https://bit.ly/3LymHGv

After 30 Years, Genetic Study Confirms Sarin Nerve Gas As Cause of Gulf War Illness

Troops who had genes that help metabolize sarin nerve gas were less likely to develop symptoms.

For three decades, scientists have debated the underlying cause of Gulf War illness (GWI), a collection of unexplained and chronic symptoms affecting veterans of the Persian Gulf War. Now researchers led by Robert Haley, M.D., Professor of Internal Medicine and Director of the Division of Epidemiology at The University of Texas Southwestern Medical Center (UT Southwestern), have solved the mystery, showing through a detailed genetic study that the nerve gas sarin was largely responsible for the syndrome.

The findings were published on May 11, 2022, in *Environmental Health Perspectives*, a peer-reviewed journal supported by the National Institute of Environmental Health Sciences, with an accompanying editorial on the paper by leading environmental epidemiologists.

Dr. Haley's research group not only identified that veterans with exposure to sarin were more likely to develop GWI, but also found that the risk was modulated by a gene that normally allows some people's bodies to better break down the nerve gas. Gulf War soldiers with a weak variant of the gene who were exposed to sarin were more likely to develop symptoms of GWI than other exposed veterans who had the strong form of the gene.

"Quite simply, our findings prove that Gulf War illness was caused by sarin, which was released when we bombed Iraqi chemical weapons storage and production facilities," said Dr. Haley, a medical epidemiologist who has been investigating GWI for 28 years. "There are still more than 100,000 Gulf War veterans who are not getting help for this illness and our hope is that these findings will accelerate the search for better treatment."

In the years immediately following the Gulf War, more than a quarter of the U.S. and coalition veterans who served in the war began reporting a range of chronic symptoms, including fatigue, fever, night sweats, memory and concentration problems, difficulty finding words, diarrhea, sexual dysfunction, and chronic body pain. Since then, both academic researchers and those within the military and Department of Veterans Affairs have studied a list of possible causes of GWI, ranging from stress, vaccinations, and burning oil wells to exposure to pesticides, nerve gas, anti-nerve gas medication, and depleted uranium.

Over the years, these studies have identified statistical associations with several of these, but no cause has been widely accepted. Most recently, Dr. Haley and a colleague reported a large study testing veterans' urine for depleted uranium that would still be present if it had caused GWI and found none.

"As far back as 1995, when we first defined Gulf War illness, the evidence was pointing toward nerve agent exposure, but it has taken many years to build an irrefutable case," said Dr. Haley, who holds the U.S. Armed Forces Veterans Distinguished Chair for Medical Research, Honoring Robert Haley, M.D., and America's Gulf War Veterans.

Sarin is a toxic man-made nerve agent, first developed as a pesticide, that has been used in chemical warfare; its production was banned in 1997. When people are exposed to either the liquid or gas form, sarin enters the body through the skin or breathing and attacks the nervous system. High-level sarin often results in death, but studies on survivors have revealed that lower-level sarin exposure can lead to long-term impairment of brain function. The U.S. military has confirmed that chemical agents, including sarin, were detected in Iraq during the Gulf War. In particular, satellite imagery documented a large debris cloud rising from an Iraqi

chemical weapons storage site bombed by U.S. and coalition aircraft and transiting over U.S. ground troop positions where it set off thousands of nerve gas alarms and was confirmed to contain sarin.

Previous studies have found an association between Gulf War veterans who self-reported exposure to sarin and GWI symptoms. However, critics have raised questions of recall bias, including whether veterans with GWI are simply more likely to remember and report exposure due to their assumption that it may be linked to their illness. "What makes this new study a game-changer is that it links GWI with a very strong gene-environment interaction that cannot be explained away by errors in recalling the environmental exposure or other biases in the data," Dr. Haley said.

In the new paper, Dr. Haley and his colleagues studied 508 deployed veterans with GWI and 508 deployed veterans who did not develop any GWI symptoms, all randomly selected from more than 8,000 representative Gulf War-era veterans who completed the U.S. Military Health Survey. They not only gauged sarin exposure – by asking whether the veterans had heard chemical nerve gas alarms sound during their deployment – but also collected blood and DNA samples from each veteran.

The researchers tested the samples for variants of a gene called *PON1*. There are two versions of *PON1:* the Q variant generates a blood enzyme that efficiently breaks down sarin while the R variant helps the body break down other chemicals but is not efficient at destroying sarin. Everyone carries two copies of *PON1*, giving them either a QQ, RR or QR genotype.

For Gulf War veterans with the QQ genotype, hearing nerve agent alarms – a proxy for chemical exposure – raised their chance of developing GWI by 3.75 times. For those with the QR genotype, the alarms raised their chance of GWI by 4.43 times. And for those with two copies of the R gene, inefficient at breaking down sarin, the chance of GWI increased by 8.91 times. Those soldiers with both the RR genotype and low-level sarin exposure were over seven times more likely to get GWI due to the interaction per se, over and above the increase in risk from both risk factors acting alone. For genetic epidemiologists, this number leads to a high degree of confidence that sarin is a causative agent of GWI.

"Your risk is going up step by step depending on your genotype, because those genes are mediating how well your body inactivates sarin," said Dr. Haley. "It doesn't mean you can't get Gulf War illness if you have the QQ genotype, because even the highest-level genetic protection can be overwhelmed by higher intensity exposure."

This kind of strong gene-environment interaction is considered a gold standard for showing that an illness like GWI was caused by a particular environmental toxic exposure, he added. The research doesn't rule out that other chemical exposures could be responsible for a small number of cases of Gulf War illness. However, Dr. Haley and his team carried out additional genetic analyses on the new data, testing other factors that could be related, and found no other contributing causes.

"There's no other risk factor coming anywhere close to having this level of causal evidence for Gulf War illness," said Dr. Haley.

The team is continuing research on how GWI impacts the body, particularly the immune system, whether any of its effects are reversible, and whether there are biomarkers to detect prior sarin exposure or GWI.

References:

"Evaluation of a Gene–Environment Interaction of PON1 and Low-Level Nerve Agent Exposure with Gulf War Illness: A Prevalence Case–Control Study Drawn from the U.S. Military Health Survey's National Population Sample" by Robert W. Haley, Gerald Kramer, Junhui Xiao, Jill A. Dever and John F. Teiber, 11 May 2022, Environmental Health Perspectives. DOI: 10.1289/EHP9009

"Invited Perspective: Causal Implications of Gene by Environment Studies Applied to Gulf War Illness" Marc G. Weisskopf and Kimberly A. Sullivan, 11 May 2022,

Environmental Health Perspectives. [DOI: 10.1289/EHP11057](DOI: 10.1289/EHP11057)
Other UTSW researchers who contributed to this study include John Teiber, Gerald Kramer, and Junhui Xiao. The U.S. Military Health Survey was a collaborative effort of UTSW and a large survey research team at RTI International including Jill Dever, who also contributed to this paper. The study was funded by the U.S. Departments of Defense and Veterans Affairs. Opinions, interpretations, conclusions, and recommendations are those of the authors and are not necessarily endorsed by the U.S. Departments of Defense or Veterans Affairs.

https://bit.ly/3G1ScHy

Fecal Transplants Reverse Hallmarks of Aging in the Gut, Eyes, and Brain

In an experiment on mice, transplanting fecal microbiota from young into old reversed hallmarks of aging in the gut, eyes, and brain

In the quest for eternal youth, poo transplants may seem like an unlikely way to reverse the aging process.

However, scientists at the Quadram Institute and the University of East Anglia have provided evidence, from research in mice, that transplanting fecal microbiota from young into old mice can reverse the hallmarks of aging in the gut, eyes, and brain.

In the reverse experiment, microbes from aged mice induced inflammation in the brain of young recipients and depleted a key protein required for normal vision.

These findings show that gut microbes play a role in regulating some of the detrimental effects of aging and open up the possibility of gut microbe-based therapies to combat the decline in later life.

Prof Simon Carding, from UEA's Norwich Medical School and head of the Gut Microbes and Health Research Programme at the Quadram Institute, said: "This ground-breaking study provides tantalizing evidence for the direct involvement of gut microbes in aging and the functional decline of brain function and vision and offers a potential solution in the form of gut microbe replacement therapy."

It has been known for some time that the population of microbes that we carry around in our gut, collectively called the gut microbiota, is linked to health. Most diseases are associated with changes in the types and behavior of bacteria, viruses, fungi, and other microbes in an individual's gut.

Some of these changes in microbiota composition happen as we age, adversely affecting metabolism and immunity, and this has been associated with age-related disorders including inflammatory bowel diseases, along with cardiovascular, autoimmune, metabolic, and neurodegenerative disorders.

To better understand the effects of these changes in the microbiota in old age, scientists from the Quadram Institute transferred the gut microbes from aged mice into healthy young mice, and vice versa. They then looked at how this affected inflammatory hallmarks of aging in the gut, brain and eye, which suffer from declining function in later life.

The study, published in the journal *Microbiome*, found that the microbiota from old donors led to loss of integrity of the lining of the gut, allowing bacterial products to cross into the circulation, which results in triggering the immune system and inflammation in the brain and eyes.

Age-related chronic inflammation, known as inflammaging, has been associated with the activation of specific immune cells found in brain. These cells were also over-activated in the young mice who received aged microbiome transplants.

In the eye, the team also found specific proteins associated with retinal degeneration were elevated in the young mice receiving microbiota from old donors.

In old mice, these detrimental changes in the gut, eye and brain could be reversed by transplanting the gut microbiota from young mice.

In ongoing studies, the team is now working to understand how long these positive effects can last, and to identify the beneficial

components of the young donor microbiota and how they impact on organs distant from the gut.

The microbiota of young mice, and the old mice who received young microbiota transplants were enriched in beneficial bacteria that have previously been associated with good health in both mice and humans.

The researchers have also analyzed the products which these bacteria produce by breaking down elements of our diet. This has uncovered significant shifts in particular lipids (fats) and vitamin metabolism, which may be linked to the changes seen in inflammatory cells in the eye and brain.

Similar pathways exist in humans, and the human gut microbiota also changes significantly in later life, but the researchers caution about extrapolating their results directly to humans until similar studies in elderly humans can be performed.

A new facility for Microbiota Replacement Therapy (MRT), also known as Faecal Microbiota Transplantation (FMT) is being built in the Quadram Institute that will facilitate such trials, as well as other trials for microbiota-related conditions.

Lead author of the study, Dr. Aimee Parker from the Quadram Institute said: "We were excited to find that by changing the gut microbiota of elderly individuals, we could rescue indicators of age-associated decline commonly seen in degenerative conditions of the eye and brain.

"Our results provide more evidence of the important links between microbes in the gut and healthy aging of tissues and organs around the body. We hope that our findings will contribute ultimately to understanding how we can manipulate our diet and our gut bacteria to maximize good health in later life."

The research was funded by the Biotechnology and Biological Sciences Research Council, part of UK Research and Innovation.

'Fecal microbiota transfer between young and aged mice reverses hallmarks of the aging gut, eye, and brain' is published in the journal *Microbiome.*

Reference: "Fecal microbiota transfer between young and aged mice reverses hallmarks of the aging gut, eye, and brain" by Aimée Parker, Stefano Romano, Rebecca Ansorge, Asmaa Aboelnour, Gwenaelle Le Gall, George M. Savva, Matthew G. Pontifex, Andrea Telatin, David Baker, Emily Jones, David Vauzour, Steven Rudder, L. Ashley Blackshaw, Glen Jeffery and Simon R. Carding, 29 April 2022, Microbiome.
DOI: 10.1186/s40168-022-01243-w

https://bit.ly/3wxkwNO

COVID-19, MIS-C and Kawasaki Disease Share Underlying Molecular Patterns and Immune Response

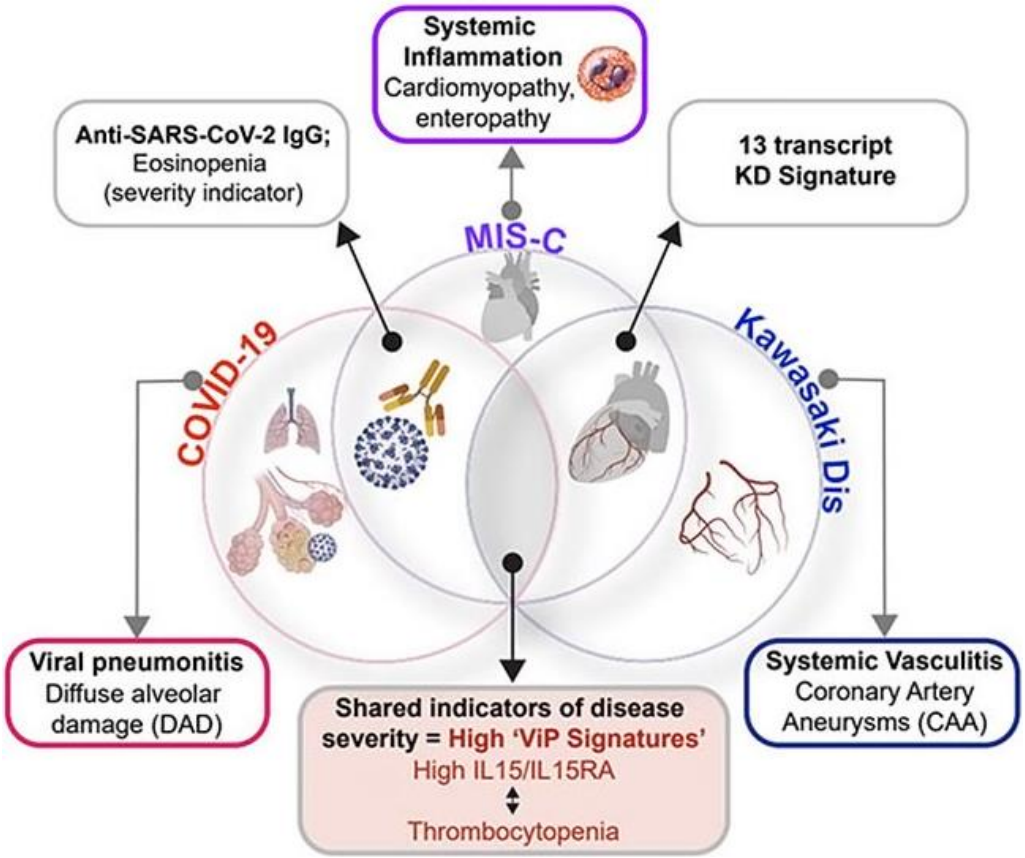
The inflammatory disorders share similar underlying molecular patterns, a University of California San Diego (UCSD) study reports; findings may improve disease diagnosis and treatment and support new drug targets for MIS-C.

When COVID-19 emerged and doctors raced to define and treat the new disease, they soon discovered it was not the only novel illness caused by SARS-CoV-2. A subset of children infected by the virus also experienced abdominal pain, headaches, rashes, and vomiting. This new set of symptoms was labeled multisystem inflammatory syndrome in children (MIS-C) and had many of its pediatric patients requiring intensive care.

As the prevalence of MIS-C increased, physicians began to note its similarities to a pre-pandemic illness, Kawasaki disease (KD), which has baffled pediatricians for more than 50 years. MIS-C and KD share many symptoms, including fever, rash, and bloodshot eyes, though KD can also lead to coronary artery aneurysms and heart attacks. Unlike MIS-C, which is associated with a specific virus, KD may be triggered by a variety of infectious and environmental stimuli.

To better understand how these inflammatory syndromes compare and contrast, researchers at the University of California San Diego School of Medicine collected blood and tissue samples from MIS-C

and KD patients. Using artificial intelligence tools, they analyzed patterns of gene expression in both conditions and compared them to gene expression markers of COVID-19.



UC San Diego researchers summarize the similarities and differences between COVID-19, MIS-C and Kawasaki disease, three conditions unified by the same immune-associated gene signature. **Credit: UC San Diego Health Sciences**

The findings, which will be published today (May 16, 2022) in the journal *Nature Communications*, reveal that MIS-C and KD are on the same immune response continuum as COVID-19, with MIS-C being a more severe version of the response than KD. Despite these underlying similarities, the conditions do diverge in several laboratory and clinical parameters. Authors said the findings could improve disease diagnosis, monitoring, and treatment in pediatric patients.

"We want our immune system to protect us from harmful stimuli, but some children are genetically predisposed to respond more intensely, leading to inflammation and unwanted symptoms across the body," said co-corresponding author Jane C. Burns, MD, a pediatrician at Rady Children's Hospital-San Diego and director of the Kawasaki Disease Research Center at UC San Diego School of Medicine. "The sooner we can identify and understand the child's inflammatory condition, the better we can tailor our delivery of life-saving support."

The research team previously identified a set of 166 genes expressed in viral respiratory diseases, including COVID-19, a subset of which also corresponded to disease severity. Researchers found that this same "gene signature" also applied to both MIS-C and KD, suggesting the conditions all stem from a similar underlying mechanism, which involves the rapid release of IL15/IL15RA cytokines.

The team then looked at a separate set of 13 genes used to identify KD, and found that a computer program trained to look for this genetic signature could not tell the KD and MIS-C samples apart.

"We were not expecting that," said co-corresponding author Pradipta Ghosh, MD, professor of medicine and cellular and molecular medicine at UC San Diego School of Medicine. "We analyzed MIS-C and KD through the lens of two distinct gene signatures, and both experiments told us these diseases are closely related."

Ghosh said the two gene signatures likely represent different parts of the same broader immune response.

While the study provides a new unifying framework for these diseases, it also identifies a few subtle differences. For example,

MIS-C patients had lower blood platelet and eosinophil counts, two features that can be measured from routine blood tests. And, while many serum cytokines were similarly elevated in both conditions, a select few were more elevated in MIS-C than in KD samples.

Authors noted that therapeutics targeting some of these cytokines, including TNFa and IL1ß, have already been approved by the U.S. Food and Drug Administration (FDA) and are being tested as novel treatments for MIS-C.

"We believe our findings have a high potential to impact clinical trial planning immediately, and also shape clinical guidelines and patient care down the line," said co-corresponding author Debashis Sahoo, PhD, associate professor of pediatrics and computer science at UC San Diego School of Medicine and UC San Diego Jacobs School of Engineering.

Reference: "An Artificial Intelligence-guided signature reveals the shared host immune response in MIS-C and Kawasaki disease" by Pradipta Ghosh, Gajanan D. Katkar, Chisato Shimizu, Jihoon Kim, Soni Khandelwal, Adriana H. Tremoulet, John T. Kanegaye and Pediatric Emergency Medicine Kawasaki Disease Research Group, 16 May 2022, Nature Communications. DOI: 10.1038/s41467-022-30357-w

Co-authors include: Gajanan D. Katkar, Chisato Shimizu, Jihoon Kim, Soni Khandelwal, Adriana H. Tremoulet, John T. Kanegaye, Pediatric Emergency Medicine Kawasaki Disease Research Group and Soumita Das, all at UC San Diego, as well as Joseph Bocchini of the Willis-Knighton Health System.

Funding: National Institutes of Health, UCOP-RGPO, iDASH, Patient Outcomes Research Institute, Gordon and Marilyn Macklin Foundation, American Association of Immunologists Intersect Fellowship Program for Computational Scientists and Immunologists, UC San Diego Stem Cell Center

https://bit.ly/3wDzHFa

Weird Link Between Parkinson's Gene and Vocal Issues Could Lead to Earlier Diagnosis

Neuroscientists found that higher levels of the alpha-synuclein protein in the brain can lead to changes in vocal production.

Parkinson's disease is likely best known for its movement-related symptoms, particularly tremors and stiffness.

However, the disease is also known to hinder vocal production, giving those with Parkinson's a soft monotonous voice. Research has suggested that those symptoms often appear much earlier in the disease's development – sometimes decades before movement-related symptoms.

New research by University of Arizona (UArizona) neuroscientists suggests that a specific gene commonly associated with Parkinson's may be behind those vocal-related issues – a finding that could help lead to earlier diagnoses and treatments for Parkinson's patients.

The research was conducted in the lab of Julie E. Miller, an assistant professor of neuroscience and of speech, language, and hearing sciences in the College of Science.

"We have this big gap here – we don't know how this disease impacts the brain regions for vocal production, and this is really an opportunity to intervene early and come up with better treatments," said Miller, who also has joint appointments in the Department of Neurology and the Graduate Interdisciplinary Program in Neuroscience, and is a member of the UArizona BIO5 Institute.

The study was published earlier this month in the scientific journal *PLOS ONE*. César A. Medina, a former Ph.D. student in Miller's lab who is now a postdoctoral scholar at Johns Hopkins University, is the paper's lead author. Also involved in the research were Eddie Vargas, a former UArizona undergraduate student who will soon attend the College of Medicine – Tucson, and Stephanie Munger, a research professional in the Department of Neuroscience.

A unique, ideal model for studying human speech

To investigate any correlation between vocal changes and the Parkinson's-related gene – known as alpha-synuclein – the researchers turned to the zebra finch, a songbird native to Australia.

The birds are an ideal model for human speech and voice pathways for several reasons, Medina said. Young finches learn their songs from older, father-like male birds, much in the same way babies learn to speak by listening to their parents. The part of a finch's

brain that deals with speech and language is also organized very similarly to its counterpart in the human brain.

"These similarities across behavior, anatomy, and genetics allow us to use the zebra finches as a model for human speech and voice," Medina said.

To see how alpha-synuclein might affect vocal production in the birds, researchers first took baseline recordings of their songs. They then introduced a copy of the gene into some of the birds; other birds were not given the gene so researchers could compare the results. All the birds' songs were recorded again immediately after introducing the gene, and then one, two, and three months later.

The researchers used computer software to analyze and compare the acoustic features of the songs over time, studying pitch, amplitude, and duration of the songs to determine whether and when the birds' vocal production changed.

Initial findings showed that alpha-synuclein did affect song production. The birds with the gene sang less after two months, and they sang less at the start of a song session three months after receiving the gene. The vocalizations were also softer and shorter, findings similar to what is seen in the human disease.

Another step toward earlier diagnoses and treatments

To determine whether the effects on speech were connected to changes in the brain, the researchers zeroed in on a section of the brain called Area X. They found that there were higher levels of the alpha-synuclein protein in Area X, helping them establish that the gene did, in fact, cause the changes in the brain that led to changes in vocal production, Medina said.

This connection, he added, had been predicted in previous Parkinson's research, but it was not conclusive.

The next step, Miller said, is figuring out how to apply these findings to human data, which could provide more answers that lead to better Parkinson's diagnoses and treatments – ones that come long before movement-related symptoms tell a patient to visit a neurologist.

The long-term goal of the Miller Lab, she said, is to partner with other researchers and private companies to develop drugs that target alpha-synuclein and other genes associated with Parkinson's.

Doing so, Medina said, would mean "we could stop the progression of Parkinson's disease before it becomes a detrimental impediment to the quality of life for the patient."

Reference: "Vocal changes in a zebra finch model of Parkinson's disease characterized by alpha-synuclein overexpression in the song-dedicated anterior forebrain pathway" by Cesar A. Medina, Eddie Vargas, Stephanie J. Munger and Julie E. Miller, 4 May 2022, PLOS ONE. DOI: 10.1371/journal.pone.0265604

This study was supported in part by funds from the Parkinson's and Movement Disorder Foundation, the University of Arizona's Accelerate for Success Program and Core Facilities Pilot Program, and departmental startup funds. The research was also supported by the National Institute of Neurological Disorders and Stroke of the National Institutes of Health under award number R21NS123512. Medina's work was supported by a National Science Foundation Graduate Research Fellowship under National Science Foundation award number DGE-1746060, the University of Arizona's Initiative for Maximizing Student Development under National Institutes of Health award number R25 GM 062584, and a University of Arizona Marshall Foundation Dissertation Scholarship. Vargas' work was supported by summer research funding through the University of Arizona Undergraduate Biology Research Program, the Border Latino American Indian Summer Exposure to Research program, the W.A. Franke Honors College and the Undergraduate Program in Neuroscience and Cognitive Science.

https://bit.ly/3lro7ry

Severe Hepatitis Spike in Children 'Linked' to Dogs, But Here Are The Facts

Data suggesting this link is probably a lot weaker than most of the alternative hypotheses

Mick Bailey, The Conversation

The recent spike in cases of sudden, severe hepatitis in children around the world has been widely reported. Recently, several news outlets have highlighted a possible link between cases and contacts with pet dogs. However, the data suggesting this link is extremely weak – in fact, probably a lot weaker than most of the alternative

hypotheses that have been proposed.

The spike in hepatitis cases in children was first noticed in the UK, but has now been reported in Europe, Asia, and the Americas. Although the numbers worldwide are still very low, the disease has been severe and some children have needed a liver transplant.

At least 11 children have died, and there are suggestions that it may continue for some time.

Hepatitis in humans is normally caused either by toxicity, such as alcohol, or by infections with one of several different viruses. However, none of the usual viruses have been identified in these children.

The UK Health Security Agency (UKHSA), the agency responsible for public health protection in the UK, is working to find the cause of the disease so that it can be effectively controlled and treated.

Dog exposure

In a recent briefing paper, the agency reported a high number of "dog exposures" in these cases of severe childhood hepatitis. However, before parents stop their children from going near their family dog, it's worth looking at the results in detail.

The UKHSA found that 70 percent of patients (64 of 92, where data was available) were from dog-owning families or had "other dog exposures".

Yet 33 percent of households in the UK own dogs, and many more children from non-dog-owning households will be exposed to dogs when they visit or play with their friends. Seventy percent exposure to dogs may be completely normal.

To suggest a link, it's important to show not only that exposure to dogs in patients is high, but that it's higher than in unaffected children. Until that's checked in what's known as a case-control study, any link is nothing more than a suggestion.

A second problem with the data is that if you ask enough questions, there's a strong probability that the answers to one or more questions may seem linked to cases.

Where we collect very large amounts of data retrospectively, this kind of spurious association can easily occur.

In fact, there's a website devoted to collecting them. Here's an example: the divorce rate in Maine between 2000 and 2009 seems to be strongly linked to per capita margarine consumption.

A spurious association. **(Tyler Vigen)**

The important point about links identified by retrospective data is that they are hypotheses. They always need to be checked by collecting further data around new cases. If the link is real, it will continue to show up in new data. If it's spurious, it won't.

One of the associations on the spurious-correlation website shows another important problem. Between 2000 and 2009, per capita cheese consumption in the US appears to be linked to deaths as a result of becoming tangled in bedsheets.

It's actually not hard to think that this might happen as a result of cheese-induced nightmares. The fact that we can think of a mechanism underlying the link gives us more confidence that it might be true, even if the mechanism is quite far-fetched.

We tend to put more weight on associations where we can think of

a reason, even when the evidence is poor.

So what are the possible causes of the spike in hepatitis cases in children, and might any of them be linked to dogs? One virus in particular, an adenovirus, has been detected in the blood of 72 percent of patients tested (for comparison, SARS-CoV-2 was detected in only 18 percent).

Where it was possible to identify the type, it was found to be adenovirus 41 (Ad41), a human type normally causing diarrhoea in children. Although dogs have their own adenoviruses that cause respiratory disease or hepatitis, they are not known to infect humans, and Ad41 has no known association with dogs.

The cases in children don't suggest that infection is passing between children – there are too few cases, too widely distributed for that.

Equally, the distribution of cases doesn't suggest that this is a novel virus being transmitted from dogs to children. Cases have appeared in other countries much faster than a dog virus would spread between dogs.

Possible causes

Are there other possible causes? It has been suggested that the severity of the hepatitis is a result of the immune system working incorrectly – either too strongly or not strongly enough.

Social distancing during the pandemic has reduced the transmission of a whole range of diseases, and a lack of exposure to them may have left some children unprepared for infections that normally wouldn't cause a problem.

Equally, the lack of exposure to dirt as a result of handwashing, sterilizing surfaces, and other hygiene measures may have predisposed children to over-reactive immune responses (as has been suggested for allergic diseases), and the hepatitis may be caused by the immune response rather than a virus.

Finally, and not surprisingly, it's been suggested that previous COVID infections may have predisposed children to hepatitis.

All of these are no more than theories at the moment, and the available data is insufficient to prioritize any of them or to use them to suggest control measures.

Fortunately, the incidence is still extremely low, and until there is better data parents should probably concentrate more on keeping an eye out for any symptoms in their children than on reducing their exposure to dogs.

Mick Bailey, Professor of Comparative Immunology, University of Bristol.

https://bit.ly/3yOU2dq

Ancient tooth of mysterious Denisovan girl possibly found

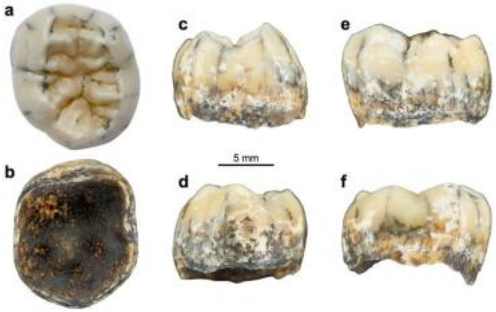
The tooth may have belonged to a 3-year-old girl.

By Charles Q. Choi

The discovery of an ancient molar — a tooth that likely belonged to young girl who lived up to 164,000 years ago in a cave in what is now Laos — is new evidence that the mysterious human lineage dubbed the Denisovans, previously known only from caves in Siberia and China, also lived in Southeast Asia, a new study finds.

"This shows that Denisovans lived in a wide range of environments and latitude and were able to adapt to extreme conditions, from the cold mountains of the Altai [in Russia] and Tibet to the tropical forests of Southeast Asia," study co-author Clément Zanolli, a paleoanthropologist at the University of Bordeaux in France, told Live Science.

"Genetic studies indicated that Denisovans were adapted to high altitude and cold climates, but now we also know that they were living in warmer and more humid climates and at low altitude," Zanolli added.



Different views of the young girl's tooth. **(Image credit: Demeter, F. et al.**

Nature Comunnications)

Although modern humans, *Homo sapiens*, are now the only surviving members of the genus *Homo* — the human family tree — other human lineages once lived on Earth. The closest extinct relatives of modern humans include the Neanderthals in Europe and Asia and the newfound Denisovan lineages of Asia and Oceania.

The research team inspects sedimentary rock, known as breccia, that they had just cut out of Cobra cave on the day of the discovery.

Previous research estimated the ancestors of modern humans split about 700,000 years ago from the lineage that gave rise to Neanderthals and Denisovans, and the ancestors of Neanderthals and Denisovans diverged from one another about 400,000 years ago. However, genetic analysis of fossils of these extinct lineages revealed they remained close enough to interbreed with modern humans.

Much remains a mystery about Denisovans. So far, researchers have discovered only five fossils linked for certain with them — three upper molars, a finger bone and a jawbone — which greatly limits what researchers know about them overall. Scientists who discovered a skull in China dubbed "Dragon Man" claimed it belonged to a newfound species, *Homo longi*, but many other researchers suspect it may be a Denisovan skull.

Where exactly Denisovans lived is also debated. The fossils unearthed to date all came from mainland Asia, but prior genetic evidence suggests people in Oceania and islands in Southeast Asia possess Denisovan heritage.

Now, the new tooth may be the first fossil evidence of Denisovans in Southeast Asia. "Any additional fossil described as a Denisovan is relevant to better understand their biology and evolution," study co-author Fabrice Demeter, a paleoanthropologist at the University of Copenhagen, told Live Science.

Scientists discovered the tooth in 2018 in a site known as Cobra Cave in the Annamite Mountains of Laos, which has an entrance located about 110 feet (34 meters) above the ground. The limestone cave, technically dubbed Tam Ngu Hao 2, was found due to its proximity to another site, where previous research unearthed ancient fossils of modern humans. (Cobra Cave also included fossils of animals, such as rhinoceros, tapirs and sambar deer.)

A view from inside Denisova cave in Russia's Altai Mountains. Notice how the vegetation and climate are different here compared with Laos. (Image credit: Mike Morley/Flinders University)

"Even if recent results of genetic studies suggested that Denisovans and modern humans met in southern Asia during the late Pleistocene [2.6 million to 11,700 years ago], we did not expect to actually find a Denisovan tooth in Laos," study co-author Laura Shackelford, a paleoanthropologist at the University of Illinois Urbana-Champaign, told Live Science.

The tooth was a molar that had not yet erupted from the left side of the lower jaw. This suggested it belonged to a child about 3.5 to 8.5 years old. Analyzing the dirt and rock surrounding the tooth with techniques such as luminescence dating, which analyzes how ago long mineral grains were last exposed to sunlight to estimate their age, and radioactive dating, which measures the age of things based on how long it takes certain chemical elements to radioactively decay, suggested the molar was between 131,000 and 164,000 years old.

By analyzing proteins in the tooth's enamel, the team confirmed it was from genus *Homo*. The absence of proteins linked with a Y chromosome suggests the tooth came from a female. (The researchers did not analyze the fossil for ancient DNA because this genetic material rarely preserves well in the type of sediment found in the cave and in tropical conditions present in Laos.)

When the scientists compared this molar to teeth from other hominins — the group that includes humans, our ancestors and our

closest evolutionary relatives such as *Australopithecus* — they found its internal and external 3D structure resembled that of Neanderthals, but fell slightly outside their known range of variation. Moreover, the tooth also differed from that of modern humans and *Homo erectus*, the first known human species to use relatively sophisticated stone tools. Although the scientists could not exclude it as belonging to a Neanderthal, they suggested its close physical similarity to a Denisovan specimen from China indicated that the molar was likely Denisovan.

"The tooth indicates that Denisovans were actually in Southeast Asia, which is significant for understanding their range," Shara Bailey, a paleoanthropologist at New York University, who did not participate in this study, told Live Science. "We know their DNA got there — it is present in recent Southeast Asian groups — but this indicates that the population was present in the area too."

Even if this new fossil turns out to not be Denisovan, any new human fossil from an area where few ancient human fossils have been unearthed so far, such as Laos, "is important, especially if it's a non-*sapiens* fossil, as this clearly seems to be," Chris Stringer, a paleoanthropologist at the Natural History Museum in London, who did not take part in this research, told Live Science.

Given that caveat, "I think it is a good study and the conclusions are strong," Bailey said. "I agree with their assessment of the tooth."

The new findings may shed light on the extent to which different human lineages may have coexisted. "Neanderthals lived in Europe and western Asia at the same time Denisovans occupied a large part of eastern Asia, together with other human groups like *Homo erectus*, *Homo floresiensis*, *Homo luzonensis* and modern humans," Shackelford said. "However, it is still unclear if, when and where all these extinct groups might have met."

These findings suggest other fossils in Asia need to be reanalyzed using modern techniques. "I believe we will find there are more Denisovans out there," Bailey said. "I know of one tooth in particular that I have seen that is probably Denisovan."

When it comes to future research, "I'm curious about how the tooth got into the cave and whether there is any human activity in the cave," Bence Viola, a palaeoanthropologist at the University of Toronto, who was not a part of this work, told Live Science. "The now-ongoing excavations should answer that."

The scientists detailed their findings online May 17 in the journal Nature Communications.

https://bit.ly/3yQIo1t

Extraterrestrial Stone Found in Egypt May Be First Evidence on Earth of Rare Supernova

Scientists think they're found the first evidence on Earth of a type Ia supernova explosion

David Nield

'Standard candle' (or type Ia) supernova explosions are some of the most energetic events in the Universe, happening when a dense white dwarf star subsumes another star. Now, scientists think they're found the first evidence on Earth of such a supernova.

The claim comes after a careful study of the extraterrestrial Hypatia stone that was found in Egypt in 1996. Tell-tale signs, including the chemical makeup and patterning of the rock, suggest that the shards contain bits of the dust and gas cloud surrounding an Ia supernova.

A 3-gram sample of the Hypatia stone. **(Romano Serra)**

Over billions of years, that mix of dust and gas would have turned into a solid, the researchers say, eventually forming the parent body that Hypatia came from sometime close to when our Solar System first came into being.

"In a sense, we could say, we have caught a supernova Ia explosion

in the act, because the gas atoms from the explosion were caught in the surrounding dust cloud, which eventually formed Hypatia's parent body," says geochemist Jan Kramers from the University of Johannesburg in South Africa.

Using detailed, non-destructive chemical analysis techniques, the team looked at 17 different targets on a tiny sample of Hypatia. From there it was a question of piecing together clues about where the stone had been and how it had formed.

Those clues included an unusually low level of silicon, chromium, and manganese, suggesting that the rock hadn't been formed in the inner Solar System. The researchers also noticed high levels of iron, sulfur, phosphorus, copper, and vanadium, again making the object distinct from anything in our particular neighborhood in space.

Looking at element concentration patterns of Hypatia, there were marked differences to what we would expect to have formed in rocks from inside the Solar System and in our arm of the Milky Way. Further analysis rules out the idea that the rock had formed from a red giant star.

The researchers were also able to show that Hypatia didn't match what would be expected if it came from a type II supernova – it has too much iron relative to silicon and calcium – and that leaves the intriguing possibility that this is a leftover from a type Ia supernova, and the first to be found on this planet.

"If this hypothesis is correct, the Hypatia stone would be the first tangible evidence on Earth of a supernova type Ia explosion," says Kramers.

"Perhaps equally important, it shows that an individual anomalous parcel of dust from outer space could actually be incorporated in the solar nebula that our Solar System was formed from, without being fully mixed in."

From what we know of type Ia supernovas, they should produce very unusual element concentration patterns in rocks such as Hypatia. Through a comprehensive search of star data and modeling, the team wasn't able to find a better match for the rock.

Of the 15 elements analyzed in the stone, several matched what would be expected if the object had come from a dense white dwarf star explosion.

However, it's not a closed case yet. A further six elements don't match type 1a supernova models: aluminum, phosphorus, chlorine, potassium, copper, and zinc. However, the researchers think something further back in the supernova's past could explain this.

"Since a white dwarf star is formed from a dying red giant, Hypatia could have inherited these element proportions for the six elements from a red giant star," says Kramers. "This phenomenon has been observed in white dwarf stars in other research."

We'll need more research to settle the science, but at this point, it certainly looks like this mysterious rock has traveled a very long way. The research has been published in *Icarus*.

https://bit.ly/3yN7ZZm

Mind-Altering Parasite May Make Infected People More Attractive, Study Suggests

Researchers found persons infected by Toxoplasma gondii were rated as more attractive and healthier-looking than non-infected individuals.

Peter Dockrill

The brain-hijacking parasite *Toxoplasma gondii* seems to be almost everywhere. The microscopic invader is thought to infect up to 50 percent of people, and a range of studies suggests it may alter human behavior, in addition to that of many other animals.

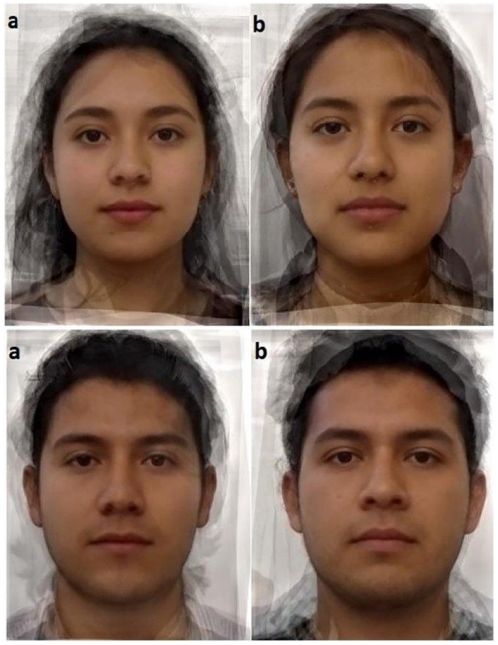
The parasite has been linked with a large range of neurological disorders, including schizophrenia and psychotic episodes, and scientists keep uncovering more mysterious effects that may result from infection.

In one such new study, researchers found that men and women

infected by the parasite ended up being rated as more attractive and healthier-looking than non-infected individuals.

On the face of it, that might sound strange and unlikely. But hypothetically speaking, the phenomenon could make sense from an evolutionary biology standpoint, scientists say.

Amidst the many neurobiological changes *T. gondii* infection appears to bring about in its hosts, researchers hypothesize some of the effects may occasionally benefit infected animals – which might then benefit the parasite too, by subsequently helping to spur its own transmission prospects.



Above: Composite images of 10 Toxoplasma-infected women and men (a), beside 10 composite images of 10 non-infected women and men (b).

"In one study, *Toxoplasma*-infected male rats were perceived as more sexually attractive and were preferred as sexual partners by non-infected females," researchers explain in a new paper led by first author and biologist Javier Borráz-León from the University of Turku in Finland.

Much research has been devoted to investigating whether similar effects can be seen in human cases of *T. gondii* infection.

The evidence is far from clear, but some evidence suggests infected men have higher levels of testosterone than non-infected men.

Arguably, men with higher levels of testosterone could be more likely to become infected by the parasite in the first place, through greater levels of risk-taking behavior associated with the hormone.

An alternative view, however, is that the parasite might be capable of subtly altering its host phenotype, manipulating chemicals in the animal's body, such as neurotransmitters and hormones, for its own subsequent ends.

Those alterations could be far-reaching, Borráz-León and his team suggest. "Some sexually transmitted parasites, such as *T. gondii*, may produce changes in the appearance and behavior of the human host, either as a by-product of the infection or as the result of the manipulation of the parasite to increase its spread to new hosts," the researchers write.

To test this hypothesis, the researchers compared 35 people (22 men, 13 women) infected with *T. gondii* against 178 people (86 men, 92 women) who did not carry the parasite.

All the participants (including the infected) were nonetheless healthy college students, who had previously had their blood tested for another study investigating *T. gondii*.

Following a number of different tests involving the participants – including surveys, physical measurements, and visual assessments, the researchers found *Toxoplasma*-infected subjects had significantly lower facial fluctuating asymmetry than the non-infected people.

Fluctuating asymmetry is a measure of deviation from symmetrical features, with lower levels of asymmetry (ie. higher symmetry) being linked with better physical health, good genes, and attractiveness, among other things.

In addition, women carrying the parasite were found to have lower body mass and lower BMI than non-infected women, and they reported both higher self-perceived attractiveness and a higher number of sexual partners.

In a separate experiment, a group of 205 independent volunteers rated photographs of the participants' faces, and the raters found the infected participants looked both significantly more attractive and healthier than the non-infected participants.

Interpreting the results, the researchers say it's possible that *T. gondii* infection might produce changes in the facial symmetry of its hosts through changes in endocrinological variables, such as testosterone levels. Further, the parasite could also be influencing metabolic rate in hosts, nudging infected people in ways that might influence their health and attractiveness perceptions.

That said, all of this is speculation at this point, and the team acknowledges other interpretations are viable too, including the idea that highly symmetrical, attractive people might somehow better afford the physiological costs related to parasitism, which in other regards are considered a burden to health.

As for which interpretation is correct, it's impossible to say for sure based on this one study alone, and the researchers acknowledge that the small sample size of their experiment is a limiting factor for its statistical analysis. For that reason, future studies with greater numbers of participants will be needed to confirm or deny their overall hypothesis. But maybe – just maybe, they say – this perplexing parasite isn't necessarily our enemy after all.

"It is possible that the apparently non-pathological and potentially beneficial interactions between *T. gondii* and some of its intermediate hosts, such as rats and humans, are the result of co-evolutionary strategies that benefit, or at least do not harm, the fitness of both the parasite and the host," the researchers write.

The findings are reported in *PeerJ*.

https://nyti.ms/3wvvGUl

Since You're Already Getting a Flu Shot, Why Not One for Covid, Too?

Scientists and federal health officials are debating plans to pair coronavirus and flu vaccinations in the fall.

By Apoorva Mandavilli

As the coronavirus morphs into a stubborn and unpredictable facet of everyday life, scientists and federal health officials are converging on a new strategy for immunizing Americans: a vaccination campaign this fall, perhaps with doses that are finely tuned to combat the version of the virus expected to be in circulation. The plan would borrow heavily from the playbook for distributing annual flu shots, and may become the template for arming Americans against the coronavirus in the years to come.

But some experts question how well a renewed vaccination push would be received by a pandemic-weary public, whether the doses can be rolled out quickly enough to reach the people who need them most — and whether most Americans need additional shots at all.

On June 28, scientific advisers to the Food and Drug Administration will meet to identify the coronavirus variant most likely to be percolating in the United States as temperatures cool. That should leave manufacturers time to decide whether the vaccines' composition needs to be revised and to ramp up production, hopefully enough to churn out hundreds of millions of doses by October.

Scientific advisers to the F.D.A. have said they would favor switching to a new version of the vaccines only if there were compelling evidence that the current ones were no longer effective and a modified version proved to be better.

The idea is that eligible Americans would be urged to seek immunization against the coronavirus and the flu at the same time this fall, and in the same places: drugstores, doctors' offices, walk-in clinics and the like. Some important details — like who would be eligible — will be sorted out next month at meetings of scientific advisers to the F.D.A. and the Centers for Disease Control and Prevention.

The plan would mark a departure from the current sequential authorizations of booster shots for various age groups. But the shortcomings of the annual approach have been apparent to flu

researchers for years.

Scientists and federal health officials usually decide on the formulation of the flu vaccine in the spring, six months before the flu season. They guess at which version of the flu virus will arrive in the United States by looking at what is already circulating in the Southern Hemisphere, among other factors.

But in some years, "by the time the vaccine is manufactured, the strains have changed, and then you might not have good matching," Dr. Ofer Levy, director of the precision vaccines program at Boston Children's Hospital and an adviser to the F.D.A., said.

Among the candidates for a fall Covid shot is a booster designed for Omicron, the odd new avatar of the coronavirus, and combinations that include it. Moderna's lead booster candidate contains 25 micrograms each of its original vaccine and one tailored to Omicron, Dr. Paul Burton, the company's chief medical officer, said.

Pfizer is also testing an Omicron-specific vaccine, but will not make a decision on its fall candidate until June, according to Jerica Pitts, a spokeswoman for the company. Even if the vaccine match isn't perfect, the boost to immunity should offer some protection against any new variant in the fall, as the flu vaccine does.

The number of Americans who have opted to get booster doses has dwindled with each newly recommended shot. While 90 percent of American adults have received at least one dose of a Covid vaccine, 76 percent opted for a second dose and just 50 percent for a third.

"Considering additional doses for a smaller and smaller return is creating an impression that we don't have a very effective vaccination program," Dr. Matthew Daley, a senior investigator at Kaiser Permanente Colorado who heads the C.D.C.'s vaccine working group, said.

A nationwide campaign for another vaccination would needlessly exhaust pharmacists, providers and public health staff, Dr. Daley and other advisers warned at a meeting of their committee last month. And the experts worry that a push for extra doses this fall, when the risks of severe illness and death are likely to be low for most Americans, might cut into the collective willingness to be immunized later if a new variant surfaces and the public urgently requires it.

Repeated immunizations may even blunt a vaccine's effectiveness. For example, people who are vaccinated against the flu in a single year develop stronger immunity than those who are vaccinated two years in a row, noted Florian Krammer, an immunologist at the Icahn School of Medicine at Mount Sinai in New York.

Despite the misgivings, federal officials are gearing up for a fall campaign. Pairing the Covid vaccine with flu every year is the simplest way to convince Americans to line up for the vaccines, Peter Marks, director of the F.D.A.'s Center for Biologics Evaluation and Research, said.

"It saves people time," Dr. Marks said. "And it may mean that more people get both vaccines, which would be a good thing."

Agency scientists are actively debating the best composition for a fall vaccine with the World Health Organization, the National Institutes of Health, and the vaccine manufacturers, Dr. Marks said.

The F.D.A. favors offering roughly the same formulations of the Pfizer-BioNTech and Moderna vaccines, in order to avoid befuddling people. Otherwise, "I worry that could actually paralyze a vaccine campaign, when the most important thing is that people get boosted at all," Dr. Marks said.

If the flu vaccine is any indication, however, many Americans will forgo another Covid shot. The Omicron variant has made it clear that preventing all infections is an unattainable goal, and many consider themselves at only a low risk of severe illness or death.

Still, Dr. Marks noted that influenza campaigns also aim to prevent loss of productivity, not just medical consequences.

Before the Omicron variant's arrival, administration officials said the Covid vaccines were intended to prevent all symptomatic infections, but they have since backed off that stance.

While the Covid vaccines blunted the spread of earlier variants by up to 70 percent, "that's clearly not true with Omicron," he said. "It would be nice to have something that did a better job."

Some experts said that instead of another round of injections, the best candidate for limiting infections would have been a nasal spray that would coat the nose and throat with antibodies to block the virus right at its entryway. But those sprays will not be available in the United States for two or three years at least.

Until Omicron came around, the F.D.A.'s scientists were so excited about mRNA vaccines that they didn't consider alternative boosters, Dr. Marks added: "We may have been temporarily blinded by the light." Still, minimizing the number of infections whenever possible is "obviously a very, very important secondary goal," Dr. Sara Oliver, who represents the C.D.C. on the Covid-19 vaccine working group, said.

Apart from curtailing the spread of the virus and societal disruption, reduced infections should reduce cases of long Covid, the constellation of symptoms that can persist for months, she said.

The new plan may revive some longstanding tensions. Disagreements about who should recommend vaccines, and for whom, have roiled these agencies for months.

Generally, the F.D.A.'s scientific advisers review the safety and effectiveness of vaccines, and recommend authorization or approval. Experts who advise the C.D.C. then issue guidelines on who should get the vaccines and when.

During the pandemic, the lines between the White House, the F.D.A. and the C.D.C. have often been blurred. "Right now, one of the challenges is that we have a lot of voices who are speaking immunization policy, and historically we've just had one voice," Dr. Daley said. When the F.D.A. authorized a second booster, for example, it did so only for adults 50 and older — a distinction that would normally have come from the C.D.C.'s vaccine advisers.

The C.D.C. also made a subtle distinction that was lost on many Americans: It recommended that adults older than 50 may get a booster if they wished to, not that they should do so. But the White House's new Covid czar, Dr. Ashish Jha, endorsed the second booster shots.

"It's not entirely clear that the White House is in the position of making vaccine recommendations per se, but nonetheless, he said that he recommended it," Dr. Camille Kotton, an infectious disease physician at Massachusetts General Hospital and a scientific adviser to the C.D.C., said of Dr. Jha.

It's unclear who would pay for a fall vaccination campaign. The stalemate in Congress over Covid-19 funding jeopardizes the government's ability to purchase and provide the vaccines to the people who are most in need.

"Without urgent additional funding, we are unable to secure enough booster shots for every American who wants one if they are needed in the fall, and we are unable to secure newer, more effective vaccines that protect against new variants," Sarah Lovenheim, assistant secretary for public affairs at the Department of Health and Human Services, said.

https://bit.ly/3wzO2CA

The role party affiliation played in getting US to grim new milestone of one million COVID deaths

Estimates suggest that more than 318,000 deaths from the disease occurred among individuals who had access to vaccines, but chose not to receive any

by Monika L. McDermott and David R. Jones, The Conversation

COVID-19 has now claimed the lives of 1 million Americans—a grim milestone made worse by the fact that probably a third of

those fatalities could have been avoided. Estimates suggest that more than 318,000 deaths from the disease occurred among individuals who had access to vaccines, but chose not to receive any. With such a devastating pandemic sweeping the country, and the globe, why would so many Americans forego a potentially life-saving vaccine?

One key answer to this question is—as with much in the U.S. today—partisan politics. Since vaccines for COVID-19 first became available, polls have consistently shown that Republicans are much less likely than Democrats to be vaccinated or to want to be vaccinated. According to monthly surveys conducted by the Kaiser Family Foundation, this partisan gap has averaged more than 30 percentage points between May 2021 and April 2022.

But the story is both more complicated and wide-ranging than it first appears. We know that party and ideology account for many of the differences in the lives of Americans.

Our research finds that not only is party affiliation a powerful predictor of vaccine willingness, it also contributes to other attitudes that promote or inhibit willingness to be vaccinated, giving it added power.

The pull of partisanship

In two surveys we conducted in March and June of 2021, we found that party affiliation affected COVID-19 vaccination preferences independently of some of the standard influences such as education, age and race. That means party alone can help determine whether a person got a vaccination.

What we also found, however, is that partisanship has additional effects on vaccination status and willingness. That's because it contributes to other factors that also affect willingness to get vaccinations, and so contributes "indirectly" to willingness as well as directly.

These indirect factors included the impact of partisanship on one's concern for contracting COVID-19 oneself; concern for others contracting it; trust in government; trust in scientists and medical professionals; and conspiracy theories surrounding the vaccine—namely that the vaccine would insert a tracking microchip into the body and that it could cause sterility.

Party affiliation influenced Americans' attitudes in each of these areas, which in turn affected a person's willingness to get a COVID-19 vaccine. This basically multiplies the effect that party affiliation has over vaccinations.

Vaccine divide

Republicans and Democrats haven't always felt this differently about potentially life-saving vaccines.

A review of historical public opinion trends during other health crises shows that in 1954, Republicans were roughly equally as likely—only 3 percentage points less—as Democrats to say they were willing to get the then-new polio vaccine.

The vaccine hesitancy gap between the parties for the Asian flu vaccine in 1957 was somewhat larger, but still a far cry from today's gap—Democrats were 9 points more likely to get that vaccine. For the swine flu vaccine in 1976, Democrats were 4 points more likely to get the vaccine.

But since 2000, there have been double-digit partisan gaps in willingness to accept other vaccines to address public health crises. When the administration of George W. Bush raised the possibility of reintroducing the smallpox vaccine in 2002, Republicans were 11 points less likely than Democrats to say they would get the vaccine. During the swine flu pandemic in 2009, this difference grew to 15 points. Most recently, initial reaction in a July 2020 Gallup Poll to the promise of a new COVID-19 vaccine produced a gap of 34 points: 81% of Democrats said they were likely to get the vaccine compared to just 47% of Republicans.

While there is no way to definitively tell if Republicans are dying

from COVID-19 at higher rates than Democrats as a result of these discrepancies, there are numbers that suggest it. An ABC News analysis shows that after vaccines became readily available, states that voted for Donald Trump in 2020 had an average of 38% higher death rates due to COVID-19 than states that voted for Joe Biden.

The partisan difference in vaccine hesitancy can be traced to a broader change in each party's attitudes toward science.

What happened?

Polling data shows that throughout the 1970s and 1980s, Republicans were consistently more likely than Democrats to report a great deal of confidence in the scientific community.

In the mid-1980s, however, prominent Republican leaders began to publicly disparage scientific input on public policy issues—initially about the acid rain debate, then expanding to other topics.

Over time, these messages discrediting science and scientists' opinions on public policy affected public opinion within the parties. In the early 2000s, the parties began to switch positions. Since 2008, Democrats have consistently displayed greater confidence in science, with the largest gap on record—30 percentage points—occurring in the most recent survey measuring it, in 2020.

The path from broader distrust in science to hesitancy toward vaccines may have a long history, but it is fairly straightforward. Scientists are the ones who research and develop vaccines, while scientifically trained doctors and nurses administer them. The most prominent talking heads in the media advocating for vaccination are from the scientific community—including, most notably, Dr. Anthony Fauci. Based on years of rhetoric from party leaders, Republican voters were already primed to distrust these figures.

Our own research demonstrates that citizens who distrust scientists and who distrust medical professionals are less likely to be vaccinated and show less willingness to consider doing so in the future.

Since these tendencies are now more prominent in the Republican Party than in the Democratic Party, this helps drive the overall partisan gap in COVID-19 vaccination and death rates among red and blue states.

Even as COVID-19 seems to be becoming less deadly, experts warn that it is not the last viral pandemic we will face.

Elected officials and other policymakers planning for future threats would be wise to keep in mind the depth of the ongoing partisan divide on vaccination.

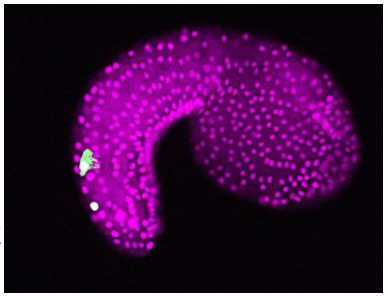
For example, while state and federal officials made a point of doing specialized outreach to boost COVID-19 vaccination rates in low-income communities and communities of color, specialized outreach may also be appropriate on the basis of partisan affiliation. Furthermore, such outreach needs to consider that a prominent hurdle to overcome among Republicans is a deficit in trust in medical professionals specifically—and science more generally.

https://bit.ly/3yR1bKd

The Evolution of a Head Has Been Traced Back Surprisingly Far Up Our Ancestral Line

What's in a head? According to new research, a little bit of our ancestors' tails.

Carly Cassella



In the early days of complex, multicellular life on Earth, animals started out without any spines or brains. They only had a network of neurons spread throughout their body. Over the course of millions of years, however, that system somehow became concentrated on one end. But how?

PIC Tunicate tadpole showing bipolar tail neurons (green). **(The University of Innsbruck)**

Tunicates, or 'sea squirts', are the closest living relatives of vertebrates, and they don't have a true head.

Their central nervous system is instead made up of clumps of neurons in the anterior and posterior parts of their body, with a dorsal strand connecting them both. As adults, these animals look like stagnant sponge-like blobs, with no clear head or tail. But as tadpole-like larvae, their cerebrum is easier to make out.

"Tunicates are like an evolutionary prototype for vertebrates," explains zoologist Ute Rothbächer from the University of Innsbruck in Austria. "Our common ancestor was probably very similar to a tunicate larva."

Not all evolutionary scientists agree with this: It's a contentious area of research. But Rothbächer and his colleagues have recently found evidence to support their ideas.

Their research has found Hmx genes, which encode for a pair of neurons in a tunicate tadpole's tail, are related to the genes that encode for clumps of neurons in a lamprey's head.

Lampreys are considered 'living fossils' because they have been around for so long with little change to their species. These marine animals are some of the first vertebrates, and they look sort-of like eels.

The evolutionary jump from tunicate life to lamprey life was a big one, but the Hmx gene seems to have made it across the divide. Its effect is just slightly different among vertebrates.

When splicing the Hmx genes of a lamprey into a tunicate species called *Ciona intestinalis*, researchers found the gene helped drive the expression of bipolar tail neurons.

In lampreys, however, the same genes helped drive the expression of sensory neurons in the cranium.

Despite impacting nerves in different parts of the body, the similar function of Hmx genes in lampreys and tunicates suggests they have a common evolutionary origin and might have played a role in the centralization of the nervous system.

"Hmx has been shown to be a central gene that has been conserved across evolution," says zoologist Alessandro Pennati, also from the University of Innsbruck.

"It has retained its original function and structure and was probably found in this form in the common ancestor of vertebrates and tunicates."

The findings suggest vertebrate brains might have once been recycled from the apparatus of their ancestors millions of years ago. And now, here we are. The study was published in *Nature*.

https://bit.ly/3PCLrAD

Monkeypox goes global: why scientists are on alert

Scientists are trying to understand why the virus, a less lethal relative of smallpox, has cropped up in so many populations around the world.

More than 120 confirmed or suspected cases of monkeypox, a rare viral disease seldom detected outside of Africa, have been reported in at least 11 non-African countries in the past week. The emergence of the virus in separate populations across the world where it doesn’t usually appear has alarmed scientists — and sent them racing for answers.

“It’s eye-opening to see this kind of spread,” says Anne Rimoin, an epidemiologist at the University of California Los Angeles, who has studied monkeypox in the Democratic Republic of the Congo for more than a decade.

Called monkeypox because researchers first detected it in laboratory monkeys in 1958, the virus is thought instead to transmit from wild animals such as rodents to people — or from infected people. In an average year, a few thousand cases occur in Africa, typically in the western and central parts of the continent. But cases outside Africa have been limited to a handful that are associated with travel to Africa or with the importation of infected animals.

The number of cases detected outside of Africa in the past week alone — which is all but certain to increase — has already surpassed the number detected outside the continent since 1970, when the virus was first identified as causing disease in humans. This rapid spread is what has scientists on high alert.

But monkeypox is no SARS-CoV-2, the coronavirus responsible for the COVID-19 pandemic, says Jay Hooper, a virologist at the US Army Medical Research Institute of Infectious Diseases in Fort Detrick, Maryland. It doesn't transmit from person to person as readily, and because it is related to the smallpox virus, there are already treatments and vaccines on hand for curbing its spread. So while scientists are concerned, because any new viral behaviour is worrying — they are not panicked.

Unlike SARS-CoV-2, which spreads through tiny air-borne droplets called aerosols, monkeypox is thought to spread from close contact with bodily fluids, such as saliva from coughing. That means a person with monkeypox is likely to infect far fewer close contacts than someone with SARS-CoV-2, Hooper says. Both viruses can cause flu-like symptoms, but monkeypox also triggers enlarged lymph nodes and, eventually, distinctive fluid-filled lesions on the face, hands and feet. Most people recover from monkeypox in a few weeks without treatment.

On 19 May, researchers in Portugal uploaded the first draft genome of the monkeypox virus that was detected there, but Gustavo Palacios, a virologist at the Icahn School of Medicine at Mount Sinai in New York City, emphasizes that it's still a very early draft, and more work needs to be done before drawing any definitive conclusions.

What researchers can tell from this preliminary genetic data is that the monkeypox virus is related to a viral strain predominantly found in western Africa. This strain causes milder disease and has a lower death rate — about 1% in poor, rural populations — compared with the one that circulates in central Africa. But exactly how much the strain causing the current outbreaks differs from the one in western Africa — and whether the viruses popping up in various countries are linked to one another — remains unknown.

Answers to those questions could help determine if the sudden uptick in cases stems from a mutation that allows this monkeypox virus to transmit more readily than those of the past, and if each of the outbreaks traces back to a single origin, says Raina MacIntyre, an infectious disease epidemiologist at the University of New South Wales in Sydney, Australia. Unlike SARS-CoV-2, a rapidly-evolving RNA virus whose variants have regularly eluded immunity from vaccines and prior infection, monkeypox virus is a relatively large DNA virus. DNA viruses are better at detecting and repairing mutations than RNA viruses, which means it's unlikely that the monkeypox virus has suddenly mutated to become adept at human transmission, MacIntyre says.

'Deeply concerning'

Still, for monkeypox to be detected in people with no apparent connection to one another suggests that the virus might have been spreading silently — a fact that Andrea McCollum, an epidemiologist who heads the US Centers for Disease Control and Prevention poxvirus team calls "deeply concerning".

Unlike SARS-CoV-2, which can spread asymptomatically, monkeypox does not usually go unnoticed when it infects a person, in part because of the skin lesions it causes. If monkeypox could spread asymptomatically, it would be especially troubling because it would make the virus harder to track, McCollum says.

Another puzzle is why almost all of the case clusters include men aged 20–50, many of whom are gay, bisexual and have sex with men (GBMSM). Although monkeypox isn't known to be sexually transmitted, sexual activity certainly constitutes close contact,

Rimoin says. The most likely explanation for this unexpected pattern of transmission, MacIntyre says, is that the virus was coincidentally introduced into a GBMSM community, and the virus has continued circulating there. Scientists will have a better idea of the origin of the outbreaks and the risk factors for infection once an epidemiological investigation is complete, which can take weeks and involves rigorous contact tracing.

Containment strategies

Scientists have been keeping an eye on monkeypox ever since an eradication campaign for smallpox, its cousin virus, wound down in the 1970s. Once smallpox was no longer a threat thanks to worldwide vaccinations, public-health officials stopped recommending smallpox inoculation — which also kept monkeypox at bay. With each year that has passed since smallpox's eradication, the population with weakened or no immunity to these viruses has grown, MacIntyre says.

There have been a few outbreaks since then. The Democratic Republic of the Congo, for example, has been grappling with monkeypox for decades, and Nigeria has been experiencing a large outbreak, with about 500 suspected and more than 200 confirmed cases, since 2017, when the country reported its first case in more than 39 years. The United States also reported an outbreak in 2003, when a shipment of rodents from Ghana spread the virus to pet prairie dogs in Illinois and infected more than 70 people.

Yet public-health authorities are not powerless against monkeypox. As a precaution against bioterrorism, countries such as the United States maintain a supply of smallpox vaccines, as well as an antiviral treatment thought to be highly effective against the virus. The therapies probably wouldn't be deployed on a large scale, though, McCollum says. Health-care workers would probably instead use a method called 'ring vaccination' to contain the spread of monkeypox: this would vaccinate the close contacts of people who have been infected with monkeypox to cut off any routes of transmission.

On the basis of the data that she has seen so far, McCollum thinks the current outbreaks probably won't necessitate containment strategies beyond ring vaccination. "Even in areas where monkeypox occurs every day," she says, "it's still a relatively rare infection." *doi: https://doi.org/10.1038/d41586-022-01421-8*

https://bit.ly/3LCPAkw

Environment scientists close in on 'golden spike' to define Anthropocene

Major step in search for a "golden spike" to formally define humanity's current geological period—and acknowledge human impact on our planet

Leicester researchers searching for a "golden spike" to formally define humanity's current geological period—and acknowledge human impact on our planet—have announced a major step in their analysis at an international conference on Wednesday.

University of Leicester Professors Jens Zinke, Mark Williams and Jan Zalasiewicz and Ph.D. researcher Stephen Himson presented multiple candidates for unique reference points to define the Anthropocene at Haus der Kulturen der Welt's "Unearthing the Present" conference in Berlin.

The Anthropocene—the suggestions that human impact has driven Earth into the conditions of a new geological period or "epoch"—has been one of the most influential concepts of the last decade in geological research, with Leicester researchers playing a leading role in its analysis.

Search for a "golden spike" is a key concept in Anthropocene study, which would provide a unique reference point—chosen somewhere in the world—to mark the beginning of the Anthropocene, that might ultimately allow it to be formally defined as part of the Geological Time Scale.

Researchers' attention is focused on the mid-20th century, a transformational "Great Acceleration" in our planet's history that included massive burning of fossil fuels and its climate effects, the worldwide spread of human-made radioactive elements such as plutonium and of plastic debris and other pollutants, as well as rapid and dramatic changes to Earth's ecosystems.

Currently, research teams are making detailed studies of a dozen potential sites around the globe, ranging from a core of Antarctic snow and ice, to a peat bog in Poland, to a stalagmite deep underground in the Italian Alps.

Among the candidate sites are two being studied by University of Leicester teams: a living coral on Australia's Flinders Reef, the annual growth layers of which are being analyzed by a team led by Professor Zinke of the School of Geography, Geology and the Environment; and the mud layers of San Francisco Bay, studied by a team led by Stephen Himson and Professor Williams within the same School, which contain a biological chronometer in the form of the remains of many recently invasive organisms in the Bay.

The full list of candidate sites includes:

- Beppu Bay (marine sediments), Kyushu Island, Japan
- Crawford Lake (lake muds), Ontario, Canada
- Ernesto Cave (cave deposits), Italy
- Flinders Reef (coral), Coral Sea, Australia
- Gotland Basin (marine sediments), Baltic Sea
- Palmer Ice Core (ice sheet), Antarctic Peninsula
- San Francisco Estuary (marine sediments), California, U.S.
- Searsville Reservoir (lake muds), California, U.S.
- Sihailongwan Lake (lake muds), Jilin province, China
- Śnieżka Bog (peat layers), Poland
- Vienna Museum Excavation (urban soil), Austria
- West Flower Garden Bank (coral), Gulf of Mexico

Results of these studies were unveiled for the first time at the meeting in Berlin, to begin the discussion of which of these sites might have the most precise and complete record of Earth's global changes, to allow it to represent the Anthropocene's chosen beginning.

Announcement of these results are a major new development in study of the Anthropocene, and the potential springboard to its acceptance as a universally acknowledged new phase in our planet's history.

Over the five days of the Berlin event the scientists will also interact with artists, scholars, activists and the public in open discussion forums, via a series of online essays on various kinds of human impact, and by the opening of an exhibition, Earth Indices. This will provide unique insights into the processes of developing a geological archive of humans' home planet.

Professor Zinke, whose research examines the role of massive corals and sedimentary archives from tropical oceans as recorders of environmental change, says that "coral provide the highest resolution archive of anthropogenic impacts on the tropical oceans and they do that over several centuries of continuous upward growth."

"Massive corals at Flinders Reef provided a continuous record of environmental change for more than 300 years, starting in 1710, giving us information how anthropogenic activity has modified the environment in remote coral reefs."

"The Flinders Reef corals recorded a clear spike in radiocarbon between 1959 and 1963 short after the nuclear bomb testing began in the 1950s. This is a unique signature of the Anthropocene."

"The burning of fossil fuels has left a clear signature in the coral skeleton in their isotopic composition of Carbon which started to decline around 1850. The coral show us that light carbon from fossil fuel burning has been taken up by the surface oceans."

Professor Williams, whose work focuses on human-induced

changes to life and how human-built environments affect the delicate balance of natural ecosystems on our planet, says that "the ecosystem of the San Francisco Estuary has been wholly changed by organisms introduced from as far afield as Japan."

"Sometimes the new arrivals completely dominate their adopted ecologies, their shells accumulating in the recent fossil record and leaving a clear geological signature of human impacts on the planet." "Although San Francisco Estuary is very well studied, the same patterns, from introduced species, are becoming widespread on our planet."

The Leicester research team have also contributed to a feature on their findings, "Biological and Palaeontological signatures of the Anthropocene," published by *Anthropocene Curriculum*.

More information: *Publication: www.anthropocene-curriculum.or ... -of-the-anthropocene*

https://bit.ly/3lB0s8d

Researchers Just Found That Kidneys Act on Blood Differently Than We Thought Before

Kidney cells are pumps, not filters, and they are generating forces

Mike Mcrae

By this time tomorrow, every drop of blood in your body will have passed through your kidneys dozens of times. With each pass, water saturated with waste is removed to form urine, and freshly cleaned blood then returns back into circulation.

We might imagine this vital task as a kind of force-fed filtration driven by the thumping pressures of our heartbeat. But, according to a new study co-authored by Johns Hopkins mechanical engineer Sean Sun, that description isn't quite as accurate as once thought.

"Everyone hears that kidneys filter blood, but conceptually that is incorrect," says Sun.

"What we showed is that kidney cells are pumps, not filters, and they are generating forces."

It's not for lack of looking that we happened to miss this peculiar mechanical activity, either. Anatomists have known about the kidney's structure and its role in producing urine from blood since the 17th century.

The organ's ability to mix passive physics of osmosis with active shunting of various chemicals in order to balance our body's salts, wastes, and water has also been extensively studied inside and outside of the body.

Yet each kidney consists of kilometers of channels and tubules crammed into a space no bigger than your fist, potentially making for some weird plumbing deep inside.

Studies have shown that the cells lining those tubules can sense changes in hydrostatic pressure, and even respond; however, it's not clear how or even whether those changes push back in some way.

Working out how fluids swish through those itty-bitty pipes isn't easy, either. Any experiment to study the hydraulics at work inside individual tubules would need some pretty impressive technology to screen out stray forces.

Which is precisely what Sun and colleagues from across the US came up with. Their micro-fluidic kidney pump (MFKP) consists of patterned blocks and porous membranes capable of containing a culture of cells that line kidney tubules.

Once the cells had settled into place and were subjected to a range of tests for electrical resistance and permeability, the researchers measured variations in pressure across the tissue in response to squirts of fluid from a syringe.

They noticed the movement of fluids near the cells dropped in accordance with a rise in hydraulic pressure, which was greater towards one end of the tissue than the other. Just as we'd expect if the tubules acted like a pump.

A close look at the proteins the cells were churning out revealed that small changes in the pressure of fluids entering the tissues

changed the arrangements of ion channels and its supporting structure, altering its shape and function.

For most of us, this means fluids passing from the blood into the kidney's network of tubules moves in part under the mechanical direction of the cells themselves, adding a subtle new layer of operation that could help to explain a range of renal disorders.

To see how this behavior unfolds inside less-functional kidneys, the researchers used cells taken from individuals with the renal disorder autosomal dominant polycystic kidney disease, or ADPKD.

In this condition, thanks to the way the cells lining the kidney tubules change shape, cysts commonly form, distorting the tissue and raising the risk of kidney stones and urinary tract infections. But, according to the team's work, there's more to the story. The researchers observed the cells pumping in reverse, with the pressure gradient flipped from one end to the other.

When the FDA-approved ADPKD treatment tolvaptan was applied to the cells, their pressure gradients smoothed out, suggesting the drug works by reducing stress on the tissues and thereby slowing the rate at which cysts might form.

With this in mind, it's possible other tissues might also have their own versions of a mechanical pumping system adjusting fluid pressures at their convenience. Sun and his team aim to modify their device to test other tissues and organs.

This research was published in *Nature Communications*.

https://bit.ly/3wCDHqS

New study estimates how long mined metals circulate before being lost

In some cases, we're throwing out one metal in the process of extracting another.

John Timmer

Almost every aspect of modern society relies on materials of limited quantity on Earth. In order to live within the limits set by our planet, we have to figure out how to make the most of what we extract and reuse whatever we have extracted. A new study released this week looks into how close we are to reaching that ideal for 61 different metals.

Along the way, its authors figure out how long different metals stay in circulation before they're lost and identify the stage at which those losses take place. While a lack of recycling is a major roadblock on the way to a circular economy, it's far from the only one. For many metals, including some critically important ones, we discard huge amounts that are present in the ores that we mine for different elements.

Mind your metals

Tracking that many metals through their entire life cycle is a huge task, but the authors were able to build on previous work by Japanese researchers who developed a software model called MaTrace. The model is designed to track the flow of materials from production to loss, estimating losses at each stage of the material's life cycle based on empirical data.

Losses are tracked at a number of points in a material's life cycle. For metals, these include the production of a raw material from ores, the metal's use in the fabrication of products, and its loss during the product's use. Finally, at the end-of-life stage of any product, the metal is either recycled or discarded as waste. MaTrace can also track the flow of the material through the recycling process (with its inevitable losses) and back into additional products.

To put this in concrete terms, we can turn to something simple like iron, which is mined from ores that are then processed. Both steps involve some loss of iron and any other metals that happen to be in the same ore. The iron is eventually incorporated into products, a process that can again involve losses as extraneous material is cut away—some of the excess here is also sent into the recycling

process. There's also loss during use, which can be as simple as a fraction of the iron rusting away into the environment. Ultimately, a fraction of the iron-based products will be recycled, with the remainder being discarded into the environment.

Some of the numbers needed to track the fate of metals, like the efficiency of converting ore to metal, are easy to come by. Others, like the percentage of indium that ends up in electronics, are necessarily rougher estimates, and the researchers caution against treating any number here as a definitive estimate.

For their analysis, the researchers start with a kilogram of material and send it through MaTrace for either 1,000 years or until all of the metal is lost—whichever comes first. The authors performed individual analyses for each of the 61 metals and aggregated them into a number of groups: ferrous metals (iron and its relatives), non-ferrous metals, specialty metals, and precious metals. This allowed the researchers to pick up general trends for materials that are often used in specialized industries.

Even when grouped into these four large categories, there's no single story to our use of metals. Driven largely by the ease of recycling iron, ferrous metals have an average lifetime of about 150 years from extraction to when they're lost to the environment. On the low side, specialty metals only take about 12 years to exit the use/recycling cycle.

Losses at different stages of a metal's life cycle also varied widely. We're very good at extracting most metals from ores so that most of the losses are incidental—that is, some of the metal happens to be present in an ore we use for other materials. For example, iron ore may contain something like manganese at low concentrations, but the amount of ore we process means that a lot of manganese will end up being thrown away. Overall, these losses tended to be in the area of 15 percent, with the exception of specialty metals, which averaged about 25 percent.

Both those averages obscure some fairly horrifying losses. About half of the cobalt, which is highly desired for many types of batteries, ends up being lost during production. Indium, used in many semiconductor products, sees losses hit 70 percent. And many metals have production losses of 95 percent or higher: arsenic, gallium, germanium, hafnium, scandium, selenium, and tellurium.

Losses in manufacturing are much less scary; they're generally a rounding error compared to the losses in extraction. Manufacturing produces the smallest losses for over half the metals analyzed, and there's none for which it's the highest. Even the worst rate of loss (among non-ferrous metals) only reaches 6 percent. It's clear that manufacturing has been very good at avoiding waste.

Once in use, most metals suffer minimal losses, with averages of about 5 percent or less for everything but specialty metals. But those specialty metals see losses that average over 30 percent during use. Some of them, notably strontium and barium, primarily end up in single-use products that are permanently lost to the environment (they're part of the mud injected into wells during gas and oil drilling). Those two, along with mercury, are the only three for which use is the largest source of loss.

For 43 of the metals, the largest source of loss came at a product's end-of-life period. Losses here were in the area of 70–85 percent for everything but specialty metals (remember, those are mostly lost during use, so they never reach their end of life). Even metals like aluminum, copper, and iron, which are frequently recycled, saw large losses to disposal over time, simply because even the most efficient recycling rarely reached 90 percent efficiency. Expensive platinum relatives are mostly used for catalytic converters, and those aren't systematically recycled. The same goes for the use of europium and terbium in lighting applications.

In the loop

Based on this tracking, the researchers were able to estimate how

long an average bit of metal will remain in circulation before it's lost. The range was pretty high, from less than a year for gallium and selenium to nearly 200 years for gold. Iron has the second-longest average life at just over 150 years. Since iron accounts for 97 percent of the ferrous metals, it dragged the category's average lifespan up considerably. If you exclude iron, only about 4 percent of the rest of the ferrous metals would still be in circulation in a century.

These numbers were also distorted by a few long-lived products. Boron, for example, is largely used for glass-based building insulation, which has an average lifetime of about 50 years. So even though it's rarely recycled, it outlasts metals that are used in relatively short-lived catalytic converters and see significant levels of recycling.

Again, it's important to emphasize that these are all estimates; the degree of accuracy will vary from metal to metal. And the data represents a snapshot of things as they stand in recent years, so it will likely become outdated quickly for at least some materials. For example, we're likely to see a surge of lithium batteries reaching end-of-life in the coming decades, and there are a number of companies gearing up to recycle them.

Despite these limitations, however, this could be a very valuable study if we choose to act on this information. For example, the paper identifies some low-hanging fruit, like catalytic converters, where instituting a more organized recycling program could lead to marked improvements in the lifespan of a number of very expensive metals. Longer-term, it also has the potential to help with improving our ability to approach a circular economy for a variety of materials by identifying the largest or easiest-to-correct points of loss.

Nature Sustainability, 2022. DOI: 10.1038/s41893-022-00895-8 (About DOIs).

https://bit.ly/3Py95hv

Do bees really die if they sting you?

Do all of the roughly 20,000 species of bee even have stingers?

By Joe Phelan

It's an oft-spouted legend: If a bee stings you, it will die as a result. But is this tale, introduced to most of us in childhood and something many of us have recounted at one time or another, really true?

In a word, no. While some bees undoubtedly do die, others don't. Not all bee species are even capable of stinging.

"There are an estimated 20,000 species of bees across the globe, and not all of them sting," Allyson Ray, a doctoral student of molecular cellular and integrative biosciences at Penn State, told Live Science in an email.

"There is a group of bees called the 'stingless bees' (tribe Meliponini) as well as the 'mining bees' (family Andrenidae), which do have stingers, but are so reduced as to be mostly ineffective."

There are more than 500 species of stingless bees, found mainly in the tropics. Rather than stinging, they bite, "and frequently have elaborate nest entrances to deter invaders," said Nicholas Naeger, a molecular biologist at Washington State University, who has been studying bees for over two decades.

But what about those bees that *do* sting? What enables some to survive after they unleash their defensive weapon, and what causes others to perish?

"Honeybees will most often die as a consequence of stinging [humans or other mammals]," Ray said. "This is due to the anatomy of their stinger. It is barbed, which catches within the skin, allowing the stinger to remain in place and continue to pump venom into the unfortunate sting recipient."

Honeybees — of which there are around 10 species, according to Naeger — do not tend to die when stinging other insects or spiders,

which tends to happen only if the bee thinks its hive is being invaded.

This is because the stinger is generally able to pierce an insect's relatively thin exoskeleton and can be extracted without incurring damage. (This isn't the case with Asian giant hornets (*Vespa mandarinia*), colloquially known as murder hornets, whose thick outer skin shields them from Japanese honeybees' (*Apis cerana japonica*) stings; instead, these honeybees swarm an invading Asian giant hornet, using the heat generated from fluttering their wings to "slow cook" their rival.)

Human skin, however, is much thicker than most insects' exoskeletons, meaning "the stingers become lodged," Ray said.

"When the bee flies away after stinging a person, the stinger remains, and the organs of the gut are pulled and detached, effectively disemboweling the individual," Ray explained. The bee, now with a hole in its abdomen "might live for several hours after stinging, but eventually it will succumb to fluid loss and internal organ failure," Naeger added.

Naeger once carried out research to confirm that honeybees — which are the most common bee species worldwide, according to MyBeeLine, a network for beekeepers and bee enthusiasts — are incapable of surviving after stinging a human-like target.

"I marked and returned over 200 bees that had stung [the target], and I never witnessed a single case of a bee being alive the following morning," he said. "The act truly is deadly."

Other bees, however, are able to survive after stinging a human, as they have different stingers to honeybees. Bumblebees have a "smooth stinger, and are therefore able to sting multiple times without dying," Ray said.

Other flying stinging insects, such as hornets and wasps, have a similarly smooth stinger, which enables them to attack a target multiple times without dying.

Why do bees sting?

With that in mind, what encourages honeybees to go on the offensive? Are they naturally aggressive creatures, or are they somewhat misunderstood?

"Honeybees, like most bees, are timid when they are away from their hive and have nothing to protect," Naeger said. "The only two significant ways to get a bee to sting you is to provoke the sting by grabbing or squishing [the bee] so it does not have the option to flee, or by going too near its home nest."

Rather, the bee's reputation as a combative insect has potentially been sullied by another winged stinger.

"A significant number of insect stings that are blamed on bees are actually committed by wasps, which tend to be bolder and more aggressive than bees," Naeger noted.

It is also worth noting that not all members of the "stinging" bee species actually have the ability to sting. "Any stinging bee is going to be female, as the stinger is actually a modified ovipositor," or a tubular organ via which a female insect deposits its eggs, Ray added.

Female bees tend to massively outnumber their male counterparts. According to a 2019 study published in the journal PLOS One, the average bee population has a female-to-male ratio of around 5 to 1.

And female bees are very happy to fight as a team when necessary.

If any perceived threat is considered too large for a solitary female bee to manage on her own, she is able to "call on her sisters for help," said Dr. Marley Iredale, a veterinarian at the University of Florida.

"She does this by releasing an alarm pheromone that her sisters recognize as a cue to defend the colony," Iredale told Live Science in an email. "This pheromone in honeybees actually includes the molecule that makes bananas smell ripe (isoamyl acetate), so an upset honeybee colony can smell strongly of bananas."

To bee, or not to bee

Given the dire fate that awaits a honeybee once it stings a human or other thick-skinned mammal, is there any chance the bee is aware of what the outcome will be? Are they cognisant of the fact that once their stinger pierces the skin, they are essentially signing their own death certificate?

"I do not think that honeybees understand that they are going to die when they sting, but under the right circumstances, they are very willing to give up their lives for defense of the colony," Naeger said. "When it comes to protecting the colony or making sure that genes are passed to the next generation, the instincts that drive those behaviors clearly outweigh any concern that the bees might have for their individual selves."

This is something both Iredale and Ray support.

"Whether they are 'aware' of the influences driving their decision-making and the personal consequences of their stinging behavior is not obvious," Ray said.

Iredale agreed that bees are unlikely to be aware of the consequences of stinging a human. "I think knowledge of one's mortality might be a burden that only highly derived organisms, such as primates, experience," Iredale said. "But, if the bees are aware, I genuinely think they would sacrifice themselves willingly for the good of the colony."