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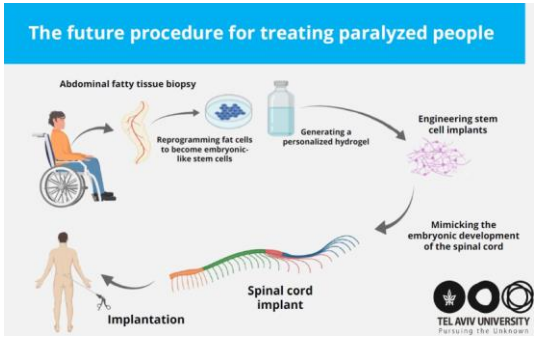
Human Spinal Cord Implants: Breakthrough May Enable People With Paralysis To Walk Again

In world-first, Tel Aviv University researchers engineer human spinal cord implants for treating paralysis.

For the first time in the world, researchers from Sagol Center for Regenerative Biotechnology at Tel Aviv University have engineered 3D human spinal cord tissues and implanted them in lab model with long-term chronic paralysis. The results were highly encouraging: an approximately 80% success rate in restoring walking abilities.

Now the researchers are preparing for the next stage of the study: clinical trials in human patients. They hope that within a few years the engineered tissues will be implanted in paralyzed individuals enabling them to stand up and walk again.



Visualization of the next stage of the research – human spinal cord implants for treating paralysis. **Credit: Sagol Center for Regenerative Biotechnology**

The groundbreaking study was led Prof. Tal Dvir's research team at the Sagol Center for Regenerative Biotechnology, the Shmunis School of Biomedicine and Cancer Research, and the Department of Biomedical Engineering at Tel Aviv University. The team at Prof. Dvir's lab includes PhD student Lior Wertheim, Dr. Reuven Edri, and Dr. Yona Goldshmit. Other contributors included Prof. Irit Gat-Viks from the Shmunis School of Biomedicine and Cancer Research, Prof. Yaniv Assaf from the Sagol School of Neuroscience, and Dr. Angela Ruban from the Steyer School of Health Professions, all at Tel Aviv University.

The results of the study were published in the prestigious scientific journal *Advanced Science.*

Prof. Dvir explains: "Our technology is based on taking a small biopsy of belly fat tissue from the patient. This tissue, like all tissues in our body, consists of cells together with an extracellular matrix (comprising substances like collagens and sugars). After separating the cells from the extracellular matrix we used genetic engineering to reprogram the cells, reverting them to a state that resembles embryonic stem cells – namely cells capable of becoming any type of cell in the body. From the extracellular matrix we produced a personalized hydrogel, that would evoke no immune response or rejection after implantation. We then encapsulated the stem cells in the hydrogel and in a process that mimics the embryonic development of the spinal cord we turned the cells into 3D implants of neuronal networks containing motor neurons."

The human spinal cord implants were then implanted in lab models, divided into two groups: those who had only recently been paralyzed (the acute model) and those who had been paralyzed for a long time – equivalent to a year in human terms (the chronic model). Following the implantation, 100% of the lab models with acute paralysis and 80% of those with chronic paralysis regained their ability to walk.

Prof. Dvir: "The model animals underwent a rapid rehabilitation process, at the end of which they could walk quite well. This is the first instance in the world in which implanted engineered human tissues have generated recovery in an animal model for long-term chronic paralysis – which is the most relevant model for paralysis treatments in humans. There are millions of people around the world who are paralyzed due to spinal injury, and there is still no effective treatment for their condition. Individuals injured at a very young age are destined to sit in a wheelchair for the rest of their

lives, bearing all the social, financial, and health-related costs of paralysis. Our goal is to produce personalized spinal cord implants for every paralyzed person, enabling regeneration of the damaged tissue with no risk of rejection.

Based on the revolutionary organ engineering technology developed at Prof. Dvir's lab, he teamed up with industry partners to establish Matricelf (matricelf.com) in 2019. The company applies Prof. Dvir's approach in the aims of making spinal cord implant treatments commercially available for persons suffering from paralysis.

Prof. Dvir, head of Sagol Center for Regenerative Biotechnology, concludes: "We hope to reach the stage of clinical trials in humans within the next few years, and ultimately get these patients back on their feet. The company's preclinical program has already been discussed with the FDA. Since we are proposing an advanced technology in regenerative medicine, and since at present there is no alternative for paralyzed patients, we have good reason to expect relatively rapid approval of our technology."

Reference: "Regenerating the injured spinal cord at the chronic phase by engineered iPSCsderived 3D neuronal networks" by Lior Wertheim,Reuven Edri, Yona Goldshmit, Tomer Kagan, Nadav Noor, Angela Ruban, Assaf Shapira, Irit Gat-Viks, Yaniv Assaf and Tal Dvir, 7 February 2022, Advanced Science.
DOI: 10.1002/advs.202105694

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Chimpanzees apply insects to wounds, a potential case of medication use?

For the first time, chimpanzees observed to apply insects to wounds

A research team from Osnabrück University and the Ozouga Chimpanzee Project has, for the first time, observed chimpanzees applying insects to their own wounds and the wounds of conspecifics. The new findings have been published under the title "Application of insects to wounds of self and others in chimpanzees in the wild" in the journal *Current Biology*.

Chimpanzees are found across equatorial Africa including the Loango National Park in Gabon which has been home to the Ozouga Chimpanzee Project, led by primatologist Dr. Tobias Deschner and cognitive biologist Prof. Dr. Simone Pika at Osnabrück University. In Loango, the researchers investigate the behavior of a community of about 45 chimpanzees with a special focus on their social relationships, interactions and disputes with other groups, their hunting behavior, tool-use and their cognitive and communicative skills.

"Self-medication—where individuals use plant-parts or non-nutritional substances to combat pathogens or parasites—has been observed across multiple animal species including insects, reptiles, birds and mammals," says Pika. "For instance, our two closest living relatives, chimpanzees and bonobos, swallow leaves of plants with anthelmintic properties and chew bitter leaves that have chemical properties to kill intestinal parasites."

However, despite research spanning decades from other long-term field sites in west and east Africa, external application of animal matter on open wounds has, until now, never been documented. "Our observations provide the first evidence that chimpanzees regularly capture insects and apply them onto open wounds. We now aim to investigate the potential beneficial consequences of such a surprising behavior," says primatologist Tobias Deschner.

Alessandra Mascaro, at the time a volunteer at the project, recalls her first observation: "In 2019, I was following a female chimpanzee named Suzee, and watched as she tended to the injured foot of her adolescent son, Sia. I noticed that she appeared to have something between her lips that she then applied to the wound on Sia's foot. Later that evening, I re-watched my videos and saw that Suzee had first reached out to catch something which she put between her lips and then directly onto the open wound on Sia's

foot. Discussing these observations and the possible function of the behavior with the team members, we realized that we had never seen such a behavior and that it had also never been documented before."

A week later, Ph.D. student Lara Southern observed an adult male, Freddy, demonstrating a similar behavior. The team worked out that the tiny objects were most likely flying insects, given where and how they were caught. During the following year, the researchers began to watch and film all individuals with injuries. They gradually built up a record of 22 events, mostly involving individuals applying insects to their own wounds.

Almost a year after Mascaro's observation of the first insect application to another individual's wound, Southern observed another event. "An adult male, Littlegrey, had a deep open wound on his shin and Carol, an adult female, who had been grooming him, suddenly reached out to catch an insect," says Southern. "What struck me most was that she handed it to Littlegrey, he applied it to his wound and subsequently Carol and two other adult chimpanzees also touched the wound and moved the insect on it. The three unrelated chimpanzees seemed to perform these behaviors solely for the benefit of their group member."

The authors from the Ozouga Chimpanzee Project and Osnabrück suggest that the applied insects might have anti-inflammatory or antiseptic properties. The use of insects for therapeutic purposes has been dated back in humans to 1,400 BCE and is still popular across human populations covering a variety of insect species with scientifically proven antibiotic and anti-viral effects. Alternatively, another explanation may be that such a behavior does not have any beneficial consequences but is part of the local chimpanzee culture, just as a large number of medical treatments are in human societies.

"For me, being interested in the cognitive skills of chimpanzees, it was particularly striking to witness that individuals not only treat their own but also the wounds of other non-related individuals. Such examples of clear prosocial behaviors are rarely observed in nonhuman species, but these observations may now also convince the skeptics," says Pika.

As a next step, the researchers aim to recover remaining insect parts to identify the species and to subsequently carry out bioassays investigating the potential pharmaceutical properties. Furthermore, the team will also focus on the social dimension of the behavior, such as who are the main actors and who are the main receivers of the "treatment," as well as the social learning processes that allow for its transmission.

"It is just fascinating to see that after decades of research on wild chimpanzees they still surprise us with unexpected new behaviors" says Deschner. "Our study shows that there is still a lot to explore and discover about our closest living relatives, and we therefore need to still put much more effort into protecting them in their natural habitat."

More information: *Simone Pika, Application of insects to wounds of self and others by chimpanzees in the wild, Current Biology (2022). DOI: 10.1016/j.cub.2021.12.045. www.cell.com/current-biology/f ... 0960-9822(21)01732-2*

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Big data imaging shows rock's big role in channeling earthquakes in Japan

Mountain-size rock buried miles beneath the coast of southern Japan could act as a lightning rod for the region's megaquakes

Thanks to 20 years of seismic data processed through one of the world's most powerful supercomputers, scientists have created the first complete, 3D visualization of a mountain-size rock called the Kumano Pluton buried miles beneath the coast of southern Japan. They can now see the rock could be acting like a lightning rod for the region's megaquakes, diverting tectonic energy into points along its sides where several of the region's largest earthquakes have

happened.

Scientists have known about the pluton for years but were aware of only small portions of it. Thanks to new research by an international team of scientists led by The University of Texas at Austin, researchers now have a view of the entire subterranean formation and its effect on the region's tectonics.

The findings will provide critical information for a major new Japanese government-funded project to find out whether another major earthquake is building in the Nankai subduction zone, where the pluton is located, said Shuichi Kodaira, director of the Japan Agency for Marine-Earth Science and Technology and a co-author of the study published Feb. 3 in the journal *Nature Geoscience*.

"We cannot predict exactly when, where, or how large future earthquakes will be, but by combining our model with monitoring data, we can begin estimating near-future processes," said Kodaira, who was among the scientists who first spotted signs of the Kumano Pluton in 2006.

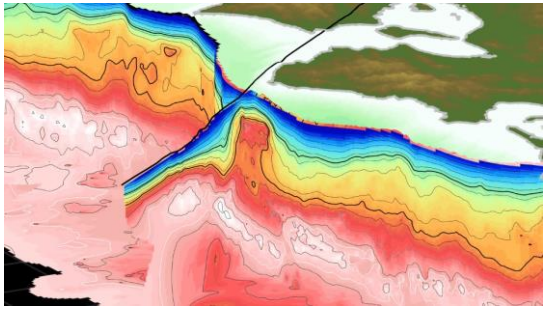
"That will provide very important data for the Japanese public to prepare for the next big earthquake."

The full extent of the Kumano Pluton was revealed using the LoneStar5 supercomputer at UT's Texas Advanced Computing Center to piece together 20 years of seismic data into a single high-definition 3D model.

"The fact that we can make such a large discovery in an area that is already well studied is, I think, eye opening to what might await at places that are less well monitored," said Adrien Arnulf, a research assistant professor at the University of Texas Institute for Geophysics and the study's lead author.

The model shows the region around the Nankai subduction zone, with the Earth's crust bending under the pluton's weight. In another unexpected finding, the pluton was seen diverting buried groundwater into the Earth's interior. The researchers think the pluton's interference with the wider subduction zone is influencing the tectonic forces that cause earthquakes.

Seismic imaging uses sound waves to create pictures of the Earth's subsurface. Over the years, Japan's vast network of sensors has collected millions of seismic recordings from thousands of locations along the Nankai subduction zone.



The Kumano Pluton in southern Japan appears as a red bulge (indicating dense rock) in the center of a new 3D visualization by The University of Texas at Austin. The pluton is large enough to interfere with the nearby Nankai subduction zone and the region's earthquakes. **Credit: Adrien Arnulf.**

The sensors are primarily used to record earthquakes and tremors, but the team widened their search to include chance recordings of passing scientific surveys using a technique Arnulf and coauthor Dan Bassett, a research scientist at GNS Science, had perfected while working on small-scale projects in New Zealand. The researchers compiled the massive amounts of information into a single data set and turned it into a 3D model with the help of LoneStar5.

In addition to shedding light on how the pluton may be influencing how and where earthquakes occur, the study is a major demonstration of how big data could revolutionize earthquake science. Arnulf envisions the same methods being used to make regional-scale images in other areas, such as northeast Japan, New Zealand, and Cascadia in the U.S. Pacific Northwest—all of which have subduction zones known to host the Earth's largest earthquakes.

More information: *Adrien F. Arnulf et al, Upper-plate controls on subduction zone geometry, hydration and earthquake behaviour, Nature Geoscience (2022). DOI: 10.1038/s41561-021-00879-x*

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Chemists develop radical way to make it easier, more profitable to recycle plastic

Method developed to break down plastics to create a new material that is stronger and tougher than the original

The United States generates more plastic trash than any other country—about 46.3 million tons of it—or 287 pounds per person a year, according to a 2020 study. The country's 9% rate of recycling will never keep up. Why so low? The chemistry of today's plastics makes most difficult to recycle. Even thermoplastics that can be melted down weaken with each re-use. And that leads to the real barrier to recycling—economics. There's just no profit incentive.

But now a group of chemists at the University of North Carolina at Chapel Hill have turned the tables by discovering a method to break down plastics to create a new material that is stronger and tougher than the original—meaning it's potentially more valuable.

"Our approach views plastic waste as a potentially valuable resource for the production of new molecules and materials," said Frank Leibfarth, assistant professor of chemistry in the UNC College of Arts & Sciences. "We hope this method could drive an economic incentive to recycle plastic, literally turning trash into treasure." Leibfarth and UNC-Chapel Hill professor Erik Alexanian, who specializes in chemical synthesis, describe the approach that could close the loop on plastic recycling in the journal *Science*.

Carbon-hydrogen bonds are some of the strongest chemical bonds in nature. Their stability makes it difficult to turn natural products into medicines and challenging to recycle commodity plastics.

But by modifying the carbon-hydrogen bonds that are common in polymers, the building blocks for modern plastic used in grocery bags, soda and water bottles, food packaging, auto parts and toys, the life span of polymers could be expanded beyond single-use plastic.

With a newly identified reagent that could strip hydrogen atoms off medicinal compounds and polymers, the UNC chemists were able to make new bonds in places previously considered unreactive.

"The versatility of our approach is that it enables many valuable transformations of carbon-hydrogen bonds on such a wide range of important compounds," Alexanian said.

Turning trash into treasure

The Leibfarth Group at Carolina is focused on designing polymers that are smarter, more functional and more sustainable.

With the support of the NC Policy Collaboratory, the team developed a super-absorbent polymer capable of removing dangerous chemicals from drinking water. Researchers envisioned using the innovative approach to help transform difficult-to-recycle plastic waste into a high-value class of polymers.

They started with plastic foam packaging used to protect electronics during shipping that otherwise ends up in landfills. Samples of post-consumer foam were provided by High Cube LLC, a Durham, N.C., recycling company. The foam is made of a low-density plastic called a commercial polyolefin.

By selectively pulling hydrogen atoms from polyolefin, the chemists came up with a way to expand the life of the single-use plastic into a high-value plastic known as an ionomer. A popular ionomer is Dow's SURLYN, a go-to material used in a wide variety of food packaging.

Most recycled plastic is "downcycled" into lower quality products like carpet or polyester clothing, that may still end up in landfills. Discarded plastics in waterways endanger sea life if turtles mistake ocean plastic for food. But if the chemistry can be repeatedly applied to polymers to help recycle them over and over again, "it could change the way we look at plastic," Leibfarth said.

Study co-authors include Timothy Fazekas, Jill W. Alty, Eliza K. Neidhart and Austin S. Miller.

More information: *Timothy J. Fazekas et al, Diversification of aliphatic C–H bonds in small molecules and polyolefins through radical chain transfer, Science (2022).* *DOI: 10.1126/science.abh4308*

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Mysterious Link Between Vitamin D And COVID-19 Reaffirmed in 'Striking' New Findings

"Striking" differences in chances of getting seriously ill from COVID-19 between patients who had sufficient vitamin D levels

Catherine Schuster-Bruce, Business Insider

Israeli scientists said they found "striking" differences in the chances of getting seriously ill from COVID-19 when they compared patients who had sufficient vitamin D levels prior to contracting the disease, with those who didn't.

A study published Thursday in research journal *PLOS One* found that about half of people who were vitamin D deficient before getting COVID-19 developed severe illness, compared to less than 10 percent of people who had sufficient levels of the vitamin in their blood.

We know vitamin D is vital for bone health, but its role in protecting against severe COVID-19 is less-well established.

The latest research was the first to examine vitamin D levels in individuals prior to them contracting COVID-19, the study authors said.

Dr. Amiel Dror, a study author and physician at the Galilee Medical Center, said of the findings: "We found it remarkable, and striking, to see the difference in the chances of becoming a severe patient when you are lacking in vitamin D compared to when you're not," per the *Times of Israel*. The findings come from 253 people admitted to Galilee Medical Center in Nahariya, Israel between 7 April 2020 and 4 February 2021 – a period before the highly-infectious Omicron variant emerged.

Dror said the findings suggested vitamin D helped bolster the immune system to deal with viruses that attack the respiratory system. "This is equally relevant for Omicron as it was for previous variants," Dror said.

The research doesn't prove vitamin D protects against COVID-19 and isn't a green light to avoid vaccines and take vitamins instead. Vaccines cut the risk of Omicron hospitalization, particularly after a booster, by up to 90 percent, according to the UK Health Security Agency.

Most vitamin D comes from direct sunlight on the skin. It's also found in foods such as fatty fish, mushrooms, and egg yolks as well as supplements. Vitamin D levels of more than 20 nanograms per milliliter are considered sufficient for most people, according to the Centers for Disease Control and Prevention – which is the benchmark used by the researchers from Bar-Ilan University and Galilee Medical Center.

Research compiled before the emergence of COVID-19 and published in *The Lancet*, found vitamin D cut the risk of other respiratory infections, compared with dummy drugs.

But for COVID-19, early findings have been inconsistent – some studies have found a link between low vitamin D levels and severe COVID-19, whilst others concluded the vitamin wasn't protective.

It wasn't clear – even from those studies with results showing a positive correlation between low vitamin D levels and severe COVID-19 – if depleted vitamin D came before or after people got sick, the Israeli researchers said.

Despite the new Israel data, we still don't know if low vitamin D levels cause people with COVID-19 to develop serious disease.

Underlying conditions that reduce vitamin D can also make people more vulnerable to severe COVID-19, for example.

The Israeli researchers cautioned vitamin D was "one piece of the complex puzzle" underlying severe COVID-19, in addition to comorbidities, genetic predisposition, dietary habits, and

geographic factors.

"Our study warrants further studies investigating if and when vitamin D supplementation among vitamin D deficient individuals in the community impacts the outcome of an eventual COVID-19 episode," they said.

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Self-cleaning bioplastics repel liquid and dirt

RMIT Ph.D. researcher Mehran Ghasemlou, lead author of the study published in Science of the Total Environment, said the new bioplastic was ideal for fresh food and takeaway packaging.

"Plastic waste is one of our biggest environmental challenges but the alternatives we develop need to be both eco-friendly and cost-effective, to have a chance of widespread use," Ghasemlou said.

"We designed this new bioplastic with large-scale fabrication in mind, ensuring it was simple to make and could easily be integrated with industrial manufacturing processes."

Ghasemlou said nature was full of ingeniously-designed structures that could inspire researchers striving to develop new high-performance and multifunctional materials.

"We've replicated the phenomenally water-repellent structure of lotus leaves to deliver a unique type of bioplastic that precisely combines both strength and degradability," he said.

The bioplastic is made from cheap and widely-available raw materials—starch and cellulose—to keep production costs low and support rapid biodegradability. The fabrication process does not require heating or complicated equipment and would be simple to upscale to a roll-to-roll production line, Ghasemlou said.

Naturally compostable

While biodegradable plastics are a growing market, not all bioplastics are equal. Most biodegradable or compostable plastics require industrial processes and high temperatures to break them down.

The new bioplastic does not need industrial intervention to biodegrade, with trials showing it breaks down naturally and quickly in soil.

"There are big differences between plant-based materials—just because something is made from green ingredients doesn't mean it will easily degrade," Ghasemlou said. "We carefully selected our raw materials for compostability and this is reflected in the results from our soil studies, where we can see our bioplastic rapidly breaks down simply with exposure to the bacteria and bugs in soil.

"Our ultimate aim is to deliver packaging that could be added to your backyard compost or thrown into a green bin alongside other organic waste, so that food waste can be composted together with the container it came in, to help prevent food contamination of recycling."

Lotus-inspired structures

Lotus leaves are renowned for having some of the most water-repellent surfaces on earth and are almost impossible to get dirty.

The secret lies in the leaf's surface structure, which is composed of tiny pillars topped with a waxy layer.

Any water that lands on the leaf remains a droplet, simply rolling off with the help of gravity or wind. The droplets sweep up dirt as they slide down, keeping the leaf clean.

To make their lotus-inspired material, the RMIT team of science and engineering researchers first synthetically engineered a plastic made of starch and cellulosic nanoparticles.

The surface of this bioplastic was imprinted with a pattern that mimics the structure of lotus leaves, then coated with a protective layer of PDMS, a silicon-based organic polymer.

Tests show the bioplastic not only repels liquids and dirt effectively, but also retains its self-cleaning properties after being scratched with abrasives and exposed to heat, acid and ethanol.

Corresponding author, Professor Benu Adhikari, said the design

overcomes key challenges of starch-based materials.

"Starch is one of the most promising and versatile natural polymers, but it is relatively fragile and highly susceptible to moisture," Adhikari said. "Through our bio-inspired engineering that mimics the 'lotus effect,' we have delivered a highly-effective starch-based biodegradable plastic."

Ghasemlou is currently working with a bioplastic company, which is evaluating further development of these novel water repellant materials. The RMIT research team is keen to collaborate with other potential partners on commercial applications for the bioplastic. "Biodegradation of novel bioplastics made of starch, polyhydroxyurethanes and cellulose nanocrystals in soil environment" is published in *Science of the Total Environment*.

More information: *Mehran Ghasemlou et al, Biodegradation of novel bioplastics made of starch, polyhydroxyurethanes and cellulose nanocrystals in soil environment, Science of The Total Environment (2022). DOI: 10.1016/j.scitotenv.2021.152684*

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Eating Dinner Late Ups Diabetes Risk; Melatonin Involved

Eating dinner close to bedtime when endogenous melatonin levels are high is associated with decreased insulin secretion and decreased glucose tolerance, which increase the risk of type 2 diabetes.

Marlene Busko

And people who are carriers of the G allele of the melatonin receptor-1b gene (*MTNR1B*) have greater impairment in glucose tolerance after eating a late dinner.

"In natural late eaters [in Spain], we simulated early and late dinner timing by administering a glucose drink and compared effects on blood sugar control over 2 hours," said senior author Richa Saxena, PhD, a principal investigator at the Center for Genomic Medicine at Massachusetts General Hospital, Boston.

The study also compared outcomes in carriers and noncarriers of the G allele variant of the melatonin receptor gene, Saxena pointed out, in a press release from the hospital.

"We found that late eating disturbed blood sugar control in the whole group," added lead author Marta Garaulet, PhD.

"This impaired glucose control was predominantly seen in genetic risk variant carriers, representing about half of the cohort," said Garaulet, professor of physiology and nutrition, University of Murcia, Spain.

The study results "may be important in the effort towards prevention of type 2 diabetes," according to co-senior author Frank A.J.L. Scheer, PhD.

"Our findings are applicable to about a third of the population in the industrialized world who consume food close to bedtime, as well as other populations who eat at night, including shift workers, or those experiencing jetlag or night-eating disorders, as well as those who routinely use melatonin supplements close to food intake," said Scheer, director of the Medical Chronobiology Program at Brigham and Women's Hospital, Boston, Massachusetts.

The results suggest people should not eat within 2 hours of bedtime, say the researchers.

"Notably, our study does not include patients with diabetes, so additional studies are needed to examine the impact of food timing and its link with melatonin and receptor variation in patients with diabetes," Scheer said.

The findings, from the *MTNR1B* SNP*Food Timing Interaction on Glucose Control (ONTIME-MT) randomized crossover study, were recently published in *Diabetes Care*.

Melatonin Plays a Key Role in Glucose Metabolism

Melatonin, a hormone primarily released at night that helps control the sleep–wake cycle, typically rises around 2 hours before bedtime, the researchers explain.

The discovery of *MTNR1B* as a type 2 diabetes-associated gene "suggests that beyond sleep and circadian regulation, melatonin plays a key role in glucose metabolism," they note.

However, whether melatonin improves or impairs glucose control is controversial, and the effect of *MTNR1B* genotypes on glucose control is not clear. "We decided to test if late eating that usually occurs with elevated melatonin levels results in disturbed blood sugar control," Saxena explained.

To investigate this, researchers enrolled 845 adults in Spain who were 18-70 years old and did not have diabetes.

Participants were a mean age of 38 years and 71% were women. They had a mean body mass index (BMI) of 25.7 kg/m^2 and 18% had obesity. On average, they typically ate dinner at 21:38 (9:38 PM) and went to bed at 24:32 (12:32 AM).

DNA analysis from participants' blood samples determined that 50% had the CC genotype of the *MTNR1B* gene, 40% had the CG genotype, and 10% had the GG genotype.

Each participant underwent two oral glucose tolerance tests.

They fasted for 8 hours and then had a 2-hour 75-g oral glucose tolerance test either 1 hour before bedtime (simulating a late dinner) or 4 hours before bedtime (simulating an early dinner). Then they repeated the test at the opposite dinner time on another night.

The average serum melatonin values were 3.5-fold higher after the late dinner than after the early dinner, resulting in 6.7% lower insulin area under the curve (AUC) and 8.3% higher glucose AUC.

Genotype differences in glucose tolerance were attributed to reductions in beta-cell function. "Our results confirm that late eating acutely impairs glucose tolerance through a defect in insulin secretion," the researchers reiterate.

ONTIME-MT was funded by the National Institutes of Health, the Spanish Government of Investigation, Development, and Innovation, and the Seneca Foundation. The researchers have reported no relevant financial disclosures.

Diabetes Care. Published online January 10, 2022. Abstract

https://bit.ly/3oDHWhm

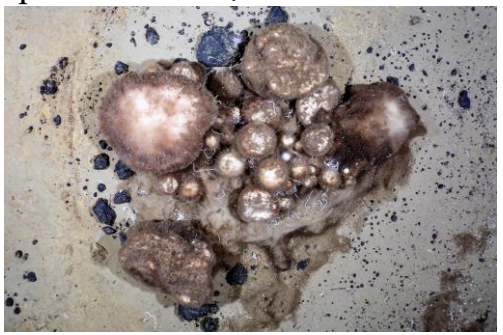
These sponges survive the deep sea by feeding on remains of long-dead animals

Massive sponge community cycles nutrients from fossils into the Arctic Ocean ecosystem

By Tess Joosse

It can be hard to find food in the central Arctic Ocean. The water is frigid and the surface is blanketed in ice, making it nearly impossible for the tiny organisms that power many marine food chains to photosynthesize. Now, researchers have unraveled how a gigantic, newly discovered sponge garden gets around the lack of nutrients: by feeding on the fossilized remains of other underwater invertebrates that lived thousands of years ago. Some of the sponges have apparently survived on such a diet for more than 300 years

"It's a really cool" finding, says Stephanie Archer, a marine ecologist at the Louisiana Universities Marine Consortium who wasn't involved in the study. The work, she says, reveals how rarely studied deep Arctic ecosystems continue to function, even as melting sea ice threatens to disrupt them.



These 300-year-old sponges feed on fossilized remains in the deep Arctic Ocean. **Alfred Wegener Institute/PS101 AWI OFOS system**

Sponges have been around for at least 600 million years and were likely the first multicellular organisms on Earth. They filter water through their pores, digesting microscopic photosynthesizing organisms called phytoplankton and other food particles to help cycle nutrients such as carbon, nitrogen, and phosphorus through the underwater ecosystem. "They're very opportunistic and can tap

into food sources that others cannot," says Jasper de Goeij, a marine ecologist at the University of Amsterdam, also not involved with the study.

But sponges weren't necessarily top of mind when Antje Boetius, a marine biologist at the Max Planck Institute for Marine Microbiology and one of the study's co-authors, set out on a research mission to the central Arctic Ocean in 2016. Among other projects, she planned to survey and map the Langseth Ridge, a V-shaped, 125-kilometer-long underwater mountain range located north of Svalbard at the top of the globe. "We thought we might see some rocks and maybe one or two" deep-sea sponges, Boetius says of the effort.

She and her colleagues devised an underwater sledge packed with equipment to measure and sample the ocean floor. The rig included cameras, lights, sensors, and other devices encased in a steel frame about as large as a Volkswagen Beetle. While traversing the underwater peaks and valleys of the Langseth Ridge, the rig came across a dense patch of sponges stretching for at least 15 square kilometers, nearly the size of 3000 U.S. football fields—a total shock, Boetius says.

"Imagine yourself going into the desert, and you find the most spectacular oasis where everyone has told you there is no life," she explains. The sponge ecosystem sat as far as 1000 meters below a thick sheet of ice through which no sunlight could penetrate. Boetius and her colleagues wondered how the animals could survive in such an inhospitable home.

In many parts of the deepest ocean, life congregates around seeps—vents in the sea floor where gasses leak out from Earth's innards and fuel microbial growth, attracting communities of deep-sea invertebrates. But there was no such gas source along this ridge and no currents or upwelling that could be carrying nutrients or particles to the sponges, explains study co-author Teresa Morganti, who studies sponges at Max Planck. The water was still and stripped of food, but the sponges were thriving.

So the researchers extracted samples of the underwater sponge "oasis" to figure out how the animals were surviving—some were several centuries old, carbon dating revealed. The sponges, some as wide as dinner plates, were growing on a curious substrate: a blackened tangle of fossilized siboglinid tube worms, which are deep-sea worms that live in clusters of tubes stuck to the ocean floor. The team measured the carbon and nitrogen isotopes of the samples and sequenced the DNA of microbes that colonize the sponges and help them process their food.

The sponges were replete with microbes that digest organic matter, the team reports today in *Nature Communications*. This suggests the animals were pulling nutrients from the fossilized layer below them, essentially eating the 1000-year-old dead invertebrates with help from their symbiotic bacteria, the team says.

The former tube worms likely sprung up around gaseous vents that were active thousands of years ago but then closed, leaving the fossilized husks ready for the taking by the hungry sponges. It's the first time such an eating strategy has been observed for sponges, Morganti believes.

Goeij is cautious, however, noting the analyses come from just a few chunks of the ocean floor. Still, he says, it's complicated to obtain these samples, and "this is a really good basis" for the hypothesis that sponges are capable of this strategy.

Both he and Archer say the finding makes clear how important the often-underestimated animals are in building biological hot spots. Because sponges help cycle nutrients through their environment, everything they eat and do has "consequences for the rest of the ocean," Archer says. "Every time we think we have sponges figured out," she says, "a paper like this comes along and there's something new they can do."

https://wb.md/3rEv2BB

'Substantial' CVD Risks, Burden Up to a Year After COVID-19

Increased risk for and 12-month burden of cardiovascular disease (CVD) that is substantial

Patrice Wendling

People who have had COVID-19 have an increased risk for and 12-month burden of cardiovascular disease (CVD) that is substantial and spans an array of cardiovascular disorders, a deep dive into federal data suggests.

"I went into this thinking that this is most likely happening in people to start with who have a higher risk of cardiovascular disorders, smokers, people with high BMI, diabetes, but what we found is something different," Ziyad Al-Aly, MD, told *theheart.org | Medscape Cardiology*. "It's evident in people at high risk, but it was also as clear as the sun even in people who have no cardiovascular risk whatsoever."

Rates were increased in younger adults, never smokers, White and Black people, males and females, he said. "So the risk confirmed by the SARS-CoV-2 virus seems to spare almost no one."

Although cardiovascular outcomes increased with the severity of the acute infection, the excess risks and burdens were also evident in those who never required hospitalization, a group that represents the majority of people with COVID-19, observed Al-Aly, who directs the Clinical Epidemiology Center at the Veterans Affairs St. Louis Health Care System.

"This study is very important because it underscores not just the acute cardiovascular risk associated with COVID but the increased risk of chronic cardiovascular outcomes as well," cardiologist C. Michael Gibson, MD, professor of medicine, Harvard Medical School, Boston, told Medscape via email. "Given the number of patients in the US who have been infected with COVID, this could represent a significant chronic burden on the healthcare system, particularly as healthcare professionals leave the profession."

For the study, the investigators used national VA databases to build a cohort of 153,760 veterans who were alive 30 days after testing positive for COVID-19 between March 1, 2020 and January 2021. They were compared with a contemporary cohort of 5.6 million veterans with no evidence of SARS-CoV-2 infection and a historical cohort of 5.8 million veterans using the system in 2017 prior to the pandemic. Median follow-up was 347, 348, and 347 days, respectively.

As reported in *Nature Medicine*, the risk for a major adverse cardiovascular event, a composite of myocardial infarction, stroke, and all-cause mortality, was 4% higher in people who had been infected with COVID-19 than in those who had not.

"People say 4% is small, but actually it's really, really big if you think about it in the context of the huge number of people who have had COVID-19 in the United States, and also globally," Al-Aly said.

Compared with the contemporary control group, people who had COVID-19 had an increased risk (hazard ratio [HR]) and burden per 1000 people at 1 year for the following cardiovascular outcomes:

- ***Stroke: HR, 1.52; burden, 4.03***
- ***Transient ischemic attack: HR, 1.49; burden, 1.84***
- ***Dysrhythmias: HR, 1.69; burden, 19.86***
- ***Ischemic heart disease: HR, 1.66; burden, 7.28***
- ***Heart failure: HR, 1.72; burden, 11.61***
- ***Non-ischemic cardiomyopathy: HR, 1.62; burden 3.56***
- ***Pulmonary embolism: HR, 2.93; burden, 5.47***
- ***Deep vein thrombosis: HR, 2.09; burden, 4.18***
- ***Pericarditis: HR, 1.85, burden, 0.98***
- ***Myocarditis: HR, 5.38; burden, 0.31***

Recent reports have raised concerns about an association between COVID-19 vaccines and myocarditis and pericarditis, particularly

in young males. Although very few of the participants were vaccinated prior to becoming infected, as vaccines were not yet widely available, the researchers performed two analyses censoring participants at the time of the first dose of any COVID-19 vaccine and adjusting for vaccination as a time-varying covariate.

The absolute numbers of myocarditis and pericarditis were still higher than the contemporary and historical cohorts. These numbers are much larger than those reported for myocarditis after vaccines, which are generally around 40 cases per 1 million people, observed Al-Aly.

The overall results were also consistent when compared with the historical control subjects.

"What we're seeing in our report and others is that SARS-CoV-2 can leave a sort of scar or imprint on people, and some of these conditions are likely chronic conditions," Al-Aly said. "So you're going to have a generation of people who will bear the scar of COVID for their lifetime and I think that requires recognition and attention, so we're aware of the magnitude of the problem and prepared to deal with it."

With more than 76 million COVID-19 cases in the United States, that effort will likely have to be at the federal level, similar to President Joe Biden's recent relaunch of the "Cancer Moonshot," he added. "We need a greater and broader recognition at the federal level to try and recognize that when you have an earthquake, you don't just deal with the earthquake when the earth is shaking, but you also need to deal with the aftermath."

Gibson pointed out that this was a study of predominantly males and, thus, it's unclear if the results can be extended to females. Nevertheless, he added, "long COVID may include outcomes beyond the central nervous system and we should educate patients about the risk of late cardiovascular outcomes."

The authors also note the largely White, male cohort may limit generalizability of the findings. Other limitations include the possibility that some people may have had COVID-19 but were not tested, the datasets lacked information on cause of death, and possible residual confounding not accounted for in the adjusted analyses.

The research was funded by the US Department of Veterans Affairs and two American Society of Nephrology and Kidney Cure fellowship awards. The authors declare no competing interests. Gibson reports having no relevant conflicts of interest.

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https://bit.ly/3LkT7oS

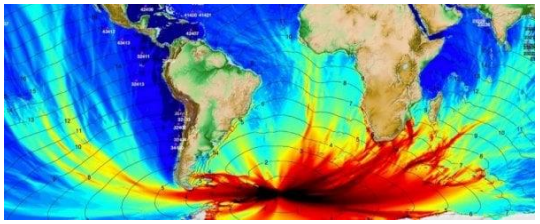
Mystery Tsunami That Spread Around The World in 2021 Can Finally Be Explained

Last year in August, a surprise tsunami in the South Atlantic Ocean spread over 10,000 kilometers, rippling through the North Atlantic, the Pacific, and the Indian Oceans.

Carly Cassella

Last year in August, a surprise tsunami in the South Atlantic Ocean mushroomed to distances over 10,000 kilometers (more than 6,000 miles) away, rippling through the North Atlantic, the Pacific, and the Indian Oceans.

It was the first time a tsunami had been recorded in three different oceans since the 2004 Indian Ocean earthquake, and scientists have only just now figured out how the waves were triggered.



The 2021 mystery tsunami. **(NOAA Center for Tsunami Research)**

The epicenter of the August earthquake was measured 47 kilometers (about 30 miles) below the ocean floor, which is much too deep to initiate a significant tsunami, even one with relatively small waves between 15 and 75 centimeters tall (6 to 30 inches).

As it turns out, however, this tsunami wasn't just the product of a

single 7.5-magnitude earthquake. A fresh look at the seismological data suggests it was actually a series of five sub-quakes, and in their midst, was hiding a much larger and shallower rumble that was probably what set loose the global tsunami.

This 'invisible' third quake struck just 15 kilometers below the Earth's surface at a magnitude of 8.2. Yet in the crowd of quakes, our monitoring systems completely missed it.

"The third event is special because it was huge, and it was silent," explains seismologist Zhe Jia from the California Institute of Technology.

"In the data we normally look at [for earthquake monitoring], it was almost invisible."

Cutting up the seismological data into longer periods of 500 seconds, Jia and his colleagues were able to reveal the presence of a shallow and slow earthquake not seen before.

Between clusters of other regular ruptures, they found a 3-minute rumble that ruptured a 200-kilometer section of the plate interface. Altogether, this one event made up over 70 percent of the total seismic moment recorded.

"Thus," the authors conclude, "the South Sandwich Island earthquake appears to be a hybrid of deep rupture and slow tsunamigenic slip; this explains the somewhat unusual combination of the relatively large depth and the globally observed tsunami."

The findings suggest our earthquake and tsunami warning systems need to be updated. If we are to warn coastal communities about similar events, then our systems need to read between the seismological lines to see the bigger quakes.

Otherwise, the true size of complex earthquakes could continue to slip by us unnoticed. Today, earthquake monitoring systems tend to focus on short- and medium-periods of seismological waves, but it seems like the longer periods also hold important information.

"It's hard to find the second earthquake because it's buried in the first one," says Jia.

"It's very seldom complex earthquakes like this are observed... And if we don't use the right dataset, we cannot really see what was hidden inside."

Geologist Judith Hubbard, who works for the Earth Observatory of Singapore and who was not involved in the current research, says she is grateful that others are digging into the data of unexpected tsunamis to better understand where they came from.

"With these complex earthquakes, the earthquake happens and we think, 'Oh, that wasn't so big, we don't have to worry.' And then the tsunami hits and causes a lot of damage," says Hubbard.

"This study is a great example of how we can understand how these events work, and how we can detect them faster so we can have more warning in the future."

The study was published in *Geophysical Research Letters*.

https://bit.ly/3BfqkNJ

3 paralyzed men can walk again after getting electrode implant

The device stimulates specific spinal nerves.

By Nicoletta Lanese

Three men with paralyzing spinal cord injuries can now stand, walk and cycle after electrodes were implanted into their spinal cords.

The electrodes deliver electrical pulses to specific regions of the spinal cord and thus activate muscles in the trunk and legs, according to a new study, published Monday (Feb. 7) in the journal Nature Medicine. The soft, flexible device lies directly on top of the spinal nerves, beneath the vertebrae, and can be controlled wirelessly with software, operated from a tablet, and a handheld clicker.

The software communicates with a pacemaker-like device in the abdomen, which then directs the activity of the nerve-bound electrodes on the spinal cord. So, with the tap of a touch screen, the

user of the implant can prompt their device to generate a precise pattern of stimulation. These stimulation patterns translate to patterns of muscle activity, allowing the user to walk, cycle, or swim, for instance. Users can also manually switch between these stimulation patterns with their clicker.

"All three patients were able to stand, walk, pedal, swim and control their torso movements in just one day, after their implants were activated," co-senior author Grégoire Courtine, a neuroscientist and professor at the Swiss Federal Institute of Technology Lausanne (EPFL), said in a statement. The three patients were men, ages 29 to 41, but the study authors also expect that the device will work in women, The Guardian reported.

After the initial implantation, the patients underwent extensive training to get used to using the device and regain muscle mass and motor control, co-senior author Dr. Jocelyne Bloch, an associate professor of neurosurgery at Lausanne University Hospital, told The Guardian. "It was not perfect at the beginning, but they could train very early to have a more fluid gait," she said. Eventually, the patients progressed from using the implants only in a controlled lab setting to using them out and about in their daily lives.

After four months of training, one patient, Michel Roccati, was able to walk about 0.6 mile (1 kilometer) outside the lab and without stopping, with only a frame for balance, AFP reported. He can now continuously stand for about two hours. Like the other participants in the trial, Roccati has a complete spinal cord injury, meaning the nerves below his site of injury cannot communicate with the brain at all. He was injured in a motorcycle accident in 2019 and lost both feeling and motor control in his legs.

"It was a very emotional experience," Roccati said of the first time the electrical pulses were activated and he took a step, AFP reported. Now, the device is "a part of my daily life," he told The Guardian. At a news conference, Roccati said he's regained some feeling in his legs; he can feel his body making contact with the ground and his muscles engaging when he walks, STAT reported.

The new device builds on existing technology called spinal cord stimulators, which are already used to alleviate pain, according to NBC News. The team modified these stimulators to target specific nerves involved in controlling muscles of the legs and lower trunk, they wrote in their report. In addition, in the trial, the team custom-fit each implant to match the length of the spinal cord and the position of the nerves in different participants, according to STAT.

"That gives us precise control over the neurons regulating specific muscles," Bloch said in the statement. "Ultimately, it allows for greater selectivity and accuracy in controlling the motor sequences for a given activity."

The device will now be tested in a large-scale trial in the U.S. and Europe, according to STAT. The team hopes to test the device in people with relatively recent injuries; in the three-person trial, all of the participants were at least a year out from their injuries. "The next step is to start earlier, just after the injury, when the potential for recovery is much larger," Bloch told NBC News. Animal studies hint that electrical stimulation may help the spinal cord heal after injury, according to STAT; so patients could potentially regain more sensation and motor control if their implant is placed soon after injury.

The team is also investigating whether a similar stimulator could be implanted directly into the motor cortex, a key region of the brain for controlling voluntary movement, Courtine told NBC News. Such a device could allow people with paralysis to direct their movements without the aid of a tablet or clicker.

The treatment's accessibility has limitations, however: Placement of the implant requires invasive surgery, and patients must undergo extensive monitoring and rehabilitation after the implantation, ABC Science reported.

"The challenge for the future is not only improving these approaches and developing other approaches, but to manage the application of these interventions so that many individuals can benefit, given that the access to high levels of technology may be an impediment," Reggie Edgerton, a professor at the University of California, Los Angeles who oversaw some of Courtine's postdoctoral work, told STAT.

https://wb.md/3LvsGNw

Not as Silent as We Thought: The Symptoms of Early-Stage Ovarian Cancer

Many patients presented with one or more symptoms

Andrew M. Kaunitz, MD

Ovarian cancer represents the most lethal gynecologic malignancy in US women. During training, I was taught that ovarian cancer is a silent killer. Indeed, most cases are diagnosed in women in their 50s or 60s who have advanced disease, and to date, screening for this uncommon but dreaded disease has not been found to reduce ovarian cancer mortality. Prior studies conducted to assess whether symptoms are present in women with ovarian cancer have focused on patients with late-stage disease.

The lead article in the February issue of American College of Obstetricians and Gynecologists' (ACOG's) Green Journal (*Obstetrics & Gynecology*) addressed the prevalence of symptoms in women with early-stage ovarian cancer. Investigators used data collected at the time of enrollment in a trial that assessed different chemotherapy strategies for women with stage I or II disease.

Among 419 patients evaluated, some three fourths presented with one or more symptoms. Of these, approximately one half had one symptom and one third had multiple symptoms. The most common symptoms were abdominal or pelvic pain, followed by fullness or increased abdominal girth. Other symptoms included abnormal bleeding as well as urinary and gastrointestinal complaints.

An important limitation of this report is that participants in the trial had already been diagnosed with ovarian cancer. We know that patients already diagnosed with disease are more likely to report prior symptoms than before disease diagnosis. Given this potential for recall bias, the study likely overestimated symptom prevalence in women with early-stage ovarian cancer.

Nonetheless, we should counsel women in their 50s or older to contact us if they experience persistent abdominal or pelvic pain, increased abdominal fullness or girth, or abnormal uterine bleeding. When such symptoms are identified, arranging for a vaginal ultrasound represents a prudent next step.

I am Andrew Kaunitz. Please take care of yourself and each other.

https://wb.md/3rGyHPb

Docs React: NyQuil Chicken and Endless Eye Mucus

It's the season of love. In that spirit, we're offering you a bouquet of absurd TikTok health trends that physicians love to hate — and explain the absurdity of.

Jay Lankau

Lean in and get a whiff of the latest good, bad, and ugly videos making the rounds on the internet's most perplexing platform. But don't get too close; these videos are especially ripe.

The Good: Can You Fart Yourself Blind? Doc Explains

It's something we've all wondered about, right?

TikTok and YouTube's mainstay plastic surgeon Anthony Youn, MD, took it upon himself to reply to a comment saying "I once farted so hard I went blind for 3 minutes." This phenomenon, according to Youn, is very rare, but not impossible, though we wouldn't exactly want to try it for ourselves.

In the humorous (but very informative!) video, Youn explains that particularly pungent flatulence can contain large amounts of hydrogen sulfide, a gas that is known for smelling like rotten eggs. According to the Occupational Safety and Health Administration,

hydrogen sulfide is produced in a number of industries, like oil and gas refining, mining, and paper processing. Exposure to higher concentrations of hydrogen sulfide can be dangerous, with prolonged exposure at a 2-5 parts per million (ppm) concentration causing nausea, headaches, and airway problems in some asthma patients. At very high concentrations, it can be fatal.

Thankfully, a person's gas is not at all that dangerous. When it comes to the commentor's claim, Youn says that something else hydrogen sulfide can do is reduce blood pressure.

"If it reduces blood pressure to the central retinal artery," Youn says, "your silent but deadly toot could theoretically make you go blind."

Thank goodness we can lay that question to rest.

The Bad: NyQuil Chicken

You know something bad has happened when your TikTok search ends with a warning from the app that says "Learn how to recognize harmful trends and hoaxes." That's what shows up now when you try to find out what the "NyQuil chicken" or "sleepy chicken" trend is (or was) all about.

TikTok videos, including this one from TikTok user @janelleandkate, show users trying out a trend meant to cook up a meal that will also cure your cold symptoms. The trend involves cooking chicken in a pan full of the cold and flu medicine NyQuil. The NyQuil chicken idea stems from a Twitter meme from 2017, so it is possible that some of the recent videos are fake (blue food coloring is easy to get, people). However, in the instance that people believe the videos to be real and want to try the trend out, it is important to warn that this shouldn't be attempted.

Aaron Hartman, MD, assistant clinical professor of family medicine at Virginia Commonwealth University, told the website Mic about the trend's dangers: "When you cook cough medicine like NyQuil, however, you boil off the water and alcohol in it, leaving the chicken saturated with a super concentrated amount of drugs in the meat. If you ate one of those cutlets completely cooked, it'd be as if you're actually consuming a quarter to half a bottle of NyQuil."

And that's not good for anyone. What ever happened to an old fashioned herb marinade?

The Ugly: Eye Boogers from Hell

Get a look at this!

This video from @mikaylaadiorr has amassed over 8 million likes and over 89,000 comments, and shows someone, who we can assume is Mikayla, pulling some sort of long string-like material out of the corner of her eye. It's like a clown's never-ending handkerchief, only goopy.

These mucus eye strings are caused by untreated eye conditions, like dry eye or pink eye (conjunctivitis), but pulling the mucus out is actually a symptom of what is called *mucus fishing syndrome*. As you know, our eyes are covered in layers of mucus and tears, which keeps our eyeballs lubricated and also protects us from bacteria and viruses. It's possible to dry out the eyes by pulling some mucus off, but our eyes aren't big fans of that, so they'll create more mucus to keep from drying out.

A person who might get a bit addicted to pulling the strings out has likely developed mucus fishing syndrome, which is considered a body-focused repetitive behavior (BFRB); other BFRBs include skin-picking (dermatillomania) or picking hairs out (trichotillomania).

Popular TikToker and Oregon ophthalmologist Will Flanary, MD, aka Dr. Glaucomflecken, responded to the videos, which have been encouraging others to try it.

"This is called mucus fishing syndrome," the ophthalmologist explained via text captions in his video. "The trauma from pulling mucus out of your eye causes more mucus to form. You get caught in a never-ending cycle that gets worse over time. So…stop it."

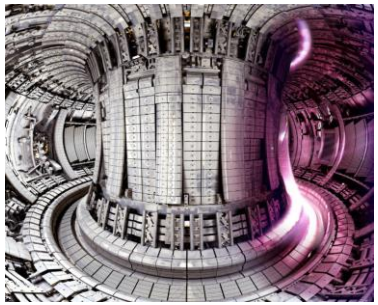
Fingers off the mucus, people.

https://bit.ly/3BeqVzc

Five seconds, 59 megajoules: A new record for tokamak fusion

The Joint European Torus takes a major step in preparing for work at ITER.

John Timmer



Enlarge / The interior of JET, configured as a scale model for ITER, overlaid with an image of a plasma present in the tokamak during experiments. EUROfusion

On Wednesday, the EUROfusion consortium announced that the Joint European Torus (JET), located near Oxford in the UK, had set a new record for released energy. Over the course of a five-second "pulse," 59 megajoules of energy were released, double the previous record for tokamak fusion set at JET in 1997.

Despite the impressive numbers, the results are still well short of the break-even point where the fusion energy released would match the energy input required to trigger the fusion. Still, the work provides an important validation of the approach being taken at the next major fusion project, the International Thermonuclear Experimental Reactor, or ITER.

Two ways to fuse

Fusion takes place when atomic nuclei are brought close enough together that they merge, creating a heavier element. It's the process that powers stars, and it could produce vast amounts of energy from small amounts of hydrogen isotopes if we could reproduce the temperatures and pressures found in stars here on Earth. So far, we've taken two main approaches to the process.

In the first, many high-powered lasers deliver an extremely intense burst of energy that crushes and heats a small pellet of hydrogen isotopes, producing a short burst of fusion. This is the approach taken at the National Ignition Facility, which has put up some impressive results in terms of the amount of energy produced. But the released energy comes in an extremely short burst, after which the lasers need to be re-cycled and the target needs to be replaced. By the time the system is ready to create another burst of fusion, all the heat generated by the first has dissipated. It's not clear how to create the sort of sustained release of energy that will be needed for something like a power plant.

The alternative approach involves creating a high-energy hydrogen plasma and then using intense magnetic fields to contain and compress it. This is generally done in a toroidal structure called a tokamak, an approach developed in the Soviet Union (though there are alternative structures). While it doesn't produce the same sort of burst of fusion, a tokamak contains a lot more fuel and has the potential to sustain fusion reactions for long enough to extract useful energy.

Right now, the most powerful tokamak on the planet is JET, which holds the record for highest output: 22 megajoules, set during an experimental run in 1997. In recent years, JET has been used as a testbed for the technologies and materials that will go into ITER, a much larger tokamak that is expected to finally reach break-even and pave the way for the first demonstration fusion power plant.

As such, successes at JET provide important indications that ITER is likely to achieve the milestones expected of it.

World records

While it's possible to run sustained reactions in tokamaks, JET isn't large enough to reach this sort of stable state. Instead, it is being operated in five-second pulses in which it creates conditions where fusion can start and then ramps back down again. This setup allows researchers to test materials for the tokamak and different configurations of its magnets to determine how they affect this

pulse of fusion. Since the design is largely similar to that of ITER, these pulses can give real-world data to validate the models we have of what will happen inside ITER once it is switched on.

And that's why this energy milestone is important. Set up to reflect the design of ITER, and with the mix of deuterium and tritium fuel that will be used there, JET made the largest sustained fusion reaction yet.

"The record—and more importantly, the things we've learned about fusion under these conditions and how it fully confirms our predictions—shows that we are on the right path to a future world of fusion energy," said Tony Donné, the program manager at EUROfusion, which runs JET. "If we can maintain fusion for five seconds, we can do it for five minutes and then five hours as we scale up our operations in future machines."

After years of delays, ITER is now expected to begin experimental runs in 2025. Unlike JET, ITER is expected to go well past the break-even point and host self-sustaining fusion reactions in which the energy produced remains above the energy needed to control the reaction.

https://wb.md/3Jpr4D5

Dairy a Risk Factor for Parkinson's?

Dairy intake may increase risk of Parkinson's disease in men, according to investigators.

Will Pass

Men of European ancestry with a genetic marker predicting dairy consumption had significantly greater risk of Parkinson's disease than individuals without the marker, suggesting a causal relationship between dairy intake and Parkinson's disease, lead author Cloé Domenighetti, MSc, a PhD student at UVSQ, Université Paris Sud, and colleagues reported.

"Previous studies highlighted dairy intake as a risk factor of Parkinson's disease," the investigators wrote in Movement Disorders. "A meta-analysis of prospective studies reported a 40% increased Parkinson's disease risk in participants with the highest intake. It is unclear whether the association is causal or explained by confounding or reverse causation, given the long prodromal phase of Parkinson's disease."

A Mendelian Randomization Study

The investigators evaluated this link by comparing 9,823 cases of Parkinson's disease with 8,376 controls, all individuals of European ancestry from the Courage-Parkinson's disease consortium, comprising 23 studies. Data were analyzed by two-sample Mendelian randomization, a technique that uses genotype to predict behavior, thereby replacing conventional methods of capturing behavior, such as questionnaires. In this case, the investigators screened all participants for rs4988235, a single-nucleotide polymorphism (SNP) upstream of the lactase gene that is well documented to predict dairy intake among individuals of European ancestry.

"Mendelian randomization uses genetic variants associated with exposures as instrumental variables to estimate causal relationships between exposures and outcomes," the investigators wrote. "Mendelian randomization analyses are less likely to be biased by confounding or reverse causation than observational studies if a set of assumptions are met."

The approach uncovered a significant association between rs4988235 and Parkinson's disease, with a 70% increase in disease risk per one serving of dairy per day (odds ratio, 1.70; 95% confidence interval, 1.12-2.60; P = .013). Further analysis revealed that this finding was driven by men, who had a 2.5-fold increased risk of Parkinson's disease per one serving per day (OR, 2.50; 95% CI, 1.37-4.56; P = .003) versus women, among whom there was no significant association (OR, 1.04; 95% CI, 0.56-1.92; P = .91). No significant associations were observed among individuals grouped

by age or Parkinson's disease duration.

"Our findings suggest that dairy intake increases Parkinson's disease risk," the investigators concluded. "Therefore, diets with limited milk intake (e.g., Mediterranean diet) may be beneficial with respect to Parkinson's disease."

Further Evidence Supporting a Link Between Diet and Parkinson's Disease

According to Silke Appel-Cresswell, MD, Marg Meikle Professor for Parkinson's Research at the University of British Columbia, Vancouver, the findings align with previous prospective cohort studies demonstrating an increased risk of Parkinson's disease with greater consumption of dairy.

"What the current study adds," Appel-Cresswell said, "is a complementary approach to assess the association where the risk of reverse causation and of confounding are minimized. Like in some of the previous studies, the authors find sex differences with an increased risk for men but not women."

Appel-Cresswell noted that an increasing body of evidence supports a link between diet and Parkinson's disease, including a study of her own published last year, which showed later onset of Parkinson's disease among individuals with a Mediterranean-style diet.

"We are accumulating evidence for a role of diet (or more broadly, the food exposome) for the risk to develop Parkinson's disease," Appel-Cresswell said, noting that "key pieces are still missing, including mechanisms underlying associations, clinical trials in individuals with established Parkinson's disease and — eventually — preventive interventions. This research is urgently needed and analyses will need to take sex differences and a large range of potential other factors into account."

A "Modest" Contributing Factor?

Vikas Kotagal, MD, associate professor of neurology at the University of Michigan, Ann Arbor, offered a perspective on the study methodology, and suggested that a causal link between dairy intake and Parkinson's disease, if present, is likely minimal.

"Limitations to the study include the fact that participants weren't actually asked or tested for how much dairy they truly consumed," Kotagal said. "Their dairy intake was estimated based on their genetic background — there are certainly many assumptions baked into this analytic approach which may or may not be true. It is also worth noting the fact that this causal association was seen in men and not women, suggesting that even if dairy intake was truly causal, it is likely to be a modest contributing factor and not a significant cause of Parkinson's disease in the broader population in general."

Still, Kotagal agreed with Appel-Cresswell that underlying mechanisms need further investigation. "The biggest takeaway here is to heighten the urgency for researchers and funders to explore whether factors that might cluster with dairy intake — including pesticide exposure in milk or even the make-up of bacterial populations in different peoples' intestines — might deserve closer scrutiny as a missing link connecting dairy consumption to increased Parkinson's disease risk," Kotagal said.

Dietary Advice

Considering all available evidence, Appel-Cresswell offered some dietary advice with benefits that may extend beyond prevention of Parkinson's disease.

"From a clinical point of view, I suggest to limit dairy intake to a moderate amount," she said. "Mediterranean diets so far have the best supporting evidence for a lower Parkinson's disease risk, although data is lacking for benefits in established Parkinson's disease. Given the low risk of the Mediterranean diet and the established benefits for a host of other medical conditions, this is generally a safe and delicious recommendation whether one is living with Parkinson's or not."

The study was supported by the European Union Joint Program for Neurodegenerative Disease Research, the National Centre of Excellence in Research on Parkinson's Disease, the National Institutes of Health, and others. The investigators disclosed additional relationships with Astellas Pharma, Sanofi, Pfizer, and others. Kotagal and Appel-Cresswell reported no relevant conflicts of interest.
This story originally appeared on MDedge.com, part of the Medscape Professional Network.

https://bit.ly/3HLFZXN

Ebola Lurking in Brain Fluid Kills Monkeys Weeks After Recovery

New research reveals where the virus was hiding and hints at how to truly purge it from the body.

Dan Robitzski

A new study in macaques sheds light on how the Ebola virus can persist in the brains of survivors even after they've been vaccinated, treated with FDA-approved monoclonal antibody therapies, or both. There's a growing body of evidence suggesting that Ebola can lurk in the body for long periods of time, evading the immune system as well as available therapeutics.

Reports from Ebola outbreaks document survivors that relapse, falling ill and sometimes dying months or even years after they've recovered from their acute illness. Macaque and human studies have also shown that the Ebola virus can persist long-term in the eyes, brain, and testes of survivors. Research published today (February 9) in *Science Translational Medicine* sheds new light on this process: scientists found the virus in the ventricles—cavities in the brain that produce and circulate cerebrospinal fluid (CSF)—of several macaques that were treated for and appeared to have made complete recoveries from Ebola.

Over the course of the study, Zeng and his team infected 36 rhesus macaques (*Macaca mulatta)* with Ebola, treated them with monoclonal antibodies, and monitored their plasma and CSF for the presence of Ebola RNA using quantitative reverse transcription PCR (RT-qPCR).

According to those RT-qPCR analyses, seven of the macaques had elevated levels of Ebola RNA and Ebola antigens in their CSF two and four weeks after initial virus exposure, indicating dormant or persistent infections. Two of those seven macaques suddenly fell ill, dying 30 and 39 days, respectively, after being infected with the virus and roughly two weeks after having made what seemed like a complete recovery. Meanwhile, most macaques in the experiment survived for about four months after infection, then were euthanized.

After the macaques were euthanized, the researchers stained samples from their brains and those of the two monkeys that had died of Ebola. They observed the presence of Ebola RNA and Ebola antigens in the brain ventricles of the seven macaques with persistent infections.

In the two monkeys that died of the disease, the virus seemed to be gone about 12 days after first exposure, says lead study author Xiankun Zeng, a researcher at the United States Army Medical Research Institute of Infectious Diseases (USAMRIID), but "several days before their deaths, the monkeys got a fever." The pathology was only in the ventricular system of the brain, he explains, where the researchers observed "massive infections" and "massive tissue damage and inflammation." All other organs were normal.

Macaque models are considered the gold standard for Ebola research, Zeng explains, and any new therapeutics must be tested on the monkeys rather than mice or other animals due to the macaques' close biological similarity to humans.

While there has yet to be a study showing that Ebola lurks in the ventricles of a human brain, Zeng explains that at least one relapse case linked to the virus in a survivor's brain has been reported. Thus, he says he's confident that in humans as well as in macaques,

the virus invades cerebrospinal fluid in the brain.

The discovery has important implications for both public health initiatives and clinical care for individual patients, says Zeng. He explains that multiple devastating Ebola outbreaks from the past decade have been linked to persistent infections from a previous one. For example, an Ebola outbreak in 2021 began after the disease re-emerged from a survivor who initially became sick five years prior, a recent *Nature* study found. A better understanding of how such relapse infections occur could lead to more effective strategies for preventing future outbreaks.

Furthermore, the macaques in Zeng's study were treated with the same monoclonal antibody cocktails currently approved for use in humans. That could suggest that current treatment protocols need to be updated to completely root out the virus from the body.

Miles Carroll, an emerging viruses researcher at the University of Oxford who didn't work on the study, tells *The Scientist* over email that the paper "provides unique insights into the cell types within the brain environment, that support [Ebola] persistence."

However, he says there are higher priorities than individual relapsing infections when it comes to containing Ebola, noting that "the more likely route of [Ebola virus disease] survivor human-to-human transmission has been shown to be sexual transmission, mediated by infected semen."

University College Cork biochemist Anne Moore, who also didn't work on the new study, has a different take, telling *The Scientist* over email that "if this persistent [Ebola] infection, that occurs in about 20% of [monoclonal antibody]–treated animals, is reflected in even a fraction of human cases, then this warrants serious attention, given that these [antibodies] are authorized for use."

Moore adds that she'd like to see follow-up research to further clarify the molecular dynamics at play, suggesting that researchers replicate the experiment using macaque monoclonal antibodies instead of human ones to see if it alters the outcomes.

"Our study highlights the importance of careful, long-term follow-up of disease survivors to prevent, diagnose, or treat recrudescent disease that comes at an enormous individual and public health cost," Zeng says.

Zeng adds that public health officials and others handling the follow-up work will need to take great care to avoid further stigmatizing survivors. A 2015 letter in the *International Journal of Health Policy Management* describes how fear and stigma represent major challenges to understanding Ebola and bringing outbreaks under control. Additionally, the authors argue that Western researchers have put local communities in Liberia, Guinea, and Sierra Leone—all nations affected by Ebola outbreaks—on edge by taking approaches rooted in colonialism and by failing to share new medical knowledge with the regions that are actually being hit by the disease. In order to conduct the long-term study that Zeng recommends, researchers would need to win public trust in regions affected by Ebola.

Down the road, Zeng suggests that a new, improved combination of therapeutics, likely monoclonal antibodies coupled with an antivirus treatment with better penetration, "may help clear Ebola persistency from the brain, eyes, and testes" and prevent the kind of relapse he uncovered in his study. Moore adds that perhaps the antibodies could be re-engineered in order to reduce the risk of persistent infections.

Carroll agrees with Zeng, saying that "there is an urgent need to develop practical in vivo models to assess the efficacy of small molecule therapeutics to penetrate immune privileged sites, especially the testes, and inactivate persistent [Ebola]. In the absence of such therapies, [Ebola virus disease] survivors may continue to be a potential source of future human-to-human transmission."

https://go.nature.com/3GIhXeN

Earth-like planet spotted orbiting Sun's closest star

Shifts in starlight from Proxima Centauri, observed over more than 2 years, reveal its third planet.

Davide Castelvecchi

Astronomers have discovered a third planet orbiting Proxima Centauri, the star closest to the Sun. Called Proxima Centauri d, the newly spotted world is probably smaller than Earth, and could have oceans of liquid water.

"It's showing that the nearest star probably has a very rich planetary system," says Guillem Anglada-Escudé, an astronomer at the Institute of Space Sciences in Barcelona, Spain, who led the team that, in 2016, discovered the first planet to be seen orbiting Proxima Centauri.

Astronomer João Faria and his collaborators detected Proxima Centauri d by measuring tiny shifts in the spectrum of light from the star as the planet's gravity pulled at it during orbit. The team used a state-of-the art instrument called the Echelle Spectrograph for Rocky Exoplanets and Stable Spectroscopic Observations (ESPRESSO) at the Very Large Telescope, a system of four 8.2-metre telescopes at the European Southern Observatory in Cerro Paranal, Chile. The results were published on 10 February in *Astronomy & Astrophysics*[1].

This 'wobble' technique look for changes in the star's motion along the line of sight from Earth; ESPRESSO can detect variations of just 10 centimetres per second. The total effect of the planet's orbit, which takes only 5 days, is about 40 centimetres per second, says Faria, who is at the Institute of Astrophysics and Space Sciences of the University of Porto in Portugal. "I knew that ESPRESSO could do this, but I was still surprised to see it showing up." .

To find the wobble, the team made more than 100 observations of Proxima Centauri's spectrum over a little more than 2 years. ESPRESSO is kept in a special room at the observatory, inside a tank that keeps its pressure and temperature constant. This ensures that its measurements are consistent and repeatable over years. ESPRESSO can measure the wavelength of spectral lines with a precision of 10^{-5} ångströms, or one-ten-thousandth of the diameter of a hydrogen atom, Faria says.

Provisional planet

So far, researchers consider Proxima Centauri d only a 'planet candidate': astronomers conventionally wait for independent confirmation before officially introducing a new world into their catalogues. But the ESPRESSO team has high confidence in the detection, says Faria. From its effects on the star's spectrum, the team estimates that the planet is probably smaller than Earth, but no less than 26% of our planet's mass.

ESPRESSO was built mainly to search for extrasolar planets, as well as to study light from extremely bright but distant objects called quasars. The most exciting thing about the latest discovery is that it shows that the instrument works as advertised, says Anglada-Escudé. "ESPRESSO is the new instrument which everyone wants to use and play with," he says.

Proxima Centauri has a special place in astronomers' hearts, he adds. "It always has a little bit of mystique, being the closest one."

"It is fascinating to know that our Sun's nearest stellar neighbour is the host to three small planets," says Elisa Quintana, an astrophysicist at NASA's Goddard Space Flight Center in Greenbelt, Maryland. "Their proximity make this a prime system for further study, to understand their nature and how they likely formed."

Faria admits that even though interstellar travel is still in the realm of science fiction, the dream that people could one day visit our nearest star motivates him to look for Earth-like planets there. "It does make you wonder," he says.

doi: https://doi.org/10.1038/d41586-022-00400-3

Updates & Corrections

Correction 11 February 2022*: An earlier version of this article said that the planet was orbiting in Proxima Centauri's habitable zone. The planet is in fact outside the habitable zone as defined in this paper.*

References *1. Faria, J. P. et al. Astron. Astrophys.* ***658****, A115 (2022).* *Article Google Scholar Download references*

https://bit.ly/3uMjIoU

Catalyst turns carbon dioxide into gasoline 1,000 times more efficiently

Ruthenium-based catalyst produces longer chain hydrocarbons, like butane, propane and ethane

by Andrew Myers, Stanford University

Engineers working to reverse the proliferation of greenhouse gases know that in addition to reducing carbon dioxide emissions we will also need to remove carbon dioxide from power plant fumes or from the skies. But, what do we do with all that captured carbon? Matteo Cargnello, a chemical engineer at Stanford University, is working to turn it into other useful chemicals, such as propane, butane or other hydrocarbon fuels that are made up of long chains of carbon and hydrogen.

"We can create gasoline, basically," said Cargnello, who is an assistant professor of chemical engineering. "To capture as much carbon as possible, you want the longest chain hydrocarbons. Chains with eight to 12 carbon atoms would be the ideal."

A new catalyst, invented by Cargnello and colleagues, moves toward this goal by increasing the production of long-chain hydrocarbons in chemical reactions. It produced 1,000 times more butane—the longest hydrocarbon it could produce under its maximum pressure—than the standard catalyst given the same amounts of carbon dioxide, hydrogen, catalyst, pressure, heat and time.

The new catalyst is composed of the element ruthenium—a rare transition metal belonging to the platinum group—coated in a thin layer of plastic. Like any catalyst, this invention speeds up chemical reactions without getting used up in the process. Ruthenium also has the advantage of being less expensive than other high-quality catalysts, like palladium and platinum.

Cargnello and his team describe the catalyst and the results of their experiments in their latest paper, published this week in the journal *Proceedings of the National Academy of Sciences*.

Cargnello and his team took seven years to discover and perfect the new catalyst. The hitch: The longer the hydrocarbon chain is, the more difficult it is to produce. The bonding of carbon to carbon requires heat and great pressure, making the process expensive and energy intensive.

In this regard, the ability of the new catalyst to produce gasoline from the reaction is a breakthrough, said Cargnello. The reactor in his lab would need only greater pressure to produce all the long-chain hydrocarbons for gasoline, and they are in the process of building a higher pressure reactor.

Gasoline is liquid at room temperature and, therefore, much easier to handle than its gaseous short-chain siblings—methane, ethane and propane—which are difficult to store and prone to leaking back into the skies.

Cargnello and other researchers working to make liquid fuels from captured carbon imagine a carbon-neutral cycle in which carbon dioxide is collected, turned into fuel, burned again and the resulting carbon dioxide begins the cycle anew.

Perfecting the polymer

The key to the remarkable increase in reactivity is that layer of porous plastic on the ruthenium, explained lead student author Chengshuang Zhou, a doctoral candidate in Cargnello's lab, who conducted the search and experimentation needed to refine the new coating.

An uncoated catalyst works just fine, he said, but only produces methane, the shortest chain hydrocarbon, which has just a single atom of carbon bonded to four hydrogens. It's not really a chain at all.

"An uncoated catalyst gets covered in too much hydrogen on its surface, limiting the ability of carbon to find other carbons to bond with," Zhou said.

"The porous polymer controls the carbon-to-hydrogen ratio and allows us to create longer carbon chains from the same reactions. This particular, crucial interaction was demonstrated using synchrotron techniques at SLAC National Laboratory in collaboration with the team of Dr. Simon Bare, who leads Co-Access there."

While long-chain hydrocarbons are an innovative use of captured carbon, they are not perfect, Cargnello acknowledges.

He is also working on other catalysts and similar processes that turn carbon dioxide into valuable industrial chemicals, like olefins used to make plastics, methanol and the holy grail, ethanol, all of which can sequester carbon without returning carbon dioxide to the skies.

"If we can make olefins from CO_2 to make plastics," Cargnello noted, "we have sequestered it into a long-term storable solid. That would be a big deal."

More information: *Chengshuang Zhou et al, Steering CO2 hydrogenation toward C–C coupling to hydrocarbons using porous organic polymer/metal interfaces, Proceedings of the National Academy of Sciences (2022). DOI: 10.1073/pnas.2114768119*

https://bit.ly/3uGqu6u

Sauro-Throat! Study finds first evidence indicating dinosaur respiratory infection

Fossilized remains of an immature diplodocid may provide the first evidence of a unique respiratory infection in a dinosaur

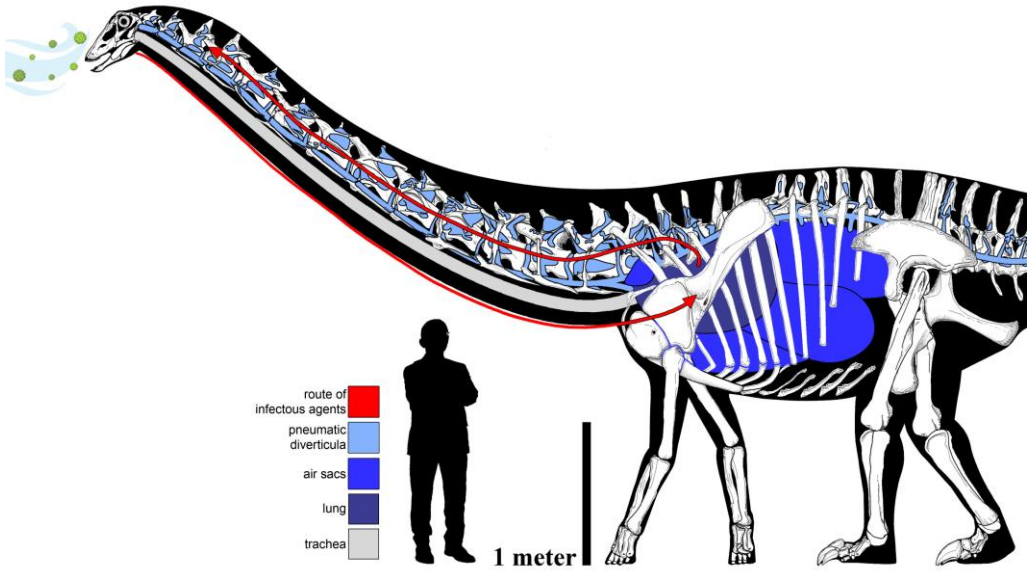
The fossilized remains of an immature diplodocid—a large, long-necked herbivorous sauropod dinosaur, like Brontosaurus—may provide the first evidence of a unique respiratory infection in a dinosaur, according to a study published in *Scientific Reports*. The findings increase our understanding of the illnesses that affected dinosaurs.

The specimen, nicknamed "Dolly," was discovered in southwest Montana, U.S., and dates back to the Late Jurassic Period of the Mesozoic Era (approximately 150 million years ago). Cary Woodruff of the Great Plains Dinosaur Museum in Malta, along with his colleagues, examined three of the cervical vertebrae (the bones from the neck) from Dolly and identified never-before-seen abnormal bony protrusions that had an unusual shape and texture. These protrusions were located in an area of each bone where they would have been penetrated by air-filled sacs. These air sacs would have ultimately connected to Dolly's lungs and formed part of the dinosaur's complex respiratory system. CT imaging of the irregular protrusions revealed that they were made of abnormal bone that most likely formed in response to an infection.

"Given the likely symptoms this animal suffered from, holding these infected bones in your hands, you can't help but feel sorry for Dolly," Woodruff said. "We've all experienced these same symptoms—coughing, trouble breathing, a fever, etc. – and here's a 150-million-year-old dinosaur that likely felt as miserable as we all do when we're sick."

Based on the location of these abnormal bony protrusions, the researchers suggest that they formed in response to a respiratory infection in Dolly, which ultimately spread into these neck vertebrae via the air sacs and caused the irregular bone growths. The authors speculate that this respiratory infection could have been caused by a fungal infection similar to aspergillosis, a common respiratory illness that affects birds and reptiles today and can lead to bone infections. In addition to documenting the first occurrence of such a respiratory infection in a dinosaur, this fossilized infection

also has important anatomical implications for the respiratory system of sauropod dinosaurs.



The elaborate and circuitous pulmonary complex of the sauropod, with the hypothetical route of infectious pathway in MOR 7029. Human scale bar is the profile of a man standing 170cm tall. **Credit: Woodruff, et al., and Francisco Bruñén Alfaro.**

"This fossil infection in Dolly not only helps us trace the evolutionary history of respiratory-related diseases back in time, but gives us a better understanding of what kinds of diseases dinosaurs were susceptible to," Woodruff said.

The researchers suggest that if Dolly had been infected with an aspergillosis-like respiratory infection, it likely experienced flu or pneumonia-like symptoms such as weight loss, coughing, fever, and breathing difficulties. As aspergillosis can be fatal in birds if untreated, a potentially similar infection in Dolly could have ultimately caused the death of the animal, they add.

In addition to Woodruff, the research team included a paleopathologist/veterinarian, Ewan Wolff (University of New Mexico); a veterinarian, Sophie Dennison (TeleVet Imaging Solutions, Oakton, Va.); and two paleontologists who are also medical anatomists, Mathew Wedel (Western University of Health Sciences, Pomona, Calif.) and Lawrence Witmer (Ohio University Heritage College of Osteopathic Medicine, Athens, Ohio).

More information: *Cary Woodruff, The first occurrence of an avian-style respiratory infection in a non-avian dinosaur, Scientific Reports (2022). DOI: 10.1038/s41598-022-05761-3. www.nature.com/articles/s41598-022-05761-3*

https://bit.ly/3sCeAkB

Research team finds clue to possible extraterrestrial origin of peptides

Researchers show that peptides can form on dust under conditions such as those prevailing in outer space

by Friedrich Schiller University of Jena

Dr Serge Krasnokutski studies the formation of biomolecules at low temperature in a vacuum. Credit: Jens Meyer/University of Jena

Researchers from the Friedrich Schiller University Jena and the Max Planck Institute for Astronomy have discovered a new clue in the search for the origin of life, by showing that peptides can form on dust under conditions such as those prevailing in outer space. These molecules, which are one of the basic building blocks of all life, may therefore not have originated on our planet at all, but possibly in cosmic molecular clouds.

Chains of amino acids

All life as we know it consists of the same chemical building blocks. These include peptides, which perform various completely different functions in the body—transporting substances, accelerating reactions or forming stabilizing scaffolds in cells. Peptides consist of individual amino acids arranged in a specific order. The exact order determines a peptide's eventual properties.

How these versatile biomolecules came into being is one of the questions about the origin of life. Amino acids, nucleobases and various sugars found in meteoroids, for example, show that this origin could be extraterrestrial in nature. However, for a peptide to be formed from individual amino acid molecules requires very

special conditions that were previously assumed to be more likely to exist on Earth.

The first step requires water, while for the second step, there must be no water

"Water plays an important role in the conventional way in which peptides are created," says Dr. Serge Krasnokutski of the Laboratory Astrophysics and Cluster Physics Group of the Max Planck Institute for Astronomy at the University of Jena. In this process, individual amino acids combine to form a chain. For this to happen, one water molecule must be removed each time. "Our quantum chemical calculations have now shown that the amino acid glycine can be formed through a chemical precursor—called an amino ketene—combining with a water molecule. Put simply: In this case, water must be added for the first reaction step, and water must be removed for the second."

With this knowledge, the team led by the physicist Krasnokutski has now been able to demonstrate a reaction pathway that can take place under cosmic conditions and does not require water.

"Instead of taking the chemical detour in which amino acids are formed, we wanted to find out whether amino ketene molecules could not be formed instead and combine directly to form peptides," says Krasnokutski, describing the basic idea behind the work. He adds, "And we did this under the conditions that prevail in cosmic molecular clouds, that is to say, on dust particles in a vacuum, where the corresponding chemicals are present in abundance: Carbon, ammonia and carbon monoxide."

In an ultra-high vacuum chamber, substrates that serve as a model for the surface of dust particles were brought together with carbon, ammonia and carbon monoxide at about one quadrillionth of normal air pressure and minus 263 degrees Celsius.

"Investigations showed that under these conditions, the peptide polyglycine was formed from the simple chemicals," Krasnokutski says. "These are therefore chains of the very simple amino acid glycine, and we observed different lengths. The longest specimens consisted of eleven units of the amino acid."

In this experiment, the German team was also able to detect the suspected amino ketene. "The fact that the reaction can take place at such low temperatures at all is due to the amino ketene molecules being extremely reactive. They combine with each other in an effective polymerization. The product of this is polyglycine."

Quantum mechanical tunneling effect might play a role

"It was nevertheless surprising to us that the polymerization of amino ketene could happen so easily under such conditions," says Krasnokutski. "This is because an energy barrier actually has to be overcome for this to happen. However, it may be that we are helped in this by a special effect of quantum mechanics. In this special reaction step, a hydrogen atom changes its place. However, it is so small that as a quantum particle, it could not overcome the barrier but was simply able to cross it, so to speak, through the tunneling effect."

Now that it is clear that not only amino acids, but also peptide chains, can be created under cosmic conditions, we may have to look not only to Earth but also more into space when researching the origin of life.

More information: *Sergiy Krasnokutski, A pathway to peptides in space through the condensation of atomic carbon, Nature Astronomy (2022). DOI: 10.1038/s41550-021-01577-9. www.nature.com/articles/s41550-021-01577-9*

https://bit.ly/3Bqd0ZG

Long COVID Could Be Linked to the Effects of SARS-CoV-2 on the Vagus Nerve

Could be linked to the effect of the virus on one of the most important multi-functional nerves in the body

New research to be presented at this year's European Congress of Clinical Microbiology and Infectious Diseases (ECCMID 2022,

Lisbon, April 23-26) suggests that many of the symptoms connected to post-COVID syndrome (PCC, also known as long COVID) could be linked to the effect of the virus on the vagus nerve – one of the most important multi-functional nerves in the body. The study is by Dr. Gemma Lladós and Dr. Lourdes Mateu, University Hospital Germans Trias i Pujol, Badalona, Spain, and colleagues.

The vagus nerve extends from the brain down into the torso and into the heart, lungs, and intestines, as well as several muscles including those involved in swallowing. As such, this nerve is responsible for a wide variety of bodily functions including controlling heart rate, speech, the gag reflex, transferring food from the mouth to the stomach, moving food through the intestines, sweating, and many others.

Long COVID is a potentially disabling syndrome affecting an estimated 10-15% of subjects who survive COVID-19. The authors propose that SARS-CoV-2-mediated vagus nerve dysfunction (VND) could explain some long COVID symptoms, including dysphonia (persistent voice problems), dysphagia (difficulty in swallowing), dizziness, tachycardia (abnormally high heart rate), orthostatic hypotension (low blood pressure) and diarrhea.

The authors performed a pilot, extensive morphological and functional evaluation of the vagus nerve, using imaging and functional tests in a prospective observational cohort of long COVID subjects with symptoms suggestive of VND. In their total cohort of 348 patients, 228 (66%) had at least one symptom suggestive of VND. The current evaluation was performed in the first 22 subjects with VND symptoms (10% of the total) seen in the Long COVID Clinic of University Hospital Germans Trias i Pujol between March and June 2021. The study is ongoing and continues to recruit patients.

Of the 22 subjects analyzed, 20 (91%) were women with a median age of 44 years. The most frequent VND-related symptoms were: diarrhea (73%), tachycardia (59%), dizziness, dysphagia and dysphonia (45% each), and orthostatic hypotension (14%). Almost all (19 subjects, 86%) had at least 3 VND-related symptoms. The median prior duration of symptoms was 14 months. Six of 22 patients (27%) displayed alteration of the vagus nerve in the neck shown by ultrasound – including both thickening of the nerve and increased 'echogenicity' which indicates mild inflammatory reactive changes.

A thoracic ultrasound showed flattened 'diaphragmatic curves' in 10 out of 22 (46%) subjects (which translates a decrease in diaphragmatic mobility during breathing, or more simply abnormal breathing). A total of 10 of 16 (63%) assessed individuals showed reduced maximum inspiration pressures, showing weakness of breathing muscles.

Eating and digestive function was also affected in some patients, with 13 of 18 assessed (72%) having a positive screen for self-perceived oropharyngeal dysphagia (trouble swallowing). An assessment of gastric and bowel function performed in 19 patients revealed 8 (42%) had their ability to deliver food to the stomach (via the esophagus) impaired, with 2 of these 8 (25%) reporting difficulty in swallowing. Gastroesophageal reflux (acid reflux) was observed in 9 of 19 (47%) individuals; with 4 of these 9 (44%) again having difficulty delivering food to the stomach and 3 of these 9 (33%) with hiatal hernia – which occurs when the upper part of the stomach bulges through the diaphragm into the chest cavity.

A Voice Handicap Index 30 test (a standard way to measure voice function) was abnormal in 8/17 (47%) cases, with 7 of these 8 cases (88%) suffering dysphonia.

The authors say: "In this pilot evaluation, most long COVID subjects with vagus nerve dysfunction symptoms had a range of

significant, clinically-relevant, structural and/or functional alterations in their vagus nerve, including nerve thickening, trouble swallowing, and symptoms of impaired breathing. Our findings so far thus point at vagus nerve dysfunction as a central pathophysiological feature of long COVID."

Meeting: The European Congress of Clinical Microbiology & Infectious Diseases (ECCMID 2022)

https://bit.ly/3oLd8vh

Frequent Use of Aspirin, Advil, or Tylenol Associated With Higher Risk of Tinnitus

Frequent use of moderate-dose aspirin was associated with a 16 percent higher risk among women under 60

Over-the-counter (OTC) analgesics, such as aspirin, non-steroidal anti-inflammatory drugs (NSAIDS), and acetaminophen, are some of the most commonly used medications, widely available without a prescription, and perceived to be safe. But frequent use — including inadvertently exceeding a recommended dose when taking cold and sinus medications that contain these analgesics — can potentially cause harm.

Very high doses of aspirin can lead to reversible tinnitus, but a new longitudinal study, led by investigators at Brigham and Women's Hospital, investigated whether frequent use of typical doses of common analgesics, including low-dose and moderate-dose aspirin, NSAIDs and acetaminophen, or use of prescription COX-2 inhibitors, is independently associated with the risk of developing chronic persistent tinnitus.

In a paper published in the *Journal of General Internal Medicine*, the researchers report that frequent use of NSAIDs or acetaminophen, or regular use of COX-2 inhibitors, was associated with higher risk of tinnitus. Low-dose aspirin use did not elevate risk, but frequent moderate-dose aspirin use was associated with higher risk of persistent tinnitus among women under 60.

"Our findings suggest that analgesic users may be at higher risk for developing tinnitus and may provide insight into the precipitants of this challenging disorder," said lead author Sharon Curhan, MD, ScM, of the Brigham's Channing Division of Network Medicine. "Even though these analgesics are widely available without a prescription, these are still medications, and there are potential side effects. For anyone who is considering taking these types of medications regularly, it is advisable to consult with a health care professional to discuss the risks and benefits and to explore whether there are alternatives to using medication."

Millions of Americans experience tinnitus, often to a disabling degree. Tinnitus is the perception of sound when no actual external noise is present. Commonly described as "ringing in the ears," tinnitus can also be experienced as many different perceptions of sound, such as buzzing, hissing, whistling, swooshing, and clicking. Tinnitus can be transient or temporary, or it can be a persistent, long-term condition.

According to Curhan, tinnitus is a common condition, potentially disabling, yet difficult to treat. In the US, about 20 million people struggle with burdensome chronic tinnitus, and approximately 3 million individuals are severely disabled by it. Among most individuals with tinnitus, the cause of their tinnitus is unknown, and the effectiveness of treatments is limited.

Curhan and colleagues conducted their research among 69,455 women who were participants in the Nurses' Health Study II (NHSII) as part of the Conservation of Hearing Study (CHEARS), a large, ongoing longitudinal investigation that examines risk factors for hearing loss and tinnitus among participants in several large, ongoing prospective cohort studies. Women were between the ages of 31 and 48 at the time of enrollment and were followed for over 20 years.

The primary outcome examined was incident (new onset) persistent

tinnitus, defined as tinnitus that was experienced by the participant several days per week or more. The team also examined alternative definitions of tinnitus, including persistent tinnitus lasting 5 minutes or longer and tinnitus experienced every day.

Participants answered questions (before the development of tinnitus) about their use of over-the-counter pain medications as well as use of COX-2 inhibitors, a prescription NSAID with similar properties to other NSAIDS but with less gastrointestinal side effects.

The team found:

** Frequent use (6 to 7 days per week) of **moderate-dose aspirin** was associated with a 16 percent higher risk of tinnitus among women aged less than 60 but not among older women.*

** Frequent **low-dose aspirin** (=100 mg) was not associated with elevated risk of developing tinnitus.*

** Frequent use of **NSAIDs** or frequent use of **acetaminophen** was associated with an almost 20 percent higher risk of developing tinnitus, and the magnitudes of the elevated risks tended to be greater with more frequent use.*

** Regular use (2 or more days per week) of **COX-2 inhibitors** was associated with a 20 percent higher risk of developing tinnitus as well.*

The authors note that information on tinnitus and on analgesic use was self-reported by participants. Due to the nature of the condition, subjective tinnitus is perceived only by the individual, so the researchers needed to rely on self-reporting. The observational design of the study did not permit them to assign causality. The study population was primarily white, and all participants were female, so additional study of non-white populations and men is needed.

"Based on these findings, it will be informative to examine whether avoidance of analgesics may help alleviate tinnitus symptoms," said Curhan. "OTC analgesics clearly have benefits with short-term use. However, frequent use of these medications and use over long periods of time may increase the risk of tinnitus and may cause other adverse health effects. Therefore, it is important to take these medications mindfully and to limit their use as much as possible, and to discuss any change in medication use, whether prescription or non-prescription, with your health-care provider."

Reference: "Longitudinal Study of Analgesic Use and Risk of Incident Persistent Tinnitus" by Sharon G. Curhan MD, ScM, Jordan Glicksman MD, MPH, Molin Wang PhD, Roland D. Eavey MD, SM and Gary C. Curhan MD, ScD, 7 February 2022, Journal of General Internal Medicine. DOI: 10.1007/s11606-021-07349-5

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https://bit.ly/3sA5h4N

New Drug Could Prevent Tumor Metastasis by Putting Cancer Cells to Sleep

Therapeutic approach prevents growth of metastatic tumors in mice by forcing cancer cells into a dormant state

A new therapeutic approach prevents the growth of metastatic tumors in mice by forcing cancer cells into a dormant state in which they are unable to proliferate. The study, published in the *Journal of Experimental Medicine* (*JEM*), could lead to new treatments that prevent the recurrence or spread of various cancer types, including breast cancer and head and neck squamous cell carcinoma (HNSCC).

Many cancer patients relapse, often years or decades after their initial treatment, and develop new tumors that regrow in the same location or metastasize (spread) to other parts of the body.

These secondary tumors are often resistant to treatment and are produced by individual tumor cells that may remain dormant for long periods before being reactivated to start proliferating again.

Patient relapse might therefore be prevented if researchers could find a way to keep remaining cancer cells in a dormant state.

In a previous study, Maria Soledad Sosa from the Icahn School of Medicine at Mount Sinai and Julio A. Aguirre-Ghiso, now at Albert Einstein College of Medicine, discovered that the ability of cancer cells to remain dormant is controlled by a protein called NR2F1 (Nuclear Receptor Subfamily 2 Group F Member 1).

This receptor protein can enter the cell nucleus and turn numerous genes on or off to activate a program that prevents the cancer cells from proliferating. NR2F1 levels are usually low in primary tumors but are elevated in dormant disseminated cancer cells.

Levels of the NR2F1 protein then decline once more when cancer cells start proliferating again and form recurrent or metastatic tumors.

"We therefore thought that activating NR2F1 using a small molecule could be an attractive clinical strategy to induce cancer cell dormancy and prevent recurrence and metastasis," Aguirre-Ghiso explains.

In the new *JEM* study, Sosa and Aguirre-Ghiso's teams used a computer-based screening approach to identify a drug, named C26, that activates NR2F1. The researchers found that treating patient-derived HNSCC cells with C26 boosted the levels of NR2F1 and arrested cell proliferation.

The researchers then tested whether C26 would prevent metastasis in mice. Animals injected with patient-derived HNSCC cells typically form large primary tumors that spread to the lungs after the original tumor is surgically removed. Treatment with C26 reduced the size of primary tumors, and, after surgery, further doses of C26 completely blocked the growth of metastatic tumors. Instead, the rodent's lungs contained just a few dormant disseminated cancer cells unable to proliferate even after cessation of the treatment.

Sosa and Aguirre-Ghiso's teams determined that, by activating NR2F1, C26 forces cancer cells into a long-lived state of dormancy characterized by a unique pattern of gene activity.

Cancer patients whose tumors display a similar pattern of gene activity tend to go longer without relapsing, suggesting that inducing this dormancy program with C26-type drugs could be effective in humans.

"Drugs that activate NR2F1 might be particularly useful in breast cancer," says Sosa. "NR2F1 is highly enriched in ER-positive tumors when compared to ER-negative tumors, and activating NR2F1 might be able to suppress reawakening of dormant cancer cells kept in that state by anti-estrogen therapies."

However, because C26 treatment elevates the levels of NR2F1, the approach may also be useful for other cancers with inherently low levels of the receptor protein.

"Overall, our study reveals a mechanism-based and rationally designed strategy to exploit NR2F1-activated dormancy as a therapeutic option to prevent metastatic relapse," Aguirre-Ghiso says.

Reference: "An NR2F1-specific agonist suppresses metastasis by inducing cancer cell dormancy" by Bassem D. Khalil, Roberto Sanchez, Tasrina Rahman, Carolina Rodriguez-Tirado, Stefan Moritsch, Alba Rodriguez Martinez, Brett Miles, Eduardo Farias, Mihaly Mezei, Ana Rita Nobre, Deepak Singh, Nupura Kale, Karl Christoph Sproll, Maria Soledad Sosa and Julio A. Aguirre-Ghiso, 23 November 2021, Journal of Experimental Medicine. DOI: 10.1084/jem.20210836

https://bit.ly/3HJyqAK

Book Excerpt from *On the Trail of the Jackalope*

In chapter 8, "Dr. Shope's Warty Rabbits," author Michael P. Branch describes the scientist who unearthed the viral cause of strange growths on wild rabbits.

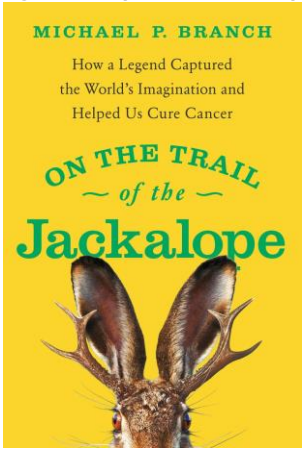
Michael P. Branch

In 1932, virologist Richard E. Shope became aware of stories of wild cottontails stricken with a disease that resulted in unusual

growths on the animals that, he wrote, were "referred to popularly as 'horned' or 'warty' rabbits." Like Richard Shope, fellow virologist Ludwik Gross was a proponent of the then-controversial theory that some cancers are caused by viruses. In his 1961 book *Oncogenic Viruses* (the first history of tumor virology), Gross included the following story, told in Shope's own words, reprinted with Shope's permission from his unpublished notes:

The father of the wife of one of our staff members was visiting his daughter in Princeton shortly after I had started my experiments with the rabbit fibroma. This old gentleman was from Iowa and was quite a hunter out there. Because of this, his daughter had asked me if I would show her father the tumor that I had gotten from one of our New Jersey rabbits.

I showed him what I considered a good example. He looked at it disdainfully and said that this was nothing compared with the sort of things that they had in the Iowa rabbits. He said he had shot rabbits with horns out of the side of their heads like Texas steers, or out of the top of their noses like a rhinoceros. Naturally, I was intrigued by this colorful description and speculated as to what the character of these growths might be.



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When the hunter (T. A. McKichan, of Cherokee, Iowa) reported that such beasts were not uncommon in his home state, Shope traveled to back Iowa with him and spent several days hunting for horned rabbits. Failing to shoot any diseased cottontails, Shope initiated a contingency plan:

We had a young boy by the name of Cliff Peck hunting with us, so when at the end of four days I had to return to Princeton empty-handed, I left a bottle of glycerol and a five dollar bill with Cliff and told him that if he would get me the horns of one of these rabbits and send them to me in glycerol, I would give him another five dollars. Needless to say, Cliff really scoured the underbrush for rabbits and within the course of a week I had my bottle of glycerol back and in it were several so-called horns from a cottontail rabbit shot near Cherokee.

Having studied the horns, sent to him in a 50 percent glycerol solution, Shope asked his contacts in Iowa and Kansas to procure him specimens of the anomalous rabbits if they could. A frantic search for diseased rabbits must have ensued, as a shipment of a dozen wild cottontails soon arrived in Princeton from Kansas, and before long Shope had received a total of seventy-five cottontails from the Midwest. Upon investigation, he discovered that eleven of those seventy-five animals were stricken with the same naturally occurring disease.

Shope now turned his full attention to the mystery of the "warty" rabbits. First, he devised a relatively simple experiment to test his unorthodox theory that the rabbits' odd "horns" were tumors caused by an unidentified virus. He removed and pulverized the horns, mixing the resulting material in a solution, which he strained through a porcelain filter so fine as to allow only viruses to pass through. If no virus was present in the resulting filtered solution, the solution would remain sterile. But when Shope rubbed the material that had passed through the filter onto the scarified skin of healthy rabbits—both cottontails and domestic rabbits—they subsequently grew horns! The results of this research on the diseased cottontails, published in his landmark 1933 article "Infectious Papillomatosis of Rabbits" published in *The Journal of Experimental Medicine*, demonstrated clearly that the grotesque excrescences on the cottontails were indeed caused by a previously unknown viral infection.

Shope had proven that the "horn" of the diseased rabbit resulted

from infection by what would come to be called Shope papillomavirus. But he went further, documenting in detail the powerful neutralizing properties of the sera from infected rabbits. In a series of over one hundred wild and domestic rabbits which were experimentally administered the virus, not a single animal displayed natural immunity. Once rabbits were infected, however, they developed antibodies capable of resisting the virus. It was an immensely important finding. In the conclusion to his trailblazing 1933 article, Shope wrote that "Rabbits carrying experimentally produced papillomata are partially or completely immune to reinfection and, furthermore, their sera partially or completely neutralize the causative virus." Shope had not only discovered and isolated the virus that caused the growth of the rabbit's horns, he had also proven that the antibodies produced by stricken rabbits could effectively prevent reinfection. This latter discovery would open the door to new and even more exciting possibilities.

Shope's research on the warty rabbits suggested that the virus-induced growths were actually a keratinous carcinoma: a potentially invasive tumorous cancer. The importance of Shope's horned rabbit research was not simply that it revealed the viral etiology of the diseased animals' mysterious growths, but that it established a crucial link between viruses and cancer in a mammal. His related studies on antibodies and resistance to viral reinfection hinted that the same virus that causes a certain type of cancer in a mammal might light the way toward development of an antiviral cancer vaccine. The work that followed from Shope's studies, carried out by researchers including Nobel laureates Peyton Rous and Harald zur Hausen, would ultimately prove what had been a controversial proposition: viruses cause some types of cancer. The eventual result of this line of research would be the human papillomavirus (HPV) vaccine, which, according to the American Cancer Society, can prevent more than 90% of HPV-caused cancers, including cancers of the cervix, vulva, vagina, penis, anus, mouth, tonsils, or throat.