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A Common Infection Could Be a Trigger For Multiple Sclerosis, Large Study Finds

Glandular fever (infectious mononucleosis) during the teenage years really is a risk factor for subsequent MS.

Scott Montgomery, *The Conversation*

For most of the time since the [first description](#) of multiple sclerosis (MS) in 1868, the causes of this disabling disease have remained uncertain. Genes have been identified as important, which is why having other family members with MS is associated with a greater risk of developing the disease.

A [recent study](#) my colleagues and I conducted found that several types of infection during the teenage years are associated with MS after age 20. Our study didn't investigate whether people who are more likely to have genetic risks for MS were also more likely to have worse infections. This might explain why people with MS also have more infections that need hospital treatment.

If this were the explanation, the infection would not be a risk factor triggering MS, it would only identify those more likely to have MS, anyway. Our new study, [published in JAMA Network Open](#), examines this and shows that [glandular fever](#) (one of the infections most associated with MS risk) during the teenage years really is a risk factor for subsequent MS.

Some scientists have suggested that infections like glandular [fever](#) (also called infectious mononucleosis "mono" or "kissing disease") might be worse in people who will go on to develop MS because their immune system is already different.

But another explanation – the one that our study investigated – is that the infection triggers MS. It has also been argued that families with more infections are different in other ways from families who have fewer infections. Perhaps the differences between these families – not the infections themselves – are what helps to explain

MS risk.

To confirm that infections are a true risk factor for MS, triggering the MS disease process, our latest study compared siblings in the same family. Siblings share much of their genetic make-up and have similar family lives.

If one sibling develops glandular fever and goes on to develop MS, while the other does not develop glandular fever and does not develop MS, that would suggest that it is the glandular fever rather than any genetic predisposition that led to the MS. (On the other hand, if only one developed glandular fever but they both later developed MS, that would suggest a genetic predisposition was to blame.) If we see the same pattern in many families, we can be much more certain that that's the case.

We looked at glandular fever at different ages, as the teenage years may be a time when exposures are most likely to increase MS risk. The study involved 2.5 million people living in Sweden. Just under 6,000 had a diagnosis of MS after age 20.

We found that glandular fever between ages 11 and 19 was associated with a significantly increased MS risk after age 20 years, in an analysis that compared siblings with each other in every family separately, and then the results were combined.

This design was to make sure the results are not because people susceptible to MS are also more likely to have more severe infections because of this susceptibility. The results confirm that glandular fever, and [almost certainly other infections](#), are important risk factors for MS and able to trigger the disease.

The new study also made it possible to look in greater detail at when an infection is more likely to trigger MS. Glandular fever in earlier childhood was less of a risk for MS than when it occurred after age 11 years. The highest risk for MS was seen for infections between ages 11 and 15 years (around the time of puberty), with the risk dropping with increasing age and almost completely

disappearing by age 25. Changes in the brain and immune system as people age may help explain this.

MS develops very slowly

Even though glandular fever may be triggering MS, most often around puberty, it can be many years before MS is diagnosed. Many who had the infection between ages 11 and 15 years did not have an MS diagnosis until after they were 30. This is because the damage to the brain caused by MS develops slowly until it makes someone sick enough to receive a diagnosis of MS.

Glandular fever during the teenage years may trigger MS because it can get into the brain. And the damage it causes to nerve cells may cause the immune system to start attacking a part of the nerves that insulates them – called the myelin sheath.

When the immune system is activated in this way, the process is called autoimmunity. Once started, it can damage nerves in the brain that can become progressively worse over the years. Fortunately, [modern treatments](#) are becoming increasingly effective in slowing this process.

This study provides stronger evidence that a severe bout of glandular fever (and likely other serious infections) during the teenage years – particularly around puberty - can trigger MS, even though, often, MS may not be diagnosed for at least ten years after the infection.

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Mysterious, extinct Japanese wolf may hold clues to origins of dogs

The two may share a common ancestor—a long-extinct population of wolves

By [David Grimm](#)

If you were walking through a dark forest in ancient Japan, you might hope to run into an okuri-ōkami, a wolf that would escort you safely to your destination. This creature of folklore may be based

on the Japanese wolf, a border collie-size animal with short legs and stubby ears that lived in Japan for thousands of years until humans wiped it out in the early 20th century.

Now, scientists studying ancient DNA from this wolf's bones say they may have solved the long-standing mystery of where it came from: a vanished population of gray wolves in East Asia that also gave rise to modern dogs.



An illustration of a Japanese wolf dating to the early 19th century Carl Hubert de Villeneuve/Wikimedia Commons

“It’s a very meticulous study,” says Peter Savolainen, a geneticist at the Royal Institute of Technology in Stockholm who was not involved. The research, he says, adds evidence to the idea that dogs arose in East Asia, as he and other researchers suspect, rather than in Europe or the Middle East, as some experts have proposed.

All of today’s dogs likely descend from a single population of gray wolves. But exactly where and when those wolves lived has long been a source of [contentious debate](#). Part of the problem is that although the species persists, that original population has likely vanished, wiping out genetic clues about doggy origins.

Enter the Japanese wolf (*Canis lupus hodophilax*). Described by some as [one of the greatest mysteries in the history of Japanese zoology](#), the animal’s origins are unclear, as is the route it took to reach Japan. A genetic analysis of remains from a single Japanese wolf published earlier this year found it was [closely related to a lineage of Siberian wolves](#), long thought extinct. Recent evidence also suggests [dogs may have arisen in Siberia](#). Might Japanese wolves and dogs share more than just geography?

To find out, Yohey Terai, an evolutionary biologist (and dog lover)

at Graduate University for Advanced Studies in Hayama, Japan, and colleagues extracted and sequenced the complete genomes of nine Japanese wolves, including museum specimens and skulls found on the roofs of old houses, where people used to place them for protection. The researchers also sequenced the genomes of 11 Japanese dogs, including popular breeds like [shiba inus](#). They compared all of these sequences with the available genomes of a variety of canids, such as foxes, coyotes, dingos, various wolves, and modern dogs from around the world.

The [Japanese wolves stood out as their own group](#), separate from the other species, the team reported last week on the preprint server bioRxiv. “They are distinct from any other wolf or dog,” Terai says. Yet when Terai and his colleagues constructed evolutionary trees, they found that the branch containing the Japanese wolf lineage lay closer to that of dogs than to any other animal. “It’s a sister relationship,” Terai says.

“If true, this is very important,” says Laurent Frantz, an evolutionary geneticist at the Ludwig Maximilian University of Munich who was not involved with the work. “It’s the first time we’ve seen a wolf population that’s close to dogs.”

Most importantly, the data suggest dogs and Japanese wolves share the same ancestor: a vanished population of gray wolves that lived somewhere in East Asia, given the likely trajectories of both Japanese wolves and early dogs. That supports two conflicting theories about canine domestication. Savolainen has long argued that dogs arose in Southeast Asia, whereas Frantz and his colleagues have suggested northeastern Siberia. The new study doesn’t provide enough data to say who is right, Savolainen says, but it does argue against other proposed regions of dog domestication, including Western Europe or the Middle East.

Not all dogs have equal genetic overlap with Japanese wolves, however. Terai and his colleagues found that eastern dogs—a group

that includes relatively ancient canines like the dingo and New Guinea singing dog, as well as modern Japanese breeds—shared as much as 5% of their DNA with Japanese wolves. Yet western dogs like German shepherds and Labrador retrievers shared far less genetic material. The team speculates that Japanese wolves bred with dogs that were moving east after a hypothesized [east-west split](#). Later, those eastern dogs bred with western dogs, leaving only a dilute Japanese wolf signature in western dogs.

As for how Japanese wolf DNA influences modern dogs, Terai can only speculate. His team found four genes from Japanese wolves in Japanese dogs, but it’s unclear what they do or why they have stuck around. A mutant version of one causes mice to binge food, Terai says. Voracious eating habits could have been beneficial for Japanese dogs living in ancient farming villages, where rice and vegetables were plenty, but meat was not. “These dogs would have had to eat a lot to get the nutrients they needed.” Other genes may have changed the shape of dogs’ bodies or faces; shiba inus, for example, have the peaked ears of wolves, not the floppy ears of many western breeds.

Despite the new findings, both Savolainen and Frantz argue more data will be needed to say for sure that dogs and Japanese wolves share the same direct ancestor—or whether another population of wolves gave rise to man’s oldest friend. “This is a really good step forward,” Frantz says. “Wolves are the key to understanding dogs, so it’s going to be really exciting to see where this goes.”

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There Could Be a Curious Link Between Psychedelics And Improved Heart Health

Emerging hypothesis suggests classic psychedelics could have a positive impact on heart health that is remarkably long-lasting

[Carly Cassella](#)

In recent years, a promising and exciting research avenue has been

the potential of psychedelics to provide some unexpected health benefits. Now, researchers might have a new lead in the cardiovascular department. [Magic mushrooms](#) have been [deemed a 'breakthrough therapy'](#) for treating [depression](#), LSD has [emerged as a possible new way to reduce our perception of pain](#), and [MDMA-assisted therapy](#) could soon become a legal way to [treat post-traumatic stress disorder](#) (PTSD) in the United States.

It's still early days, but the findings are so promising, scientists have begun to expand the scope of their research.

An emerging hypothesis suggests classic psychedelics, like DMT, ayahuasca, LSD, mescaline, peyote, or psilocybin, could have a positive impact on heart health that is remarkably long-lasting.

In early 2021, an [analysis](#) of the United States National Survey on Drug Use and Health found those who had tried a psychedelic at least once in their life had higher odds of greater self-reported overall health and lower odds of being overweight. What's more, these respondents had lower odds of having a heart condition, [like high blood pressure](#), in the past year.

The association prompted researchers to dig further. Using data from the same national survey between 2005 and 2014, the authors once again found those who had tried psychedelics at least once in their life had lower odds of heart disease and lower odds of [diabetes](#) in the previous year.

This was true even when researchers controlled for age, gender, marital status, race, household income, level of education, engagement in risky behavior, and other drug use.

It's an interesting correlation, but there are still other confounding factors that might not have been taken into account. And we still don't know whether it's the psychedelic use specifically that is impacting positive heart health, or the other way around.

"The direction of causality remains unknown," Otto Simonsson from the University of Oxford [told](#) PsyPost.

"Future trials with double-blind, randomized, placebo-controlled designs are needed to establish whether classic psychedelic use may reduce the risk of cardiometabolic diseases and, if so, through which mechanisms."

Clearly, we still have a lot of questions left to answer, but there are real reasons to suspect psychedelics can have an impact on heart health as well as brain health. First of all, depression, anxiety and other mental health issues are [closely tied to cardiovascular health](#), which means psychedelics could be having an indirect impact on physical health through improving mental health.

Or it could be happening simultaneously. The very receptors that psychedelics work on in the brain are linked not only to mental health but also to cardiometabolic health. Other drugs that attach to these serotonin receptors actually [show improved glucose tolerance in animal models](#) of obesity and type 2 diabetes.

Secondly, classic psychedelics like ayahuasca have been shown to have some [possible anti-inflammatory and immunomodulatory properties](#), which are also linked to better heart health.

All of these possible mechanisms need to be further explored before we can say with any certainty what is going on, or if these associations are more than just a fluke. The current analysis is limited in what conclusions it can draw.

"The regression models controlled for several potential confounders, but the associations could have been affected by latent variables that were not included in the dataset and could not be controlled for (e.g., a common factor that predisposes respondents to classic psychedelic use might also predispose them to salubrious lifestyle behaviors associated with cardiometabolic health)," the authors [write](#).

For now, the potential long-term effects of psychedelics on cardiovascular health remain largely a mystery, but it's a tantalizing one to solve. *The study was published in [Scientific Reports](#).*

<https://bit.ly/2Zb1jof>

Precision Medicine Data Dive Shows “Water Pill” Could Potentially Be Repurposed To Treat Alzheimer’s

NIH-funded research reveals clinical trial candidate for those with genetic risk.

A commonly available oral diuretic pill approved by the U.S. Food and Drug Administration may be a potential candidate for an Alzheimer’s disease treatment for those who are at genetic risk, according to findings published in *Nature Aging*. The research included analysis showing that those who took bumetanide — a commonly used and [potent diuretic](#) — had a significantly lower prevalence of Alzheimer’s disease compared to those not taking the drug. The study, funded by the National Institute on Aging (NIA), part of the National Institutes of Health, advances a [precision medicine](#) approach for individuals at greater risk of the disease because of their genetic makeup.

The research team analyzed information in databases of brain tissue samples and FDA-approved drugs, performed mouse and human cell experiments, and explored human population studies to identify bumetanide as a leading drug candidate that may potentially be repurposed to treat Alzheimer’s.

“Though further tests and clinical trials are needed, this research underscores the value of big data-driven tactics combined with more traditional scientific approaches to identify existing FDA-approved drugs as candidates for drug repurposing to treat Alzheimer’s disease,” said NIA Director Richard J. Hodes, M.D.

Knowing that one of the most significant [genetic risk factors](#) for late-onset Alzheimer’s is a form of the apolipoprotein E gene called APOE4, researchers analyzed data derived from 213 brain tissue samples and identified the Alzheimer’s gene expression signatures, the levels to which genes are turned on or off, specific to APOE4 carriers. Next, they compared the APOE4-specific Alzheimer’s

signatures against those of more than 1,300 known FDA-approved drugs. Five drugs emerged with a gene expression signature that the researchers believed might help neutralize the disease. The strongest candidate was [bumetanide](#), which is used to treat fluid retention often caused by medical problems such as heart, kidney, and liver disease.

The researchers validated the data-driven discoveries by testing bumetanide in both mouse models of Alzheimer’s and [induced pluripotent stem cell](#)-derived human neurons. Researchers found that treating mice which expressed the human APOE4 gene reduced learning and memory deficits. The neutralizing effects were also confirmed in the human cell-based models, which led to the hypothesis that people already taking bumetanide should have lower rates of Alzheimer’s. To test this, the team pared down electronic health record data sets from more than 5 million people to two groups: adults over 65 who took bumetanide and a matching group who did not take bumetanide. The analysis showed that those who had the genetic risk and took bumetanide had a ~35% to 75% lower prevalence of Alzheimer’s disease compared to those not taking the drug.

“We know that Alzheimer’s disease will likely require specific types of treatments, perhaps multiple therapies, including some that may target an individual’s unique genetic and disease characteristics — much like cancer treatments that are available today,” said Jean Yuan, M.D., Ph.D., Translational Bioinformatics and Drug Development program director in the NIA Division of Neuroscience. “The data in this paper make a good case to conduct a proof-of-concept trial of bumetanide in people with genetic risk.”

The research team was led by scientists at Gladstone Institutes, San Francisco, the University of California, San Francisco, and the Icahn School of Medicine at Mount Sinai, New York City. This group is one of more than 20 teams supported by NIA through a

[program](#) encouraging the researcher community to seek, through big data approaches, drugs that could potentially be repurposed.

The research was funded by NIH grants R01AG057683, R01AG048017, F31AG058439, R01AG061150, F31AG057150, R21TR001743, and K01ES028047.

<https://go.nature.com/3E7wShE>

COVID reinfections likely within one or two years, models propose

Estimates based on viral evolution forecast a 50% risk 17 months after a first infection without measures such as masking and vaccination.

[Lynne Peeples](#)

People who have been infected with SARS-CoV-2 can expect to become reinfected within one or two years, unless they take precautions such as getting vaccinated and [wearing masks](#). That's the prediction of modelling based on the genetic relationships between SARS-CoV-2 and other coronaviruses¹.

The findings also warn that people could be reinfected in just a few months if they are not vaccinated. "Immunity is relatively short-lived," says study co-author Jeffrey Townsend, a bioinformatician at the Yale School of Public Health in New Haven, Connecticut. "You should still get vaccinated even if you got infected."

Further data over the coming months, and years, will be necessary to know precisely how long natural immunity lasts. "But we don't want to wait for that. And we don't have to," says Townsend.

To estimate the durability of SARS-CoV-2 immunity, he and his colleagues wanted to understand how [antibody levels](#) from a previous infection affect the risk of reinfection. Data from an earlier study² allowed the team to chart this effect over years for 'endemic', or continually circulating, coronaviruses that cause the common cold. But SARS-CoV-2 is too new for such long-term data to be available.

To fill the gap, the scientists combined genetic data from SARS-

CoV-2, three endemic coronaviruses and the closely related coronaviruses SARS-CoV and MERS-CoV to build a viral family tree. The authors then used that tree to model how viral traits have evolved over time. Together, these traits provided an estimate of the decline in antibody levels after SARS-CoV-2 infection, and of other factors needed to understand reinfection risk.

The results suggest that the average reinfection risk rises from about 5% four months after initial infection to 50% by 17 months. Overall, natural protection seems to last for less than half as long as it does for the three common-cold coronaviruses.

Townsend says he was "surprised and daunted" by his findings, which suggest that COVID-19 is likely to transition from a pandemic disease to one that's [endemic](#).

COVID-19 wild cards

Still, many unknowns remain, including the probable severity of disease when someone is reinfected. Individuals can also vary significantly in both their susceptibility to reinfection and, if reinfected, their disease course — including whether they are likely to get [long COVID](#).

Sarah Cobey, an evolutionary biologist at the University of Chicago in Illinois, cautions that the new research relies on the assumption that viruses' genetic similarities predict similarities in traits relevant to reinfection. She notes that it might be too soon to make a confident statement about how quickly protection declines after a SARS-CoV-2 infection. But she adds that the science suggests that protection will indeed wane: "Nobody would expect immunity to last that long with a virus that is specifically evolving to escape immunity."

Cobey also underscores the need for people who have been infected to bolster their protection with a vaccine — a point driven home by research published by the US Centers for Disease Control and Prevention in August. The study looked at people who got COVID-

19 in 2020, some of whom became reinfected in May or June 2021. It found that those who had not had a vaccine were more than twice as likely to get reinfected in that period as those [who had both the virus and a vaccine](#)³.

doi: <https://doi.org/10.1038/d41586-021-02825-8>

References

1. Townsend, J. P. et al. *Lancet Microbe* [https://doi.org/10.1016/S2666-5247\(21\)00219-6](https://doi.org/10.1016/S2666-5247(21)00219-6) (2021). [PubMed](#) [Article](#) [Google Scholar](#)

2. Edridge, A. W. D. et al. *Nature Med.* **26**, 1691–1693 (2020). [PubMed](#) [Article](#) [Google Scholar](#)

3. Cavanaugh, A. M., Spicer, K. B., Thoroughman, D., Glick, C. & Winter, K. *Morb. Mortal. Wkly Rep.* **70**, 1081–1083 (2021). [PubMed](#) [Article](#) [Google Scholar](#)

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<https://bit.ly/3mc5Wrf>

Your gut bacteria may be hoarding your medication

Researchers have observed this effect in petri dishes and nematodes

[Madeline Barron](#)

When we take medications, we generally do two things: first, we swallow some pills, then we wait for them to kick in. Whether or not they do, however, may be tied to our gut microbes.

Intestinal bacteria influence the availability and activity of therapeutic drugs in the body. For instance, some bacteria metabolically convert, or ‘[biotransform](#),’ drugs into their active forms; others [inactivate](#) them. And some, according to [a new report](#) published in *Nature*, don’t chemically manipulate drug molecules — they hoard them.

In this study, researchers incubated 25 representative strains of gut bacteria with 12 orally administered drugs, including those used to treat asthma, high cholesterol, and diarrhea. By measuring drug levels in the growth medium before and after 48 hours of incubation, the scientists identified 29 novel bacteria-drug pairs in which the drug was depleted from the medium. Comparing drug concentrations in the medium alone with that of the total culture

revealed that, in most cases, the drug was absent from the medium but recoverable from the total culture. These results suggest the medications were accumulating inside the bacteria.

The question is: When bacteria vacuum up drug molecules, does this alter the drug’s effect on the host?

To explore this, the researchers incubated *Caenorhabditis elegans*, a nematode and model organism, with duloxetine, an antidepressant that was accumulated by several bacterial strains. While duloxetine alone decreased nematode motility, adding a duloxetine-accumulating strain of *E. coli* to the culture reduced this effect.

These findings indicate that bacterial hoarding of medications may affect the way those drugs affect their targets. Ultimately, more research is required to determine whether a similar scenario plays out in the human gut, and in the context of other drugs. Greater insight into the interplay between medications and gut microbes could expand our understanding of drug bioavailability and efficacy, and how they may vary from one person (and gut microbiome) to the next.

<https://bit.ly/3B2DmMV>

New Model Stanford Researchers Points to Solution to Global Blood Shortage

A mathematical model of the body’s interacting physiological and biochemical processes shows that it may be more effective to replace red blood cell transfusion with transfusion of other fluids that are far less in demand.

By Danielle Torrent Tucker, Stanford University

Blood transfusions save lives, yet the precious fluid is in desperately short supply, not just in the U.S. but around the globe. But what if transfusions don’t always require blood?

A new mathematical model of the body’s interacting physiological and biochemical processes – including blood vessel expansion, blood thickening and flow-rate changes in response to the

transfusion of red blood cells – shows that patients with anemia, or blood with low oxygen levels, can be effectively treated with transfusions of blood substitutes that are more readily available.

The research, co-authored by scientists at Stanford University and the University of California, San Diego (UCSD), was published on October 14, 2021, in the *Journal of Applied Physiology*.

Using a different fluid could also eliminate a harmful consequence of blood transfusion: Blood use has been observed to [lower lifespan](#) by 6 percent per unit transfused per decade because of its adverse side effects.

“Instead of real blood, we can use a substitute that can lower the costs and eliminate blood transfusion’s negative effects,” said lead study author Weiyu Li, a PhD student in energy resources engineering at Stanford’s School of Earth, Energy & Environmental Sciences (Stanford Earth).

Transfusion is a common procedure for transferring blood components directly to anemic patients’ circulation. Red blood cells are uniquely equipped to perform the function of carrying oxygen, which is why they are used for transfusions for patients experiencing anemia. But the process of obtaining, storing and delivering the correct, sanitary blood type for each patient is also intensive and costly. Moreover, the supply of blood that is available falls far short of the demand: The global deficit across all countries without enough supply totals about 100 million units of blood per year.

“You could deliver more goods, in this case, oxygen, with less – that’s actually the basic idea of sustainability,” said senior study author Daniel Tartakovsky, a professor of energy resources engineering at Stanford Earth. “It’s all about how to do more with less.”

Transfusion of red blood cells is done to improve the likelihood that oxygen vital to organ and tissue function will be delivered.

However, the process also thickens the blood, and that increased viscosity can be a problem, according to the research. The new model shows that during transfusion, some patients’ blood vessels do not dilate and, since their blood has been thickened by additional red blood cells, it is more viscous and does not circulate as easily to deliver oxygen. For these patients, treating anemia with a 2-unit transfusion – currently, the most frequently used transfusion quantity – would reduce blood flow, regardless of the state of anemia, according to the model.

However, for many people, transfusion causes blood vessels to dilate, thereby increasing circulation and delivering more oxygen to the body. The findings reveal the advantage of anemic patients whose blood vessels dilate during transfusion. The model suggests that either abstaining from transfusion or transfusing alternative fluids known as plasma expanders, which prompt blood vessels to dilate, may be a more effective way to increase oxygen delivery. Plasma expanders consist of solutions of high-molecular-weight starch dissolved in normal saline; they have been in use in transfusion medicine for several decades and have proven to be effective in experimental studies.

“At present, blood transfusion is determined by addressing the wrong target, namely restoring oxygen-*carrying* capacity,” said co-author Marcos Intaglietta, a professor and founder of the bioengineering discipline at UCSD. “But the logical target of a blood transfusion is restoring oxygen-*delivery* capacity.”

Projections of the team’s results show that safe and low-cost blood substitutes can decrease the overall cost of blood transfusion by 10 times, while significantly lowering the negative aspects of the process. Their model of the body’s circulatory processes was derived from previously published experiments on how mammals react to transfusion.

“Our mathematical model identifies natural physiological processes

that explain the conclusion of multiple observational studies: People can get the benefit of blood transfusion without using blood,” Tartakovsky said. “But nothing really comes out of modeling alone – it has to be grounded in observations, investigational studies and experience.”

The co-authors hope their findings will lead to clinical trials that test the capacity for non-blood alternatives to increase oxygen delivery. To date, there have not been consistent results from rigorous medical trials that support the notion that small amounts of blood are more effective than just adding human plasma, according to the study authors.

“This is the first model to consider all of these effects,” Li said. “I hope people have a chance to see our results and decide whether they could be used to treat patients.”

Reference: “A model of anemic tissue perfusion after blood transfusion shows critical role of endothelial response to shear stress stimuli” by Weiyu Li, Amy G. Tsai, Marcos Intaglietta and Daniel M. Tartakovsky, 14 October 2021, Journal of Applied Physiology.

[DOI: 10.1152/jappphysiol.00524.2021](https://doi.org/10.1152/jappphysiol.00524.2021)

Tartakovsky is also a member of Bio-X. Amy Tsai of UC San Diego is a co-author on the paper.

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<https://bit.ly/2ZchLEy>

Durability, docility genes solve domestic horse origins mystery

Humans tamed horses some 4,200 years ago in the northern Caucasus region of what is today southwestern Russia

by Natalie Handel

Humans tamed horses some 4,200 years ago in the northern Caucasus region of what is today southwestern Russia, a study said Wednesday, solving the centuries-old mystery of where and when the process began that led to today's domesticated equine population.

Taming wild horses changed the way humans moved, fought,

communicated and traded.

But it also meant domesticated mares and stallions would come to replace all the wild populations in existence—from western Europe to Mongolia—within the span of about five centuries.

To pinpoint the beginning of this process, an international team led by Ludovic Orlando of the Centre for Anthropology and Genomics in Toulouse sequenced DNA from the remains of nearly 300 ancient horses from across Europe.

According to the study in *Nature*, their hunt led to a gene and a genomic region that may have influenced key traits in today's horses: docility and a strong back. "Our data show a rapid expansion (of this horse) right from the start," Orlando told AFP. "This implies that people were really motivated to create a new vehicle."

Dead end in Kazakhstan

Until recently the most promising evidence pointed to domestic horse origins in northern Kazakhstan.

There, archaeologists unearthed ceramics with traces of mare milk, horse feces in pens, and huge quantities of old horse bones and teeth that seemed to show harness use. "This reasonably made us conclude that this was where domestication happened," Orlando said of the 5,500 year old discoveries. "We started our search there by sequencing the genomes of this horse, expecting they would turn out to be the direct ancestors of domestic horses" he said.

Instead, they ended up ruling out the settlement as evidence of a failed attempt at domestication with the remains linked to a kind of horse that has since become virtually extinct.

"We had to take another approach," Orlando said.

'From Iberia to Siberia'

Rather than look at one possible location for evidence of domestication, Orlando said his team decided to sequence them all "from Iberia to Siberia".

With a team of over 150 scientists, they looked at samples dating from 2,000 to 50,000 years ago in order to include all horse lineages known to exist within that timeframe. They used cutting-edge sequencing technology and spent years hunting for similarities between ancient DNA and the horses of today.



Horse mandible excavated from the Ginnerup archaeological site, Denmark, June 2021. (This site was included in the study "The origins and spread of domestic horses from the Western Eurasian steppes" led by Ludovic Orlando, CNRS). Credit: © Lutz Klassen, East Jutland Museum.

Finally, about a year ago, a match surfaced in southwestern Russia concentrated in an area about 500 kilometers wide. "It was very, very clear: the number of genetic differences found outside the region was much, much greater than within," Orlando said.

Once they had localized the genome of interest, they used radio carbon dating to discover when these horses roamed, within one or two centuries.

Within their DNA, a particular gene and genomic region stood out: one associated with spinal strength, and one with anxiety.

The study says human preference for horses with these genes "suggests shifting use toward horses that were more docile, more resilient to stress and involved in... endurance running, weight bearing and/or warfare".

Mapping the various horse genomes over time, the researchers saw a mosaic of wild horse populations that persisted for millennia.

But as soon as domestication by man occurred, the map changed drastically. "The colorful map became one solid color," Orlando said. One horse genome, the ancestor of today's domestic horse population, took over. "At first that horse was very confined and then suddenly it spread across Eurasia like wildfire."

More information: Ludovic Orlando, *The origins and spread of domestic horses from the Western Eurasian steppes*, *Nature* (2021). [DOI: 10.1038/s41586-021-04018-9](https://doi.org/10.1038/s41586-021-04018-9).

www.nature.com/articles/s41586-021-04018-9

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

Injectable Patch Shows Promise for Heart Attack

Recovery

Injectable patch conducts electricity and keeps its shape once grafted to heart muscle

Lisa Rapaport

After a heart attack, the damaged area of the heart often becomes scar tissue that can't receive electrical messages to contract and pump blood to the body.

The result is a weakened heart that could get an irregular beat, known as an arrhythmia, or go into failure.

Right now, doctors have two imperfect options for repairing this damaged tissue.

One is to surgically implant a scaffold that conducts electrically and bridges the heart's signaling system past the dead tissue.

But these implants require open-chest surgery, which is risky and can lead to other heart problems.

Clinicians can use an approach that avoids opening the chest, but the patch used for these procedures may not hold its shape when grafted to damaged tissue.

Now, scientists may be working on a fix that promises the best of both worlds: an injectable patch that conducts electricity and keeps its shape once grafted to heart muscle.

The patch hasn't been tested in humans — any such trials are still a long way off — but early results in animals show potential.

This experimental patch can be rolled up, threaded into a catheter or a syringe, and injected into damaged heart tissue, where it unfurls and attaches to the muscle.

Once in place, the patch supports normal heart function, according to results from studies using rats and pigs.

The findings were published in [Nature Biomedical Engineering](#). When researchers placed the patch on damaged heart muscle in rats, they found this fix resulted in a return to mostly normal heart function within 4 weeks.

Results were similar when scientists tested the patch in a small number of pigs, which are considered to resemble humans more closely than rodents.

The patched hearts did a better job in pumping oxygen-rich blood to the body, and the amount of heart tissue that wasn't getting enough oxygen also declined.

Source: Nature Biomedical Engineering: "Injectable and conductive cardiac patches repair infarcted myocardium in rats and minipigs."

<https://bit.ly/3pmF4GS>

Scientists Are Closely Tracking a New Delta Subtype Spreading in The UK

Scientists worldwide are closely tracking a descendent of the [highly infectious Delta variant](#) that is spreading in the UK.

Catherine Schuster-Bruce, Business Insider

England's public-health authority said in a report on [Friday](#) that it was monitoring a subtype of the [Delta variant](#) called AY.4.2, which had infected more and more people recently.

Francois Balloux, director at the University College London Genetics Institute, said on [Twitter on Saturday](#) that data about AY.4.2 suggested it could be 10 percent more transmissible than the most common [Delta variant](#) in the UK, called AY.4.

"As such, it feels worthwhile keeping an eye on it," he said.

As of 27 September, 6 percent of UK sequenced tests were AY.4.2, Public Health England (PHE) said in its report on Friday, adding that estimates could be imprecise because it was difficult to sequence the variant's mutations.

Dr. Scott Gottlieb, the former Food and Drug Administration commissioner, said that the new variant wasn't an "immediate cause

for concern," but called for "urgent research" to work out if it was more infectious or able to avoid the body's immune response.

"We should work to more quickly characterize these and other new variants. We have the tools," he said on Twitter [on Sunday](#), adding that a coordinated, global response was required.

Dr Jeffrey Barrett, medical genomics group leader at the Wellcome Trust Sanger Institute, [said on Twitter on Tuesday](#) that AY.4.2 was the only Delta descendant that was steadily increasing, suggesting a "consistent advantage" over Delta.

Barrett cautioned that AY.4.2 was replacing Delta at a much slower rate than Delta had replaced the formerly-dominant Alpha variant. The Delta variant is estimated to be about 60 percent more infectious than Alpha.

The same pattern for AY.4.2 hasn't yet been seen in other countries. Balloux said in a statement on Tuesday that the variant was "rare" outside of the UK, with only three cases detected in the US so far. "In Denmark, the other country that besides the UK has excellent genomic surveillance in place, it reached a 2 percent frequency but has gone down since," he said.

New mutations

The [virus](#) that causes [COVID-19](#) gets about two new mutations per month, and there are now 56 Delta descendants, [according to Scripps University's Outbreak.info](#), which includes data from the Centers for Disease Control and Prevention. Before AY.4.2, PHE had tended to group Delta and its descendants together.

AY.4.2 has two new mutations in the part of the virus that attaches to human cells, which is called the spike protein. It's not yet clear how these mutations will affect the virus' behavior.

Balloux said neither of these mutations had been found in other variants of concern.

<https://bit.ly/30HvtOw>

Earth Tipped on Its Side 84 Million Years Ago, New Evidence Suggests

New study presents evidence of one such tilting event that occurred around 84 million years ago

David Nield

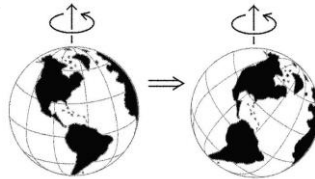
We know that [true polar wander](#) (TPW) can occasionally tilt whole planets and moons relative to their axes, but it's not entirely clear just how often this has happened to Earth.

Now a new study presents evidence of one such tilting event that occurred around 84 million years ago – when [dinosaurs](#) still walked the Earth.

Researchers analyzed limestone samples from Italy, dating back to the Late Cretaceous period (100.5 to 65.5 million years ago), looking for evidence of shifts in the magnetic record that would point towards an occurrence of TPW.

Bacteria fossils trapped in the rock, forming chains of the mineral [magnetite](#), offer some of the most convincing evidence yet of true polar wander in the Late Cretaceous – and it may help settle a scientific debate that's been going on for decades.

"This observation represents the most recent large-scale TPW documented and challenges the notion that the spin axis has been largely stable over the past 100 million years," the researchers explain in their [paper](#).



How true polar wander looks. (Victor C. Tsai/Wikimedia Commons/Public Domain)

Earth is made up of a solid metal inner core and a liquid metal outer core, with a solid mantle and crust (the surface) moving slowly around on top of the liquid metal.

Earth's magnetic field, generated by the outer core, is recorded in

rocks like the ones studied here.

True polar wander is when the geographic poles shift substantially, so the outer wrapping of Earth tilts over.

Nothing actually changes in terms of Earth's magnetic field, but the shifting rocks will record different [paleomagnetic data](#) as they move. That data reveals the distance to the North and South geographic poles, enabling researchers to plot where these poles actually are.

A fully vertical field means a rock was at the pole, while a fully horizontal field indicates it was at the equator.

"Imagine looking at Earth from space," [says geologist Joe Kirschvink](#), from the Tokyo Institute of Technology in Japan.

"True polar wander would look like the Earth tipping on its side, and what's actually happening is that the whole rocky shell of the planet – the solid mantle and crust – is rotating around the liquid outer core."

According to the study, there was around a 12 degree tilt on Earth around 84 million years ago, which was corrected relatively quickly – within about 5 million years, the equivalent of a "cosmic yo-yo" in the words of the researchers.

What that means is that these rocks – and Italy itself – took a journey towards the equator before tipping back.

The team says that [previous studies](#) hinting that true polar wander didn't happen during the Late Cretaceous simply didn't gather enough data from the geological record – something that can't be said about the latest research.

"That is one reason why it is so refreshing to see this study with its abundant and beautiful paleomagnetic data," [says geophysicist Richard Gordon](#), from Rice University in Houston, who wasn't involved in the study.

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

<https://bit.ly/3Bc4uta>

First Viking settlement in North America dated to exactly 1000 years ago

Felled trees and cosmic rays reveal when L'Anse aux Meadows was occupied

By [Michael Price](#)

The first permanent settlement of Vikings in North America—a seaside outpost in Newfoundland known as L'Anse aux Meadows—has tantalized archaeologists for more than 60 years. Now, scientists at last have a precise date for the site: Tree rings show a Viking ax felled trees on the North American continent exactly 1000 years ago, in 1021 C.E. The result is a star example of a relatively new dating method using a spike in solar radiation that left its mark in tree rings around the world.



The L'Anse aux Meadows site in Newfoundland, which researchers have now dated to 1021 C.E., contains a reconstruction of the seaside Viking settlement. Glenn Nagel Photography

“The precision is astounding,” says Rachel Wood, a radiocarbon scientist at the Australian National University who wasn’t involved in the new study. “The idea to use these short-term sharp fluctuations in radiocarbon ... has been around for a few years, but it is great to see it actually being used to date an important archaeological site.”

The Vinland sagas, a pair of Icelandic texts written in the 13th century, describe the Norse explorer Leif Erikson’s expeditions to a land referred to as Vinland. Although the texts contain their fair share of embellishment, most historians agree the sagas show Vikings sailed southwest from Greenland and reached the North

American continent sometime at the turn of the millennium. The discovery of a Viking-era archaeological site in 1960 featuring the remains of distinctive Norse-style buildings, a bronze cloak pin, iron nails, and other Viking artifacts bolstered such evidence.

Scientists have previously dated bits of wood from the site using radiocarbon dating, which measures the decay of the radioactive isotope carbon-14 in organic material and often gives dates within a couple hundred years. Early radiocarbon-dating efforts at L'Anse aux Meadows dated the artifacts to between 793 and 1066 C.E.—not much help to historians looking for an accurate timeline of the Vikings’ arrival in North America.

A breakthrough in 2012 promised to refine those dates [with the help of abnormally strong cosmic ray bursts](#). In the year 993 C.E., a large cosmic burst—probably a solar flare—caused a pulse in the production of carbon-14 in Earth’s atmosphere, which was taken up by plants around the world through photosynthesis. Every tree that was alive in 993 C.E. has a telltale ring with higher than usual carbon-14 content. By counting out from that ring, researchers can arrive at the precise year a tree died. A similar cosmic burst in 775 C.E. has already helped scientists precisely date [the construction of a chapel in Switzerland](#) and [a volcanic eruption on the Chinese–North Korean border](#).

In the new study, researchers led by radiocarbon scientist Michael Dee at the University of Groningen applied this technique to a collection of wooden chunks that had been excavated from L'Anse aux Meadows through the 1960s and '70s. Based on cut marks in the wood, archaeologists know they were chopped by metal axes, suggesting Vikings, rather than Indigenous people of North America, were responsible. For decades, those chunks were kept in a freezer by co-author Birgitta Wallace, an archaeologist with Parks Canada who has spent her career at site.

“[The artifacts] are not some beautiful objects or Viking artwork or

anything like that,” Dee says. “They are really just the offcuts or refuse of Viking activity. ... It’s a real tribute to [Wallace] that she had the foresight to do such a thing.”

Working with three chunks of wood with recognizable edges, the researchers radiocarbon dated the rings in each piece, looking for a telltale spike in carbon-14. In all three pieces, they found it in the 29th ring from the edge, indicating the trees had stopped growing 28 years after the 993 C.E. solar flare, [or the year 1021 C.E.](#), the researchers report today in *Nature*. Of course, that just confirms the Vikings were present in North America by that year, Dee notes, and it’s possible they arrived even earlier.

Another possibility is that the Vikings simply cut up wood that had been lying on the ground for years. But that’s unlikely, Dee says, because fallen wood quickly loses its strength—and historians think Vikings were seeking timber to bring back to relatively treeless Greenland. “There was no reason for them to pick up something and whack at it, rather than just cut down a brand new, solid tree.”

Lukas Wacker, a physicist who studies radiocarbon dates at ETH Zurich’s Laboratory of Ion Beam Physics, agrees that’s the most likely explanation. “[It’s convincing] that different artifacts—not all from the same tree—gave consistently the same result,” he says. “It is very unlikely that just by chance they have the same age.”

doi: 10.1126/science.acx9403

<https://go.nature.com/3nreuto>

Ivory hunting drives evolution of tuskless elephants

In Mozambique, the selective poaching of elephants with tusks has led to a higher number of females being born without them.

[Nicola Jones](#)

African elephants have evolved towards tusklessness in an area where they were intensively hunted for ivory, finds a study of elephants’ traits and genetics in Mozambique.

The results, published on 21 October in *Science*¹, could have

implications for the recovery of elephant populations in the country. Ivory trading was used to finance a civil war in Mozambique from the late 1970s to early 1990s. Poaching caused the elephant population in the country’s Gorongosa National Park to crash by more than 90%, from more than 2,500 animals down to around 200 in the early 2000s.

Before the war, about 18.5% of females were naturally tuskless — a trait that made them undesirable to poachers. Among the 91 female elephants that have been born since the war, the researchers show, that fraction has risen to 33%.



Elephants without tusks had an advantage in areas where ivory poaching was prevalent. Credit: Peter Chadwick/Getty

Mathematical modelling by evolutionary biologist Shane Campbell-Staton at Princeton University in New Jersey and his colleagues has confirmed that this shift is the result of hunting pressure: the selective killing of elephants with tusks has led to the birth of more tuskless offspring.

Fast evolution

Hunting has been blamed for causing rapid change in animals before. The size of horns on bighorn sheep (*Ovis canadensis*) in Alberta, Canada, for example, dropped by 20% over 20 years of trophy hunting². And fishing is thought to have reduced the sizes of some fish species.

But it has proved hard to pin down exactly what’s happening genetically in these populations, and difficult to unpick the importance of evolutionary pressure from hunting compared with other environmental factors, such as climate change. “It’s hard to prospect for these genes,” says Chris Darimont, a conservation scientist at the University of Victoria, Canada. “There’s controversy about whether harvest pressure matters in the first place; a lot of

[wildlife] managers don't want to hear that." If hunting does cause significant genetic changes to a small population of animals, Darimont notes, it can be very hard to restore the original traits.

Campbell-Staton and his colleagues noted that tusklessness is seen only in female elephants. This, and the pattern of inheritance of the trait, suggested that it is caused by a mutation on the X chromosome that is fatal to males and dominant in females — just one copy of a mutation is needed to cause it. The researchers searched through the elephants' genomes looking for regions on the X chromosome that differed between those with and without tusks, and showed signs of recent selection pressure. They identified two likely candidate genes: *AMELX* and *MEP1a*. In people, these genes are known to be involved with the growth of incisor teeth (the human equivalent of tusks).

The work offers strong evidence that hunting has caused this change, says Darimont. "They have this very compelling genomic data," he says. "This is a wake-up call in terms of coming to grips with humans as a dominant evolutionary force on the planet."

For the elephants, selection for tuskless females could have other knock-on effects. By looking at DNA in elephant faeces, the researchers learnt that tusked and tuskless animals eat different plants. "Because elephants are keystone species, changes in their diet can change the whole landscape," notes study co-author Robert Pringle, a biologist at Princeton. And because the tuskless trait is fatal to male offspring, it is likely that fewer elephants will be born overall, which could slow population recovery even though poaching has now been stopped in the park. "Tusklessness might be advantageous during a war," says Pringle, "but that comes at a cost." doi: <https://doi.org/10.1038/d41586-021-02867-y>

References

1. Campbell-Staton S. C. et al. *Science* **374**, 483–487 (2021). [Article](#) [Google Scholar](#)
2. Allendorf F. W. and Hard J. J. *Proc. Natl. Acad. Sci. U.S.A.* **106** (Supplement 1) 9987–9994 (2009). [PubMed](#) [Article](#) [Google Scholar](#) [Download references](#)

<https://bit.ly/3E8RvKv>

Some of the world's oldest rubies linked to early life

Carbon residue that was once ancient life found encased in a 2.5 billion-year-old ruby

While analyzing some of the world's oldest colored gemstones, researchers from the University of Waterloo discovered carbon residue that was once ancient life, encased in a 2.5 billion-year-old ruby.



Photo of the ruby that this study looks at. Credit: University of Waterloo

The research team, led by Chris Yakymchuk, professor of Earth and Environmental Sciences at Waterloo, set out to study the geology of rubies to better understand the conditions necessary for ruby formation. During this research in Greenland, which contains the oldest known deposits of rubies in the world, the team found a ruby sample that contained [graphite](#), a mineral made of pure [carbon](#). Analysis of this carbon indicates that it is a remnant of early life.

"The graphite inside this ruby is really unique. It's the first time we've seen evidence of ancient life in ruby-bearing rocks," says Yakymchuk. "The presence of graphite also gives us more clues to determine how rubies formed at this location, something that is impossible to do directly based on a ruby's color and [chemical composition](#)."

The presence of the graphite allowed the researchers to analyze a property called isotopic composition of the carbon atoms, which measures the relative amounts of different carbon atoms. More than 98 per cent of all carbon atoms have a mass of 12 atomic mass units, but a few carbon atoms are heavier, with a mass of 13 or 14 atomic mass units.

"Living matter preferentially consists of the lighter carbon atoms because they take less energy to incorporate into cells," said

Yakymchuk. "Based on the increased amount of carbon-12 in this graphite, we concluded that the carbon [atoms](#) were once ancient life, most likely dead microorganisms such as cyanobacteria."

The graphite is found in rocks older than 2.5 billion years ago, a time on the planet when oxygen was not abundant in the atmosphere, and life existed only in microorganisms and algae films.

During this study, Yakymchuk's team discovered that this graphite not only links the gemstone to [ancient life](#) but was also likely necessary for this ruby to exist at all. The graphite changed the chemistry of the surrounding rocks to create favorable conditions for ruby growth. Without it, the team's models showed that it would not have been possible to form rubies in this location.

The study, [Corundum \(ruby\) growth during the final assembly of the Archean North Atlantic Craton, southern West Greenland](#), was recently published in *Ore Geology Reviews*. A companion study, [The corundum conundrum: Constraining the compositions of fluids involved in ruby formation in metamorphic melanges of ultramafic and aluminous rocks](#), was published in the journal *Chemical Geology* in June.

More information: Chris Yakymchuk et al, *Corundum (ruby) growth during the final assembly of the Archean North Atlantic Craton, southern West Greenland*, *Ore Geology Reviews* (2021). [DOI: 10.1016/j.oregeorev.2021.104417](https://doi.org/10.1016/j.oregeorev.2021.104417)

Vincent van Hinsberg et al, *The corundum conundrum: Constraining the compositions of fluids involved in ruby formation in metamorphic melanges of ultramafic and aluminous rocks*, *Chemical Geology* (2021). [DOI: 10.1016/j.chemgeo.2021.120180](https://doi.org/10.1016/j.chemgeo.2021.120180)

<https://bit.ly/3b2ClKp>

Rapid Climate Change Wiped Out Woolly Mammoths, Study Confirms

It was not just the climate changing that was the problem, but the speed of it.

In a large-scale environmental DNA metagenomic study of ancient plant and mammal communities, an international team of

researchers have analyzed 535 permafrost and lake sediment samples from across the Arctic spanning the past 50,000 years.

"Scientists have argued for 100 years about why mammoths went extinct," said Professor Eske Willerslev, a researcher at the University of Cambridge and director of the Lundbeck Foundation GeoGenetics Centre at the University of Copenhagen.

"Humans have been blamed because the animals had survived for millions of years without climate change killing them off before, but when they lived alongside humans they didn't last long and we were accused of hunting them to death."

"We have finally been able to prove was that it was not just the climate changing that was the problem, but the speed of it."

"They were not able to adapt quickly enough when the landscape dramatically transformed and their food became scarce."

"As the climate warmed up, trees and wetland plants took over and replaced the mammoth's grassland habitats."

"And we should remember that there were a lot of animals around that were easier to hunt than a giant [woolly mammoth \(*Mammuthus primigenius*\)](#) — they could grow to the height of a double decker bus!"

Woolly mammoths and their ancestors lived on Earth for approximately 5 million years. During this period, herds of these huge animals as well as reindeers and woolly rhinoceroses thrived in the cold and snowy conditions.

Despite the cold, a lot of vegetation grew to keep the various species of animals alive — grass, flowers, plants, and small shrubs would all have been eaten by the vegetarian mammoths who probably their tusks to shovel snow aside and are likely to have used their trunks to uproot tough grasses. They were so big because they needed huge stomachs to digest the grass.

Mammoths could travel a distance equivalent of going around the world twice during their lifetime and fossil records show they lived

on all continents except Australia and South America.

Populations were known to have initially [survived](#) the end of the latest Ice Age in small pockets off the coasts of Siberia and Alaska — on Wrangel Island and St Paul Island — but the new research found they actually lived longer elsewhere too and the breeds of mammoths on both the islands were closely related despite being geographically separated.

The authors also sequenced the DNA of 1,500 Arctic plants for the very first time to be able to draw these globally significant conclusions. “The most recent Ice Age ended 12,000 years ago when the glaciers began to melt and the roaming range of the herds of mammoths decreased,” said Dr. Yucheng Wang, a researcher in the Department of Zoology at the University of Cambridge.

“It was thought that mammoths began to go extinct then but we also found they actually survived beyond the Ice Age all in different regions of the Arctic and into the Holocene — the time that we are currently living in — far longer than scientists realised.”

“We zoomed into the intricate detail of the environmental DNA and mapped out the population spread of these mammals and show how it becomes smaller and smaller and their genetic diversity gets smaller and smaller too, which made it even harder for them to survive.”

“When the climate got wetter and the ice began to melt it led to the formation of lakes, rivers, and marshes.”

“The ecosystem changed and the biomass of the vegetation reduced and would not have been able to sustain the herds of mammoths.”

“We have shown that climate change, specifically precipitation, directly drives the change in the vegetation — humans had no impact on them at all based on our models.”

The team’s [results](#) appear today in the journal *Nature*.

Y. Wang et al. Late Quaternary dynamics of Arctic biota from ancient environmental genomics. Nature, published October 20, 2021; doi: 10.1038/s41586-021-04016-x

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

Sleep Apnea Linked to Lower Stroke Mortality After Thrombectomy

[Obstructive sleep apnea](#) (OSA) is associated with a decreased risk for mortality and in-hospital complications in patients who undergo thrombectomy, new research suggests.

Daniel M. Keller, PhD

In a cross-sectional study of patients who were treated with endovascular mechanical thrombectomy (MT) for an acute [ischemic stroke](#) (AIS), the patients with OSA were at significantly lower risk for death than the patients without OSA. The rate of [intracranial hemorrhage](#) was also lower among the OSA group than the non-OSA group.

“Our goal was to determine whether the use of MT as a definitive reperfusion therapy could reduce the disparity in outcomes often observed in OSA vs non-OSA AIS patients,” lead author Justin Lepow, a medical student at New York Medical College, in Valhalla, New York, told meeting attendees.

He presented the findings at the XXV World Congress of Neurology (WCN), which was held online.

Cross-Sectional Analysis

Previous studies showed that patients with OSA and AIS had poorer outcomes and that mortality was increased in comparison with patients with stroke but without OSA, Lepow told meeting attendees.

The investigators used the National Inpatient Sample (NIS) to conduct a cross-sectional analysis of patients with AIS treated with MT from 2010 to 2018. During that period, MT was accepted as an effective therapy for AIS but had not been evaluated for patients with OSA.

The NIS is the largest inpatient database in the United States. It represents 20% of all US community hospital discharges annually.

The researchers used International Classification of Diseases-9-Clinical Modification (ICD-9-CM) and ICD-10-CM codes to identify patients treated with MT after AIS.

The investigators employed a battery of stroke severity indices to evaluate baseline characteristics and used other measures to rate severity of illness. Outcomes included in-hospital complications and discharge disposition. In addition, a multivariable model was constructed to evaluate the independent association of OSA status and mortality after adjusting for baseline covariates.

Of the total cohort of 101,093 patients with AIS who were evaluated, 6412 (6.3%) had OSA. At baseline, the OSA group was younger than the non-OSA group (mean age, 65.6 years, vs 68.5 years). There were fewer women in the OSA group (33.5% vs 50.5%), and there were fewer non-White patients (22.3% vs 29.7%; all comparisons, $P < .001$). Also, more of the patients in the OSA group had strokes from 2016 to 2018, which was after the MT clinical trial era (68.8% vs 63.8%; $P = .001$).

There were also differences in the rate of comorbid conditions at baseline. The percentage of patients with [obesity](#) was higher in the OSA group than in the non-OSA group (41.4% vs 10.5%), as was the percentage with [atrial fibrillation](#) (47.1% vs 42.2%), [hypertension](#) (87.4% vs 78.5%), and diabetes mellitus (41.2% vs 26.9%; all comparisons, $P \leq .001$).

Lower Mortality Risk, Fewer Complications

There was no difference between the groups in incidence of [patent foramen ovale](#). There was no significant difference in the composite stroke severity score or the illness severity score, and there was no significant difference in the use of IV [thrombolytics](#).

The rate of in-hospital complications was lower for the OSA group. "We surprisingly found that intracranial hemorrhage was lower in the OSA group" than in the non-OSA group (9.1% vs 21.8%; $P = .017$), Lepow reported.

Other in-hospital complications favoring the OSA group were mortality (9.7% vs 13.5%, $P < .001$) and external ventricular drain or ventriculoperitoneal shunt placement for hydrocephalus (0.3% vs 1.1%, $P = .009$).

No other neurologic or medical complications that were assessed differed between the groups, and the hospital length of stay was the same, at 8.19 days. In the multivariable analysis, "OSA was found to be independently associated with lower in-hospital mortality after treatment," Lepow said.

Mortality risk was 22% lower for the OSA patients than the non-OSA patients (odds ratio, 0.78; 95% CI, 0.63 – 0.96; $P = .02$).

The association of lower mortality with OSA persisted after controlling for obesity, atrial fibrillation, hypertension, diabetes, age, gender, severity of illness, and stroke severity.

"The Jury's Still Out"

Commenting on the findings for *Medscape Medical News*, Louise McCullough, MD, PhD, chair of the Department of Neurology at the University of Texas Medical Center, Houston, Texas, called the study interesting and well done.

However, one of the problems with the NIS dataset is that it does not include the National Institutes of Health stroke scale, said McCullough, who was not involved with the research. Still, "they have done a pretty good job trying to control for stroke severity," she added.

McCullough said she found the lower mortality rate among the OSA group somewhat surprising and paradoxical and offered some possible explanations. She noted that the investigators tried to control for several variables, including age and sex.

"But these might be very important factors" she said. "The patients with OSA were younger and were more often male."

Another possible cause of the lower mortality in the OSA group is cerebral preconditioning. The bouts of hypoxia during sleep may

have induced preconditioning, which experimental models have shown to be protective.

"So possibly, the fact that they have intermittent apnea may protect them when they have a stroke," McCullough hypothesized. Preconditioning may induce the production of growth factors, such as hypoxia inducible factor, angiogenic factors, or others in response to hypoxia, leading to formation of robust collateral vessels and smaller strokes, she said.

Studies have been conducted on the use of such factors acutely for [neuroprotection](#), but McCullough warned that "the jury's still out on whether OSA itself is protective. Certainly, we know OSA, especially if it's untreated, is detrimental."

She also cautioned that use of the NIS has its limitations. In this study, many members of the non-OSA group could have had undiagnosed OSA, skewing the results.

"So I'm sure in that 100,000 patient population, there probably were patients that had OSA that weren't coded that way," she said. The patients themselves may not have known they had OSA, she added. McCullough also cautioned that the study could not control for every possible variable that may affect mortality, such as infections, deep vein thromboses, or the possibility that some patients may have had many more comorbidities.

*Lepow and McCullough have reported no relevant financial relationships
XXV World Congress of Neurology (WCN 2021): Presented October 3–7, 2021.*

<https://bit.ly/3m7rZ1T>

Strong Evidence That COVID-19 Is a Seasonal Infection – And We Need “Air Hygiene”

New research provides strong evidence that COVID-19 is a seasonal infection linked to low temperatures and humidity, much like seasonal influenza.

A new study led by the Barcelona Institute for Global Health (ISGlobal), an institution supported by “la Caixa” Foundation,

provides robust evidence that COVID-19 is a seasonal infection linked to low temperatures and humidity, much like seasonal influenza. The results, published in *Nature Computational Science*, also support the considerable contribution of airborne SARS-CoV-2 transmission and the need to shift to measures that promote “air hygiene.”

A key question regarding SARS-CoV-2 is whether it is behaving, or will behave, as a seasonal virus like influenza, or whether it will be equally transmitted during any time of the year. A first theoretical modeling study suggested that climate was not a driver in COVID-19 transmission, given the high number of susceptible individuals with no immunity to the virus. However, some observations suggested that the initial propagation of COVID-19 in China occurred in a latitude between 30 and 50° N, with low humidity levels and low temperatures (between 5° and 11 °C).

“The question of whether COVID-19 is a genuine seasonal disease becomes increasingly central, with implications for determining effective intervention measures,” explains Xavier Rodó, director of the Climate and Health program at ISGlobal and coordinator of the study. To answer this question, Rodó and his team first analyzed the association of temperature and humidity in the initial phase of SARS-CoV-2 spread in 162 countries across five continents, before changes in human behavior and public health policies were put into place. The results show a negative relationship between the transmission rate (R0) and both temperature and humidity at the global scale: higher transmission rates were associated with lower temperatures and humidity.

The team then analyzed how this association between climate and disease evolved over time, and whether it was consistent at different geographical scales. For this, they used a statistical method that was specifically developed to identify similar patterns of variation (i.e. a pattern-recognition tool) at different windows of time. Again, they

found a strong negative association for short time windows between disease (number of cases) and climate (temperature and humidity), with consistent patterns during the first, second, and third waves of the pandemic at different spatial scales: worldwide, countries, down to individual regions within highly affected countries (Lombardy, Thüringen, and Catalonia) and even to the city level (Barcelona).

The first epidemic waves waned as temperature and humidity rose, and the second wave rose as temperatures and humidity fell. However, this pattern was broken during summertime in all continents. “This could be explained by several factors, including mass gatherings of young people, tourism, and air conditioning, among others,” explains Alejandro Fontal, researcher at ISGlobal and first author of the study.

When adapting the model to analyze transient correlations at all scales in countries in the Southern Hemisphere, where the virus arrived later, the same negative correlation was observed. The climate effects were most evident at temperatures between 12° and 18°C and humidity levels between 4 and 12 g/m³, although the authors warn that these ranges are still indicative, given the short records available.

Finally, using an epidemiological model, the research team showed that incorporating temperature into the transmission rate works better for predicting the rise and fall of the different waves, particularly the first and third ones in Europe. “Altogether, our findings support the view of COVID-19 as a true seasonal low-temperature infection, similar to influenza and to the more benign circulating coronaviruses,” says Rodó.

This seasonality could contribute importantly to the transmission of SARS-CoV-2, since low humidity conditions have been shown to reduce the size of aerosols, and thereby increase airborne transmission of seasonal viruses such as influenza. “This link warrants an emphasis on ‘air hygiene’ through improved indoor

ventilation as aerosols are capable to persist suspended for longer times,” says Rodó, and highlights the need to include meteorological parameters in the evaluation and planning of control measures.

Reference: “Climatic signatures in the different COVID-19 pandemic waves across both hemispheres” by Fontal A, Bouma MJ, San José A, Lopez L, Pascual M, Rodó X, 21 October 2021, *Nature Computational Science*. DOI: 10.1038/s43588-021-00136-6

<https://bit.ly/3E8kr5m>

Early dinosaurs may have lived in social herds as early as 193 million years ago

The prehistoric creatures lived in herds much earlier than previously thought

by Jennifer Chu, [Massachusetts Institute of Technology](#)

To borrow a line from the movie "Jurassic Park:" Dinosaurs do move in herds. And a new study shows that the prehistoric creatures lived in herds much earlier than previously thought.

In a paper appearing in *Scientific Reports*, researchers from MIT, Argentina, and South Africa detail their discovery of an exceptionally preserved group of early dinosaurs that shows signs of complex herd behavior as early as 193 million years ago—40 million years earlier than other records of dinosaur herding.

Since 2013, members of the team have excavated more than 100 [dinosaur eggs](#) (about the size of chicken eggs) and the partial skeletons of 80 juvenile and adult dinosaurs from a rich [fossil](#) bed in southern Patagonia.

Using X-ray imaging, they were able to examine the eggs' contents without breaking them apart, and discovered preserved embryos within, which they used to confirm that the fossils were all members of *Mussaurus patagonicus*—a plant-eating dinosaur that lived in the early Jurassic period and is classified as a sauropodomorph, a predecessor of the massive, long-necked sauropods that later roamed the Earth.

Surprisingly, the researchers observed that the fossils were grouped by age: Dinosaur eggs and hatchlings were found in one area, while skeletons of juveniles were grouped in a nearby location. Meanwhile, remains of adult dinosaurs were found alone or in pairs throughout the field site.

This "age segregation," the researchers believe, is a strong sign of a complex, herd-like social structure. The dinosaurs likely worked as a community, laying their eggs in a common nesting ground. Juveniles congregated in "schools," while adults roamed and foraged for the herd.

"This may mean that the young were not following their parents in a small family structure," says team member Jahandar Ramezani, a research scientist in MIT's Department of Earth, Atmospheric and Planetary Sciences. "There's a larger community structure, where adults shared and took part in raising the whole community."

Ramezani dated ancient sediments among the fossils and determined that the dinosaur herd dates back to around 193 million years ago, during the early Jurassic period. The team's results represent the earliest evidence of social herding among dinosaurs.

Living in herds may have given *Mussaurus* and other social sauropodomorphs an evolutionary advantage. These early dinosaurs originated in the late Triassic, shortly before an extinction event wiped out many other animals. For whatever reason, sauropodomorphs held on and eventually dominated the terrestrial ecosystem in the early Jurassic.

"We've now observed and documented this earliest social behavior in dinosaurs," Ramezani says. "This raises the question now of whether living in a herd may have had a major role in dinosaurs' early evolutionary success. This gives us some clues to how dinosaurs evolved."

A fossil flood

Since 2013, paleontologists on the team have worked in the Laguna

Colorada Formation, a site in southern Patagonia that is known for bearing fossils of early sauropodomorphs. When scientists first discovered fossils within this formation in the 1970s, they named them *Mussaurus* for "mouse lizard," as they assumed the skeletons were of miniature dinosaurs.

Only much later did scientists, including members of the Argentinian team, discover bigger skeletons, indicating *Mussaurus* adults were much larger than their rodent namesakes. The name stuck, however, and the team has continued to unearth a rich collection of *Mussaurus* fossils from a small, square kilometer of the formation.



*New research on a vast fossil site in Patagonia shows that some of the earliest dinosaurs, the *Mussaurus Patagonicus*, lived in herds and suggests that this behavior may have been one of the keys to the success of dinosaurs.*

Credit: Jorge Gonzalez

The fossils they have identified so far were found in three sedimentary layers spaced close together, indicating that the region may have been a common breeding ground where the dinosaurs returned regularly, perhaps to take advantage of favorable seasonal conditions.

Among the fossils they uncovered, the team discovered a group of 11 articulated juvenile skeletons, intertwined and overlapping each other, as if they had been suddenly thrown together. In fact, judging from the remarkably preserved nature of the entire collection, the team believes this particular herd of *Mussaurus* died "synchronously," perhaps quickly buried by sediments.

Based on evidence of ancient flora in the nearby outcrops, the Laguna Colorada Formation has long been assumed to be relatively old on the dinosaur timescale. The team wondered: Could these

dinosaurs have been herding from early on?

"People already knew that in the late Jurassic and Cretaceous, the large herbivore dinosaurs exhibited social behavior—they lived in herds and had nesting spots," Ramezani says. "But the question has always been, when was the earliest time for such herding behavior?"

A gregarious line

To find out, Diego Pol, a paleontologist at the Egidio Feruglio Paleontological Museum in Argentina who led the study, looked for samples of volcanic ash among the fossils to send to Ramezani's lab at MIT. Volcanic ash can contain zircon—mineral grains containing uranium and lead, the isotopic ratios of which Ramezani can precisely measure. Based on uranium's half-life, or the time it takes for half of the element to decay into lead, he can calculate the age of the zircon and the ash in which it was found. Ramezani successfully identified zircons in two ash samples, all of which he dated to around 193 million years old.

Since the volcanic ash was found in the same sediment layers as the fossils, Ramezani's analyses strongly suggest that the dinosaurs were buried at the same time the ash was deposited. A likely scenario may have involved a flash flood or windblown dust that buried the [herd](#), while ash from a distant eruption happened to drift over and, luckily for science, deposit zircons in the sediments.

Taken together, the team's results show that *Mussaurus* and possibly other dinosaurs evolved to live in complex social herds as early as 193 million years ago, around the dawn of the Jurassic period.

Scientists suspect that two other types of early dinosaurs—*Massospondylus* from South Africa and *Lufengosaurus* from China—also lived in herds around the same time, although the dating for these dinosaurs has been less precise. If multiple separate lines of dinosaurs lived in herds, the researchers believe the social

behavior may have evolved earlier, perhaps as far back as their common ancestor, in the late Triassic.

"Now we know herding was going on 193 million years ago," Ramezani says. "This is the earliest confirmed evidence of gregarious behavior in [dinosaurs](#). But paleontological understanding says, if you find social behavior in this type of dinosaur at this time, it must have originated earlier."

This research was supported, in part, by National Science Foundation in the U.S. and the National Scientific and Technical Research Council of Argentina.

More information: Diego Pol, *Earliest evidence of herd-living and age segregation amongst dinosaurs*, *Scientific Reports* (2021). DOI: [10.1038/s41598-021-99176-1](https://doi.org/10.1038/s41598-021-99176-1). www.nature.com/articles/s41598-021-99176-1

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

When and why did human brains decrease in size 3,000 years ago? Ants may hold clues

Researchers hypothesize that brain shrinkage parallels the expansion of collective intelligence in human societies

The brain is the most complex organ in the human body. Now, a new study has brought us closer to understanding some of its evolution. It shows that human brains decreased in size approximately 3,000 years ago. By studying ants as models to illustrate why brains may increase or decrease in size, the researchers hypothesize that brain shrinkage parallels the expansion of collective intelligence in human societies.

Studying and understanding the causes and consequences of brain [evolution](#) helps us understand the nature of humanity. It is well documented that [human brains](#) have increased in size over the course of our evolutionary history. Less appreciated is the fact that human brains have decreased in size since the Pleistocene. When exactly these changes happened, or why, was not well known.

"A surprising fact about humans today is that our brains are smaller compared to the brains of our Pleistocene ancestors. Why our brains have reduced in size has been a big mystery for

anthropologists," explained co-author Dr. Jeremy DeSilva, from Dartmouth College.

To disentangle this mystery, a team of researchers from different academic fields set out to study the historical patterns of human brain evolution, comparing their findings with what is known in ant societies to offer broad insights.

"A biological anthropologist and a behavioral ecologist and evolutionary neurobiologist began sharing their thoughts on brain evolution and found bridging research on humans and ants might help identify what is possible in nature," said co-author Dr. James Traniello, from Boston University.

Their paper, published in *Frontiers in Ecology and Evolution*, sheds new light on the evolution of our brain.

A recent size decrease

The researchers applied a change-point analysis to a dataset of 985 fossil and modern human crania. They found that human brains increased in size 2.1 million years ago and 1.5 million years ago, during the Pleistocene, but decreased in size around 3,000 years ago (Holocene), which is more recent than previous estimates.

"Most people are aware that humans have unusually large brains—significantly larger than predicted from our body size. In our deep evolutionary history, human brain size dramatically increased," said Traniello. "The reduction in human brain size 3,000 years ago was unexpected."

The timing of size increase coincides with what is previously known about the early evolution of Homo and the technical advancements that led to; for example, better diet and nutrition and larger social groups.

As for the decrease in brain size, the interdisciplinary team of researchers propose a new hypothesis, finding clues within ant societies.

What could ants teach us about human brain evolution?

"We propose that ants can provide diverse models to understand why brains may increase or decrease in size due to social life. Understanding why brains increase or decrease is difficult to study using only fossils," explained Traniello.

Studying computational models and patterns of worker ant brain size, structure, and energy use in some ant clades, such as the *Oecophylla* weaver ant, *Atta* leafcutter ants, or the common garden ant *Formica*, showed that group-level cognition and division of labor may select for adaptive brain size variation. This means that within a social group where knowledge is shared or individuals are specialists at certain tasks, brains may adapt to become more efficient, such as decreasing in size.

"Ant and human societies are very different and have taken different routes in social evolution," Traniello said. "Nevertheless, [ants](#) also share with humans important aspects of social life such as group decision-making and division of labor, as well as the production of their own food (agriculture). These similarities can broadly inform us of the factors that may influence changes in human brain size."

Brains use up a lot of energy, and smaller brains use less energy. The externalization of knowledge in [human societies](#), thus needing less energy to store a lot of information as individuals, may have favored a decrease in [brain](#) size.

"We propose that this decrease was due to increased reliance on collective intelligence, the idea that a group of people is smarter than the smartest person in the group, often called the 'wisdom of the crowds,'" added Traniello.

DeSilva concluded, "We look forward to having our hypothesis tested as additional data become available."

More information: *Jeremy DeSilva et al, When and Why Did Human Brains Decrease in Size? A New Change-Point Analysis and Insights from Brain Evolution in Ants, Frontiers in Ecology and Evolution (2021). DOI: [10.3389/fevo.2021.742639](https://doi.org/10.3389/fevo.2021.742639)*

<https://wb.md/3GdFs0i>

COVID Vaccination Rates Vary By People's Zodiac Sign

COVID-19 vaccination rates vary dramatically by astrological sign, with Leos at the top of the list and Scorpios at the bottom, according to [The Salt Lake Tribune](#).

Carolyn Crist

The Salt Lake County Health Department calculated the rates based on anonymous birth dates from the county's vaccination data and then compared those figures to national estimates for the overall population represented by each sign.

"Now that Mercury is not in retrograde, we're just going to leave this here ... (and yes, this is based on data)," the Health Department wrote [in a Twitter post](#) on Tuesday.

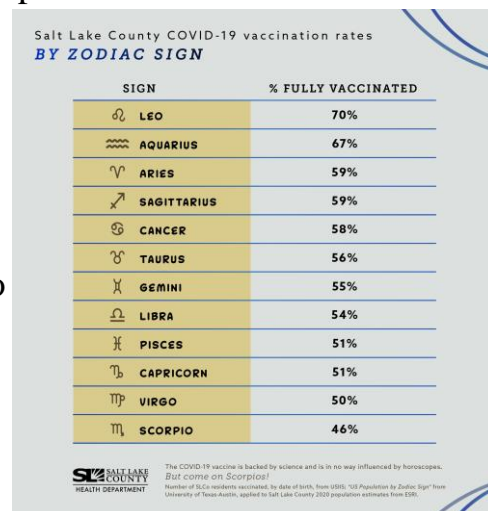
"The COVID-19 vaccine is backed by science and is no way influenced by horoscopes," the department continued. "But come on Scorpios!"

According to the graphic, 70% of those with the Leo sign are fully vaccinated, followed by Aquarius at 67%, and Aries and Sagittarius both at 59%.

The other signs range from 58% to 50%, in descending order: Cancer, Taurus, Gemini, Libra, Pisces, Capricorn, and Virgo. Scorpio sits at the bottom of the list, with 46% fully vaccinated.

Notably, three of the top four signs are elemental fire signs, *The Salt Lake Tribune* noted.

"We are overachievers," Jeff Eason, an Aries and the department's bureau manager of population health and informatics, who did the



analysis, told the newspaper.

The Health Department's post sparked positive and negative feedback across social media, with some musing about their own sign's inclinations and others scoffing at astrology altogether.

"What we're really doing is finding new and different ways to keep our community talking about vaccination when there is significant message fatigue around this topic," the department wrote in the comments.

The range of vaccination rates was startlingly wide, Eason told *The Salt Lake Tribune*. But he noted that the difference "could all come down to denominators."

Each sign's vaccination rate was ranked almost exactly inverse to its share of the overall population, the newspaper reported. Scorpios and Virgos make up 9.4% and 9.3% of the U.S. population, respectively, as compared with 7.1% for Leos and 6.3% for Aquarians.

If the 12 astrological signs were more evenly distributed in Salt Lake County than nationally, Eason said, the range of vaccinations rates wouldn't be as wide as the analysis shows.

"Obviously, it's not super scientific because we are talking astrology," Nicholas Rupp, a spokesman for the health department and a vaccinated Scorpio, told the newspaper.

Still, Health Department officials wanted to do the analysis as a fun way to start conversations and promote vaccinations. About 59% of Salt Lake County residents are fully vaccinated, and about 54% of Utah residents are fully vaccinated.

"We do have message fatigue around vaccines," Rupp said.

Sources:

The Salt Lake Tribune: "Salt Lake County calculated COVID-19 vaccination rates by zodiac sign. The news is not good for Scorpios."

Twitter: @SaltLakeHealth, Oct. 19, 2021.

<https://bit.ly/3CbR2GJ>

Your Cat Could Carry 'Good' Bacteria That Fight Resistant Staph Infections

*Bacteria from healthy cats have been shown to produce **antibodies** with some impressive skin healing properties... in mice.*

[David Nield](#)

A new study on these properties indicates we could one day harness such antibodies to potentially treat infections on humans as well as other animals. This approach is a type of [bacteriotherapy](#) – using 'good' bacteria known to provide various health benefits to help protect against 'bad' bacteria (or pathogens). It's a balance that scientists are constantly getting [new insights into](#).

Here, researchers used cat bacteria to protect against the methicillin-resistant [Staphylococcus pseudintermedius](#) or MRSP pathogen in mice: this bacterium is often found on domesticated animals, and can proliferate out of control when they're sick or injured.

The results of the study suggest that good bacteria found on cats offer strong protection against MRSP – not just in mice, as was shown in this case, but potentially also in human beings who can pick up the good bacteria as well.

"It may even be possible that living with a healthy cat provides humans with some protection against MRSP," [says medical scientist Richard Gallo](#), from the University of California San Diego. "So this may be an argument in support of pet ownership."

MRSP can jump between species – it's been known to cause eczema in dogs, cats, and humans, for example. As you can tell from the "methicillin-resistant" part, common antibiotics don't work on it, and it's difficult to treat.

The team put together a library of bacteria normally found on dogs and cats, and then grew them alongside MRSP. This enabled them to identify a strain called *Staphylococcus felis*, which blocked

MRSP growth.

It seems as though the multiple antibiotics naturally produced by *S. felis* are enough to disrupt the walls of MRSP cells, killing off the pathogen. Upon closer analysis, *S. felis* proved to be a very effective biological fighting machine.

"The potency of this [*S. felis*] species is extreme," [says Gallo](#). "It is strongly capable of killing pathogens, in part because it attacks them from many sides – a strategy known as polypharmacy. This makes it particularly attractive as a therapeutic."

Tests with *S. felis* on mice that had been infected with MRSP showed a reduction in redness and the size of the infection. Further observation showed fewer viable MRSP bacteria left on the skin after treatment. What's more, this bacterium is especially effective against antibiotic resistance: it produces four distinct antimicrobial peptides, which work together to make it more difficult for the MRSP pathogen to fight back.

There's still some way to go to get this working as a potential treatment for humans; as a next step, the researchers want to test their work in dogs. But if the findings on *S. felis* can be developed into a protective product, the possibilities are endless – it could eventually be applied as a spray, cream or gel, and we don't even have to be worried about accidentally washing it off the skin.

"Skin has evolved to protect the good bacteria, so soap and detergents don't usually wash the good guys off," [says Gallo](#).

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

<https://bit.ly/3CbwAG0>

The dead of aconite

Whether human, witch or werewolf, beware a flower known as the queen of poisons

By [Raychelle Burks](#)

Plants of the genus [Aconitum](#) have a [long history](#) full of witchcraft, [werewolves](#) and wicked deeds.^{1,2} Fantastical stories were built on

the [factual pharmacological effects](#) of *Aconitum* alkaloids³ like [aconitine](#), mesaconitine, hyaconitine and jesaconitine. Aconitine is most feared – and with good reason. It has been described as 100 times more lethal than strychnine, with an oral dose just shy of [2mg](#) reportedly enough to kill a 68kg person.⁴

[Aconitine](#) likely serves as a defensive tool for the plants that produce it, discouraging predators with its deadly action. It acts quickly on sodium ion signalling channels, opening them and preventing their closure. ‘To use a car analogy, if the valves in your car’s engine open up, but then won’t close, it’s dead in the water,’ [wrote toxicologist Justin Bower](#). ‘Just like aconitine victims.’

The danger of *Aconitum* plants, commonly referred to as aconite, has long been known. ‘For all things under the heaven, nothing is more vicious than the poison of aconite,’ asserted the second century BCE text *Masters of Huainan* (the *Huainanzi*), continuing: ‘Yet a good doctor packs and stores it, because it is useful.’⁵ Like other famous plants and their alkaloids, such as *Strychnos nuxvomica* and [strychnine](#) or *Atropa belladonna* and [atropine](#)⁶, aconite and aconitine were considered both threat and treatment. They still are.⁷⁻⁹ Aconite alkaloids have pain-relieving, fever-reducing, local anaesthetic and cardiotoxic (increasing the contractile power of the muscular tissue of the heart) effects. Aconite was treated as a cure-all for thousands of years, featuring as an ingredient in a range of second century BCE medicinal formulations excavated from Mawangdui in modern Hunan, China, with purposes from the mundane to the magical.⁵

A kind of magic

Sorcery and witchcraft include aconite in a number of [potions](#).¹ Aconite was reportedly a main ingredient of witches’ flying ointment, with its alkaloids’ anaesthetic and cardiotoxic roles perhaps explaining the sensation of flying reported by those that imbibed it.¹ Works of fiction and lore cast aconite – under one of its

alternative names, wolfsbane – as either the trigger or treatment for [werewolf transformation](#). This too is based on aconite’s real action. Aconite found use as [bait poison](#), reportedly added to raw meat to lure carnivores – including wolves – to their doom.

From mythical transformations to real pharmacological effects, the difference in blood concentration at which aconitine is an effective drug and when it’s toxic is narrow as a razor’s edge.^{3,8} The sobriquet ‘[queen of poisons](#)’ is justifiably earned.

In ancient Rome, aconite was known as both the stepmother’s poison and the mother-in-law’s poison.¹⁰ In ancient Greece and India, archers reportedly used aconite to poison their arrows, with [similar practices](#) seen in modern aconitine-treated projectiles.¹¹ In 1883, analysis by University of Virginia chemistry professor John Mallet pointed to aconitine playing a role in a highly suspicious [mass poisoning](#) at the then Western Lunatic Asylum in Virginia, US, that saw seven patients fall ill and six die. Roughly 12 years ago, the high profile UK ‘[curry poison killer](#)’ case showed the viciousness of aconite once again, when a woman murdered her former lover with an adulterated curry. But for all its infamy, aconite and aconitine can still operate covertly. As [Xiangting Gao and colleagues](#) at Soochow University in China wrote last year, aconitine ‘is not detected routinely for common toxicology analysis in present forensic practice’.⁸ One might even get away with murder.

Deadly secret

In a case detailed in the *International Journal of Legal Medicine*,¹² a man was found dead behind the wheel of his car, which was found parked adjacent to a ‘deep pitch’ (ravine) and showed signs that someone had attempted to burn it. An autopsy showed signs of ‘blunt traumatic violence on his head, face, back, arms and legs’ plus signs of strangulation. Routine toxicological analysis of blood, urine, gastric contents, liver and kidney tissue

samples found some alcohol in the blood and urine, but ‘no other drugs or toxic agents were initially detected’.

Only five years later were events clarified, when the man’s wife confessed all. Boiling the leaves and stalks of three *Aconitum napellus* plants, she had made a poisonous brew and added it to a bottle of red wine. A few hours later, thinking her husband dead, she dragged him about their home and finally to the car using ropes about his neck and chest. She then moved the car, attempting to destroy the evidence through fire and pushing it into the pitch.

Analysts returned to pathology evidence to confirm her story. Additional toxicological analysis via liquid chromatography–tandem mass spectrometry (LC-MS-MS) revealed aconitine in the urine, liver and kidney samples. Forensic analysts and investigators think aconitine poisoning contributed to the man’s death, although possible ligature strangulation suggests he was not yet dead as his wife began to drag him around their home. Whether committing crimes or casting spells, one might think they’ve been successful until chemistry reveals all.

References

- 1 A Been, *Pharm. Hist.*, 1992, **34**, 35 ([jstor.org/stable/41111425](https://doi.org/10.1016/j.pharmhist.1992.03.001))
- 2 P Wexler (ed.), *Toxicology in Antiquity*. Academic Press, 2018
- 3 F Veit et al, *Forensic Sci. Int. Rep.*, 2020, **2**, 100158 (DOI: [10.1016/j.fsir.2020.100158](https://doi.org/10.1016/j.fsir.2020.100158))
- 4 J H Bock and D O Norris, *Introduction to Forensic Plant Science*. In J H Bock and D O Norris (eds), *Forensic Plant Science*. Academic Press, 2016, p1
- 5 Y Liu, *Poisonous Medicine in Ancient China*. In P Wexler (ed), *Toxicology in Antiquity (Second Edition)*. Academic Press, 2019, p431
- 6 J Emsley, *Molecules of murder: Criminal molecules and classic cases*. Royal Society of Chemistry, 2015
- 7 Y S Cho et al, *Forensic Sci. Med. Pathol.*, 2020, **16**, 330 (DOI: [10.1007/s12024-019-00211-5](https://doi.org/10.1007/s12024-019-00211-5))
- 8 X Gao et al, *Forensic Sci. Res.*, 2020, **5**, 25 (DOI: [10.1080/20961790.2018.1452346](https://doi.org/10.1080/20961790.2018.1452346))
- 9 Q Liu et al, *Forensic Sci. Int.*, 2011, **212**, e5 (DOI: [10.1016/j.forsciint.2011.05.009](https://doi.org/10.1016/j.forsciint.2011.05.009))
- 10 L Cilliers and F Retief, *Poisons, Poisoners, and Poisoning in Ancient Rome*. In P Wexler (ed), *Toxicology in Antiquity (Second Edition)*. Academic Press, 2019, p231
- 11 Y Gaillard, P Regenstreif and L Fanton, *Am. J. Forensic Med. Pathol.*, 2014, **35**, 258 (DOI: [10.1097/PAF.0b013e318288abe8](https://doi.org/10.1097/PAF.0b013e318288abe8))
- 12 A A Van Landeghem et al, *Int. J. Legal Med.*, 2007, **121**, 214 (DOI: [10.1007/s00414-006-0119-5](https://doi.org/10.1007/s00414-006-0119-5))

<https://bit.ly/3b4WKO0>

Fighting Multiple Sclerosis With Cold, Depriving the Immune System of Its Energy

Scientists at UNIGE are demonstrating how cold could alleviate the symptoms of multiple sclerosis by depriving the immune system of its energy.

In evolutionary biology, the “Life History Theory,” first proposed in the 1950s, postulates that when the environment is favorable, the resources used by any organism are devoted for growth and reproduction. Conversely, in a hostile environment, resources are transferred to so-called maintenance programs, such as energy conservation and defense against external attacks.

Scientists at the University of Geneva (UNIGE) developed this idea to a specific field of medicine: the erroneous activation of the immune system that causes autoimmune diseases.

By studying mice suffering from a model of multiple sclerosis, the research team succeeded in deciphering how exposure to cold pushed the organism to divert its resources from the immune system towards maintaining body heat.

Indeed, during cold, the immune system decreased its harmful activity which considerably attenuated the course of the autoimmune disease. These results, highlighted on the cover of the journal *Cell Metabolism*, pave the way for a fundamental biological concept on the allocation of energy resources.

Autoimmune diseases occur when the immune system attacks the body own organs. Type 1 diabetes, for example, is caused by the erroneous destruction of insulin-producing pancreatic cells. Multiple sclerosis is the most common autoimmune disease of the central nervous system (consisting of the brain and spinal cord). The disease is characterized by the destruction of the myelin, which is a protective insulation of nerve cells and is important for the correct and fast transmission of electrical signals. Its destruction

thus leads to neurological disability, including paralysis.

“The defense mechanisms of our body against the hostile environment are energetically expensive and can be constrained by trade-offs when several of those are activated. The organism may therefore have to prioritize resource allocation into different defense programs depending on their survival values,” explains Mirko Trajkovski, professor in the Department of Cellular Physiology and Metabolism and the Diabetes Centre at the Faculty of Medicine of the UNIGE, and lead author of the study.

“We hypothesized that this can be of particular interest for autoimmunity, where introducing an additional energy-costly program may result in milder immune response and disease outcome. In other words, could we divert the energy expended by the body when the immune system goes awry?”

A drastic reduction in symptoms

To test their hypothesis, the scientists placed mice suffering from experimental autoimmune encephalomyelitis, a model of human multiple sclerosis, in a relatively colder living environment — about 10°C — following an acclimatization period of gradually decreasing the environmental temperature.

“After a few days, we observed a clear improvement in the clinical severity of the disease as well as in the extent of demyelination observed in the central nervous system,” explains Doron Merkler, professor at the Department of Pathology and Immunology and the Centre for Inflammation Research at the UNIGE Faculty of Medicine and co-corresponding author of the work.

“The animals did not have any difficulty in maintaining their body temperature at a normal level, but, singularly, the symptoms of locomotor impairments dramatically decreased, from not being able to walk on their hind paws to only a slight paralysis of the tail.”

The immune response is based, among other things, on the ability of so-called antigen-presenting monocytes to instruct T cells how to

recognize the “non-self” elements that must be fought. In autoimmune diseases, however, the antigens of the “self” are confused with those of the “non-self.” “We show that cold modulates the activity of inflammatory monocytes by decreasing their antigen presenting capacity, which rendered the T cells, a cell type with critical role in autoimmunity, less activated,” explains Mirko Trajkovski.

By forcing the body to increase its metabolism to maintain body heat, cold takes resources away from the immune system. This leads to a decrease in harmful immune cells and therefore improves the symptoms of the disease.

“While the concept of prioritizing the thermogenic over the immune response is evidently protective against autoimmunity, it is worth noting that cold exposure increases susceptibility to certain infections. Thus, our work could be relevant not only for neuroinflammation, but also other immune-mediated or infectious diseases, which warrants further investigation,” adds Mirko Trajkovski.

Autoimmune diseases on the rise

The improvement in living conditions in Western countries, which has been noticeable over the past decades, has gone hand in hand with an increase in cases of autoimmune diseases.

“While this increase is undoubtedly multifactorial, the fact that we have an abundance of energy resources at our disposal may play an important but as yet poorly understood role in autoimmune disease development,” concludes Doron Merkler.

The researchers will now pursue their research to better understand whether their discovery could be developed in clinical applications.

Reference: “Cold Exposure Protects from Neuroinflammation Through Immunologic Reprogramming” 22 October 2021, Cell Metabolism. DOI: 10.1016/j.cmet.2021.10.002

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

Discovery Points to a Crucial Role Red Blood Cells Play in Our Immune Systems

Red blood cells also play a critical role in inflammation

[Mike McRae](#)

The job description for a red blood cell isn't considered to be overly complicated. Pick up oxygen, drop off oxygen. Wash, rinse, repeat. But when it comes to protecting the body against infection, it's their white cell sisters that we've been giving all the credit to.

However, a new study led by researchers from the University of Pennsylvania in the US has confirmed red blood cells also play a critical role in inflammation, one that could make a life-or-death difference.

As far back as the [middle of last century](#) scientists had their suspicions that red cells played some kind of role in keeping invaders at bay. By the 1990s, researchers were [uncovering receptors](#) on red blood cells that responded to inflammatory messenger chemicals called cytokines.

It all pointed to something afoot. Meanwhile, there was also the inexplicable loss of blood cells – anemia – that often comes with sepsis.

"Acute inflammatory anemia is often seen early after an infection such as parasitic infections that cause [malaria](#)," [says](#) pulmonologist Nilam Mangalmurti, the senior author on the recent investigation.

"For a long time we haven't known why people, when they are critically ill from sepsis, trauma, [COVID-19](#), a bacterial infection, or parasite infection, develop an acute anemia."

[Just a few years ago](#) Mangalmurti and her team showed how red blood cells could scavenge the free-floating scraps of mitochondrial DNA that spilled from injured tissues, triggering a response that helps regulate inflammatory responses in the lungs.

But missing pieces of the puzzle remained. How does a fragment of

DNA from our own body turn an oxygen-carrying cell into an infection-fighting machine? And why do they disappear?

A major key could be found in the protein that grabs onto the DNA. Called [toll-like receptors](#) (TLR), they're normally found on sentinels like the microbe-munching macrophages, where they respond to the short sequences as a sign that the body is under invasion.

Initial tests on human and chimpanzee blood confirmed they also existed on red blood cells. Thanks to their recent analysis of blood samples taken from sepsis and COVID-19 patients, the researchers now know that the number of receptors, specifically TLR9, increases during infections.

The TLR9 receptor readily mops up the released pieces of DNA, some of which contain sequences that bear an uncanny resemblance to those in many [virus](#) and bacterial segments of nucleic acid.

Under carefully managed laboratory conditions, these DNA-triggered red blood cells looked shockingly abnormal: Their typically concave 'donut' shape was warped.

This change in morphology is a check-box for sepsis, so seeing it so obvious under these lab conditions was a clear sign that the team was on the right path.

In no time, the malformed red blood cells began to disappear, swallowed up by macrophages. The engulfing in turn set off a chain reaction of inflammatory messengers that would effectively sound the alarm for the immune system to act in haste.

Tests carried out on mice infected with parasites backed up what they were seeing outside of the body. Sure enough, mitochondrial DNA was elevated on the mice's red cells, compared with those from non-infected animals.

Triggering inflammation in parts of the body that otherwise aren't in any danger of infection can be bad news, especially in people with autoimmune disorders. So finding ways to prevent red blood cells

from overreacting to the presence of free-floating mitochondrial DNA would be immensely helpful.

It would also save lives for those at risk of acute anemia.

"Right now when patients in the ICU [intensive care unit] become anemic, which is almost all of our critically ill patients, the standard is to give them blood transfusions, which has long been known to be accompanied by a host of issues including acute lung injury and increased risk of death," [says](#) Mangalmurti.

"Now that we know more about the mechanism of anemia, it allows us to look at new therapies for treating acute inflammatory anemia without transfusions, such as blocking TLR9 on the red blood cells."

This research was published in [Science Translational Medicine](#).

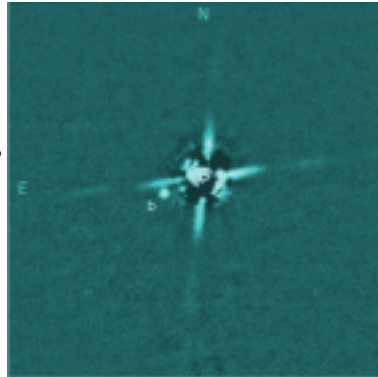
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Jaw-Dropping Direct Image Shows a Baby Exoplanet Over 400 Light-Years Away

Just over 400 light-years away, a baby exoplanet is making its way into the Universe.

[Michelle Starr](#)

This, in itself, is not so unusual. We've detected [thousands of exoplanets](#) – planets outside the Solar System. Presumably they all had to be newborn at some point too. What makes this exoplanet special is that astronomers obtained a direct image of it – an almost vanishingly rare feat.



The direct image of exoplanet 2M0437b. (Subaru Telescope)

It's named 2M0437b, and it's [one of the youngest](#) exoplanets for which we have ever obtained a direct image. This could give us a new window into the planet formation process, which in turn could help us understand how the Solar System was born and evolved.

"This serendipitous discovery adds to an elite list of planets that we

can directly observe with our telescopes," [said astronomer Eric Gaidos](#) of the University of Hawai'i at Mānoa.

"By analyzing the light from this planet we can say something about its composition, and perhaps where and how it formed in a long-vanished disk of gas and dust around its host star."

There are some very excellent reasons we can't easily directly image exoplanets. Compared to the stars they orbit, exoplanets are very small and dim, which means they are usually too faint to be seen with our current telescope technology.

Instead, we usually detect exoplanets based mainly on two effects they have on their host stars. If the exoplanet passes between us and the star on its orbital path, we can detect small, periodic changes in the star's light.

In addition, an exoplanet will exert a faint gravitational effect on the star too (as the bodies orbit a mutual center), causing the star to "wobble" slightly on the spot, causing the wavelength of its light to shift slightly.

These signals are easier to detect when the planet is very massive and very close to the star, so the majority of confirmed exoplanets are massive and on close orbits. But exoplanets on very close orbits are difficult to image directly, because they tend to be vastly outshone by their host stars.

2M0437b as imaged by the Subaru Telescope in infrared. (Subaru Telescope)

The exoplanet 2M0437b is quite large, but it's also quite far from its host star, 2M0437 – around 100 astronomical units (Pluto is around 40 astronomical units from the Sun). Usually, exoplanets this distant from their star are too cool to give off infrared radiation, but here's where 2M0437b's youth plays a role.

Because it's just a few million years old, the baby exoplanet is still relatively warm from the intense planetary formation processes, around 1,400 to 1,500 Kelvin (1,127 to 1,227 degrees Celsius, or

2,060 to 2,240 degrees Fahrenheit). This means that it glows faintly in infrared, enough to be seen at a distance of 417 light-years away. It was spotted in 2018 using the Subaru Telescope in Hawaii, and follow-up observations in near-infrared were conducted using the W. M. Keck Observatory. For three years, the research team tracked the star as it moved across the sky, and were able to confirm that 2M0437b was moving with it.

"The exquisite data from the Keck Observatory allowed us to confirm that the faint neighbor is moving through space along with its star, and thus is a true companion," [said astronomer Adam Kraus](#) of the University of Texas at Austin.

"Eventually, we might even be able to measure its orbital motion around the star."

The team believes that the young system would be an excellent candidate for follow-up observations using the Hubble Space Telescope. To date, the star and its exoplanet have been observed using Earth-based observatories, which need to correct for the warping effect of Earth's atmosphere on starlight. Hubble does not have this problem.

Such observations should be able to help constrain the properties of the star. We don't know exactly how old it is, or its mass. And they might even be able to detect chemical signatures in the atmosphere of 2M0437b – which in turn could reveal much more information about how it formed.

"We are all looking forward to more such discoveries, and more detailed studies of such planets with the technologies and telescopes of the future," astronomer Michael Liu of the University of Hawai'i [said](#).

The research has been accepted into the *Monthly Notices of the Royal Astronomical Society*, and is available on [arXiv](#).