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Common plant disease found to defend its host against pests

Ergot is toxic to humans and spoils the yields. However, it can be a beneficial protector for the plant.

Scientists from University of Turku observed that ergot, a common plant disease on rye, defended its host plant chemically against grass feeding insects. The ergot disease in grains spoils the yield and causes seed loss to the plant. Based on this, it is classified as harmful from the human perspective. A new study states that the ergot appears to be a beneficial protector for its host plant capable of even increasing plant fitness.

On an experimental field at the University of Turku Subarctic research station Kevo, the research team studied fungal symbionts of grasses and their effects on plant biotic threats such as herbivorous aphids and ergot disease.

In the study, scientists used a widely distributed grass species, red fescue, and its fungal [endophyte](#) in the genus *Epichloë*. Fungal endophytes are fungi living entirely or part of their life cycle inside their [host plants](#). This [symbiotic relationship](#) is commonly described as defensive mutualism which is characterized by [plants](#) providing nutrients to the fungus in exchange for protection against herbivory.

"*Epichloë* fungi are largely depending on their host plant for reproduction via the plant seeds. The fungal hyphae grows inside the plant up into the developing seeds, where it is spread to the developing new plant individuals. An endophyte like this would not survive without its host plant, which is why the plant wellbeing is in the interest of the symbiotic fungus," explains doctoral candidate Miika Laihonen.

Endophyte symbiosis increased the ergot infections of plant seeds—but the plant might benefit

The team observed whether the fungal endophyte affected the occurrence of herbivorous insects and fungal ergot infections in the study plants. The ergot fungus causes the ergot disease in grasses, including cereals. Thereby, the plant loses few of its seeds to the disease. The ergot-contaminated grain is toxic to humans and the ergot fungus is an unwelcomed guest on farmlands.

The researchers found that pest insect occurrence was not directly affected by the fungal endophyte but the ergot was more commonly detected on the plants with a fungal endophyte. Further analyses revealed that aphids rarely colonized plants infected by the ergot fungus. Thus, the endophyte indirectly repelled aphid herbivores by promoting ergot symbiosis. This was supported by the chemical analysis of the plants.

"Our first impression was that the fungal endophyte was harmful for the plant as it increased the probability of the plant getting infected by the ergot fungus. When we realized that the aphids avoided the ergot, we saw the results in a new light. Possibly the benefits of the ergot outweigh the harms," Laihonen says.

This is not the only time the ergot was found to repel animals in nature. An earlier study found that grazing sheep were avoiding feeding the inflorescences from plants that were infected by ergot. Thus, hosting the ergot fungus provides protection for the majority of viable [plant seeds](#) and may ultimately be a fitness advantage for the plant and the associated *Epichloë* endophyte.

"As humans, we have a natural tendency to judge the organisms from our own point of view. However, by doing so, we can miss a bigger picture. We classify the ergot [fungus](#) as a harmful plant pathogen because that is what it is for us. For the plant though, it can be a savior: by occupying very few seeds, the ergot can safeguard the rest of the next plant generation," explains Laihonen.

More information: Miika Laihonen et al, *Epichloë Endophyte-Promoted Seed Pathogen Increases Host Grass Resistance Against Insect Herbivory*, *Frontiers in Microbiology* (2022). [DOI: 10.3389/fmicb.2021.786619](https://doi.org/10.3389/fmicb.2021.786619)

<https://bit.ly/354cp0V>

430-year-old ninja weapons possibly identified

Several could be the forerunners to the well-known throwing star.

By [Owen Jarus](#)

Artifacts found in Japan may be ninja weapons, including several that look like they were the forerunner to the well-known throwing star, have been found at several sites, including two castles, scientists say.



Weapons found in two castles in Japan could be ninja weapons, with some of the weapons possibly being the forerunners to the throwing star. Here, a hand-colored illustration of mid-18th century Japan and two ninjas. (Image credit: Pictures From History/Universal Images Group via Getty Images)

Archaeologists excavated the artifacts between 1960 and 2010 at several Japan sites, including two castles — Iwatsuki Castle and Hachioji Castle. The possible ninja artifacts date to the Siege of Odawara which took place in 1590. During this siege, the Toyotomi and Tokugawa clans defeated the Hojo clan, which had controlled a sizable portion of Japan, and captured both castles.

The siege took place during the Sengoku period (1467-1615), a time when Japan was divided between several warlords who battled for power. Historical texts mention ninjas as spies and saboteurs during this time and they likely took part in the siege.

The artifacts include flat throwing stones that may have been the predecessor of the shuriken throwing star and clay caltrops that may be an early form of the makibishi caltrop — a spiky weapon that could injure the feet of soldiers and horses. These artifacts were likely the weapons of a "battle group which can move into action as ninjas," Iwata Akihiro, an archaeologist and curator at the Saitama Prefectural Museum of History and Folklore, told Live Science in

an email.

These weapons, Ahikiro told Live Science, were likely hastily constructed prior to the siege.

[This photo shows 430 year-old artifacts](#) that may be crude weapons associated with the ninja. (Image credit: Courtesy of Hachioji City History Museum)



Despite their hasty construction, however, both weapons would likely have been effective. The flat throwing stones "were used to stop the movement of the enemy who was going to attack [a soldier] at any moment, and while the enemy froze the soldier escaped," said Ahikiro. Meanwhile the clay caltrops could "stop the movement of the enemy who invaded the castle," Ahikiro said.

Despite being armed with the weapons, the Hojo clan's ninja were unable to save the castles, as they both fell to the far larger armies of the Toyotomi and Tokugawa clans. In 1615, the Tokugawa clan would succeed in uniting all of Japan under their rule, forming a shogunate that would hold power for centuries.

Live Science contacted several scholars not involved with the research; however, they either declined comment or did not respond at time of publication.

<https://bit.ly/36kSlbw>

West megadrought worsens to driest in at least 1,200 years

American West is now the driest in at least 1,200 years and is a worst-case climate change scenario

by Seth Borenstein

The American West's megadrought deepened so much last year that playing out live, a new study finds.

A dramatic drying in 2021—about as dry as 2002 and one of the driest years ever recorded for the region—pushed the 22-year drought past the previous record-holder for megadroughts in the

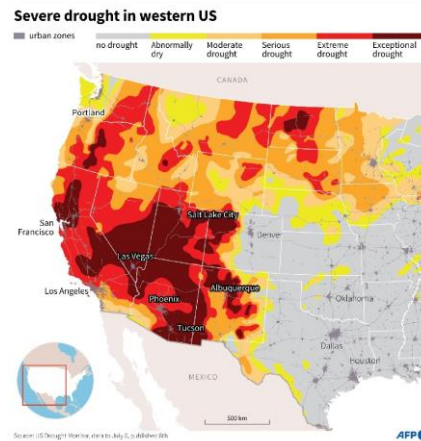
late 1500s and shows no signs of easing in the near future, according to a study Monday in the journal *Nature Climate Change*. The study calculated that 42% of this megadrought can be attributed to human-caused climate change.

"Climate change is changing the baseline conditions toward a drier, gradually drier state in the West and that means the worst-case scenario keeps getting worse," said study lead author Park Williams, a climate hydrologist at UCLA. "This is right in line with what people were thinking of in the 1900s as a worst-case scenario. But today I think we need to be even preparing for conditions in the future that are far worse than this."

Williams studied soil moisture levels in the West—a box that includes California, Wyoming, Utah, Nevada, Arizona, most of Oregon and Idaho, much of New Mexico, western Colorado, northern Mexico, and the southwest corners of Montana and Texas—using modern measurements and tree rings for estimates that go back to the year 800. That's about as far back as estimates can reliably go with tree rings.

A few years ago, Williams studied the current drought and said it qualified as a lengthy and deep "megadrought" and that the only worse one was in the 1500s. He figured the current drought wouldn't surpass that one because megadroughts tended to peter out after 20 years. And, he said, 2019 was a wet year so it looked like the western drought might be coming to an end.

Map showing drought intensity in the western United States.



But the region dried up in late 2020 and 2021.

All of California was considered in official drought from mid-May until the end of 2021, and at least three-quarters of the state was at

the highest two drought levels from June through Christmas, according to the U.S. drought monitor. "For this drought to have just cranked up back to maximum drought intensity in late 2020 through 2021 is a quite emphatic statement by this 2000s drought saying that we're nowhere close to the end," Williams said. This drought is now 5% drier than the old record from the 1500s, he said. The drought monitor says 55% of the U.S. West is in drought with 13% experiencing the two highest drought levels.

This megadrought really kicked off in 2002—one of the driest years ever, based on humidity and tree rings, Williams said.

"I was wondering if we'd ever see a year like 2002 again in my life and in fact, we saw it 20 years later, within the same drought," Williams said. The drought levels in 2002 and 2021 were a statistical tie, though still behind 1580 for the worst single year.

Climate change from the burning of fossil fuels is bringing hotter temperatures and increasing evaporation in the air, scientists say.

Williams used 29 models to create a hypothetical world with no human-caused warming then compared it to what happened in real life—the scientifically accepted way to check if an extreme weather event is due to climate change. He found that 42% of the drought conditions are directly from human-caused warming. Without climate change, he said, the megadrought would have ended early on because 2005 and 2006 would have been wet enough to break it. The study "is an important wake-up call," said Jonathan Overpeck, dean of environment at the University of Michigan, who wasn't part of the study. "Climate change is literally baking the water supply and forests of the Southwest, and it could get a whole lot worse if we don't halt climate change soon."

Williams said there is a direct link between drought and heat and the increased wildfires that have been devastating the West for years. Fires need dry fuel that drought and heat promote.

Eventually, this megadrought will end by sheer luck of a few good

rainy years, Williams said. But then another one will start.

Daniel Swain, a UCLA climate scientist who wasn't involved in the study, said climate change is likely to make megadrought "a permanent feature of the climate of the Colorado River watershed during the 21st century."

More information: A. Park Williams et al, *Rapid intensification of the emerging southwestern North American megadrought in 2020–2021*, *Nature Climate Change* (2022). DOI: 10.1038/s41558-022-01290-z

<https://nyti.ms/3LRLRkP>

A 2,700-Year-Old Figurine Revives a Weighty Mystery *A bronze statuette recovered from a river in Germany may have been part of an early Scandinavian weight system, some archaeologists believe.*

By Franz Lidz

Two summers ago, while snorkeling in the marshy streams of the Tollense River on Germany's Baltic coast, a 51-year-old truck driver named Ronald Borgwardt made a startling discovery.

Poking around in the peat, he picked up a six-inch-tall bronze figurine with an egg-shaped head, looped arms, knobby breasts and a nose that would make an anteater envious.



A small bronze figurine retrieved from the Tollense River in Germany in 2020, one of 13 found there since 1840. Credit...Volker Minkus

The statuette, sporting a belt and a neck ring, was only the second of its kind unearthed in Germany, though the 13th found near the Baltic Sea. The first turned up around 1840. All are similar in shape and proportion.

"The most recent statuette poses an archaeological riddle," said Thomas Terberger, an archaeologist and head of research at the Lower Saxony State Office for Cultural Heritage, in Germany. "What was it, how did it get there and what was it used for?"

Remarkably, 24 years earlier, while paddling through the same swamp, Mr. Borgwardt's father had spied a bunch of bones jutting from a bank. He fetched his son and together they scavenged in the muck. Among their finds were a human arm bone pierced by a flint arrowhead, and a two-and-a-half-foot-long wooden club that resembled a Louisville Slugger.

More exploration of the area yielded the skeletons of a half-dozen horses, scores of military artifacts and the remains of more than 140 individuals, most of them men between the ages of 20 and 40 who showed signs of blunt trauma. Virtually all the relics have been traced to around 1,250 B.C., suggesting that they stemmed from a violent episode that may have played out over a single day.

A 2013 geomagnetic survey revealed that this narrow stretch of the Tollense Valley was once part of a trade route bisected by a 400-foot stone-and-wood causeway that had been used to transport amber to points on the Mediterranean and Adriatic Sea. The amber road predated the bloodshed by at least five centuries.

Today the area is considered Europe's oldest battlefield site. "Although the region was sparsely populated 3,270 years ago, upward of 2,000 people were involved in the conflict," said Dr. Terberger, who helped start a series of excavations based on the Borgwardts' original discoveries.

In a paper published Feb. 12 [in the archaeological journal *Praehistorische Zeitschrift*](#), Dr. Terberger and five colleagues propose that the statuette found by the younger Mr. Borgwardt dated to the seventh century B.C. and was either a balance weight, an object of worship or a combination of both.

"The unanswered question is why the figurine wound up in a river valley along a trade route hundreds of years after a large battle took place there," Dr. Terberger said. "Did this happen by accident, or was the setting a place of commemoration for a 13th-century B.C. conflict still present in the oral history of the Late Bronze Age

people? And if the statuette depicted a goddess, did she play a role in a primitive weight system?”

Eat your heart out

Lorenz Rahmstorf, a professor of Prehistoric Archaeology at the University of Göttingen and a co-author of the study, said weights and scales first came into use around 3,000 B.C. as trade developed in Egypt and Mesopotamia; the first weighing devices were a simple system to assess the value of goods, consisting of two plates attached to an overhead beam fixed on a central pole. Sumerian texts feature the earliest mentions of a weight unit, the mina, which tipped the scales at about 500 grams, or 18 ounces.

Balance scales spread to the Aegean in the west and to the Indus Valley culture of South Asia in the east. By the middle of the second millennium B.C., weight systems turned up in Italy, and, by 1,350 B.C., north of the Alps.

“Sets of small bronze weights and balance beams in bone were mixed together in bags, and placed next to the dead in a number of graves from Eastern France and Southern Germany,” Dr. Rahmstorf said. “We do not yet have clear evidence for when weighing equipment was introduced to North Germany and Scandinavia.”

No ancient civilization attached stronger symbolic and spiritual significance to scales than the Egyptians from the second millennium B.C. to the Roman Period. Their most solemn otherworldly moment was the Weighing of the Heart.

It was the Egyptian belief that after a person died, Anubis, the jackal-headed god of embalming, led the deceased to the judgment hall of Osiris, where the dead heart was weighed against a feather of Maat, the personification of truth, justice and the cosmic order.

If a heart was pure, it would be as light as the feather, and the deceased was deemed worthy to enter the afterlife. Thoth, master of knowledge and patron of scribes, stood by to record the final verdict, and under the balance, Ammut the devourer — head of a

crocodile, forepart of a lion, hindquarters of a hippopotamus — sat ready to consume the damned.

“Balance had to be reached so that your heart didn’t get eaten by dear Ammut,” said Kara Cooney, a professor of Egyptian art and architecture at the University of California, Los Angeles.

The first definitive weights are pebbles from the Second Dynasty of ancient Egypt, which lasted from 2,890 B.C. to 2,686 B.C. “Some of the stones were engraved with parallel incisions, some with hieroglyphic inscriptions,” Dr. Rahmstorf said. “Metal weights became common only in the following millennium.”

A wealth of goddesses

A majority of the 13 bronze figurines were recovered in or around rivers near the Baltic coast — six turned up on the Öresund, a strait that separates the Danish island of Zealand from the Swedish province of Scania. The statuette found in the Tollense by Mr. Borgwardt is the largest and, at 155 grams, or about 5.5 ounces, the heaviest.

It was long believed that the economy of northern Europe during the Bronze Age had been based on gift exchange rather than trade. The idea that the bronze figurines represented measurements of an early Scandinavian weight system was advanced in 1992 by the Swedish archaeologist Mats Malmer.

After figuring in erosion and weight loss, Dr. Malmer analyzed the 12 existing “Goddesses of Wealth” for weight consistency and proportionality. His calculations indicated that the weight of the statuettes could be expressed in grams as multiples of a common denominator, 26.

On a recent afternoon in his office at the University of Göttingen, Dr. Terberger reeled off the weights of some of the figurines: 55 grams, 85 grams, 102 grams, 103 grams, 103 grams, 104 grams, 106 grams, 110 grams, 132 grams, 133 grams. From across the room, his departmental colleague Dr. Rahmstorf said, “Not every

figurine fit the scheme perfectly, but most were quite close.”

Although the units of weight seem to have been standardized, Dr. Rahmstorf doubts that the statuettes were used as weights. “It is possible that they were weight-regulated,” he said. “By which I mean the amount of metal used may have been weighed out.”

Still, the sample of figurines is small. And so far, unambiguous weights and scales from Northern Germany and Southern Scandinavia are missing. But some objects from the Late Bronze Age in these regions are possible candidates for weights: stone discs with a horizontal groove.

Dr. Rahmstorf’s initial analyses with his colleague Nicola Ialongo are promising, but he cautioned, “these would be heavy weights of over 100 to several thousand grams.” Because there are no texts and inscriptions from that era of northern Europe, “currently, the existence of weights and scales in that area is likely but still only hypothetical.”

Weight watchers

Back when Dr. Malmer came out with his theory, the statuettes were widely dismissed as artistically inferior to other figurines from the Late Bronze Age. “The hypothesis has been put forward that these statuettes are cheap mass products, owned by poor people as household gods,” he wrote in the journal *Antiquity*.

Dr. Terberger demurs. “All in all, 13 figures of this type do not support the idea that the statuettes were cheap household gods,” he said. “In the past they were interpreted as goddesses, but they don’t match any deities widely worshiped at that time.”

On the other hand, Flemming Kaul, a senior researcher at the National Museum of Denmark, is not persuaded that the statuettes were weight-regulated. “For me, the gram numbers seem much too random, and the ‘statistical material’ too low to draw any such conclusion,” he said.

Dr. Kaul speculated that the statuettes were divinities, although not

necessarily part of a defined pantheon. “These figurines may have possessed magical powers tied to the ability to produce offspring,” he said. “They could very well be seen as charms or votive pieces related to childbirth — the most dangerous time in a woman’s life.” How might the Borgwardt figurine have ended up at the bottom of the river? “On the Tollense trade route, with Nordic amber, a traveler offered up her amulet to the local water nymphs for further good luck on the voyage,” Dr. Kaul said. “Perhaps she parted with the talisman as a token of friendship or perhaps to promote life, fertility and cosmological order in the — for us — mysterious world of Bronze Age religion.”

For now, the riddle remains unsolved.

<https://bit.ly/3BtYJII>

Chewing sugar-free gum reduced preterm births in a large study

The idea was inspired by the connection between poor oral health and preterm birth

By [Aimee Cunningham](#)

Chewing a sugar-free gum daily reduced preterm births in a large study in Malawi. The oral intervention was inspired by past research linking poor oral health and preterm birth. The gum contains xylitol — a chemical that can boost oral health — in place of regular sugar.

Among women who chewed the xylitol gum, [549 out of 4,349 pregnancies, or 12.6 percent, were preterm](#), researchers reported February 3 at the Society for Maternal-Fetal Medicine’s Annual Pregnancy Meeting. That’s a 24 percent reduction compared with the group who didn’t receive the gum. Among those women, 878 out of 5,321 pregnancies, or 16.5 percent, of the babies were born before 37 weeks.

The oral health of gum users also improved. About 4,000 of the women had an initial dental exam and a later checkup. The women

who chewed the gum had less periodontal disease, a condition in which the tissue surrounding the teeth becomes infected and inflamed, compared with those who didn't get the chewing gum.

"The findings are very encouraging," says Kim Boggess, a maternal-fetal medicine specialist at the University of North Carolina School of Medicine in Chapel Hill who was not involved with the study. The researchers "are approaching a very complex problem in a low-resource area by trying to use a low-tech, easily applicable intervention." It would take more research to see if this could work in other settings, she says.

For the new study, researchers enrolled around 10,000 women across eight health centers in the greater Lilongwe area of Malawi before they were pregnant or in early pregnancy. All of the women received tailored information on pregnancy, preventing preterm birth and improving oral health from community health workers. Roughly half of the women also received the gum.

The study was part of a decade-long project in the region surrounding Lilongwe, which has [a preterm birth rate estimated at 19.3 percent](#), one of the highest globally. First, the research team talked with community members to learn what problems related to pregnancy the community was concerned about and wanted to solve.

In the Chichewa language spoken in Malawi, preterm birth is *kuchila masika asankwane*, which means "born too soon." In focus groups conducted early in the project, "all participants knew of many women who had suffered 'born too soon,'" says team member Kjersti Aagaard, a maternal-fetal medicine specialist at the Baylor College of Medicine and Texas Children's Hospital in Houston. Babies born prematurely can have complications that impair their lungs, neurodevelopment and more, with long-term health risks, and they are more likely to die in their first year of life than babies born to term.

Along with learning about [the community's perceptions of preterm birth](#), researchers also assessed [the rate of cavities and gum disease](#) among pregnant and postpartum women, which was in the 70 percent range. And they asked the community if chewing xylitol gum was "something that would be palatable — both truly palatable as well as acceptable," Aagaard says.

Studies finding a [link between periodontal disease and preterm birth](#) go back a couple of decades. The inflammatory disease has also been associated with [atherosclerosis and other ailments](#) (*SN: 4/6/16*). The diversity and size of the microbial community in the mouth is second only to the gut. With periodontal disease, there is a shift in the composition of that oral microbial community, giving way to bacteria that cause inflammation and damage gum tissue. From there, the bacteria may enter the bloodstream to reach other organs, perhaps including the placenta.

Chewing xylitol gum appears to be a check on that shift in the oral microbial community. Previous studies have shown that chewing [xylitol gum leads to fewer cavities](#) and suggest it [can reduce inflammation](#). Aagaard and her colleagues are planning more research on what's going on at the microbial level to understand how better oral health reduces preterm birth.

The team also wants to track the neurodevelopment of the children born early and those born on time in the study. "No matter how cost-effective an intervention may be, we still want to make sure you're making a difference in somebody's life," Aagaard says, "and the ultimate outcome is how do those kiddos do."

<https://bit.ly/3HVINSb>

No venom resistance in snake-eating birds: 'They just don't need it'

To eat or get eaten. It describes the evolutionary race of snakes versus the mammals and birds that prey on these snakes.

by Amber Verhaar, [Leiden University](#)

Muzaffar Ali Khan devoted his Ph.D. to investigating the molecular mechanisms play of the evolutionary arms race, and has his promotion 16 February. What makes mammals and birds successful in their snake hunting?

"I grew up in Pakistan, a part of the world where some farmers keep peacocks. Peacocks are famous for their ability to attack and kill snakes," Khan says. "I wanted to know more about animals that are capable of killing dangerous snakes and know how they do it." Under the supervision of Michael Richardson at the Institute of Biology Leiden (IBL), Khan analyzed the molecular resistance against cobra venom and found considerable differences in resistance between animals groups.

Genetic resistance in mammals differs

Khan looked at several mammals that eat snakes, such as the Asian mongoose, the European hedgehog, and the honey badger. He determined that only mammals that shared territory with snakes have evolved some form of resistance. The resistance made [snake](#) venom less potent, by making the toxins unable to bind to its target in the [mammal](#) body.

Even more interesting, the changes Khan found in the DNA were not the same in all animals. Khan: "That means that different animals evolved the resistance in their own way, without a [common ancestor](#) that already was resistant in the first place. It shows that it is essential for some mammals to have protection against cobra venom. If they didn't, the snakes won and killed them."

No genetic resistance in birds

With this in mind, Khan also looked at several [birds](#) of prey and other snake-eating birds. Hawks, eagles, the secretary bird, and peacocks, the red-legged seriema among others, were investigated. But when Khan analyzed their DNA, he was amazed. None of these snake-eaters were even slightly resistant, in genetic terms, to snake venom. "That finding was fascinating. What makes these birds able

to kill snakes?"

Khan and supervisor Richardson do have a theory. "Some birds attack snakes with impunity, even though they have no resistance," Richardson says. "It seems that the resistance is redundant: There is no selection pressure for it. Birds have feathers, scaly legs, excellent vision, are very intelligent, and are very agile. The snakes don't stand a chance against all these adaptations, so birds just don't need to be resistant."

A race of life and death

Khan adds: "They kill snakes with their speed and know how to distract the snake. They open their wings to divert the snakes' attention and then try to peck the back of the neck, away from the fangs. It is like an action movie. It is a race of life and death."

Treatment for snake bites

Both researchers hope to continue their study on differences in resistance to [snake venom](#). "For example, we also found that snakes that live in the same territory as other snake species, often have evolved some form of molecular [resistance](#) against each other," Khan explains. "We want to understand the genetic variation between animal groups. Every year, thousands of people worldwide die from snake bites, especially in Asia and Africa. One day, we hope to use our knowledge to develop a genetic treatment. That can potentially save the lives of a lot of people."

<https://bit.ly/3LHLSHP>

American Woman Appears to Be Entirely Cured of HIV After Unique Medical Treatment

Her cure gives hope to dozens of patients like her each year

[Mike McRae](#)

Ten years ago, an unnamed American woman was diagnosed with [HIV](#). Like the [tens of thousands](#) of people who test positive in the US each year, she faced a lifetime of anti-retroviral therapies to keep the [virus](#) from obliterating her immune system.

Today, that's no longer the case.

The patient is part of an extremely exclusive club of individuals who appear to have purged the virus entirely from their bodies. What's more, the means to her cure gives hope to dozens of patients like her each year.

A team of researchers in the US working as part of the International Maternal Pediatric Adolescent [AIDS Clinical Trials Network \(IMPAACT\)](#) [recently reported](#) the middle-aged patient to be virus-free more than four years after a revolutionary treatment for blood [cancer](#).

Just two other cases of total HIV remission have ever been satisfactorily confirmed, both following transplants of bone marrow from donors with HIV-blocking mutations in treatment of leukemia. One, a Caucasian male known as the "[Berlin patient](#)", was in remission for more than a decade before [passing away in 2020](#) from his cancer. [The other](#), a Latino male dubbed the "London patient", has been virus-free now for more than two years.

Just like these two renowned patients, the woman at the center of this latest case was also diagnosed with a blood cancer. In 2017, tests confirmed she had [acute myelogenous leukemia](#) (AML), a life-threatening condition affecting bone marrow.

Had the woman been White, she would have had a higher chance of finding a tissue match within the Caucasian-dominated library of willing donors. Instead, given her mixed-race heritage, specialists turned to another source of [stem cells](#) that could potentially provide the seeds for new, healthy bone marrow – umbilical cord blood.

Unlike most tissue transplants, [blood from a newborn's umbilicus doesn't require](#) a perfect immunological match between the host and donor. Since the 1990s, [more than 35,000 leukemia patients](#) around the world have received a cord blood donation.

While it's a prime choice of treatment for AML, cord blood takes weeks to settle in and generate sufficient white cells to keep

infections at bay. This makes it a rather poor option for anybody dealing with a persistent deadly infection.

To circumvent this problem, the patient's medical team devised a two-pronged strategy – receive infusions of blood from a compatible relative to provide her with a temporary defense, and cord stem cells that can slowly generate white cells. As an added fortune, the cord cells the patient received came with a bonus talent. Their DNA carried two copies of the CCR5 delta-32 mutation.

This small genetic difference alters the expression of the CCR5 co-receptor, the doorway most strains of HIV use to gain entry into the body's cells. Without easy access into white blood cells, the virus can't slide inside and destroy them.

Around three months after her transplant, all of the patient's T white blood cells and myeloid cells (white cells that gobble up invaders) were derived not from her old marrow, or her relative's blood, but from the stem cells in the cord blood.

That means they all featured the protective version of the CCR5 co-receptor, locking out her HIV for good.

Since then the patient has stopped all anti-retroviral medication, showing no signs of active HIV particles.

Cord blood stem cells have a lot going for them as a form of leukemia therapy, compared with more traditional forms of blood stem cells from a donor. For one thing, there appears to be a [reduced risk of relapse](#).

What's more, side-effects that are common among marrow transplants, such as [graft versus host disease](#), are less likely. In fact, the patient in this case left hospital just 17 days after her treatment.

Most excitingly, the fact that umbilical cord blood is more forgiving in terms of compatibility between donors and hosts means people from diverse ethnic and racial backgrounds could at last be eligible.

The researchers presented their preliminary findings at the [2022](#)

[Conference on Retroviruses and Opportunistic Infections](#), though are yet to publish or make their research publicly available.

For now, the study poses an exciting possibility for curing a fraction of the people with HIV – an ongoing [pandemic](#) that currently affects almost [40 million people around the globe](#).

This isn't to say this new therapy would be available to all people living with HIV, at least not any time soon. The risks involved still mean it's an option only available for treating life-threatening blood cancers, with the chance of curing HIV a prospective bonus.

But for those handfuls of eligible patients hit with both a cancer and HIV diagnosis, it's a thin silver lining that gives hope for a slightly brighter future.

<https://nyti.ms/3BtbS57>

An Undiscovered Coronavirus? The Mystery of the 'Russian Flu'

Scientists are grasping for any example that could help anticipate the future of Covid, even a mysterious respiratory pandemic that spread in the late 19th century.

By [Gina Kolata](#)

In May 1889, people living in Bukhara, a city that was then part of the Russian Empire, began sickening and dying. The respiratory virus that killed them became known as the Russian flu. It swept the world, overwhelming hospitals and killing the old with special ferocity.

Schools and factories were forced to close because so many students and workers were sick. Some of the infected described an odd symptom: a loss of smell and taste. And some of those who recovered reported a lingering exhaustion.

The Russian flu finally ended a few years later, after at least three waves of infection. Its patterns of infection and symptoms have led some virologists and historians of medicine to now wonder: Might the Russian flu actually have been a pandemic driven by a

coronavirus? And could its course give us clues about how our pandemic will play out and wind down?

If a coronavirus caused the Russian flu, some believe that pathogen may still be around, its descendants circulating worldwide as one of the four coronaviruses that cause the common cold. If so, it would be different from flu pandemics whose viruses stick around for a while only to be replaced by new variants years later that cause a new pandemic.

An 1889 wood engraving in a French newspaper, during the time of the Russian flu pandemic, which swept all over the world. Credit...Wellcome

Collection

If that is what happened to the Russian flu, it might bode well for the future. But there is another scenario. If today's coronavirus behaves more like the flu, immunity against respiratory viruses is fleeting. That might mean a future of yearly Covid shots.

But, some historians voice caution about the Russian flu hypothesis. "There is very little, almost no hard data" on the Russia flu pandemic, said Frank Snowden at Yale.

There is, though, a way to solve the mystery of the Russian flu. Molecular biologists now have the tools to pull shards of old virus from preserved lung tissue from Russian flu victims and figure out what sort of virus it was. Some researchers are now on the hunt for such preserved tissue in museums and medical schools that might have old jars of specimens floating in preservative fluid that still contain fragments of lung.

The Russian Flu

Tom Ewing of Virginia Tech, one of the few historians who has



studied the Russian flu, can't help noticing striking parallels with today's coronavirus pandemic: Institutions and workplaces shut down because too many people were ill; physicians overwhelmed with patients; and waves of infection. "I would say, maybe," Dr. Ewing said when asked if the Russian flu was a coronavirus.

Dr. Scott Podolsky, a professor of global health and social medicine at Harvard Medical School, called the idea "plausible."

And Dr. Arnold Monto, professor of public health, epidemiology and global health at the University of Michigan, considered it "a very interesting speculation. We have long wondered where coronaviruses came from," Dr. Monto said. "Has there ever been a coronavirus pandemic in the past?"

Harald Bruessow, a retired Swiss microbiologist and editor of the journal *Microbial Biotechnology*, points to [a paper published in 2005](#) concluding that another coronavirus circulating today, known as OC43, which causes severe colds, may have jumped from cows to humans in 1890. Three other less virulent coronaviruses circulate, too. Perhaps one of those viruses, or OC43, is a variant left over from the Russian flu pandemic.

Dr. Bruessow, while acknowledging the uncertainties, would bet that the [Russian flu was caused by a coronavirus](#). His work, which involved delving into old newspaper and journal articles, and public health reports on the Russian flu, uncovered that some patients had complained about conditions like a loss of taste and smell and long Covid-like symptoms.

Some historians speculated that the 19th century's *fin de siècle* lassitude might actually have been caused by sequelae of the Russian flu. Such symptoms are not typical of flu pandemics.

Like Covid, Dr. Bruessow reports, the Russian flu seems to have preferentially killed older people but not children. Dr. Ewing, examining 1890 records from the State Board of Health in Connecticut, found [a similar pattern](#). If true, that would make the

1890 virus unlike influenza viruses which kill the very young as well as the very old.

But historical records cannot readily answer the question of whether a coronavirus caused the Russian flu.

And Dr. Snowden of Yale cautioned that any lessons he could draw from that pandemic that could apply to a world in which the novel coronavirus has shaken societies would be "fantasy."

At this point, the idea that the Russian flu might have been caused by a coronavirus remains speculative, said Peter Palese, a flu researcher and professor of medicine at the Icahn School of Medicine at Mount Sinai in New York. There is nothing, he said, that clearly ties the Russian flu pandemic to a coronavirus and excludes influenza.

But for those seeking hints to how the current coronavirus pandemic might end, some think those past two pandemics could offer a clue. As the Russian flu pandemic waned, said J. Alexander Navarro, a historian at the University of Michigan, "people rather quickly went on with their lives." It was the same with the 1918 flu pandemic. Newspaper stories about it dwindled. And, he said, "grieving was almost entirely a private affair."

"I highly suspect that the same will occur today," Dr. Navarro said.

"In fact, in many ways, I think it already has."

When Pandemics Burn Out

Quite a few pandemics — at least in the past 100 years when their causes can be known — have been caused by respiratory viruses. Recent exceptions are Zika and chikungunya — old mosquito-borne viruses — and H.I.V., which is spread by sexual intercourse and sharing needles.

Great plagues terrorized humanity in ancient and pre-modern times, most notably the bubonic plague. It was mostly spread by rat fleas, and it ushered in a horrendous period, [killing multitudes among the European population](#) from 1347 to 1352. So many died that they

were buried in pits, in piles.

The bubonic plague kept returning to Europe for centuries after it first emerged. But how that plague ended offers few relevant lessons for today's pandemic.

Researchers have also been unable to find answers in animal studies. They have tried for decades to find general laws to predict how pandemics progress by infecting hundreds of thousands of mice with various viruses and bacteria, said Dr. George Davey Smith, professor of clinical epidemiology at the Bristol Medical School in England. The experiments went on year after year in England, Germany, the United States and Australia. All looked for ways to predict when and how an epidemic could end.

None were found.

"They couldn't predict what was going to happen," Dr. Davey Smith said. So researchers trying to understand how respiratory pandemics conclude can only study the flu and the current coronavirus pandemic.

Only the flu pandemics have ended. That, said Dr. David Morens, a flu researcher and senior adviser to the director of the National Institute of Allergy and Infectious Diseases, is a real limitation in trying to understand the natural history of respiratory disease pandemics. "We have only 104 years and four different pandemics to make predictions from," he said.

Flu pandemics are also baffling. The first of the four flu pandemics for which the virus is known began in 1918. The pandemic waned after three waves of infections and that virus, H1N1, remained in circulation, in a less virulent form until 1957, when it disappeared.

"As far as we could tell, in 1957, that virus was gone forever," Dr. Morens said. Then H2N2 emerged. It was substantially different from H1N1 and caused a pandemic. That pattern repeated itself with H3N2 emerging in 1968.

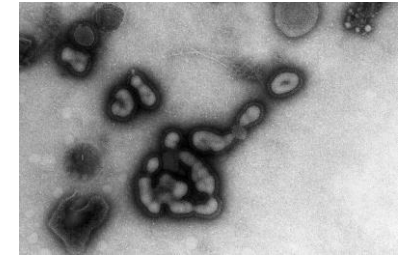
But in 1977, something strange happened. H1N1 came back after

being gone for two decades. It and another virus, H3N2, have been circulating ever since.

"Until 1977, we never had two subtypes circulating at the same time," Dr. Monto said. "We don't understand why one subtype pushed out the other and why it didn't happen in 1977."

The H1N1 strain of influenza, magnified 189,000 times, which was found circulating in people in 1977 after seemingly disappearing 20 years earlier.

Credit...Science Source



And in 2009, the H1N1 that had re-entered the human population in 1977 was displaced by a genetically distinct version that came from pigs, causing another pandemic.

But why would a new variant make the previous one go away?

That, Dr. Morens said, "is another mystery."

At least there are vaccines which are useful against the flu. But they have to be administered every year because of waning immunity. In [a study in England](#) with common cold coronaviruses, researchers found that immunity from infections with these viruses also diminishes within a year.

"Would we need a Covid vaccine every year?" asked Dr. Jeffery Taubenberger, chief of the viral pathogenesis and evolution section at the National Institute of Allergy and Infectious Diseases. "That's the direction we're heading."

Then there is the question of why the Russian flu, and now the Covid pandemic produced waves of escalating and declining mortality. "We are pretty clueless, and this extends to the waves we are seeing over the past two years with Covid," Dr. Morens said. The evolution of viruses is not the full answer, he added.

"There are no good explanations I know of."

Hunting Russian Flu Samples

The mysteries about the evolution of flu viruses and flu pandemics

lead back to the mystery of the Russian flu and the coronavirus hypothesis.

Some, like Dr. Navarro, the historian at the University of Michigan, said that he finds the evidence for the “interesting hypothesis” about the Russian flu “circumstantial at best.”

Dr. Taubenberger predicts better evidence will emerge. He and John Oxford, emeritus professor of virology at the University of London, have been looking for flu or coronavirus in old lung tissue from patients who were ill with a respiratory disease in the years before the 1918 flu. They had hoped to find them embedded in tiny blocks of paraffin no bigger than a pinky fingernail in the Royal London Hospital, a place that has tissue from patients dating back to around 1906.

“We sampled hundreds of tissues,” Dr. Taubenberger said, without finding viruses. “We continue to look,” he said.

But, he said, with renewed interest in the 1890 pandemic, he hopes some tissues containing the Russian flu virus — whatever it is — might be found, perhaps lying unnoticed in the basements of museums or medical schools in different corners of the world.

Finding the tissue, though, has been challenging.

“The people running institutions in which they might be housed very likely would have no way to easily access records about them,” Dr. Taubenberger said. “Paradoxically, genetic analysis of these samples would be less difficult than locating them in the first place.”

Dr. Podolsky of Harvard and Dominic W. Hall, the curator of the Warren Anatomical Museum at Harvard, are also looking for tissue archives that might have lung tissue from that era. Mr. Hall has been reaching out to those in charge of collections of tissue samples. On Thursday, he spoke with Anna Dhody, director of the research institute at the Mütter Museum, a collection of anatomical specimens and items from medical history in Philadelphia. She

thinks items in the museum’s climate-controlled storage room may help.

The archive contains jars of tissue from the late 19th century, including a few whole lungs, all floating in jars of pale yellow liquid, the alcohol that was used as a preservative.

With funding and the right technology, she says outside researchers may be able to analyze the specimens.

The work, Ms. Dhody said, “is so imperative.”

“It’s life and death information.”

<https://bit.ly/3rXD1tC>

Orangutans instinctively use hammers to strike and sharp stones to cut

Captive orangutans can complete two major steps in the sequence of stone tool use

Untrained, captive orangutans can complete two major steps in the sequence of stone tool use: striking rocks together and cutting using a sharp stone, according to a study by Alba Motes-Rodrigo at the University of Tübingen in Germany and colleagues, publishing February 16 in the open-access journal *PLOS ONE*.

The researchers tested tool making and use in two captive male orangutans (*Pongo pygmaeus*) at Kristiansand Zoo in Norway. Neither had previously been trained or exposed to demonstrations of the target behaviors. Each orangutan was provided with a concrete hammer, a prepared stone core, and two baited puzzle boxes requiring them to cut through a rope or a silicon skin in order to access a food reward. Both orangutans spontaneously hit the hammer against the walls and floor of their enclosure, but neither directed strikes towards the stone core. In a second experiment, the orangutans were also given a human-made sharp flint flake, which one [orangutan](#) used to cut the silicon skin, solving the puzzle. This is the first demonstration of cutting behavior in untrained, unenculturated orangutans.

To then investigate whether apes could learn the remaining steps from observing others, the researchers demonstrated how to strike the core to create a flint flake to three female orangutans at Twycross Zoo in the UK. After these demonstrations, one female went on to use the hammer to hit the core, directing the blows towards the edge as demonstrated.

This study is the first to report spontaneous stone tool use without close direction in orangutans that have not been enculturated by humans. The authors say their observations suggest that two major prerequisites for the emergence of stone [tool](#) use—striking with stone hammers and recognizing sharp stones as cutting tools—may have existed in our last common ancestor with orangutans, 13 million years ago.

The authors add: "Our study is the first to report that untrained orangutans can spontaneously use sharp stones as cutting tools. We also found that they readily engage in lithic percussion and that this activity occasionally leads to the detachment of sharp [stone](#) pieces."

More information: Motes-Rodrigo A, McPherron SP, Archer W, Hernandez-Aguilar RA, Tennie C (2022) Experimental investigation of orangutans' lithic percussive and sharp stone tool behaviours. *PLoS ONE* 17(2): e0263343.

doi.org/10.1371/journal.pone.0263343

<https://bit.ly/3p2xtMJ>

The True Source of Earth's Water Could Be Wildly Different to What You Think

Nothing on Earth can live without water. The origin of water on Earth, therefore, is the origin of life in the Solar System (and the Universe) as we know it.

[Michelle Starr](#)

Figuring out where and how our world [obtained its water](#) might be key to finding life on other worlds, but the truth is we don't know for sure where it came from.

Nonetheless, it's commonly accepted that one potential mechanism for water delivery was bombardment from water-bearing asteroids

and comets when Earth as we know it today was much younger.

But a new analysis of rocks collected from [the Moon](#) and brought to Earth during the Apollo era suggests that this might not actually be the case. Rather, according to a team of researchers at Lawrence Livermore National Laboratory, the likeliest explanation is that Earth formed with its water. In other words, it was here all along.

"Earth was either born with the water we have, or we were hit by something that was basically pure H₂O, with not much else in it," [explains cosmochemist Greg Brennecka](#) of LLNL.

"This work eliminates meteorites or asteroids as possible sources of water on Earth and points strongly toward the 'born with it' option." The Moon might seem a strange sort of place to look for Earth's water. It's dusty, dry, and extremely not wet at all.

As it turns out, though, the Moon is a great place to study Earth's history. The Moon formed when two massive objects – one roughly the size of [Mars](#), the other a little smaller than our own world – [smacked together](#) and reformed into blobs that would become Earth and its Moon.

Earth's memory of this event has weathered over time, but because the Moon has no plate tectonics or weather, geological evidence doesn't erode the same way.

That's not to say that there are no processes at all up there. Impacts from other objects and previous volcanic activity can alter the lunar surface. There are, however, some samples in [the Apollo collection](#) that are relatively unchanged.

Now, according to the [giant-impact hypothesis](#), that giant smash-up 4.5 billion years ago actually depleted Earth and the Moon of their volatiles.

That's why, under that model, the Moon is so dry; and, compared to other objects in the Solar System that have water, [the bulk of Earth is pretty dry too](#), especially once you take its size into account.

To understand the history of the Earth-Moon system prior to the

giant impact, the team looked at three lunar samples that crystallized 4.3 to 4.35 billion years ago, examining two isotopes: volatile and radioactive isotope rubidium-87 (^{87}Rb), and the isotope it decays into, strontium-87 (^{87}Sr).

The latter especially is thought to be a good proxy for understanding the long-term volatile budget of the Moon, and relative abundances of moderately volatile elements, such as rubidium, reflect the behavior of more volatile species, like water.

Interestingly, the team's analysis revealed that there was very little ^{87}Sr in the Earth-Moon system, even prior to the giant impact. This suggests that both proto-Earth and the impactor, Theia, were strongly depleted in volatile elements, suggesting that volatile depletion was not a result of the giant impact after all.

This means that the different volatile distributions on Earth and the Moon were inherited from Earth and Theia, which could explain why Earth is wetter. It also suggests that both bodies probably formed in the same general region of the Solar System, rather than Theia forming farther out and migrating in, and that the impact couldn't have happened earlier than 4.45 billion years ago.

Although this challenges some accepted views of the formation of Earth and the Moon, it neatly explains the origins of volatiles in the Earth-Moon system, the researchers say. It accounts for differences in their volatile proportions, and explains the similarities in isotope ratios.

"There were only a few types of materials that could have combined to make the Earth and Moon, and they were not exotic," [explains cosmochemist Lars Borg](#) of LLNL.

"They were likely both just large bodies that formed in approximately the same area that happened to run into one another a little more than 100 million years after the Solar System formed...but lucky for us, they did just that."

The research has been published in [PNAS](#).

<https://bit.ly/3s2m4hS>

Scientists Convert Donor Lungs to Universal Blood Type in a Medical First

The blood type of donated lungs could be altered before transplant, creating a bigger pool of universal donor lungs

[David Nield](#)

Patients can wait a long time for potentially life-saving lung transplants, since the need to find close matches complicates the process. One of the characteristics that need to be matched is patient and donor blood type.

Now new research shows that the blood type of some donated lungs could be altered before transplant, which means there is a bigger pool of universal donor lungs and less time on the waiting list for those in need.

The process works via a pair of enzymes – specifically, FpGalNAc deacetylase and FpGalactosaminidase – that in combination remove the antigens that distinguish red blood cells, converting blood type A lungs into universal type O.

"There are about 100,000 patients on US organ transplant waiting lists," the researchers write in their [published paper](#). "These patients require organs that must be compatible to their major cell surface antigens. The process to find compatible organs is not trivial."

"Because of this, patients with progressively failing organs often wait years for a life-saving transplant, and some will die, never receiving an optimally matched organ. In 2017, less than one-third of patients on the lung transplant waiting list received an organ in the United States." The difficulty of finding matches means not just longer waiting times but also donated lungs going to waste.

Under lab conditions, scientists treated eight blood type A lungs with the enzyme combination, reporting that 97 percent of blood type A antigens were removed within four hours. What's more, the conversion was achieved without any observable toxicity.

Three of the newly 'neutral' lungs were then placed in plasma to simulate an actual transplant. Observed [antibody](#) damage was minimal, meaning the converted lungs were accepted rather than rejected, at least in the crucial, early stages.

The team estimates that the procedure could eventually increase the number of blood group O donor lungs from the current 55 percent to more than 80 percent in the future.

"The treatment of donor lungs minimized antibody binding, complement deposition, and antibody-mediated injury as compared with control lungs," [write the researchers](#). "This strategy has the potential to expand ABO-incompatible lung transplantation and lead to improvements in fairness of organ allocation."

At the moment, transplanting lungs of the wrong blood type leads to a rapid immune response and the rejection of the organ by the body. For example, patients with blood type O have a 20 percent greater risk of dying while waiting for a suitable donor. The procedure stops that auto-immune response from happening by removing the blood type A antigens.

More research is required before this process is approved as safe to use with actual people, but the early signs are promising. Next, the researchers want to run tests on mice to further test their lung blood type conversion process.

"As next steps, we plan to use similar transgenic mice to study antigen reexpression kinetics and long-term post-transplant effects of the organ donor enzymatic treatment," [write the researchers](#).

The research has been published in [Science Translational Medicine](#).

<https://bit.ly/3gYZOip>

The Quest to Reacquaint Japan With Its Forgotten Native Citrus

Once revered by royals and celebrated by poets, the tachibana is now endangered.

by [Florentyna Leow](#)

It's early December, and somewhere on a mountain on the Japanese island of Shikoku, there's a citrus tree laden with golden-yellow fruit, each one no larger than a kumquat. There aren't many of them in the wild. This one might have grown from a large seed, dropped by a bird feasting on the fruit of its cousin from elsewhere. These rare trees cannot survive unless their surroundings are just right, with plenty of sun, space, well-drained soil, and warm temperatures. Scratch the peel of one of those tiny fruits, and you'll release a remarkably powerful fragrance, full of zesty, spicy, bitter notes, a dozen citrus distillates into a single whiff. Its flesh is an electric burst of tart and bitter flavors, far more intense than a lemon or grapefruit, followed by a barely detectable undertone of sweetness.

This delicate little citrus is the *tachibana*. It is one of only two citrus native to Japan—the other being the Okinawan shequasar—and is extremely rare. Officially classified as an endangered species by the Ministry of the Environment, the tachibana is in the rather peculiar position of being omnipresent yet virtually unknown.

Most people encounter it daily, engraved on the face of 500-yen coins, or in miniature as a tree on the dolls' displays during Girls' Festival in March. Its flowers appear on family crests, and on the prestigious Order of Cultural Merit medal, awarded to those who have made significant contributions to Japanese culture.

Nevertheless, tracking down a tachibana is like trying to score a reservation at an invitation-only restaurant. You have to know what you're looking for, and whom to ask. Most people have never seen a tachibana in the flesh, let alone tasted one. Many Japanese citizens don't even realize it's a citrus, according to Akari Hiroi, a citrus expert based in Kagawa Prefecture.

"I've seen tachibana before, but they were always ornamental," says Hiroi, who authored *The Citrus Textbook* for the Citrus Sommelier Association. "We usually encounter them in their flower

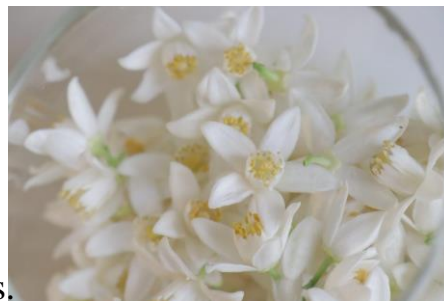
form, rather than as a fruit to be eaten out of hand, so we tend to think of it as a plant.”

Kenji Jō is trying to change that. Since 2011, the former bank employee has served as the chairman of the [Nara Tachibana Project](#). The organization’s mission is to rekindle interest and raise awareness about the citrus, preserve a forgotten piece of Japanese culture, and raise Nara’s culinary profile in the process. To help achieve that goal, Jō has spent most of his retirement planting several thousand tachibana trees and developing related citrus products such as tachibana herb tea and tachibana *koshō* (a riff on yuzu *koshō*—a seasoning that contains chili and citrus—using tachibana peel).

Jō’s work is crucial to saving this disappearing fruit tree and preserving its little-known legacy. While few people may be able to recognize the tachibana today, there was a time when the fruit and its flower both commanded reverence and respect.

Both the *Nihon Shoki* and the *Kojiki* describe its legendary origins: With one foot in the grave, Emperor Suinin (r. 29 B.C.–70 A.D.) commanded a man to venture into the underworld and bring back the fruit of immortality. Although he returned too late to save the emperor, the fruit and branches he brought back were supposedly planted at Tachibana Temple.

Although the story may be apocryphal, the temple still stands to the south of Nara City and features several tachibana trees on its grounds.



In the Heian period, aristocratic women tucked sachets of tachibana flowers in their kimono sleeves. Courtesy of Kenji Jō

According to citrus researcher and scientist Sayuri Teramoto, there’s a grain of truth to that legend. Whether it was humans, migrating birds, or even ocean currents, the first citrus seeds were

almost certainly carried over to Japan from the Chinese mainland thousands of years ago. Somewhere along the line, the imported interloper underwent several mutations that resulted in a citrus cultivar that was genetically isolated from other citrus populations in China. In short, one that was unique to Japan.

Most early references to the tachibana praise its tart, heady fragrance. During the Heian period (794–1185), women within the Japanese aristocracy perfumed themselves with tachibana, tucking sachets of its blossoms into their kimono sleeves or threading the fruits on cords and wearing them like bangles. The *Man’yōshū*, the oldest extant collection of Japanese poetry, contains 70 poems about or referencing tachibana, celebrating its beguiling perfume.

By the Edo period, the tachibana had become more accessible to classes outside the aristocracy, with many families using the fruit in household offerings to the gods. But even with its increased popularity, the tachibana still held a powerful status in royal circles: In the same era, there are references to ripe tachibana fruits being presented to the Imperial Court and the shogunate.

Despite its value, the tachibana wasn’t something people commonly ate. “I mean, you could eat it, but it wasn’t a *fruit* as such. You didn’t just eat it as is,” stresses Teramoto. “It was originally a symbolic fruit.”

The little fruit is no bigger than a kumquat. [Courtesy Noriyuki Enami/Enami Farm](#)



Historical records overwhelmingly emphasize its fragrance over its flavor. Although details on the tachibana’s culinary use throughout history are sparse, there are a few examples: The *Nihon Shoki*, for instance, briefly notes that tachibana juice was used as a sweetener and, before satsuma mandarins and bitter oranges replaced the

citrus, decorative *kagami* mochi (rice cakes) once came topped with tachibana to symbolize longevity at New Year's celebrations. And yet, while the tachibana was once the subject of poems, offerings, and reverence, few people give a second thought to the fruit that graces their money today. How did such a beloved citrus fall into near-obscurity?

Kenji Jō thinks that censorship during the postwar period is partially to blame. Following orders from the Ministry of Education in September 1945, teachers and students across Japan were obliged to erase nationalist content from wartime textbooks with ink and scissors. Because of its associations with the Imperial family (who had long cherished the tachibana as a symbol of longevity), mentions of the tachibana were likely also deleted. According to his theory, this had the effect of erasing, or at the very least vastly diminishing, the tachibana's presence in Japan's collective consciousness.

However, according to other citrus experts, there are simpler, more likely reasons for the tachibana's gradual fall into obscurity. First, the trees are very challenging to cultivate. "There are still places that protect and grow them, especially shrines and temples," says Teramoto. "But there are very precise, limited conditions under which tachibana can survive in the wild, and if these aren't just right, they won't survive at all."

More importantly, the tachibana currently lacks commercial value. According to citrus farmer Noriyuki Enami, who makes marmalade using the tachibana, the bitter citrus can be a hard sell. The increasing availability of more flavorful citruses like the satsuma mandarin as well as sugar in general has also reshaped palates to prefer sweeter fruits. The average consumer is unlikely to gravitate to new, unfamiliar fruit, let alone something as bitter as the tachibana. (It certainly doesn't help that the fruits remain ripe and edible for a week to 10 days at most before rotting; they wouldn't

last the journey to most supermarkets.)

The tachibana's symbolic weight in Japanese culture also means that not everyone thinks the drive to bring the fruit to more consumers is uniformly positive.

"I feel a little disloyal to Jō for saying this, but if many people started growing tachibana and it became popular, it would lose some of its value," muses Hiroshi Kawashima, head chef of [akordu](#), a modern Spanish restaurant in Nara. Kawashima features fruits sourced from the Nara Tachibana Project on akordu's menu. "Not everyone will care about its history as a sacred fruit the way he does, and if it does become popular, it'll become just another consumer product."

Although the citrus still isn't widely cultivated on a commercial scale, there has been a quiet-but-growing increase in culinary interest in the tachibana, thanks to the efforts of grassroots organizations in small towns across Japan, such as the Nara Tachibana Project as well as [Heda Tachibana no Kai](#), which has carried out tachibana conservation and promotion efforts in Numazu City for the last two decades.

Short of finding actual tachibana in the wild, consumers can try the rare citrus through dishes like the ones served at akordu. Kawashima's menu includes a refreshing, gently medicinal tachibana herbal tea as an aperitif as well as tempura he makes with leaves from the plant's first flush.

Beyond the restaurant, a variety of tachibana-flavored products have started popping up across Japan. [Nara kakigōri specialist Housekibaco](#) transforms tachibana into vibrant syrups for shaved ice, while Yamato Distillery's [Kikka Gin](#) uses the fruit's peels. And farther south, in Fukuoka, wagashi purveyor Fujimaru uses egg whites, sugar, and juice from the tachibana that grows at Dazaifu Tenmangu Shrine to make a dry, wafer-like sweet to be enjoyed with tea.

In 2020, Noriyuki Enami took home the Double Gold Award at the World's Original Marmalade Awards with his [tachibana marmalade](#), made from wild tachibana trees managed by the Toda Forestry Association in Numazu City. "It's pretty popular in the U.K.," he says with pride.

While the tachibana's extreme bitterness means that it's unlikely to ever achieve mainstream popularity, any recipe that promotes the little citrus is a step toward lifting it out of its endangered status. "I'd like for this level of interest to continue," says Enami. "I'd really like for more people around the world to know about tachibana."

<https://bit.ly/3sW9srT>

Wild animals prized as delicacies in China contain a bevy of threatening viruses

New study spotlights pandemic risks of the exotic game trade

By [Jon Cohen](#)

Wild animals sometimes found on the menu in Asian countries harbor a bewildering panoply of viruses, a new study has found—including many that can infect humans. Although none is closely related to the coronavirus that touched off the COVID-19 pandemic, the study sends a clear warning that other viral threats are lurking in the animal kingdom, scientists say.

Live-animal markets are known to have sparked outbreaks, such as severe acute respiratory syndrome (SARS) 2 decades ago. But the study underscores the extent of the threat, showing "there is an enormous amount of unsampled viral diversity" in the animals, says Harvard University evolutionary biologist William Hanage, who was not involved in the work. "We humans need to understand that for a virus, different mammal species can look pretty alike, provided their cells have appropriate receptors." China has clamped down on the sale of the animals sampled in the study, but other countries in the region have not.

The researchers, led by veterinarian Su Shuo of Nanjing Agricultural University, took samples from nearly 2000 animals representing 18 different species at venues in China including fur farms, zoos, and natural habitats. Most were species that are traditionally eaten as delicacies in China, including civets, raccoon dogs, badgers, bamboo rats, and porcupines. Using a "metagenomics" technique, which probes samples for RNA transcripts that viruses make when they copy themselves, they identified 102 virus species from 13 different viral families in the animals' noses, feces, and tissues. Sixty-five of the viruses had never been described before. The researchers deemed 21 as "high risk" to humans, because they had infected people in the past or simply had a history of readily jumping between species.

"Our results provide important insights to those game animals and their viruses that might lead to the next pandemic," says Su, whose group published its work online yesterday [in Cell](#).

Among the worrisome finds were several coronaviruses. For example, a hedgehog was infected with a virus resembling the one that causes Middle East respiratory syndrome in humans. Four canine coronaviruses found in raccoon dogs were about 94% similar to coronaviruses recently found in humans in Malaysia and Haiti. "These viruses can infect many animals," Su says.

Some of the species sampled in the study could act as "intermediary" hosts that bat coronaviruses infect before they make the jump to humans. Indeed, a coronavirus close to one found in bats turned up in a civet. Most researchers think both SARS-CoV-2 and SARS-CoV-1—the cause of SARS—became human pathogens after passing through an intermediate host.

The researchers also detected several influenza viruses, another family that could trigger a new pandemic. In a finding "of considerable significance," the authors write, civets and Asian badgers were found to carry H9N2, an influenza A virus that has

become increasingly common in chickens and ducks. There have been fewer than 50 documented human cases of H9N2 infection, a [February 2020 report](#) noted, because the virus does not transmit efficiently between people. But researchers fear that by replicating in other mammals it has more opportunities both to infect humans and to adapt to them. The infected badgers had runny noses and presumably could transmit to humans through the respiratory route. Other viruses detected in the study that can infect people include influenza B, Norwalk, human parainfluenza virus 2, rotaviruses, and orthoreoviruses.

Markets that sell live animals—often called “wet markets”—are ideal places for viruses to transmit to humans, both because of the density of animals and because the stress they suffer makes them prone to shedding viruses, says medical virologist Marietjie Venter of the University of Pretoria, Hatfield. The new findings “confirm that trade and consumption of these animals should be avoided and support the actions taken by China to ban the trade of many of these animals,” says Venter, who is a member of the World Health Organization’s Scientific Advisory Group for the Origins of Novel Pathogens.

After SARS, China made the sale of many of the animals sampled in the study illegal, but they were still [readily available in Wuhan markets](#) in 2019, just before the start of the pandemic, including at the Huanan Seafood Market, which had the earliest identified cluster of COVID-19 cases. Su says the government has cracked down hard on illegal sales since then. “With very strict legislation, as well as screening checks, it is now difficult to find wildlife” for sale, Su says. “What worries me is that it seems that in Southeast Asia, where the economy is lagging, this wild animal trade is continuing.”

Evolutionary biologist Edward Holmes at the University of Sydney, a co-author of the new study, “strongly suspects” SARS-CoV-2

jumped into humans at the Huanan market. As long as wild animals are sold, the risk of similar jumps remains high, he says. “It’s hard to think of a more effective way to ignite and fan the flames of an epidemic,” Holmes says. “We keep allowing these things to flourish and it’s only a matter of time before we get another outbreak and perhaps another pandemic.”

<https://wb.md/3h2pKcW>

COVID Rates Jump After Denmark Lifts All Restrictions

Since Denmark lifted its remaining coronavirus restrictions it has more COVID-19 cases per capita than other places in the world

Carolyn Crist

Since Denmark became the first major country to lift its remaining coronavirus restrictions at the beginning of February, it has recorded more COVID-19 cases per capita than most other places in the world.

COVID-19 hospitalizations and deaths have jumped by nearly a third, signaling a warning to the U.S. and other countries that are now easing mask mandates, vaccine requirements, and limits for crowded spaces such as bars and nightclubs, according [to Yahoo News](#).

"Not looking good in Denmark. Deaths are now 67% of peak with a steep ascent," Eric Topol, MD, director of the Scripps Research Translational Institute, wrote [in a Twitter post](#) this week.

He shared charts that showed sharp increases in COVID-19 cases, hospital admissions, and deaths from early February to mid-February. In a [response to comments](#), he linked to a news story from September, when Denmark previously lifted all restrictions before cases climbed again. "The world is looking to Denmark as a guide to removing all restrictions," Topol said. "It seems that we've seen this movie before."

In late January, COVID-19 cases appeared to peak in Denmark.

After the emergence of BA.2, the Omicron subvariant, cases began to rise again and reached a new all-time high on Feb. 13, surpassing the record from December 2020.

Hospitalizations also climbed in Denmark, surpassing the U.K. rate in early February and the U.S. rate this week. About 1½ times more Danes are now hospitalized with COVID-19 than ever before during the pandemic. If COVID-19 deaths continue to increase, Denmark could set a record in coming days, Yahoo News reported. But Danish health officials have pointed out that hospital burden is still low in the country, compared to former surges. Denmark also tests far more people than in the U.K. and the U.S., the news outlet reported.

In addition, about 81% of Danes are fully vaccinated, including 95% of those over age 65, and 62% have received a booster dose, according to the [latest data](#) from the Danish Health Authority. Overall, Danes have remained protected against COVID-19 and have less severe illness. "Overall mortality in Denmark in all age categories has now fallen into the normal spectrum as Omicron has become fully dominant," Søren Neermark, an official at the Danish Health Authority, wrote [in a Twitter thread](#) on Monday.

At the same time, he noted, Denmark shouldn't necessarily be used as a model for other countries. "Denmark cannot be used as a (sole) argument for lifting restrictions or maintaining restrictions in other countries," he wrote. "The capacity of the healthcare system in each country will vary and the same [with] overall vaxrate, trust, test, prior immunity etc."

In reality, countries will need to decide based on their own factors, and restrictions will likely toggle on and off in response to changing conditions, Kristian Andersen, PhD, an immunologist at the Scripps Research Institute, said [in a podcast](#) this week. Andersen, a Danish expat, said he has been watching the situation in Denmark closely in recent weeks to understand the trends.

"We have to be realistic. If we say we're not going to have restrictions, it's up to you to get your boosters and wear a face mask if you can. ... We should probably expect that for the next few years to come, most people will get infected a couple of times a year," he said. "And we should expect 200,000 to 250,000 deaths [a year] in this country alone."

To keep up with the coronavirus, countries will also need to prioritize innovation, namely with "better home testing, better masks, better vaccines, better antivirals," Andersen said.

"But it also requires that we realize [COVID] is going to be a problem we're going to continue to deal with during the next 5 to 10 years," he said. "If we say it's all over, my concern is that the innovation stops. Because then it's like, 'Well, what's the point?'"

Sources

Yahoo News: "In a warning to U.S., COVID rates soar after Denmark lifts all restrictions."

Twitter: @EricTopol, Feb. 13, 2022; @sneermark, Feb. 14, 2022.

Danish Health Authority: "Covid-19 surveillance," updated Feb. 17.

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<https://bit.ly/3H4cTS4>

Laser-Driven Light Sails Will Need to Billow Like Parachute: Study

Designing the size, shape and materials for a light sail accelerated to speeds approaching the speed of light

As part of the [Breakthrough Starshot Initiative](#), University of Pennsylvania researcher Igor Bargatin and his colleagues are designing the size, shape and materials for a light sail accelerated to relativistic speeds — speeds approaching the speed of light — by powerful lasers.

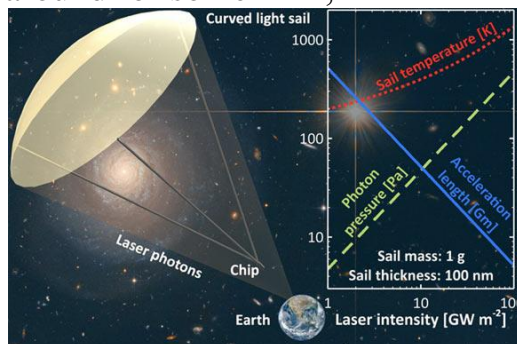
Using nanoscopically thin materials and an array of powerful lasers, such a sail [could carry](#) a microchip-sized probe at a fifth of the speed of light, fast enough to make the trip to the Alpha Centauri

system in roughly 20 years.

“Reaching another star within our lifetimes is going to require relativistic speed, or something approaching the speed of light,” Dr. Bargatin said.

“The [idea](#) of a [light sail](#) has been around for some time, but we’re just now figuring out how to make sure those designs survive the trip.”

Much of the earlier research in the field presumed that the Sun would passively provide all of the energy that light sails would need to get moving.



Campbell et al. show that the diameter and radius of curvature of a circular light sail should be comparable in magnitude, both on the order of a few meters, in optimal designs for gram-scale payloads. Image credit: Campbell et al., doi: 10.1021/acs.nanolett.1c03272.

However, the plan of the Breakthrough Starshot Initiative to get its sails to relativistic speeds requires a much more focused source of energy.

Once the sail is in orbit, a massive array of ground-based lasers would train their beams on it, providing a light intensity millions of times greater than the Sun’s.

Given that the lasers’ target would be a 3-m- (10-foot) wide structure a thousand times thinner than a sheet of paper, figuring out how to prevent the sail from tearing or melting is a major design challenge.

In two new papers published in the [journal *Nano Letters*](#), Dr. Bargatin and co-authors outlined some of those fundamental specifications.

In the [first paper](#), they demonstrated that their light sails — proposed to be constructed out of ultrathin sheets of aluminum

oxide and molybdenum disulfide — will need to billow like a parachute rather than remain flat, as much of the previous research assumed.

“The intuition here is that a very tight sail, whether it’s on a sailboat or in space, is much more prone to tears,” Dr. Bargatin explained.

“It’s a relatively easy concept to grasp, but we needed to do some very complex math to actually show how these materials would behave at this scale.”

Rather than a flat sheet, the authors suggest that a curved structure, roughly as deep as it is wide, would be most able to withstand the strain of the sail’s hyper-acceleration, a pull thousands of times that of Earth’s gravity.

“Laser photons will fill the sail much like air inflates a beach ball,” said Dr. Matthew Campbell, also from the University of Pennsylvania.

“And we know that lightweight, pressurized containers should be spherical or cylindrical to avoid tears and cracks. Think of propane tanks or even fuel tanks on rockets.”

In the [second paper](#), the researchers provided insights into how nanoscale patterning within the sail could most efficiently dissipate the heat that comes along with a laser beam a million times more powerful than the Sun.

“If the sails absorb even a tiny fraction of the incident laser light, they’ll heat up to very high temperatures,” said Dr. Aaswath Raman, a researcher at the University of California, Los Angeles.

“To make sure they don’t just disintegrate, we need to maximize their ability to radiate their heat away, which is the only mode of heat transfer available in space.”

*Matthew F. Campbell et al. 2022. Relativistic Light Sails Need to Billow. *Nano Lett* 22 (1): 90-96; doi: 10.1021/acs.nanolett.1c03272*

*John Brewer et al. 2022. Multiscale Photonic Emissivity Engineering for Relativistic Lightsail Thermal Regulation. *Nano Lett* 22 (2): 594-601; doi: 10.1021/acs.nanolett.1c03273*

<https://bit.ly/3JFw1aN>

Plants under anesthesia reveal surprising parallels with humans

The carnivorous Venus flytrap can be anesthetized with ether.

Some surprising parallels to anesthesia in humans emerge.

Medicine has a broad repertoire of anesthetics at its medication allows patients to better endure painful treatments or even sleep through them. As early as 1842, ether was first used for a dental treatment in New York. Since then, this anesthetic has served as one of the main anesthetics worldwide for over 100 years.

Remarkably, anaesthetisation is also possible in [plants](#). Claude Bernard proved in 1878 that the [touch](#)-sensitive plant *Mimosa pudica* did not react to touch under the influence of ether by closing its leaves. He concluded that plants and animals must have a common biological essence that is disturbed by anesthetics.

Ether anesthetics were used during surgery, childbirth and in palliative treatment to take away patients' pain. However, the exact mechanism of action has never been elucidated. Even with modern anesthetics, it is often unclear how and where they function. One reason for this is certainly that humans are a very delicate research subject.

Venus flytrap has a distinctive system for stimulus transmission

This is where plant researchers from Julius-Maximilians-Universität (JMU) Würzburg in Bavaria, Germany, have now stepped in. Professor Rainer Hedrich's team has been leading research on the Venus flytrap for over ten years. He has already achieved many groundbreaking insights into the life of this carnivorous plant.

"Unlike most other plants, the Venus flytrap is particularly sensitive to touch. In response to such stimuli, electrical impulses are triggered and transmitted extremely quickly to catch animal prey," Hedrich explains.

The [electrical impulses](#) (action potentials, APs) of the flytrap are comparable to those of our nervous system. It is true that plants do not have a distinct nervous system. But they do transmit electrical information in their conductive tissue, for example to close the trap at lightning speed: "In 2016, we were able to show that the Venus flytrap, like a human, can not only perceive touch, but also count and remember the APs it has fired," explains the Würzburg professor. "So it made sense to test whether and how ether affects the carnivorous plant's sense of touch."

Safety precautions against explosions had to be taken

Before anesthetizing the plant, however, there were some tricky hurdles to overcome in order to be able to use the highly explosive ether gas.

"Explosions resulting in death unfortunately occurred repeatedly in the medical use of ether. That's why we had an explosion-protected device made so that we could work safely without blowing up the whole institute," reports Dr. Sönke Scherzer with a grin.

This way, the Würzburg researchers found out that the Venus flytrap can be anesthetized, similar to a human being, and that it does not react to touch during this time. Investigations of the trap memory even showed that the trap cannot "remember" touches during anesthesia. Thus, its reaction is not different from that of a patient, as Hedrich's team reports in the journal *Scientific Reports*.

Venus flytrap provides information about the mechanism of action of ether

"Things got really exciting, however, when we discovered that the anesthetized [traps](#) can perceive touch locally, but cannot transmit it," says Sönke Scherzer, the first author of the paper.

Every touch of the sensory hairs leads to the release of the signal molecule calcium in the Venus flytrap. This molecule also plays a decisive role in the transmission of stimuli in humans.

In the plant, however, the JMU researchers were able to make the

calcium signal visible by expressing genetically encoded calcium sensors. They found that the calcium signal is still produced in the sensory hairs of anesthetized plants after a touch, but that it no longer leaves this touch sensor. Ether therefore interrupts the transmission of stimuli.

"Now we finally knew in which tissue the ether acts," says Sönke Scherzer. But in order to understand the exact mechanism of action of the anesthesia, the Würzburg researchers studied these hairs in detail and found out that only the hairs of fully-grown traps trigger the fast calcium signal when touched. Immature traps, on the other hand, do not have this signal and therefore cannot catch any prey.

What distinguishes mature traps from immature ones?

"Now we have looked at how these two developmental stages differ and have come across an interesting gene that is found exclusively in the hairs of adult traps," says Rainer Hedrich. This gene encodes a glutamate receptor, which is apparently responsible for the rapid transmission of stimuli. These receptors perceive the [neurotransmitter glutamate](#) and are also found in humans, where they are involved in the transmission of stimuli in the synapses.

Here, the plant researchers received support from Professor Manfred Heckmann, an expert on animal glutamate receptors at JMU Würzburg. "Indeed, we see calcium signals when we stimulate the traps externally with glutamate," says Heckmann. "However, this response does not occur in anesthetized traps or immature traps without the glutamate receptor expressed. Thus, the [glutamate receptor](#) appears to be a likely target in ether anesthesia. When this receptor is blocked, stimulus transmission also stops.

"Now we need to find out what the glutamate receptors of animals and plants have in common and how they differ," Heckmann outlines ongoing experimental research.

"With this paper, we show that the Venus flytrap can serve as a study object not only for plant research, but also for medicine. With

it, it could be possible to investigate the mechanism of action of drugs without having to conduct animal experiments," Scherzer holds out the prospect.

More information: Sönke Scherzer et al, *Ether anesthetics prevents touch-induced trigger hair calcium-electrical signals excite the Venus flytrap*, *Scientific Reports* (2022). [DOI: 10.1038/s41598-022-06915-z](https://doi.org/10.1038/s41598-022-06915-z)

<https://bit.ly/3JIOSC6>

Skull of 'armless' meat-eating dinosaur discovered

It likely used its head and jaws to take down prey.

By [Laura Geggel](#)

Paleontologists in Argentina have uncovered an unusual [dinosaur](#) skull that belonged to an "armless," tiny-brained carnivore that lived about 70 million years ago, a new study finds.

The newfound species — named *Guemesia ochoai* for General Martín Miguel de Güemes, a hero of the Argentine War of Independence — is a member of Abelisauridae, a clade of carnivores that roamed what is now South America, Africa and India during the dinosaur age.



The newfound dinosaur Guemesia ochoai may have looked a bit like this other abelisaurid illustrated here, the horned Carnotaurus sastrei. (Image credit: Fred Wierum; [CC BY 4.0](#) via [Wikimedia Commons](#))

It's possible that *G. ochoai* is a close relative of the ancestors of abelisaurids, the researchers said. However, *G. ochoai* is different from its abelisaurid relatives in two key ways: It lacks horns, perhaps because abelisaurid ancestors hadn't evolved these pointy skewers yet; and it likely lived in what is now northern Argentina where its skull was found, far away from most abelisaurid remains in Patagonia, southern Argentina, suggesting that this dinosaur group could live in varied ecosystems.

"This new dinosaur is quite unusual for its kind," study co-author Anjali Goswami, a research leader at the Natural History Museum in London, [said in a statement](#). "It shows that the dinosaurs that live in this region were quite different from those in other parts of Argentina, supporting the idea of distinct provinces in the [Cretaceous](#) of South America."

Abelisaurids likely preyed on long-necked titanosaurs, an impressive feat given that their tiny arms were [vestigial and essentially useless](#). They weren't the only theropod — or bipedal, mostly meat-eating dinosaurs — with short arms. [Tyrannosaurus rex](#) has embarrassingly short arms for its stature, although its arms were longer than those of abelisaurids and [unpublished research suggests](#) that the dinosaur king could use its wee arms to bring prey in close. With such puny arms, abelisaurids had to take down prey almost entirely with their skulls and fearsome jaws.

The skull is all that's left of this *G. ochoai* individual. So, after researchers uncovered it in the Los Blanquitos Formation near Amblayo, they got to work studying it. The team analyzed the dinosaur's well-preserved braincase, or the area where the brain sat. Like other abelisaurids, *G. ochoai*'s braincase was small, indicating that it had a little brain. In fact, its entire cranium is about 70% smaller than its abelisaurid relatives, suggesting that this individual was a juvenile, although this matter is not yet settled.

The research team of Argentine and U.K. scientists also noticed a unique feature called foramina, or rows of small holes at the front of the skull. These holes could have helped *G. ochoai* cool down when the animal pumped blood into the thin skin at the front of its head, where it could release heat, the researchers said.

There are already 35 other abelisaurid species described from Argentina, but nearly all of them are from Patagonia. The discovery of *G. ochoai* and other extraordinary paleo-species, such as [a huge turtle](#) with a 3-foot-long (1 meter) shell, in this northern region

suggest that it was a unique part of the world during the late Cretaceous.

Researchers hope to discover more specimens of *G. ochoai* and its relatives so they can learn more about life in ancient Argentina. The study was published online Feb. 10 in the [Journal of Vertebrate Paleontology](#).

<https://bit.ly/35esj95>

First Gene Therapy for Tay-Sachs Disease Successfully Given to Two Children

Two babies have received the [first-ever gene therapy](#) for Tay-Sachs disease after over 14 years of development.

By [Miguel Sena-Estevés](#)

[Tay-Sachs](#) is a severe neurological disease caused by a deficiency in an enzyme called HexA. This enzyme breaks down a fatlike substance that normally exists in very small, harmless amounts in the brain. Without HexA, however, this fatlike substance can accumulate to toxic levels that damage and kill neurons.

One of the symptoms of this disease was first described in 1883 by British ophthalmologist [Warren Tay](#), who saw a cherry-red spot on the back of the eye of affected infants. In 1887, American neurologist [Bernard Sachs](#) described the profound neurological symptoms of Tay-Sachs in a seminal paper:

"... Nothing abnormal was noticed until the age of two to three months, when the parents observed that the child was much more listless than children of that age. ... The child would ordinarily lay upon its back, and was never able to change its position ... it never attempted any voluntary movement ... the child grew steadily weaker, it ceased to take its food properly, its bronchial troubles increased, and finally, pneumonia set in, it died August, 1886."

This dismal description of Tay-Sachs [remains current](#), and those with the disease usually die by age five. Some people develop Tay-Sachs later in life, with symptoms starting in their teens that get

progressively worse over many decades.

[I am](#) a member of a team of researchers from UMass Chan Medical School and Auburn University who developed a gene therapy that may help get around this barrier. Our treatment uses two harmless viral vectors to deliver DNA instructions to [brain](#) cells that teach them how to produce the missing enzyme. [Similar techniques](#) have been used to treat a number of [related diseases](#) and other conditions. Unfortunately there is still no treatment for Tay-Sachs. Aggressive medical treatment can extend survival but doesn't improve neurological function. The only effective way to treat Tay-Sachs is to restore the HexA enzyme in the brain. This is difficult, however, because the [blood-brain barrier](#) prevents most molecules from passing into the [brain](#).

In the case of Tay-Sachs, these DNA instructions enter the nucleus of these cells and stay there, allowing for long-term production of HexA. Based on our previous studies successfully testing our gene therapy on [different animal species](#), we believe that delivering the treatment to a central part of the brain allows the enzyme to travel along its connections to other regions and to be distributed throughout the entire brain.

The first child who received our gene therapy treatment was age two and a half, with late-stage disease symptoms. Three months after treatment, they had better muscle control and could focus their eyes. Now at age five, the child is in stable health and is seizure-free, which usually isn't possible for patients at this age. A second child treated at age seven months had improved brain development by the three-month follow-up and remains seizure-free at a little over age two.

More testing is needed to confirm whether our treatment can fully stop disease progression. Given that this was the first time our treatment was given to humans, we used a conservative dose below the maximum therapeutic effects we saw in our animal studies. My

colleagues and I are currently conducting a follow-up clinical trial to test the safety and efficacy of increasing doses in a larger number of patients.

The [increasing cost](#) of manufacturing these treatments makes it extremely difficult, if not impossible, to develop and test gene therapy for many ultrarare diseases where the number of patients worldwide is very small and [profitability low](#).

We were able to deliver these treatments to the children in our ongoing clinical trials thanks only to funding from a generous family whose own child is a participant. This grassroots approach is a [common theme](#) in ultrarare disease research; development and testing are often supported by parents, foundations and federal grants.

Our [Translational Institute for Molecular Therapeutics](#) program at UMass Chan Medical School focuses on developing more viral vector gene therapies for an ever-expanding number of ultra-rare diseases in collaboration with families and foundations. We believe every patient afflicted with any of the approximately [7,000 rare diseases](#) worldwide deserves a chance at a normal life.

<https://bit.ly/3JKOyLI>

Study: Caffeine Impacts Expression of Genes Known to Mediate Cardiovascular Risk

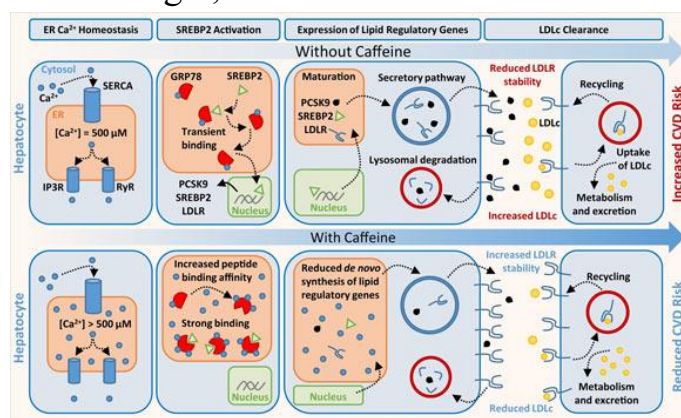
Caffeine blocks PCSK9 expression and increases LDL cholesterol clearance in hepatocytes.

Evidence suggests that caffeine reduces cardiovascular disease risk. However, the mechanism by which this occurs is still unknown. In a new study, researchers from McMaster University and elsewhere investigated the effect of caffeine on the expression of two regulators of circulating low-density lipoprotein (LDL) cholesterol — or 'bad' cholesterol — levels.

“Just two to three average-sized cups of coffee per day contains enough caffeine to trigger a cascade effect, which reduces the levels

of LDL cholesterol,” said McMaster University’s Professor Richard Austin, senior author of the study. “High bloodstream levels of LDL cholesterol are associated with an increased risk of cardiovascular disease. Regular caffeine consumption is linked to reduced blood levels of the [PCSK9](#) protein, which increases the liver’s ability to remove excess LDL cholesterol from the bloodstream. Coffee and tea drinkers have another important health reason to rejoice — minus the sugar,” he added.

“These findings now provide the underlying mechanism by which caffeine and its derivatives can mitigate the levels of blood PCSK9 and thereby reduce the risk of cardiovascular disease.”



The treatment of liver hepatocytes with caffeine increases the concentration of ER Ca²⁺; excess ER Ca²⁺ leads to an increase in the peptide binding capacity and chaperone activity of ER-resident GRP78; the result is an ER-resident GRP78-SREBP2 complex with enhanced stability; the failure of SREBP2 to quickly exit the ER leads to a net reduction in expression of lipid regulatory genes, including PCSK9, SREBP2 and PCSK9; with reduced outflow of de novo PCSK9, cell-surface LDLR exhibits increased half-life and abundance, leading in a net increase in LDL cholesterol clearance.

Image credit: Lebeau et al., doi: 10.1038/s41467-022-28240-9.

Caffeine and its derivatives can also block the activation of a protein called [SREBP2](#), which in turn reduces the levels of PCSK9 into the bloodstream. “Given that SREBP2 is implicated in a host of cardiometabolic diseases, such as diabetes and fatty liver disease, mitigating its function has far reaching implications,” Professor

Austin said. “Recent population-level studies have shown that coffee and tea drinkers have a reduced risk of death from cardiovascular disease, but a biochemical explanation of this phenomenon has previously eluded researchers,” he added.

“These findings have wide ranging implications as they connect this widely consumed, biologically active compound to cholesterol metabolism at a molecular level,” McMaster University’s Professor Guillaume Paré, co-author of the study. “This discovery was completely unexpected and shows that ordinary food and drink have many more complex effects than we think.”

The authors also developed new caffeine derivatives that potently lower blood PCSK9 levels, potentially leading to new LDL cholesterol treatments.

“We are excited to be pursuing this new class of medicines — or nutraceuticals — for the potential treatment and prevention of cardiovascular disease,” said Dr. Jakob Magolan, also from McMaster University. “It is exciting to see yet another potential clinical benefit from caffeine,” added McMaster University’s Professor Mark Tarnopolsky.

The [findings](#) are published in the journal *Nature Communications*. P.F. Lebeau et al. 2022. Caffeine blocks SREBP2-induced hepatic PCSK9 expression to enhance LDLR-mediated cholesterol clearance. *Nat Commun* 13, 770; doi: 10.1038/s41467-022-28240-9

<https://bit.ly/3LLSkNW>

Study of Over 1 Million People Reveals Heart Attacks Can Reduce Parkinson's Risk

Helpful clues linking having a heart attack with a lower risk of developing Parkinson's later

[David Nield](#)

We know the devastating effects [Parkinson's](#) disease can have, but scientists are still trying to figure out how it gets started and how to cure it.

Some new research may have found helpful clues, linking having a heart attack with a lower risk of developing Parkinson's later.

The drop in risk is around 20 percent, based on an analysis of 181,994 patients in the Danish health system who suffered a heart attack between 1995 and 2016, compared with 909,970 control subjects, matched for age and sex and the year of their heart attack diagnosis.

What's more, the chance of developing parkinsonism – which brings on the same sort of movement difficulties and other symptoms as Parkinson's, though, in this study, isn't classed as Parkinson's itself – was found to be reduced by 28 percent as well. Researchers followed up with study participants for a maximum of 21 years.

"The risk of Parkinson's appears to be decreased in these patients, in comparison to the general population," [says first author of the new paper, epidemiologist Jens Sundbøll](#) from Aarhus University Hospital in Denmark.

It's the first time research has looked at Parkinson's disease risk in heart attack survivors, and it's still early days for figuring out why the risk is lowered. Both heart attacks and Parkinson's have a complex set of risk factors, and it's possible that the answer to this relationship lies somewhere in them.

Certain classic risk factors for heart attacks – including smoking, [high cholesterol](#), high blood pressure, and type 2 [diabetes](#) – have previously been associated with a lower risk of developing Parkinson's disease, so these links may be driving the results seen in the new study.

However, other risk factors are the same. Heart attacks and Parkinson's are more likely in the elderly and less likely in people who drink more coffee and [are more physically active](#).

The new study gives doctors more guidance on where to focus their attention on people recovering from a heart attack.

"For physicians treating patients following a heart attack, these results indicate that cardiac rehabilitation should be focused on preventing ischemic stroke, [vascular dementia](#), and other cardiovascular diseases such as a new heart attack and heart failure," [says Sundbøll](#).

It would seem, however, that a reduced risk of Parkinson's disease and parkinsonism may follow after a person has had a heart attack. Further studies are needed to make sure, especially in more diverse racial and ethnic groups (though this research used a large sample, they were predominantly white).

Future research also needs to consider the impact of smoking and high cholesterol levels on the relationship between heart attack survivors and a reduced risk of Parkinson's, which wasn't closely looked at in this study.

"We have previously found that following a heart attack, the risk of neurovascular complications such as ischemic stroke [clot-caused stroke] or vascular dementia is markedly increased, so the finding of a lower risk of Parkinson's disease was somewhat surprising," [says Sundbøll](#).

The research has been published in the [Journal of the American Heart Association](#).

<https://bit.ly/3v52Zxs>

Vegetables alone not enough to reduce heart risk, study finds

Vegetables may be good for you, but eating a lot of them is unlikely to reduce your risk of a heart attack or stroke, a large UK study suggests.

What else we eat, how much exercise we do and where and how we live may have more of an impact, the researchers say.

But they emphasise that a balanced diet helps reduce the risk of many diseases, including some cancers.

Eating at least five portions of fruit and vegetables every day is

recommended by health advisers, including the NHS.

The study, from the universities of Oxford and Bristol and the Chinese University of Hong Kong, asked nearly 400,000 people who are taking part in the [UK Biobank study](#) to fill in a questionnaire about their diet, including the quantity of cooked and raw vegetables they ate each day.

On average, people said they ate two heaped tablespoons of raw vegetables, three of cooked vegetables and five in total per day.

Their health, and any heart problems that led to hospital treatment or death, was then tracked over the next 12 years.

Rich in fibre

Although the risk of dying from cardiovascular disease was around 15% lower for those eating the most vegetables - particularly those eating lots of raw veg - compared with those eating the least, the researchers said this could all be explained by other factors.

These included people's lifestyles - for example, whether they smoked and how much alcohol they drank - as well as their jobs, incomes and overall diet.

As a result, they said their study did not find evidence of "a protective effect of vegetable intake" on how often heart and circulatory problems occurred.

Dr Ben Lacey, from the University of Oxford, said: "This is an important study with implications for understanding the dietary causes of cardiovascular disease (CVD)."

But Prof Naveed Sattar, professor of metabolic medicine at the University of Glasgow, said there was "good trial evidence" that eating foods rich in fibre such as vegetables, "can help lower weight and improve levels of risk factors known to cause heart disease".

He said the study's conclusions could be debated and should not alter widespread advice to eat at least five portions of fruit and vegetables a day.

"Many living in the UK fall well short of this, sadly, and more

needs to be done to encourage better intake of vegetables," he said.

"In fact, I suspect we may have underestimated the importance of a healthy diet on health and disease in general," he added.

Other experts said measuring how much and what kinds of foods people eat over many years in order to study the effect on disease risk was prone to error.

"Unfortunately doubt has to be cast on the reliability of findings from the use of simple questions expecting users to express an average intake value," said Prof Janet Cade, from the University of Leeds.

[The study, published in *Frontiers in Nutrition*](#), says people who eat lots of raw vegetables may have a reduced heart risk because cooking vegetables removes important nutrients, such as vitamin C. Oils and fat used in cooking may also increase intake of sodium and fats, which are known risk factors for heart problems.

People eating a high-vegetable diet may eat fewer calories and less fat, while also consuming more vitamins and anti-oxidants, which can prevent damage to cells.