the lowest prices, in some cases reaching the mid-teens.

That puts wind in an incredibly competitive position. The report uses an estimate of future natural gas prices that show an extremely gradual rise of about $10/MW-hr out to 2050. But natural gas—on its own, without considering the cost of a plant to burn it for electricity—is already over $20/MW-hr. That means wind sited in the center of the US is already cheaper than fueling a natural gas plant, and wind sited elsewhere is roughly equal.



***Enlarge** / Those black bars are the price of gas. Blue circles are wind, while yellow are solar.* **US DOE**

The report notes that photovoltaics have reached prices that are roughly equivalent to wind, but those got there from a starting point of about $150/MW-hr in 2009. Thus, unless natural gas prices reverse the expected trend and get cheaper, wind and solar will remain the cheapest sources of new electricity in the US.

The levelized cost of electricity, which eliminates the impact of incentives and subsidies on the final prices, places wind below $40/MW-hr in 2018. The cheapest form of natural gas generation was roughly $10 more per MegaWatt-hour. Note that, as recently as 2015, the US' Energy Information Agency was predicting that wind's levelized cost in 2020 would be $74/MW-hr.

Built on better tech

Why has wind gotten much cheaper than expected? Part of it is in improved technology. The report notes that in 2008, there were no turbines installed in the US with rotors above 100 meters in diameter. In 2018, 99 percent of them were over 100m, and the average size was 116m. In general, the turbine's generator grew in parallel. The average capacity for 2018 installs was 2.4MW, which is up five percent from the year previous.

The area swept by the blades goes up with the square of their length. Thus, even though blade length and rated generating capacity are going up in parallel, the actual potential energy input from the blades is growing much faster. This has the effect of lowering what's called the specific power of the wind turbine. These lower specific power turbines work better in areas where the wind isn't as strong or consistent. On the truly windy days, they'll saturate the ability of the generator to extract power, while on a more typical day when the winds are lighter or erratic, they'll get more out of them.

So even though more turbines are being built at sites without the best wind resources, we're generating more power per turbine. The capacity factor—the amount of power generated relative to the size of the generator—for projects built in the previous four years has now hit 42 percent, a figure that would once have required offshore

wind. That's dragged the capacity factor of the entire US wind industry up to over 35 percent for the first time last year.

The economics of these low-wind designs are so good that 23 existing sites were "repowered," with new, larger rotors replacing older hardware on existing towers. One thing that may be encouraging this is that older plants (those a decade old or more) seem to see a small dip in capacity factor over time. But the reason for this isn't clear at this point, so it's something that will have to be tracked in the future.

Better grid management also helped the economics of wind. At times, strong winds can cause wind farms to produce an excess of power relative to demand, causing a farm's output to be reduced. This process, called curtailment, remained a small factor, with only two percent of the potential generation lost this way. Put differently, if the curtailed electricity had been used, it would have only raised the average capacity factor by 0.7 percentage points.

Overall, given these economics, it's clear that the economic case for wind energy will remain solid as the tax credits for the construction of renewable energy fade out over the next few years. But the vanishing credits are causing lots of developers to start projects sooner rather than later, so we may see a bubble in construction for the next couple of years, followed by a dramatic drop off.

http://bit.ly/2TI4lcQ

Measles killing more people than Ebola in Congo, Doctors Without Borders says

Measles has killed 2,758 people in Congo since January, more than the Ebola epidemic in a year

KINSHASA – Measles has killed 2,758 people in Congo since January, more than the Ebola epidemic in a year, medical NGO Doctors Without Borders said, and called Saturday for a "massive mobilization of funds."

The disease, preventable with a vaccine, has infected over 145,000 people in Congo between January and early August, it said in a statement. "Since July, the epidemic has worsened, with a rise in new cases reported in several provinces," said the NGO, which goes by its French acronym MSF.

"Only $2.5 million has been raised out of the $8.9 million required for the Health Cluster response plan — in stark contrast with the Ebola epidemic in the east of the country, which attracts multiple organisations and hundreds of millions of dollars in funding," it added. MSF tweeted that without a "massive mobilisation of funds and response organizations, the current measles outbreak in #DRCongo could get even worse."

The NGO said it has vaccinated 474,860 children between the ages of 6 months and 5 years since the beginning of the year, and provided care to more than 27,000 measles patients. In the country's east, Ebola has claimed more than 1,900 lives since erupting last August.

Measles is a highly contagious diseased caused by a virus that attacks mainly children. The most serious complications include blindness, brain swelling, diarrhea and severe respiratory infections. Last year, cases more than doubled to almost 350,000 from 2017, according to the World Health Organization, amid a rise in "anti-vaxxer" sentiment in some countries that can afford the vaccine, and lagging resources for the preventative measure in poor nations. Congo declared a measles epidemic in June.

http://bit.ly/2Zcixfh

Beyond 23andMe: DNA sequencing clinics for the healthy (and wealthy)

Top U.S. medical centers roll out DNA sequencing clinics for healthy (and often wealthy) clients

***By* Rebecca Robbins @rebeccadrobbins**

Seizing on the surging popularity of at-home DNA testing kits, top academic medical institutions are opening clinics that promise to probe much deeper into your DNA — if you're willing to pay hundreds or even thousands of dollars out of pocket to learn about disease risks that may be lurking in your genes.

Genomic sequencing programs that cater to apparently healthy adults have been started in the past few years at the Mayo Clinic; the University of California, San Francisco; and the HudsonAlpha Institute for Biotechnology, a nonprofit research institution in Alabama. Now, two top Boston hospitals are getting into the potentially lucrative business.

Brigham and Women's Hospital on Friday unveiled a new Preventive Genomics Clinic that will offer a menu of options for a genetic workup, with price tags ranging from $250 to $2,950, depending on how many genes are analyzed; it's the first program of its kind that will offer the sequencing to children in addition to adults. And next month, Massachusetts General Hospital plans to launch its own clinic for adults that will offer elective sequencing at a similar price range as the Brigham.

By scouring hundreds or thousands of genes — far more than most consumer genetics companies — representatives for these clinics told STAT that, in a small fraction of patients, they're helping diagnose mild genetic diseases as well as turning up markers of elevated risks for conditions both common and rare. The test results allow clinicians to offer further guidance to patients, whether that means encouraging them to take proactive steps such as getting a preventive mastectomy or counseling them to just be more diligent about a screening that was recommended anyway.

"I think there's just more and more interest from patients and families not only because of 23andMe and the like, but because there's just this understanding that if you can find out information about your health before you become sick, then really our opportunity as physicians to do something to help you is much greater," said Dr. David Bick, the clinical geneticist who directs the elective genomics program at HudsonAlpha. Close to 50 adults have each paid $7,000 for whole genome sequencing and interpretation since HudsonAlpha launched the offering in 2016, Bick said.

Dr. Robert Green, a medical geneticist leading the new clinic at the Brigham, is candid about the limitations of advanced sequencing programs. "It's clearly not been demonstrated to be cost-effective to promote this on a societal basis," he said. It's evident too, he said, that such sequencing leads to pricey follow-up testing.

"The question that's hard to answer is whether there are long-term benefits that justify those health-care costs — whether the sequencing itself, the physician visit, and any downstream testing that's stimulated will be justified by the situations where you can find and prevent disease," Green said.

Insurers sometimes cover deep genomic sequencing when there's a clear medical reason for it, such as for people with a long family history of cancer. (The soon-to-launch clinic at Mass. General will offer such medically indicated testing, too.) By contrast, insurers generally refuse to cover the elective sequencing offered at the clinics sprouting up at top academic medical centers. There's not yet strong evidence to indicate that apparently healthy people derive widespread benefits.

The result is that the new clinics generally serve only those who can afford to pay cash. That worries some in the medical community.

"The idea that genomic sequencing is only going to be accessible by wealthy, well-educated patrons who can pay out of pocket is anathema to the goals of the publicly funded Human Genome Project, and creates new disparities in our health care system," said Dr. Jonathan Berg, a genetics professor at the University of North Carolina.

As more preventive genomics clinics open their doors, some report that demand is surging.

The Mayo Clinic offers elective sequencing at its flagship sites in Minnesota, Arizona, and Florida, as part of a program that is aimed at business executives. The genomics offering soft-launched in 2014, and has gradually attracted more interest each year. But demand "really started to take off" last year, after sequencing was added to a menu of options for executives interested in a medical workup, said Teresa Kruisselbrink, a genetic counselor who manages the team at Mayo that helps patients interpret these results. More than 1,300 adults signed up to get sequenced last year.

Other clinics, though, have seen less interest.

Since UCSF opened its preventive genomics clinic in 2017, a few hundred people have paid to get genomics panels ranging from about $300 to $800, or for more thorough exome sequencing ranging from about $2,000 to $2,500. Dr. Aleksandar Rajkovic, UCSF's chief genomics officer who leads the clinic there, said he was a bit surprised that demand hasn't been higher.

One reason for the modest demand, he mused, is that UCSF hasn't heavily advertised the service. Another? "Most regular physicians are not really recommending it because at this point in time there really haven't been studies that show significant clinical utility of doing these testing in healthy populations," Rajkovic said.

One of the priciest high-end sequencing offerings is a commercial one, from Human Longevity Inc., the San Diego company founded by genomics pioneer Craig Venter. In 2015, HLI launched an extraordinarily in-depth medical workup, including genetic analysis, for $25,000. Seeking to bring in more customers, the company started offering discounts, dropping the price to $4,950 as of last summer. (HLI didn't return STAT's requests for comment on current pricing.) But that business hasn't grown as quickly as executives and investors hoped, the Wall Street Journal reported last December.

At the new clinic at the Brigham, which is expected to primarily draw people from the Boston area, Green said he's not worried about demand.

"We're not trying to make a profit — we're trying to offer a service in a medically responsible way. And so if a very modest number of people want to use it, that's fine," Green said. "What we're trying to say is that people are using this, whether it's HLI or consumer-facing laboratories over the internet, and we'd like to provide them with an alternative."

Green's new clinic at the Brigham grew out of his work on several of the most ambitious research studies aiming to assess whether thorough genomic sequencing is worth it. One was BabySeq, a study of 360 newborns that randomly assigned half of the group to get genomic sequencing and the other half to get standard screening. Another was MedSeq, a study of 200 adults that randomly assigned participants to either get their genome sequenced or their family medical history analyzed.

The Brigham's new clinic has quietly seen a couple dozen patients since a soft-launch last winter.

One of them is Nicole, a Boston-area entrepreneur in her 40s who requested her surname not be disclosed because she does not want insurers to know that her genome has been sequenced.

Nicole, who was connected to STAT by representatives from the Brigham, said she learned about the new offering at a fundraiser in New York supporting Green's research.

To decide what to order, Nicole read through a menu offering genomic sequencing and gene panel tests, including several offered by genomics companies. After weighing her options, she decided to move forward with a $2,950 offering, to be run by a laboratory

operated by the Boston area Partners HealthCare system, that would scour more than 3,700 of her genes for disease risk. She also added on a $349 test from the company OneOme that promised to analyze her DNA to see how it influences the effectiveness of certain medications. (Green is a paid adviser for several genomics companies, including Veritas Genetics, one of the companies on the Brigham clinic's menu of offerings.)

It was a bit expensive, Nicole said. But she already invests heavily in diet and exercise, and saw sequencing as one more thing she could do for her health. And she didn't want to wait for the price to go down, she said, because of the risk that disease could strike in the interim. "If there's preventative actions that I can take now as compared to later, then I'd rather know," Nicole said.

At the Brigham clinic last week, Nicole got her blood drawn and her cheek swabbed. It was part of an extensive visit that each patient goes through before the sequencing is performed, involving taking a medical history and undergoing a full physical examination meant to help guide decisions about follow-up testing and other care. She's expecting to return to the clinic in a few months to get her results — and to talk through what they mean and how to proceed.

So far, insurers have generally paid for the initial and follow-up visits to the Brigham's clinic. Without insurance, the initial visit tends to cost around $1,000, and the follow-up visit may go for a few hundred dollars.

While the Brigham's new clinic is offering people a purely clinical service, it involves an optional research component, too. Most of the Brigham clinic's first patients have agreed to participate in PeopleSeq, a study funded by the National Institutes of Health that aims to track the long-term outcomes of people who've gotten thorough genomic sequencing. (The cost of the sequencing is not waived if they agree to sign up.)

The study's goal is to follow thousands of patients across the country for as many years as they're willing to complete an annual online survey that will ask basic questions, like whether the person has developed cancer or a thickened heart wall, or faced insurance discrimination. "We have no data on so much of this," Green said. "It's all been in the realm of speculation."

http://bit.ly/2z6sobV

Inside China's Play to Become the World's CRISPR Superpower

China could soon outpace the US in CRISPR-related research papers and patents

By Marc Prosser

In some ways, Hercules is pretty standard for the course where beagles are concerned. He likes to run around and generally looks as (borderline insanely) happy as any of his floppy-eared cousins across the world. However, when it comes to muscles, Hercules is to other beagles what a prime Arnold Schwarzenegger is to, well, me.

The reason is CRISPR. Chinese scientists used the gene-editing technology to delete myostatin, which limits muscle growth, in Hercules at the embryo stage. As a result, he developed unusual muscle strength. The study could lead to new ways of treating human diseases such as muscular dystrophy and Parkinson's.

Hercules is far from alone, as China is seeing an explosion in CRISPR-based animal studies and embracing the gene-editing technology with unrivaled zest and zeal—so much so that China could soon outpace the US in CRISPR-related research papers and patents across fields such as medical research, agriculture, and industrial applications.

As Jennifer Doudna, often credited as the inventor of CRISPR, put it to *Science*, "This is a country and a culture that really values

science and technology. Their government has put very serious money into it, and they're walking the walk."

China's CRISPR Explosion

When it comes to CRISPR, there's the US, China—and everybody else. A recent analysis shows the US still holds more CRISPR-related patent applications (872 versus China's 858). For comparison, all of Europe has 186 patents. The same study shows US-based scientists have released 2,976 CRISPR-related scientific papers to their Chinese counterparts' 2,059. Japan, in third place, has 228. In some areas, such as agriculture and industrial applications, China holds more patents and has published more papers than anyone else.

Patents and papers alone do not make a science superpower. Other important factors include the backing of government organizations and educational institutions' renown. Traditionally, US universities have drawn top scientists from around the world, but for CRISPR that seems to be changing. Chinese universities have successfully enticed Chinese gene-editing scientists to return from the US, and international scientists are immigrating to China to do their research. In its latest five-year plan, the Chinese government highlighted gene editing as a focus point and committed to easing the surrounding bureaucratic framework.

The country seems to be focusing its efforts on areas such as agriculture, human medicine, and basic research. A new gene-editing technology similar to CRISPR coming out of the University of Peking is proof of the latter. Supposedly, the new technology, called LEAPER, is similar to CRISPR-Cas13 but uses arRNA instead of RNA, easing delivery of gene edits and lowering risks of unwanted cellular responses.

Monkeys, Corn, and Ethical Dilemmas

Sheer numbers seem to play a pivotal role in China's approach to CRISPR research. For example, the study with Hercules involved 27 puppies. Across China, there are at least four groups of CRISPR researchers gene editing large colonies of monkeys, while others are using dogs, mice, rats, pigs, and rabbits.

Reproductive biologist Jon Hennebold at the Oregon National Primate Research Center in Hillsboro told *Science*, "The most startling part of what is coming out of China is seeing how they have just a brute-force approach. The level of animal support they have to do those experiments is really astounding."

Some of the animals, including Hercules, seem to suffer no ill consequences, but others are given excruciating diseases. Some projects, such as the reported collaboration between Juan Carlos Izpisúa Belmonte from the Salk Institute in California and researchers in China are splicing human cells to animal embryos. The goal is to create organs, like kidneys or a liver, that can be harvested for transplantation into humans. The embryo study was carried out in China 'to avoid legal issues.'

Ethical questions abound with such studies, but, at least on the surface, they seem less prevalent in China compared to many Western countries. For comparison, US legislators could soon force the National Institutes of Health to end non-human primate experiments altogether.

The most prevalent counterargument is that such experiments can lead to cures for many diseases, including Parkinson's, Alzheimer's, and perhaps even some forms of cancer.

China's Challenges and CRISPR

China's full-speed-ahead approach on CRISPR extends beyond animal research. There are at least 20 research groups across the country using CRISPR to modify crop genes as part of a wider, technology-based push to improve agricultural output. Recent figures are hard to come by, but in 2013, China's public funding of agricultural research was close to $10 billion, more than twice that of the US, and it doesn't seem to have slowed down since.

The animal and plant-based CRISPR studies seem to be fulfilling two purposes. First, they help bolster China's position on several of the economic, political, and technological fronts where the country is squaring off with the US. Second, gene editing offers viable solutions to some of the major issues facing the world's most populous country.

Chinese authorities need to find ways of feeding 1.4 billion people out of the world's rising population. Competition for resources, including food, is increasing, so being able to produce more of it at home is imperative. At the same time, Chinese demographics are changing. The middle class is growing rapidly, leading to changes such as increased consumption of meat and higher prevalence of lifestyle diseases. It also faces stark shortages when it comes to, among other things, some healthcare supplies and services. One study suggests that 300,000 Chinese people need organ transplants, but there are just 10,000 organs available.

What China's Charge May Lead To

All this brings us to the biggest CRISPR story to come out of China over the last couple of years: He Jiankui's gene-edited babies. While the Chinese authorities have condemned the experiment, other studies that involve using CRISPR on humans are still going ahead.

Last year, Chinese scientists delivered CRISPR-edited genes into a lung cancer patient as part of a clinical trial. Carl June, a scientist working on a similar project at the University of Pennsylvania, described it to *Nature* as the possible trigger for "Sputnik 2.0, a biomedical duel on progress between China and the US."

That duel already seems well underway, with China moving toward getting the upper hand. Goldman Sachs analyst Salveen Richter, who has studied China's CRISPR efforts, pointed out that as of February 2018, there were nine registered clinical studies testing CRISPR-edited cells to treat various cancers and HIV infection in China, and only one such study in the US.

If China indeed grabs the lead on CRISPR, it could translate into a variety of advantages. As the ongoing battle over who invented CRISPR clearly illustrates, future earnings are very dependent on patent rights. Such rights are often tied to scientific studies. The combination of both is key to developing patented new solutions and products, which people across the globe will likely want to purchase, especially considering that many countries face similar challenges to China when it comes to healthcare shortages or finding ways to produce more food.

The 'Sputnik 2.0 race' is far from over, and the good news is that the competition will almost invariably lead to new discoveries and solutions that can be beneficial for all of humanity. The question then becomes what access the rest of the world will have to such solutions.

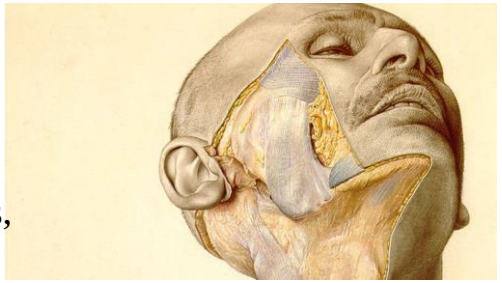
https://bbc.in/2KGJ2oR

The Nazi book of anatomy still used by surgeons

Though very expensive and detailed, few would proudly display it

By Keiligh Baker BBC News

When nerve surgeon Dr Susan Mackinnon needed help to finish an operation, she reached, as she often does, for a mid-20th Century book of anatomy.



Thanks to the complex hand-drawn illustrations - showing the human body peeled back layer by layer - Dr Mackinnon, from Washington University in St Louis, was able to complete the procedure.

An illustration from the atlas shows a man's partially dissected cheek **Erich Lepier**

The book she had used, the innocuous-sounding Pernkopf Topographic Anatomy of Man, is widely considered to be the best example of anatomical drawings in the world. It is richer in detail and more vivid in colour than any other.

Skin, muscle, tendons, nerves, organs and bone are revealed in graphic detail. It's not for the faint-hearted.

But the book, often referred to as Pernkopf's Atlas, is no longer in print and a second-hand set - there are several volumes - can sell for thousands of pounds online.

Yet despite its hefty asking price, few would proudly display it in their clinic, library or home.

That's because the book's findings came from the bodies of hundreds of people killed by the Nazis. It is their bodies - cut up and dissected - that are shown across thousands of pages.

Critics say the book is tainted by its dark past and scientists have grappled with the ethics involved in its use.

Dr Mackinnon says she feels uncomfortable with its origin, but using the book is a crucial part of being an "ethical surgeon" - and that she could not do her job without it.

Rabbi Joseph Polak - a Holocaust survivor and professor of health law - believes the book is a "moral enigma" because it is derived from "real evil, but can be used in the service of good".

The book was a 20-year project of a prominent Nazi and doctor, Eduard Pernkopf, who rose through the academic ranks in Austria thanks to his support for Adolf Hitler's party.

His colleagues described him as an "ardent" National Socialist who, from 1938, wore a Nazi uniform to work every day.

When he was made dean of the medical school at the University of Vienna, he sacked all the Jewish members of the faculty, including three Nobel laureates.

In 1939, a new Third Reich law ensured the bodies of all executed prisoners were immediately sent to the nearest department of anatomy for research and teaching purposes.

During this period Pernkopf worked 18-hour days dissecting corpses, while a team of artists created images for his book. Sometimes the anatomy institute was so full, executions had to be postponed.

Dr Sabine Hildebrandt, from Harvard Medical School, says at least half of the 800 images in the atlas came from political prisoners. They included gay men and lesbians, gypsies, political dissidents and Jews.

In the first edition of the atlas, published in 1937, the signatures of illustrators Erich Lepier and Karl Endtresser included swastikas and the double lightning bolt insignia of the SS.

Even the 1964 two-volume English language edition included the original signatures including the Nazi symbols. Later editions airbrushed out the Nazi insignia.

Thousands of copies of the atlas were sold across the world, and it was translated into five languages. Prefaces and introductions in the books describe "pictorially impressive drawings... and outstanding pieces of art" while eschewing any mention of their bloody past.

It was only in the 1990s that students and academics really began questioning who the people in the atlas were. After the brutal history was revealed, the atlas went out of publication in 1994.

The Royal College of Surgeons says the atlas is not in use in the UK, apart from being retained by libraries for historical purposes.

However a recent Neurosurgery survey of nerve surgeons found 59% were aware of Pernkopf's Atlas, with 13% currently using it.

Of those surveyed, 69% said they were comfortable using the atlas once they were made aware of its history, 15% were uncomfortable and 17% were undecided.

Dr Mackinnon says nothing else "even begins to compare" to the book's accuracy and detail, and it is particularly useful for complex surgeries because it helps her "figure out which of the many small nerves that course through our body are potentially causing the pain".

But she says she ensures everyone involved in the surgery is aware of the book's dark origins.

"When I became aware of the tainted and evil origin of this atlas I began keeping it secured away in my operating room locker," she says.

Last year, Rabbi Polak and medical historian and psychiatrist Professor Michael Grodin, prepared a Responsum (a scholarly answer based on Jewish medical ethics) on whether it is ethical to use the atlas based on Dr Mackinnon's experience.

They concluded that most Jewish authorities would allow the use of the images to save human lives - under the condition the history of the atlas was made known, so the victims were afforded some of the dignity they are owed.

Rabbi Polak, told the BBC: "Look at Dr Mackinnon - she couldn't find a nerve and she's the greatest in her field. The patient told her 'I want my leg cut off if you can't find it' - no one wants that to happen.

"So she swallowed hard and asked them to bring Pernkopf's atlas. She found the nerve in minutes because of these illustrations.

"She asked me, as a moral thinker, about the situation. And I said to her, if this is going to heal this person and give them their life back, then there is no question that the atlas can be used."

Pernkopf was arrested after the war and sacked from the university. He was held at an Allied prison of war camp for three years but was never charged with any crime.

Following his release he returned to the university and continued his work on the atlas, publishing a third volume in 1952. He died in 1955, shortly before the publication of a fourth volume.

More than 60 years later, the atlas is still one of the best resources for visual information for detailed anatomical and surgical work, according to Dr Hildebrandt, who teaches anatomy.

"Those of us who have learned to 'see' with it use it whenever we have questions. In peripheral nerve surgery some surgeons find it to be a unique and irreplaceable source of information," she says.

But, she adds: "I personally do not use the Pernkopf images in my anatomy teaching unless I have time to speak about its history."

Dr Jonathan Ives, a bioethicist from the University of Bristol, agrees the atlas is "amazingly detailed" but says it is tainted by its "horrific past".

"If we are using it and reaping the benefits it implies we are somehow complicit," he says.

"But you could also argue that in not using it, the atlas would be lost and it could not be used as a reminder of what happened."

For Dr Mackinnon, it remains an vital tool - even if its past can never be forgotten.

"I would think that as an ethical surgeon I would take it as a given that I should use whatever educational resource I thought would help me to maximize a successful outcome," she says, "and that my patient would expect that of me.

"In my experience, it would set back detailed nerve surgery tremendously if these books are lost."