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Ivermectin COVID-19 Scandal Shows How Vulnerable Science Is to Fraud

Most scientists assume they will never come across a single case of fraud in their careers

James Heathers & Gideon Meyerowitz-Katz

Haruko Obokata published two papers in January 2014 that described how regular blood cells could be turned into pluripotent stem cells.

At the time, this was a coup – it dramatically simplified a previously complicated process and opened up new vistas of medical and biological research, while neatly sidestepping the bioethical considerations of using human embryos to harvest stem cells.

Moreover, the process for this was straightforward, and involved applying a weak acid solution or mechanical pressure – oddly similar to how you'd clean a rust stain off a knife.

Within a few days, scientists noticed some of the images in the paper were irregular. And a broader skepticism began. Could it really be that simple?

As the experiments were simple and the biologists were curious, attempts to replicate the papers' findings began immediately. They failed. By February, Obokata's institute had launched an investigation. By March, some of the paper's co-authors were disavowing the methods. By July, the papers were retracted.

While the papers were clearly unreliable, there was no clarity on the center of the problem. Had the authors mislabelled a sample? Did they discover a method that worked once but was inherently unreliable?

Had they simply made up the data? It took years longer, but the scientific community got an approximate answer when further related papers by Obokata were also retracted for image manipulation, data irregularities, and other problematic issues.

The whole episode was a sterling example of science correcting itself. An important result was published, it was doubted, it was tested, investigated, and found wanting… and then it was retracted.

This is how we might hope the process of organized skepticism would always work. But, it doesn't.

In the vast majority of scientific work, it is incredibly rare for other scientists to even notice irregularities in the first place, let alone marshal the global forces of empiricism to do something about them. The underlying assumption within academic peer review is that fraud is sufficiently rare or unimportant as to be unworthy of a dedicated detection mechanism.

Most scientists assume they will never come across a single case of fraud in their careers, and so even the thought of checking calculations in reviewable papers, re-running analyses, or checking if experimental protocols were properly deployed is deemed unnecessary.

Worse, the accompanying raw data and analytical code often needed to forensically analyze a paper are not routinely published, and performing this kind of stringent review is often considered to be a hostile act, the kind of drudge work reserved only for the deeply motivated or the congenitally disrespectful.

Everyone is busy with their own work, so what kind of grinch would go to such extremes to invalidate someone else's?

Which brings us neatly to ivermectin, an anti-parasitic drug trialed as a treatment for COVID-19 after lab-bench studies early in 2020 showed it was potentially beneficial.

It rose in popularity sharply after a published-then-withdrawn analysis by the Surgisphere group showed a huge reduction in death rates for people who take it, triggering a massive wave of use for the drug across the globe.

More recently, the evidence for ivermectin's efficacy relied very

substantially on a single piece of research, which was preprinted (that is, published without peer review) in November 2020.

This study, drawn from a large cohort of patients and reporting a strong treatment effect, was popular: read over 100,000 times, cited by dozens of academic papers, and included in at least two meta-analytic models that showed ivermectin to be, as the authors claimed, a "wonder drug" for COVID-19. It is no exaggeration to say that this one paper caused thousands if not millions of people to get ivermectin to treat and/or prevent COVID-19.

A few days ago, the study was retracted amid accusations of fraud and plagiarism. A masters student who had been assigned to read the paper as part of his degree noticed that the entire introduction appeared to be copied from earlier scientific papers, and further analysis revealed that the study's datasheet posted online by the authors contained obvious irregularities.

It is hard to overstate how monumental a failing this is for the scientific community. We proud guardians of knowledge accepted at face value a piece of research that was so filled with holes that it only took a medical student a few hours to entirely dismantle.

The seriousness accorded to the results was in direct contrast to the quality of the study. The authors reported incorrect statistical tests at multiple points, standard deviations that were extremely implausible, and a truly eye-watering degree of positive efficacy – the last time the medical community found a '90 percent benefit' for a drug on a disease, it was the use of antiretroviral medication to treat people dying of AIDS.

Yet, no-one noticed. For the better part of a year, serious, respected researchers included this study in their reviews, medical doctors used it as evidence to treat their patients, and governments acknowledged its conclusions in public health policy.

No-one spent the 5 minutes required to download the data file that the authors had uploaded online and notice that it reported numerous deaths happening before the study had even begun. No one copy-and-pasted phrases from the introduction into Google, which is all it takes to notice just how much of it is identical to already-published papers.

This inattention and inaction perpetuated the saga – when we remain studiously disinterested in the problem, we also don't know how much scientific fraud there is, or where it can be readily located or identified, and consequently make no robust plans to address or ameliorate its effects.

A recent editorial in the *British Medical Journal* argued that it might be time to change our basic perspective on health research, and assume that health research is fraudulent until proven otherwise. That is to say, not to assume that all researchers are dishonest, but to begin the receipt of new information in health research from a categorically different baseline level of skepticism as opposed to blind trust.

This might sound extreme, but if the alternative is accepting that occasionally millions of people will receive medications based on unvetted research that is later withdrawn entirely, it may actually be a very small price to pay.

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Novel coronavirus discovered in British bats

It is the first time that a sarbecovirus (SARS-related coronavirus) has been found in a lesser horseshoe bat and the first to be discovered in the UK.

A coronavirus related to the virus that causes COVID-19 in humans has been found in UK horseshoe bats—according to new collaborative research from the University of East Anglia, ZSL (Zoological Society of London), and Public Health England (PHE).

However, there is no evidence that this novel virus has been transmitted to humans, or that it could in future, unless it mutates.

UEA researchers collected fecal samples from more than 50 lesser horseshoe bats in Somerset, Gloucestershire and Wales and sent them for viral analysis at Public Health England.

Genome sequencing found a novel coronavirus in one of the bat samples, which the team have named "RhGB01."

It is the first time that a sarbecovirus (SARS-related coronavirus) has been found in a lesser horseshoe bat and the first to be discovered in the UK.

The research team say that these bats will almost certainly have harbored the virus for a very long time. And it has been found now, because this is the first time that they have been tested.

Importantly, this novel virus is unlikely to pose a direct risk to humans, unless it mutates.

A mutation could happen if a human infected with COVID-19 passes it to an infected bat, so anyone coming into contact with bats or their droppings, for example those engaged in caving or bat protection, should wear appropriate PPE.

Prof Diana Bell, an expert in emerging zoonotic diseases from UEA's School of Biological Sciences, said: "Horseshoe bats are found across Europe, Africa, Asia and Australia and the bats we tested lie at the western extreme of their range.

"Similar viruses have been found in other horseshoe bat species in China, South East Asia and Eastern Europe.

"Our research extends both the geographic and species ranges of these types of viruses and suggests their more widespread presence across more than 90 species of horseshoe bats.

"These bats will almost certainly have harbored this virus for a very long time—probably many thousands of years. We didn't know about it before because this is the first time that such tests have been carried out in UK bats.

"We already know that there are different coronaviruses in many other mammal species too," she said. "This is a case of 'seek and you will find."

"Research into the origins of SARS-CoV-2, the virus that causes COVID-19 in humans, has focussed on horseshoe bats—but there are some 1,400 other bat species and they comprise 20 percent of known mammals.

"Our findings highlight the need for robust genotype testing for these types of viruses in bat populations around the world. And it raises an important question about what other animals carry these types of viruses."

Prof Andrew Cunningham, from the Zoological Society of London, said: "Our findings highlight that the natural distribution of sarbecoviruses and opportunities for recombination through intermediate host co-infection have been underestimated.

"This UK virus is not a threat to humans because the receptor binding domain (RBD) - the part of the virus that attaches to host cells to infect them—is not compatible with being able to infect human cells.

"But the problem is that any bat harboring a SARS-like coronavirus can act as a melting pot for virus mutation. So if a bat with the RhGB01 infection we found were to become infected with SARS-CoV-2, there is a risk that these viruses would hybridize and a new virus emerge with the RBD of SARS-CoV-2, and so be able to infect people.

"Preventing transmission of SARS-CoV-2 from humans to bats, and hence reducing opportunities for virus mutation, is critical with the current global mass vaccination campaign against this virus."

Prof Bell added: "The main risks would be for example a bat rehabilitator looking after a rescued animal and infecting it with SARS-CoV2—which would provide an opportunity for genetic recombination if it is already carrying another sarbecovirus.

"Anyone coming into contact with bats or their droppings, such as bat rescuers or cavers, should wear appropriate PPE—in order to reduce the risk of a mutation occurring.

"We need to apply stringent regulations globally for anyone handling bats and other wild animals," she added.

The new virus falls within the subgroup of coronaviruses called sarbecoviruses which contains both SARS-CoV-2 (responsible for the current pandemic) and SARS-CoV (responsible for the initial 2003 SARS outbreak in humans).

Further analysis compared the virus with those found in other horseshoe bat species in China, South East Asia and Europe and showed that its closest relative was discovered in a Blasius's bat from Bulgaria in 2008.

The UK discovery was made by undergraduate ecology student Ivana Murphy, from UEA's School of Biological Sciences, who collected bat droppings as part of her final year research dissertation. Jack Crook conducted the genetic analyses in partnership with other researchers at PHE.

A total of 53 bats were captured, and their feces collected in sterile bags. The research was conducted under strict Health and Safety protocols. Full PPE was worn and Ivana was regularly tested for COVID-19 to avoid any chance of cross contamination. The bats were released immediately after their droppings had been collected.

Ivana said: "More than anything, I'm worried that people may suddenly start fearing and persecuting bats, which is the last thing I would want and would be unnecessary. As like all wildlife, if left alone they do not pose any threat."

"Metagenomic identification of a new sarbecovirus from horseshoe bats in Europe" is published in the journal *Scientific Reports* on July 19, 2021.

More information: *Jack M. Crook et al, Metagenomic identification of a new sarbecovirus from horseshoe bats in Europe, Scientific Reports (2021). DOI: 10.1038/s41598-021-94011-z*

https://bit.ly/3iG7G91

When did humans start experimenting with alcohol and drugs?

Humans don't just reshape our external world – we engineer our internal worlds, and reshape our minds

Nicholas R. Longrich *

Humans constantly alter the world. We fire fields, turn forests into farms, and breed plants and animals. But humans don't just reshape our external world – we engineer our internal worlds, and reshape our minds.

One way we do this is by upgrading our mental "software", so to speak, with myths, religion, philosophy and psychology. The other is to change our mental hardware – our brains. And we do that with chemistry.

Today, humans use thousands of psychoactive compounds to alter our experience of the world. Many derive from plants and fungi, others we manufacture. Some, like coffee and tea, increase alertness; others, like alcohol and opiates, decrease it. Psychiatric drugs affect mood, while psychedelics alter reality.

We alter brain chemistry for all kinds of reasons, using substances recreationally, socially, medicinally, and ritually. Wild animals sometimes eat fermented fruit, but there's little evidence that they eat psychoactive plants. We're unusual animals in our enthusiasm for getting drunk and high. But when, where and why did it all start?

High on life in the Pleistocene

Given humanity's love of drugs and alcohol, you might assume getting high is an ancient, even prehistoric tradition. Some researchers have suggested prehistoric cave paintings were made by humans experiencing altered states of consciousness. Others, perhaps inspired more by hallucinogens than hard evidence, suggest that drugs triggered the evolution of human consciousness. Yet

there's surprisingly little archaeological evidence for prehistoric drug use.

African hunter-gathers – Bushmen, Pygmies and the Hadzabe people – likely live their lives in ways similar to ancestral human cultures. The most compelling evidence for the use of drugs by such early humans is a potentially hallucinogenic plant *!kaishe*, used by Bushmen healers, which supposedly makes people "go mad for a while". Yet how much Bushmen historically used drugs is debated, and otherwise, there's little evidence for drug use in hunter-gatherers.

The implication is that, despite Africa's diverse plants and fungi, early humans used drugs rarely, maybe to induce trances during rituals, if at all. Perhaps their lifestyle meant they rarely felt the need for escape. Exercise, sunlight, nature, time with friends and family – they're powerful antidepressants. Drugs are also dangerous; just as you shouldn't drive drunk, it's risky to get high when lions lurk in the bush, or a hostile tribe waits one valley over.

Out of Africa

Migrating out of Africa 100,000 years ago, humans explored new lands and encountered new substances. People discovered opium poppies in the Mediterranean, and cannabis and tea in Asia.

Archaeologists have found evidence of opium use in Europe by 5,700 BC. Cannabis seeds appear in archaeological digs at 8,100 BC in Asia, and the ancient Greek historian Herodotus reported Scythians getting high on weed in 450 BC. Tea was brewed in China by 100 BC.

It's possible our ancestors experimented with substances before the archaeological evidence suggests. Stones and pottery preserve well, but plants and chemicals decay quickly. For all we know, Neanderthals could have been the first to smoke pot. But archaeology suggests the discovery and intensive use of psychoactive substances mostly happened late, after the Neolithic Revolution in 10,000 BC, when we invented farming and civilisation.

The American psychonauts

When hunters trekked across the Bering Land Bridge 30,000 years ago into Alaska and headed south, they found a chemical cornucopia. Here, the hunters discovered tobacco, coca and maté. But for some reason, indigenous Americans were especially fascinated with psychedelics.

Many drugs were discovered beyond Africa. **Nicholas Longrich /Wikimedia/Google Earth, Author provided**

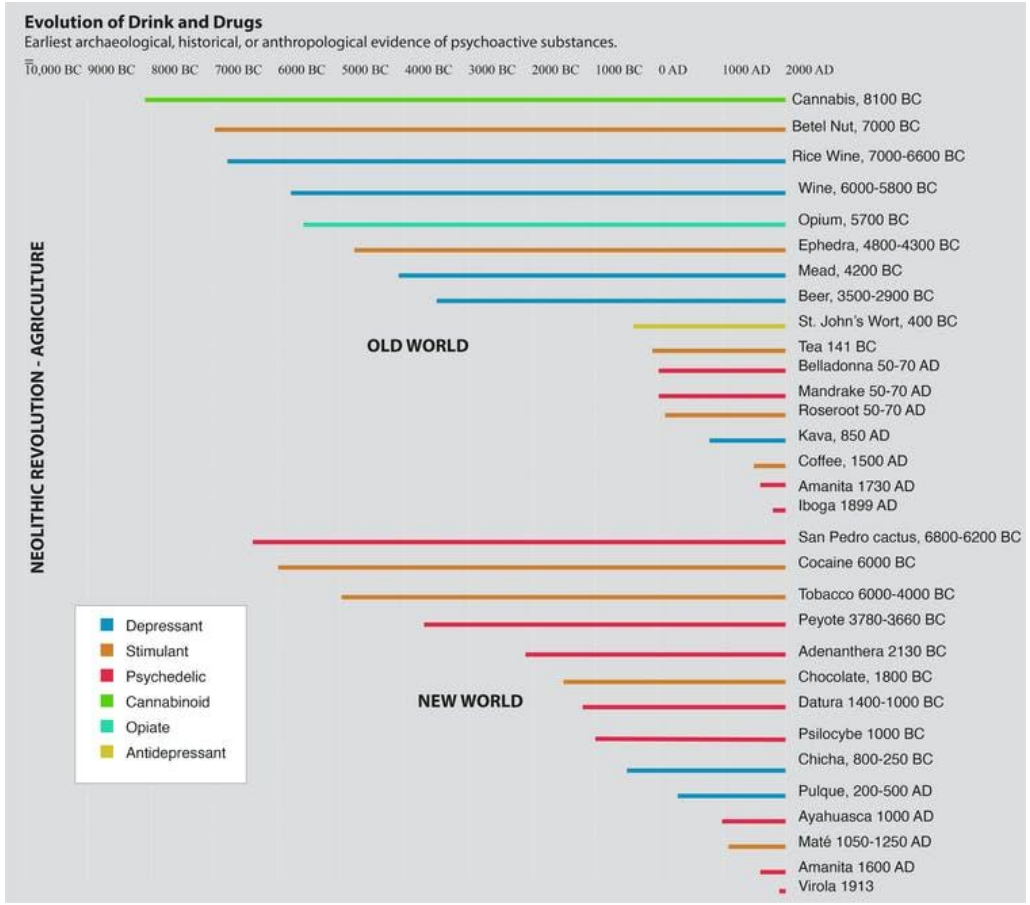
American psychedelics included peyote cactus, San Pedro cactus, morning-glory, *Datura*, *Salvia*, *Anadenanthera*, Ayahuasca, and over 20 species of psychoactive mushrooms. It was a pre-Columbian Burning Man. Indigenous Americans also invented the nasal administration of tobacco and hallucinogens. They were the first to snort drugs – a practice Europeans later borrowed.

This American psychedelic culture is ancient. Peyote buttons have been carbon-dated to 4,000 BC, while Mexican mushroom statues hint at *Psilocybe* use in 500 BC. A 1,000 year-old stash found in Bolivia contained cocaine, *Anadenanthera* and ayahuasca – and

must've been one hell of a trip.

Inventing alcohol

A huge step in the evolution of debauchery was the invention of agriculture, because farming made booze possible. It created a surplus of sugars and starches which, mashed and left to ferment, magically transformed into potent brews.



Evidence suggests human drug use came after the Neolithic Revolution.
Nicholas Longrich, Author provided

Humans invented alcohol many times independently. The oldest booze dates to 7,000 BC, in China. Wine was fermented in the Caucasus in 6,000 BC; Sumerians brewed beer in 3,000 BC. In the Americas, Aztecs made *pulque* from the same agaves used today for tequila; Incas brewed *chicha*, a corn beer.

While in America psychedelics appear to have been particularly important, Eurasian and African civilisations seem to have preferred alcohol. Wine was central to ancient Greek and Roman cultures, was served at Plato's Symposium and at the Last Supper, and remains incorporated in the Jewish Seder and Christian communion rituals.

Civilisation and intoxication

Archaeology suggests alcohol and drugs date back millennia, to early agricultural societies. But there's little evidence early hunter-gatherers used them. That implies something about agricultural societies and the civilisations they gave rise to promoted substance use. But why?

It's possible large civilisations simply drive innovation of all kinds: in ceramics, textiles, metals – and psychoactive substances. Perhaps alcohol and drugs also promoted civilisation – drinking can help people socialise, altered perspectives encourage creativity, and caffeine makes us productive. And it may just be safer to get drunk or high in a city than the savannah.

A darker possibility is that psychoactive substance use developed in response to civilisation's ills. Large societies create large problems – wars, plagues, inequalities in wealth and power – against which individuals are relatively powerless. Perhaps when people couldn't change their circumstances, they decided to change their minds.

It's a complex problem. Just thinking about it makes me want to grab a beer.

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Solar cells: Layer of three crystals produces a thousand times more power

The photovoltaic effect of ferroelectric crystals can be increased by a factor of 1,000 if three different materials are arranged periodically in a lattice.

This has been revealed in a study by researchers at Martin Luther University Halle-Wittenberg (MLU). They achieved this by creating crystalline layers of barium titanate, strontium titanate and calcium titanate which they alternately placed on top of one another. Their findings, which could significantly increase the efficiency of solar cells, were published in the journal "Science Advances".

Most solar cells are currently silicon based; however, their efficiency is limited. This has prompted researchers to examine new materials, such as ferroelectrics like barium titanate, a mixed oxide made of barium and titanium. "Ferroelectric means that the material has spatially separated positive and negative charges," explains physicist Dr Akash Bhatnagar from MLU's Centre for Innovation Competence SiLi-nano. "The charge separation leads to an asymmetric structure that enables electricity to be generated from light." Unlike silicon, ferroelectric crystals do not require a so-called pn junction to create the photovoltaic effect, in other words, no positively and negatively doped layers. This makes it much easier to produce the solar panels.

However, pure barium titanate does not absorb much sunlight and consequently generates a comparatively low photocurrent. The latest research has shown that combining extremely thin layers of different materials significantly increases the solar energy yield. "The important thing here is that a ferroelectric material is alternated with a paraelectric material. Although the latter does not have separated charges, it can become ferroelectric under certain conditions, for example at low temperatures or when its chemical structure is slightly modified," explains Bhatnagar.

Bhatnagar's research group discovered that the photovoltaic effect is greatly enhanced if the ferroelectric layer alternates not only with one, but with two different paraelectric layers. Yeseul Yun, a PhD student at MLU and first author of the study, explains: "We embedded the barium titanate between strontium titanate and calcium titanate. This was achieved by vaporising the crystals with a high-power laser and redepositing them on carrier substrates. This produced a material made of 500 layers that is about 200 nanometres thick."

When conducting the photoelectric measurements, the new material was irradiated with laser light. The result surprised even the research group: compared to pure barium titanate of a similar thickness, the current flow was up to 1,000 times stronger - and this despite the fact that the proportion of barium titanate as the main photoelectric component was reduced by almost two thirds. "The interaction between the lattice layers appears to lead to a much higher permittivity - in other words, the electrons are able to flow much more easily due to the excitation by the light photons," explains Akash Bhatnagar. The measurements also showed that this effect is very robust: it remained nearly constant over a six-month period.

Further research must now be done to find out exactly what causes the outstanding photoelectric effect. Bhatnagar is confident that the potential demonstrated by the new concept can be used for practical applications in solar panels. "The layer structure shows a higher yield in all temperature ranges than pure ferroelectrics. The crystals are also significantly more durable and do not require special packaging."

The study was supported by the Federal Ministry of Education and Research (BMBF), the Deutsche Forschungsgemeinschaft (German Research Foundation, DFG) and with funding from the European Regional Development Fund (ERDF).

Study: *Yun, Y., Mühlenbein, L., Knoche, D.S., Lotnyk, A., Bhatnagar, A. Strongly*

enhanced and tunable photovoltaic effect in ferroelectric-paraelectric superlattices. Science Advances (2021). DOI: 10.1126/sciadv.abe4206

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Coffee Not Linked to Increased Arrhythmia Risk in New Study

Habitual coffee drinking was not associated with a heightened risk of cardiac arrhythmias in a study of more than 300,000 people.

Jake Remaly

In fact, an adjusted analysis found that "each additional cup of coffee intake was associated with a 3% lower risk of incident arrhythmia," Eun-jeong Kim, MD, of the division of cardiology at the University of California, San Francisco, and colleagues reported in JAMA Internal Medicine. In addition, genetic differences that affect caffeine metabolism did not significantly influence the odds of arrhythmias, the researchers found.

Still, these findings should not necessarily encourage people to start drinking coffee if they don't already, or to guzzle additional cups with abandon, they said.

"We certainly don't want to say drink coffee and it will reduce your risk of arrhythmias," study author Gregory M. Marcus, MD, MAS, associate chief of cardiology for research at UCSF Health, said in an interview. "But rather, we think the main point is that a blanket prohibition against coffee or caffeine to reduce the risk of arrhythmias among patients who have a diagnosis of arrhythmias is likely unwarranted. And given some evidence that coffee consumption may actually have other benefits regarding diabetes, mood, and perhaps overall mortality, it may be problematic to admonish patients to avoid coffee or caffeine when it is not really warranted."

Methods and Results

The conventional wisdom that caffeine increases arrhythmic risk has not been well substantiated. To further examine whether moderate, habitual coffee drinking relates to arrhythmia risk, and whether certain genetic variants influence the association, Kim and colleagues analyzed data from the UK Biobank. They focused on longitudinal data collected between 2006 and 2018 from 386,258 people who did not have a prior diagnosis of arrhythmia.

Participants had an average age of 56 years, and about 52% were female. They provided information about their coffee consumption, and the researchers grouped the participants into eight categories based on their daily coffee intake: 0, less than 1, 1, 2, 3, 4, 5, and 6 or more cups per day.

Over an average follow-up of 4.5 years, 16,979 participants developed an incident arrhythmia. After adjusting for demographic characteristics, comorbid conditions, and lifestyle habits, the decreased risk with each cup of coffee was similar for atrial fibrillation or flutter (hazard ratio, 0.97) and supraventricular tachycardia (HR, 0.96).

Taking into account genetic variations that relate to caffeine metabolism did not modify the findings. Mendelian randomization analyses that used a polygenic score of inherited caffeine metabolism patterns "failed to provide evidence that caffeine consumption leads to a greater risk of arrhythmias," the researchers said.

Professional society guidelines have suggested staying away from caffeinated products to reduce the risk of arrhythmia, but this guidance has "relied on assumed mechanisms and a small observational study from 1980," the authors wrote. Subsequent research has indicated that coffee's reputation of increasing the risk of arrhythmia may be undeserved.

"The investigators should be commended on performing a high-quality observational study to try to further understand the association between coffee consumption and arrhythmias, or the

lack of one," commented Zachary D. Goldberger, MD, MS, with the division of cardiovascular medicine at the University of Wisconsin–Madison, who was not involved in the study. "This is not a randomized, controlled trial, and coffee consumption was self-reported, but the methods employed are rigorous, despite these and other important limitations. However, we need to be extremely cautious in how we interpret these findings, and not use these data as a prescription for more coffee. It's important to recognize that this study is not telling us to drink more coffee, or start drinking coffee, to protect against developing arrhythmias. However, it should offer more reassurance that moderate coffee consumption is not necessarily harmful, and will not always lead to arrhythmias. This is important, given the widespread notion that coffee is universally proarrhythmic."

A Call for Personalized Guidance

"As the investigators note, there are definitely biologically plausible reasons how coffee and caffeine may not cause arrhythmias, and may be possibly protective in some, despite being a stimulant," Goldberger said. "However, if your patient is reporting palpitations or symptoms of an arrhythmia, and feels they be related to coffee or caffeine, we should not use this study to tell them that coffee may not be the culprit. We need to listen to our patients, and the decision to reduce coffee consumption to reduce these symptoms needs to be personalized."

The effect size was small, and only about 4% of the participants developed an arrhythmia, Goldberger and Rodney A. Hayward, MD, wrote in an invited commentary on the study in JAMA Internal Medicine. Hayward is a professor of public health and internal medicine at the University of Michigan, Ann Arbor, and a senior investigator at the Ann Arbor Veterans Affairs Center for Clinical Management Research.

"Unfortunately, coffee consumption was self-reported at a single time point. Not only can this lead to recall bias, but subsequent and substantial changes in coffee consumption are also possible, including reductions due to new signs or symptoms," they said.

No Evidence That Coffee Ups Risk for Developing Arrhythmias

Another recent study suggests that people may alter their coffee consumption depending on their baseline cardiovascular health, according to the commentary.

Overall, the results "strengthen the evidence that caffeine is not proarrhythmic, but they should not be taken as proving that coffee is an antiarrhythmic—this distinction is of paramount importance," Goldberger and Hayward wrote. "Health care professionals can reassure patients that there is no evidence that drinking coffee increases the risk for developing arrhythmias. This is particularly important for the many patients with benign palpitations who are devastated when they think, or are told, that they have to stop drinking coffee. Given current evidence, this is entirely a patient-preference decision, not a medical one."

Marcus, a cardiac electrophysiologist, sees patients with arrhythmias all the time. They tend to "come in fairly convinced that caffeine is to be avoided when they have arrhythmias," he said. "Often, they been told by their primary care physician or their general cardiologist to avoid caffeine because they have an arrhythmia. "What I suggest to my patients is that they feel free to go ahead and experiment and try coffee," Marcus said.

Still, Marcus suspects that there are some individuals in whom caffeine is a trigger for the arrhythmia. But evidence indicates these cases likely are rare, and avoiding caffeine need not apply to the general population, particularly "given the potential health benefits of benefits of coffee and also, frankly, just the enhanced quality of life that people can enjoy drinking a good cup of coffee."

The research was conducted using the UK Biobank resource, which was established by the Wellcome Trust, the Medical Research

Council, the U.K. Department of Health, and the Scottish government. The UK Biobank has received funding from other agencies and foundations as well. Marcus disclosed grants from Baylis, Medtronic, and Eight Sleep outside the submitted work. In addition, he reported consulting for Johnson & Johnson and InCarda, and holding equity in InCarda. A coauthor received salary support from the National Institutes of Health during the study. Goldberger and Hayward disclosed no conflicts of interest.

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https://bit.ly/3eJYPSD

Study: Long-term prognosis for some patients with severe brain injury better than expected

Surprising recoveries months later may prompt physicians to delay life-support discussions

New research adds to a body of evidence indicating decisions about withdrawing life-sustaining treatment for patients with moderate-to-severe traumatic brain injury (TBI) should not be made in the early days following injury.

In a July 6, 2021, study published in *JAMA Neurology*, researchers led by UC San Francisco, Medical College of Wisconsin and Spaulding Rehabilitation Hospital followed 484 patients with moderate-to-severe TBI. They found that among the patients in a vegetative state, 1 in 4 "regained orientation" - meaning they knew who they were, their location and the date - within 12 months of their injury.

"Withdrawal of life-sustaining treatment based on early prediction of poor outcome accounts for most deaths in patients hospitalized with severe TBI," said senior author Geoffrey Manley, MD, PhD, professor and vice chair of neurological surgery at UCSF and chief of neurosurgery at Zuckerberg San Francisco General Hospital, noting that 64 of the 92 fatalities in the study occurred within two weeks of injury.

"TBI is a life-changing event that can produce significant, lasting disability, and there are cases when it is very clear early on that a patient will not recover," he said. "But results from this study show a significant proportion of our participants experienced major improvements in life functioning, with many regaining independence between two weeks and 12 months after injury."

The patients in the study were enrolled by the brain injury research initiative TRACK-TBI, of which Manley is the principal investigator. All patients were 17 and older and had presented to hospitals with level 1 trauma centers within 24 hours of injury. Their exams met criteria for either moderate TBI (approximately one third of patients) or severe TBI.

In both groups, the most common causes of injury were falls, assault and primarily car and motorcycle crashes in which the patient had been a driver/passenger, pedestrian or cyclist.

The patients, whose average ages were 35 in the severe TBI group (78 percent males) and 38 in the moderate TBI group (80 percent males), were assessed using the Glasgow Outcomes Scale Extended (GOSE), which ranges from 1 for death to 8 for "upper good recovery" and resumption of normal life. The Disability Rating Scale (DRS) was also used to categorize impairment.

At 12 Months, Small but Significant Minority of Severe TBI Patients Had No Disability

At two weeks post-injury, 93 percent of the severe TBI group and 79 percent of the moderate TBI group had moderate-to-severe disability, according to the DRS, and 80 percent had GOSE scores from 2 to 3, meaning they required assistance in basic everyday functioning.

But by 12 months, half of the severe TBI group and three-quarters of the moderate TBI group had GOSE scores of at least 4, indicating they could function independently at home for at least

eight hours per day. Moreover, 19 percent of the severe TBI group had no disability, according to the DRS, and a further 14 percent had only mild injury, the researchers noted.

Most surprising were the findings for the 62 surviving patients who had been in a vegetative state, defined as a chronic state of brain dysfunction in which a person shows no signs of awareness. All patients had recovered consciousness by the 12-month mark and 14 out of the 56 with available data (1 in 4) had regained orientation. All but one survivor in this group recovered at least basic communication ability.

"These patients made the cut for favorable outcome," said co-first author, Joseph Giacino, PhD, of Spaulding Rehabilitation Hospital, Massachusetts General Hospital and Harvard Medical School. "Their GOSE scores were 4 or higher, which meant they could be at home unsupervised for at least eight hours a day, since they were able to take care of basic needs, such as eating and toileting."

The study follows previous research that shows a significant percentage of patients with grave impairments achieve favorable functionality many months or years later. This research, led by Giacino, coincided with the recommendation in 2018 from the American Academy of Neurology that in the first 28 days after injury, clinicians should refrain from telling families that a patient's prognosis is beyond hope.

"While a substantial proportion of patients die or suffer lasting disability, our study adds to growing evidence that severe acute impairment does not portend uniformly poor long-term outcome," said Manley, who is also affiliated with the UCSF Weill Institute for Neurosciences. "Even those patients in a vegetative state - an outcome viewed as dire - may improve, since this is a dynamic condition that evolves over the first year."

Co-first author is Michael McCrea, PhD, of Medical College of Wisconsin. A full list of authors and TRACK-TBI investigators is available in the journal.

The study was supported by grants from the U.S. National Institutes of Health, National Institute of Neurologic Disorders and Stroke, U.S. Department of Defense, TBI Endpoints Development (TED) Initiative.

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How Bad Is the Bootleg Fire? It's Generating Its Own Weather.

Unpredictable winds, fire clouds that spawn lightning, and flames that leap over firebreaks are confounding efforts to fight the blaze, which is sweeping through southern Oregon.

By Henry Fountain

A towering cloud of hot air, smoke and moisture that reached airliner heights and spawned lightning. Wind-driven fronts of flame that have stampeded across the landscape, often leapfrogging firebreaks. Even, possibly, a rare fire tornado.

The Bootleg Fire in Southern Oregon, spurred by months of drought and last month's blistering heat wave, is the largest wildfire so far this year in the United States, having already burned more than 340,000 acres, or 530 square miles, of forest and grasslands.

And at a time when climate change is causing wildfires to be larger and more intense, it's also one of the most extreme, so big and hot that it's affecting winds and otherwise disrupting the atmosphere.

"The fire is so large and generating so much energy and extreme heat that it's changing the weather," said Marcus Kauffman, a spokesman for the state forestry department. "Normally the weather predicts what the fire will do. In this case, the fire is predicting what the weather will do."

The Bootleg Fire has been burning for two weeks, and for most of that time it's exhibited one or more forms of extreme fire behavior, leading to rapid changes in winds and other conditions that have caused flames to spread rapidly in the forest canopy, ignited whole stands of trees at once, and blown embers long distances, rapidly igniting spot fires elsewhere.

"It's kind of an extreme, dangerous situation," said Chuck Redman,

a forecaster with the National Weather Service who has been at the fire command headquarters providing forecasts. Fires so extreme that they generate their own weather confound firefighting efforts. The intensity and extreme heat can force wind to go around them, create clouds and sometimes even generate so-called fire tornadoes — swirling vortexes of heat, smoke and high wind.

The catastrophic Carr Fire near Redding, Calif., in July 2018 was one of those fires, burning through 230,000 acres, destroying more than 1,600 structures and leading to the deaths of at least eight people, some of which were attributed to a fire tornado with winds as high as 140 miles per hour that was captured on video.

Many wildfires grow rapidly in size, and the Bootleg Fire is no exception. In the first few days it grew by a few square miles or less, but in more recent days it has grown by 80 square miles or more. And nearly every day the erratic conditions have forced some of the nearly 2,200 firefighting personnel to retreat to safer locations, further hindering efforts to bring it under control. More than 75 homes and other structures have burned.

On Thursday night along its northern edge, the fire jumped over a line that had been treated with chemical retardant, forcing firefighters to back off. It was just the latest example of the fire overrunning a firebreak. “This fire is a real challenge, and we are looking at sustained battle for the foreseeable future,” said Joe Hessel, the incident commander for the forestry department.

And it’s likely to continue to be unpredictable.

“Fire behavior is a function of fuels, topography and weather,” said Craig B. Clements, director of the Wildfire Interdisciplinary Research Center at San Jose State University. “It changes generally day by day. Sometimes minute by minute.”

Mr. Redman said that nearly every day the fire had created tall updrafts of hot air, smoke and moisture called pyrocumulus clouds, some of them reaching up to 30,000 feet. One day, he said, they saw one of these clouds collapse, which can happen in early evening when the updraft stops.

“All that mass has to come back down,” he said, which forces air at the surface outward, creating strong, gusty winds in all directions that can spread a fire. “It’s not a good thing.”

Last Wednesday, though, conditions led to the creation of a larger, taller cloud called a pyrocumulonimbus, which is similar to a thunderhead. It likely reached an altitude of about 45,000 feet, said Neil Lareau, who studies wildfire behavior at the University of Nevada, Reno. Like a thunderhead, the huge cloud spawned lightning strikes, worrying firefighters because of their potential to start new fires. It may have also brought precipitation.

“Some of these events rain on themselves,” said John Bailey, a professor of forestry at Oregon State University.

Rain can be a good thing, by dampening some of the fuels and helping slow the fire. But by cooling the air closer to the surface, rain can also create dangerous downdrafts, Dr. Lareau said.

A fire whirl that formed during the 2019 Kincade Fire in Sonoma County, Calif. **Credit...Kent Porter/The Press Democrat, via Associated Press**

There have also been reports of fire whirls, small spinning vortexes of air and flames that are common to many wildfires and are often inaccurately described as fire tornadoes. Fire whirls are small, perhaps a few dozen feet in diameter at their largest, and last for a few seconds to a few minutes.

But Dr. Lareau said there were some indications that the Bootleg Fire might have created an actual fire tornado, which can be several thousand feet in diameter, have wind speeds in excess of 65 miles an hour, extend thousands of feet into the air and last much longer.

"It looks like it's been producing some pretty significant rotation," he said.

Fire tornadoes occur as a plume of hot air rises within a fire, which draws more air from outside to replace it. Local topography and differences in wind direction, often caused by the fire itself, can impart a spin to this in-rushing air, and stretching of the air column can cause it to rotate faster, like a figure skater pulling her arms in to increase her spin.

Mr. Redman said the incident command had not received any reports of a fire tornado. "But it's totally possible" for one to occur in a fire this big and intense, he said. "When we get these extreme events, it's stuff we've got to watch for."

Other kinds of extreme fire behavior are more common. But the duration of the extreme behavior in the Bootleg Fire has stunned some of those fighting it. "It's day after day of that extreme behavior and explosive growth," Mr. Kauffman said. "And you can't really fight fire under those conditions. It's too dangerous."

The root cause of most of the extreme behavior is the huge amount of heat the fire is pumping out. The amount of heat is related to the dryness of the fuel — trees and other vegetation, both dead and alive. And the fuels in Southern Oregon, as well as most of the West, are extremely dry, a result of the severe drought afflicting most of the region.

Dr. Clements likened it to a campfire. "You want the driest tinder and logs to get that fire going," he said. "Same thing in a forest fire. That's why we've been monitoring the drought." If vegetation is damp, some of the energy from burning is used to evaporate its moisture. If there is no moisture to evaporate, the fire burns hotter. "More heat is released," he said. "The flames are bigger."

Oregon was also hit in late June by an extreme heat wave, when record temperatures in some places were broken by as much as 9 degrees Fahrenheit. That dried out the vegetation even more. In Southern Oregon, the fuels were as dry as they'd be at the end of summer in a more normal year.

"We've had a lot of fuel that was ready to burn," Dr. Bailey said.

What would help end the extreme behavior, and eventually the fire itself, is a good, widespread rain. But that doesn't appear to be in the offing.

"We're not seeing any significant relief in the next week at least," Mr. Redman said. "But I don't think we can get any worse."

https://bit.ly/36UQ3N4

A sweeping study shows that "brain training" games are not effective

These games are popular and fun, but there is no evidence that they improve cognitive function

Kelly Cotton

In 2019, 44 percent of older Americans reported playing video games at least once a month. Part of this trend is seen in the rising popularity of game-like brain training programs such as Lumosity (which alone boasts over 75 million users), which promise improvements in memory, attention, and decision-making skills. But are these claims backed up by research?

One early study found effects of working memory training on intelligence, sparking a field of research focused on potential training benefits. After initial promising results , subsequent studies failed to replicate these findings. Often studies find some evidence of "near transfer", or a training boost to specific skills, but fail to see "far transfer", or benefits to general cognitive performance.

A 2021 study set out to determine the effectiveness of brain training programs in over 8,000 online participants, including 1,000 people who reported being active users of a brain training program. If these programs are as effective as they claim, then these active users should outperform the other participants on tests of memory, verbal ability, and reasoning skills. The participants came from a variety

of countries, education levels, genders, and ages, a major strength of this study. The self-reported brain trainers actively used at least one program, and had used programs for anywhere between two weeks and five years.

The researchers found no evidence of an effect of brain training. Active brain trainers did not perform better on any cognitive measure than people who do not use these programs. Furthermore, no effect was found for any demographic group, such as age, education or socioeconomic status, or specific brain training program, further bolstering the conclusion that these programs are not effective.

The researchers found one significant result: people who believed that brain training was effective, regardless of whether they actually used them or not, counterintuitively performed worse on cognitive tests compared to people who didn't believe these programs are effective. Whether or not people believe these games work, they seem to have little benefit to general cognitive function. Play games for enjoyment, not with any expectation of a major cognitive boost.

https://bit.ly/3rD0tL6

The climate impact of wild pigs greater than a million cars

By uprooting carbon trapped in soil, wild pigs are releasing around 4.9 million metric tons of carbon dioxide annually across the globe, the equivalent of 1.1 million cars.

An international team led by researchers from The University of Queensland and The University of Canterbury have used predictive population models, coupled with advanced mapping techniques, to pinpoint the climate damage wild pigs are causing across five continents.

UQ's Dr. Christopher O'Bryan said the globe's ever-expanding population of feral pigs could be a significant threat to the climate.

"Wild pigs are just like tractors plowing through fields, turning over soil to find food," Dr. O'Bryan said.

"When soils are disturbed from humans plowing a field, or in this case, from wild animals uprooting, carbon is released into the atmosphere. "Since soil contains nearly three times as much carbon than in the atmosphere, even a small fraction of carbon emitted from soil has the potential to accelerate climate change.

"Our models show a wide range of outcomes, but they indicate that wild pigs are most likely currently uprooting an area of around 36,000 to 124,000 square kilometers, in environments where they're not native. "This is an enormous amount of land, and this not only affects soil health and carbon emissions, but it also threatens biodiversity and food security that are crucial for sustainable development."

"Our models show a wide range of outcomes, but they indicate that wild pigs are most likely currently uprooting an area of around 36,000 to 124,000 square kilometers, in environments where they're not native," Dr. O'Bryan said. Credit: The University of Queensland

Using existing models on wild pig numbers and locations, the team simulated 10,000 maps of potential global wild pig density.

They then modeled the amount of soil area disturbed from a long-term study of wild pig damage across a range of climatic conditions, vegetation types and elevations spanning lowland grasslands to sub-alpine woodlands.

The researchers then simulated the global carbon emissions from wild pig soil damage based on previous research in the Americas, Europe, and China.

University of Canterbury Ph.D. candidate Nicholas Patton said the research would have ramifications for curbing the effects of climate change into the future. "Invasive species are a human-caused problem, so we need to acknowledge and take responsibility for their environmental and ecological implications," Mr. Patton said.

"If invasive pigs are allowed to expand into areas with abundant

soil carbon, there may be an even greater risk of greenhouse gas emissions in the future. "Because wild pigs are prolific and cause widespread damage, they're both costly and challenging to manage. "Wild pig control will definitely require cooperation and collaboration across multiple jurisdictions, and our work is but one piece of the puzzle, helping managers better understand their impacts. "It's clear that more work still needs to be done, but in the interim, we should continue to protect and monitor ecosystems and their soil which are susceptible to invasive species via loss of carbon."

More information: *Christopher J. O'Bryan et al, Unrecognized threat to global soil carbon by a widespread invasive species, Global Change Biology (2021). DOI: 10.1111/gcb.15769*

https://bit.ly/3kLQe5x

DNA pulled from thin air identifies nearby animals

Two research groups have shown the atmosphere can contain detectable amounts of DNA from many kinds of animals

By Erik Stokstad

DNA is everywhere, even in the air. That's no surprise to anyone who suffers allergies from pollen or cat dander. But two research groups have now independently shown the atmosphere can contain detectable amounts of DNA from many kinds of animals. Their preprints, posted on bioRxiv last week, suggest sampling air may enable a faster, cheaper way to survey creatures in ecosystems.

The work has impressed other scientists. "The ability to detect so many species in air samples using DNA is a huge leap," says Matthew Barnes, an ecologist at Texas Tech University. "It represents an exciting potential addition to the toolbox."

"The surprising part is that you're able to get birds and mammals—wow," says Julie Lockwood, a molecular ecologist at Rutgers University, New Brunswick. The new studies suggest "there's more than just spores; there's cells and hair and all kinds of interesting things that float through the air."

For more than a decade, researchers have analyzed those disparate sources of DNA in water to identify elusive organisms. Researchers' sampling of environmental DNA (eDNA) in lakes, streams, and coastal waters has let them identify invasive species like lionfish as well as rare organisms such as the great crested newt. More recently, some scientists have tracked insects by eDNA on leaves, and also found soil eDNA apparently left by mammals loping along a trail.

Far fewer studies have been done on animal eDNA in air. It's not obvious how much tissue wafts off animals or how long the genetic contents of those cells persist in air. Some earlier studies used metagenomic sequencing—an approach to identify mixtures of DNA—to detect microorganisms including bacteria and fungi that are abundant in air. And a 2015 study of air monitors for pathogens in the Washington, D.C., area found traces of eDNA from many kinds of vertebrates and arthropods. But it wasn't obvious how useful the technique would be, and it's not clear how terrestrial animals shed cells that float away.

Earlier this year, Elizabeth Clare, a molecular ecologist now at York University, reported in *PeerJ* that eDNA from naked mole rats could be detected in air samples taken in the laboratory. To find out whether animal eDNA could be detected outdoors, she and colleagues from Queen Mary University of London went to a zoo: There, the species are known and absent from the surrounding landscape, so the team could determine the source of airborne eDNA they found. In December 2020, Clare set up vacuum pumps with filters in 20 locations in Hamerton Zoo Park and let each run for 30 minutes.

Clare collected 72 air samples from both outside and inside zoo buildings. She used polymerase chain reaction to amplify the scant genetic fragments left on the filters into enough DNA for sequencing. "We had to take a leap of faith that it was there because

it wasn't something you can measure," she says. After sequencing the eDNA, she matched the snippets to known sequences in a database. The team identified 17 species kept at the zoo and others living near and around it, such as hedgehogs and deer. Some zoo animal DNA was found nearly 300 meters from the animals' enclosures. She also detected airborne DNA likely from the meat of chicken, pig, cow, and horse fed to captive predators indoors. All told, the team detected 25 species of mammals and birds.

Meanwhile, researchers in Denmark had pursued the same idea. Kristine Bohmann, a molecular ecologist at the University of Copenhagen, recalls inspiration struck while brainstorming proposals for a high-risk grant program. "I remember saying, it has to be crazier—like vacuuming DNA from air, that would be insane." They won the grant and sucked up air from three locations in the Copenhagen Zoo with vacuums and fans in three types of samplers. They consistently detected animals—a total of 49 species Cf vertebrate.

"These preprints are exciting and show some great data," says Kristy Deiner, a conservation ecologist at ETH Zürich. She leads an XPRIZE Rainforest team to develop airborne DNA technology for monitoring biodiversity.

Airborne DNA may help reveal the presence of otherwise hard to detect animals, such as those in dry environments, burrows, or caves, and those that fly out of sight of wildlife cameras, like some birds, Lockwood says.

She cautions that many questions remain about the approach, including the key issue of how far eDNA travels on air, which will influence how well the method can pinpoint the recent location of animals. That distance will depend on many factors, including the environment; eDNA will probably waft farther in a grassland than in a forest. Another question is how exactly animals shed the DNA. It could be when cells are freed as they scratch or rub their skin, sneeze, or do any vigorous activity like fighting or subduing prey. But even sloth eDNA turned up, says molecular ecologist Christina Lynggaard, a postdoc at the University of Copenhagen who did the sampling at the zoo.

Preventing contamination—always an issue with eDNA studies—is particularly thorny. Sampling eDNA in air, Barnes says, is like "pipetting underwater." One problem, Clare says, is how to find a negative control, or a test sample with no DNA in it. "I don't know where to buy a balloon of sterile air."

Despite the unknowns, Barnes and others have high hopes. Lockwood, who studies forest pests and has identified eDNA traces on bark and leaves, is already hoping to identify insect pests from air. "I can't wait to try it," she says.

https://bit.ly/3BByU9v

Excessive Caffeine Consumption May Increase Risk of Osteoporosis

In a double-blind clinical study, researchers examined the impact of high-dose, short-term caffeine intake on renal clearance of calcium, sodium and creatinine in healthy adults.

Enrico de Lazaro

Osteoporosis is a chronic, painful, and debilitating disease which makes bones less dense and more susceptible to fracture.

More common in women, it occurs when bones lose calcium and other minerals faster than the body can replace them.

The consumption of caffeine has been linked to osteoporosis, believed to be due to enhanced bone resorption as a result of increased calcium excretion in the urine.

However, the amount of calcium in the urine may not necessarily reflect the true effect of caffeine on calcium clearance.

"The emergence of an increasing 'coffee culture' it's important for people to understand the impacts of what they are putting into their bodies," said study co-author Dr. Hayley Schultz, a researcher at

the University of South Australia.

"Caffeine is one of the most widely used recreational drugs in the world, with 80% of adults consuming at least one caffeinated beverage per day. It's a common stimulant, consumed by professionals, parents, shift workers, and teenagers alike to start their day and stay alert — even the military use caffeine to help combat sleepines. But while coffee has its perks, it's also important to acknowledge its fallbacks — one of them being how our kidneys handle calcium."

In a double-blind clinical study, participants chewed caffeine or placebo gum for 5 minutes at two-hour intervals over a 6-hour treatment period (800 mg total caffeine).

While the primary research objective was to examine the impact of caffeine consumption on wakefulness and other factors, this sub-study aimed to evaluate the impact of caffeine consumption on the renal clearance of calcium.

"Our research found that people who consume 800 mg of caffeine over a typical working day will have a 77% increase in calcium in their urine, creating a potential deficiency that could impact their bones," Dr. Schultz said.

"Understanding the long-term impacts of high caffeine consumption is especially important for higher risk groups," added study first author Dr. Stephanie Reuter Lange, also from the University of South Australia.

"The average daily intake of caffeine is about 200 mg — roughly two cups of coffee. While drinking eight cups of coffee may seem a lot (800 mg of caffeine), there are groups who would fall into this category."

"People at risk could include teenagers who binge-consume energy drinks are at are at risk because their bones are still developing; professional athletes who use caffeine for performance enhancement; as well as post-menopausal women who often have low blood calcium levels due to hormonal changes and lack sufficient daily dietary calcium intake."

"Increasingly, we are also seeing high levels of caffeine among shiftworkers who need to stay alert over the night-time hours, as well as those in the military who use caffeine to combat sleep deprivation in operational settings."

"Caffeine in moderation certainly has its pros. But understanding how excess consumption could increase the risks of a highly preventable disease such as osteoporosis, is important."

The findings appear in the *British Journal of Clinical Pharmacology*.

Stephanie E. Reuter et al. The effect of high-dose, short-term caffeine intake on the renal clearance of calcium, sodium and creatinine in healthy adults. British Journal of Clinical Pharmacology, published online April 14, 2021; doi: 10.1111/bcp.14856

https://bit.ly/36WQhU3

Long COVID and severe COVID-19 infections associated with Epstein-Barr virus reactivation

Reactivation of Epstein-Barr virus may play a role in the development of long COVID symptoms and severe COVID-19

Two recently published studies available on the National Institutes of Health (NIH) website indicate Epstein-Barr virus (EBV) reactivation may play a role both in the development of long COVID symptoms, as well as severe COVID-19 cases.

The first evidence linking EBV reactivation to long COVID symptoms was discovered by Gold et al. (2021) and published in *Pathogens*. This study can be viewed on the NIH website here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8233978/

"We ran Epstein-Barr virus serological tests on COVID-19 patients at least 90 days after testing positive for SARS-CoV-2 infection, comparing EBV reactivation rates of those with long COVID symptoms to those who never experienced long COVID symptoms," said lead study author Jeffrey E. Gold of World

Organization. "We found over 73% of COVID-19 patients who were experiencing long Covid symptoms were also positive for EBV reactivation."

Another group of researchers, Chen et al. (2021), found EBV reactivation may also be associated with COVID-19 severity. Their report published in *Scientific Reports by Nature* is available here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8149409/

According to Gold, more than 95% of health adults will test positive for latent EBV infection, identified by testing for the presence of EBV VCA IgG and/or EBV nuclear antigen 1 (EBNA-1) IgG. EBV reactivation, on the other hand, is identified by further testing for the presence of EBV EA-D IgG, EBV VCA IgM, and/or circulating EBV DNA.

David J. Hurley, PhD, a professor and molecular microbiologist at the University of Georgia and coauthor of the *Pathogens* study said, "We found similar rates of EBV reactivation in those who had long COVID symptoms for months, as in those with long COVID symptoms that began just weeks after testing positive for COVID-19. This indicated to us that EBV reactivation likely occurs simultaneously or soon after COVID-19 infection."

According to Gold, other diseases and stressors can also trigger EBV reactivation, this is not exclusive to COVID-19. The inflammation response from SARS-CoV-2 infection, however, appears more successful than many other stressors at triggering EBV reactivation.

While EBV reactivation may not be responsible for all cases of recurring fatigue or brain fog after recovering from COVID-19, evidence indicates that it likely plays a role in many or even most cases.

The *Pathogens* study found that nearly one-third of 185 people surveyed who had tested positive for COVID-19 ended up with long haul symptoms, even some who were initially asymptomatic. This percentage of long term sequelae after COVID-19 infection was similar to the percentage found in a separate study Sequelae in Adults at 6 Months After COVID-19 Infection published in *JAMA Network Open*.

The relationship between SARS-CoV-2 and EBV reactivation described in these studies open up new possibilities for the diagnosis and treatment of initial COVID-19 infection as well as long COVID.

The researchers of the study in *Pathogens* indicated that it may be prudent to test patients newly positive for COVID-19 for evidence of EBV reactivation indicated by positive EBV EA-D IgG, EBV VCA IgM, or serum EBV DNA tests. If patients show signs of EBV reactivation, they can be treated early to reduce the intensity and duration of EBV replication, which may help inhibit the development of long COVID.

While there is no available vaccine to prevent EBV infection, on July 26, 2021 a phase 1, open-label study to evaluate the safety and immunogenicity of an EBV vaccine sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) at NIH is expected to begin.

"As evidence mounts supporting a role for EBV reactivation in the clinical manifestation of acute COVID-19, this study further implicates EBV in the development of long COVID," said Lawrence S. Young, PhD, a virologist at the University of Warwick speaking about the *Pathogens* study.

"If a direct role for EBV reactivation in long COVID is supported by further studies, this would provide opportunities to improve the rational diagnosis of this condition and to consider the therapeutic value of anti-herpesvirus agents such as ganciclovir."

Original publication: Gold, J.E.; Okyay, R.A.; Licht, W.E.; Hurley, D.J. Investigation of Long COVID Prevalence and Its Relationship to Epstein-Barr Virus Reactivation. Pathogens 2021, 10, 763. https://doi.org/10.3390/pathogens10060763

https://bit.ly/3eQdewH

This is how the visual system shows us a more persistent world

An international collaboration elucidates the mechanisms that facilitate accurate identification of moving images.

The findings have been published in *Nature Communications*

Imagine meeting a friend on the street, and imagine that with every step they take, your visual system has to process their image from scratch in order to recognize them. Now imagine if the same thing were to happen for every object and creature that moves around us. We would live in a constant state of uncertainty and inconsistency. Luckily, that is not the case. Our visual system is able to retain information obtained in motion, thereby presenting us with a more consistent picture of our surroundings. These are the findings of a study conducted by SISSA, in collaboration with the University of Pennsylvania and Katholieke Universiteit Leuven and published in *Nature Communications*, which explains the neuronal underpinnings of this phenomenon.

"One of the biggest challenges of all the sensory systems is to maintain a consistent representation of our surroundings, despite the constant changes taking place around us. The same holds true for the visual system," explains Davide Zoccolan, director of the Visual Neuroscience Laboratory at the Scuola Internazionale Superiore di Studi Avanzati (SISSA). "Just look around us: objects, animals, people, all on the move. We ourselves are moving. This triggers rapid fluctuations in the signals acquired by the retina, and until now it was unclear whether the same type of variations apply to the deeper layers of the visual cortex, where information is integrated and processed. If this was the case, we would live in tremendous confusion."

It has been known for a while that the signals produced by the retina following presentation of visual stimuli reach a set of consecutive processing stages within the visual cortex, arranged according to a finely-tuned hierarchy. It is this processing sequence that enables us to recognize an object or a face and to do so irrespective of its angle or position. This has been demonstrated in the case of static stimuli and can be explained by the invariance in the encoding of the images that is gradually built up along the cortical hierarchy.

To investigate the existence of a similar process in dynamic situations, researchers from SISSA, University of Pennsylvania (Penn), and Katholieke Universiteit Leuven (KU Leuven), led by Zoccolan, analyzed the signals produced by neurons across different visual cortical areas in rodents following presentation of dynamic visual stimuli. The findings have been published in *Nature Communications*.

"We used three distinct datasets: one collected by Liviu Soltuzu at SISSA, one collected by Kasper Vinken at KU Leuven in the group led by Hans Op de Beeck and one made freely available by the Allen Institute for Brain Science in Seattle," said the scientist. "The visual stimuli used in each were of different types. In SISSA, we created dedicated video clips showing objects moving at different speeds. The other datasets were acquired using various kinds of clips, including from films."

Next, the researchers analyzed the signals registered in the different areas of the visual cortex through a combination of sophisticated algorithms and models developed by Eugenio Piasini and Vijay Balasubramanian from Penn in collaboration with SISSA scientists (Liviu Soltuzu, Paolo Muratore and Riccardo Caramellino). The researchers developed a theoretical framework to help connect the images in the movies to the activity of specific neurons in order to determine how neural signals evolve over different time scales.

"The art in this science was figuring out an analysis method to show that the processing of visual images is getting slower as you go

deeper and deeper in the brain," explains Balasubramanian. "Different levels of the brain process information over different time scales--some things could be more stable, some quicker. It's very hard to tell if the timescales are changing across the brain, so our contribution was to devise a method of doing this."

The results remained consistent, irrespective of the nature of the visual stimuli: "We observed an increased persistence of neuronal responses recorded in deeper stages of the visual system, a sort of 'perceptual constancy' that guarantees some amount of stability in the encoding of visual information and eliminates the fluctuations observed in earlier visual areas" explains Zoccolan. "And not only that. We also noticed a form of 'intrinsic' persistence that increased along the hierarchy of visual areas. In the deeper areas, the neural response remains for a few hundred milliseconds even after the stimulus disappears, which guarantees a minimum duration for the encoding of the images, and this in turn ensures that the information is properly processed and that the reaction to the stimulus is correctly calibrated."

It appears that the visual system has developed an ideal strategy for providing us with a more consistent, safer world: limiting too-rapid fluctuations on one hand while ensuring we do not lose potentially valuable information on the other.

https://bit.ly/3x36qSk

39-Year-Old Becomes First US Patient to Receive 'Aeson' Artificial Heart Implant

Team of surgeons has successfully completed the first human implantation in the US of an artificial heart

David Nield

In the US alone, thousands are currently waiting for organ transplants, and an average of 17 people die each day because they've run out of time – and that's why the development of artificial organs is such an important field of research.

Now a team of surgeons has successfully completed the first human implantation in the US of an artificial heart device called the 'Aeson', developed by French company CARMAT. The artificial heart has two ventricular chambers and four biological valves, just like the real organ, and is powered by an external device.

Made from "biocompatible materials" including bovine tissue, the artificial heart uses a combination of sensors and algorithms to maintain its pace and keep blood circulating through the body.

"We are encouraged that our patient is doing so well after the procedure," says cardiologist Carmelo Milano from the Duke University School of Medicine. "As we evaluate this device, we are both excited and hopeful that patients who otherwise have few to no options could have a lifeline."

The patient in question is 39-year-old Matthew Moore, from Shallotte in North Carolina. Moore was initially due to have heart bypass surgery, but as his condition deteriorated the medical staff started to run out of options; he became so ill that even a regular heart transplant was too risky.

Fortunately, he was in the right place: the Aeson device is being tested at Duke University, pending approval from the US Food and Drug Administration (FDA). It's already been given the green light for use by regulators in Europe, after several years of tests in European patients, not all of which have been successful.

The artificial heart has been developed specifically to help those whose hearts can no longer pump enough blood through both chambers. It replaces the entire natural heart, although it's not intended to be permanent – it's designed to be a bridge towards a full heart transplant within six months or so.

"Because of the shortages of donor hearts, many patients die while waiting for a heart transplant," says cardiologist Jacob Schroder from Duke University School of Medicine. "We are hopeful for new options to help these patients, many like Mr Moore

who have devastating disease and cannot otherwise be considered for a transplant."

This is just one device for one particular organ: other research teams are working on other body parts that can potentially step in when particular parts of our bodies fail us. If the technology can be developed successfully and safely, the potential benefits are huge.

The FDA has approved US trials of the CARMAT artificial heart, which will involve 10 patients with end-stage biventricular heart failure, and assess whether the Aeson can act as a way of prolonging life before a heart transplant can happen.

For now, Matthew Moore will have to carry around a controller and a pack of rechargeable batteries to keep Aeson working – but he is still alive, and the technology keeping him alive could go on to save thousands of other lives in the future, if further tests of the device turn out to be positive.

"Both Matthew and I are so grateful that we've been provided an opportunity to participate in something that has the potential to have an impact on so many lives," says Matthew's wife, Rachel Moore, a practicing nurse. "We are just taking it day-by-day and hope everything continues to progress well."

https://bit.ly/2TvGhOq

The Lambda variant: is it more infectious, and can it escape vaccines? A virologist explains

The Lambda coronavirus variant was first reported in Peru in December 2020, according to the World Health Organization.

Adam Taylor *

It then spread to multiple countries in South America, where it currently accounts for over 20% of detected variants. One case of Lambda was recorded in hotel quarantine in New South Wales in April. Lambda has now been detected in more than 20 countries around the globe.

The European Centre for Disease Prevention and Control has designated Lambda a "variant under monitoring", and Public Health England regards it as a "variant under investigation".

In June this year, the WHO designated it a "variant of interest". This is due to mutations thought to affect the virus' characteristics, such as how easily it's transmitted. Though it's not yet concerning enough for the WHO to deem it a "variant of concern", such as Alpha or Delta.

Epidemiological evidence is still mounting as to the exact threat Lamda poses. So, at this stage more research is required to say for certain how its mutations impact transmission, its ability to evade protection from vaccines, and the severity of disease.

Preliminary evidence suggests Lambda has an easier time infecting our cells and is a bit better at dodging our immune systems. But vaccines should still do a good job against it.

Is Lambda more infectious? And can it escape vaccines?

Mutations affecting the spike protein of the SARS-CoV-2 virus can increase infectivity, which is the ability of the virus to infect cells.

What's more, as many of the coronavirus vaccines currently available or in development are based on the spike protein, changes to the spike protein in new variants can impact vaccine effectiveness

Lambda contains multiple mutations to the spike protein.

One mutation (F490S) has already been associated with reduced susceptibility to antibodies generated in patients who had recovered from COVID. This means antibodies generated from being infected with the original Wuhan strain of COVID aren't quite as effective at neutralising Lambda.

Another Lambda mutation (L452Q) is at the same position in the spike protein as a previously studied mutation found in the Delta variant (L452R). This mutation in Delta not only increases the ability of the virus to infect cells, but also promotes immune escape meaning the antibodies vaccines generate are less likely to

recognise it. Both mutations F490S and L452Q are in the "receptor binding domain", which is the part of the spike protein that attaches to our cells.

Preliminary data on the Lambda spike protein suggests it has increased infectivity, meaning it's more easily able to infect cells than the original Wuhan virus and the Alpha and Gamma variants. These early studies also suggest antibodies generated in people receiving the CoronaVac vaccine (developed by Chinese biotech Sinovac) were less potent at neutralising the spike protein of Lambda than they were the Wuhan, Alpha or Gamma variants.

It's worth noting infectivity is not the same as being more infectious between people. There's not enough evidence yet that Lambda is definitely more infectious, but the mutations it has suggest it's possible.

A separate small study, also yet to be reviewed by the scientific community, suggests the L452Q mutation in the Lambda spike protein is responsible for its increased ability to infect cells. Like the L452R mutation in the Delta variant, this study suggests the L452Q mutation means Lambda may bind more easily to the "ACE2 receptor", which is the gateway for SARS-CoV-2 to enter our cells.

This preliminary study suggests Lambda's spike protein mutations reduce the ability of antibodies generated by both Pfizer and Moderna's vaccines to neutralise the virus. Also, one mutation was shown to resist neutralisation by antibodies from antibody therapy to some extent.

However, these reductions were moderate. Also, neutralising antibodies are only one part of a protective immune response elicited by vaccination. Therefore, these studies conclude currently approved vaccines and antibody therapies can still protect against disease caused by Lambda.

Is it more severe?

A risk assessment released by Public Health England in July concedes there's not yet enough information on Lambda to know whether infection increases the risk of severe disease.

The risk assessment also recommends ongoing surveillance in countries where both Lambda and Delta are present be implemented as a priority. The aim would be to find out whether Lambda is capable of out-competing Delta.

With ongoing high levels of transmission of the coronavirus, there's a continued risk of new variants emerging. The Lambda variant again highlights the risk of these mutations increasing the ability of SARS-CoV-2 to infect cells or disrupt existing vaccines and antibody drugs.

The WHO will continue to study Lambda to determine whether it has the potential to become an emerging risk to global public health and a variant of concern.

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What are the Delta, Gamma, Beta and Alpha Covid variants?

The UK is seeing rising cases of coronavirus caused by a variant called Delta, which was first identified in India.

By Michelle Roberts Health editor, BBC News online

Experts say it is more transmissible than even the "UK/Kent" or Alpha variant which previously dominated here.

Delta is behind almost all new Covid infections.

What do we know about Covid variants?

There are thousands of different variants of Covid circulating across the world. One of them, called Delta or B.1.617.2, appears to be spreading more quickly in some countries, including the UK.

Viruses mutate all the time and most changes are inconsequential. Some even harm the virus. But others can make the disease more infectious or threatening - and these mutations tend to dominate.

Those with the most potentially concerning changes are called "variants of concern". They are kept under the closest watch by health officials, and include:

- Delta (B.1.617.2) which currently accounts for 99% of new Covid cases in the UK

- Alpha (B.1.1.7), first identified in the UK but which has spread to more than 50 countries and appears to be mutating again

- Beta (B.1.351), first identified in South Africa but which has been detected in at least 20 other countries, including the UK

- Gamma (P.1), first identified in Brazil but which has spread to more than 10 other countries, including the UK

Are they more dangerous?

There is no evidence that any of them cause much more serious illness for the vast majority of people.

As with the original version, the risk remains highest for people who are elderly or have significant underlying health conditions.

But a virus being more infectious and equally dangerous will in itself lead to more deaths in an unvaccinated population.

Vaccines offer high protection against severe illness with Covid-19, including infections caused by variants of concern. The shots also reduce the risk of infection. But they are not perfect and do not completely eliminate all risk.

The advice to avoid infection remains the same for all strains: wash your hands, keep your distance, wear a face covering and be vigilant about ventilation.

How are the mutants behaving?

The variants of concern have all undergone changes to their spike protein - the part of the virus which attaches to human cells.

Delta has some potentially important ones (such as L452R) that might make it spread more easily.

There is no evidence to indicate it causes more severe disease or might make current vaccines less effective, say UK officials.

One mutation, called N501Y, shared by the Alpha, Gamma and Beta, seems to make the virus better at infecting cells and spreading.

Beta and Gamma also have a key mutation, called E484K, that may help the virus sidestep some of the body's immune defences.

Experts recently found a small number of cases of Alpha with this change too.

Will vaccines still work against variants?

Current vaccines were designed for earlier versions of coronavirus, which means they may not be the ideal match for new variants and so might not work quite as well.

But experts say they are still very effective at protecting lives by cutting the risk of severe illness:

- An analysis by Public Health England found two doses of either the Pfizer or AstraZeneca vaccine was more than 90% effective against hospitalisations for Covid-19 caused by Delta

- A single dose, however, was less effective at preventing illness from Delta, compared to how well it worked against Alpha.

Doctors say it is vital that people get both doses to gain maximum protection against existing and emerging variants.

Do variants mean booster jabs are more likely?

Experts are confident existing vaccines can be redesigned to better tackle emerging mutations.

The UK government has a deal with biopharmaceutical company CureVac to develop vaccines against future variants, and has pre-ordered 50 million doses.

Depending on how variants continue to develop, these could potentially be used to offer a booster vaccine to older or clinically vulnerable people later in the year.

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Common cold virus may predate modern humans, ancient DNA hints

Inside a pair of 31,000-year-old baby teeth, scientists discovered DNA remnants from several viruses and used that genetic material to reconstruct the pathogens' evolutionary history.

By Nicoletta Lanese - Staff Writer

Their analysis suggests that human adenovirus C (HAdV-C), a species of virus that typically causes mild, cold-like illnesses in children, may have originated more than 700,000 years ago, long before *Homo sapiens* walked the Earth, the team reported in a recent study, posted June 28 to the preprint database bioRxiv, which has not yet been peer-reviewed.

Still, not everyone is convinced by the findings.

"The authors find a relatively ancient date before the emergence of our own species," said Sébastien Calvignac-Spencer, an evolutionary biologist at the Robert Koch Institute in Germany. "I think it is plausible but ... I would consider their analyses as preliminary," Calvignac-Spencer, who was not involved in the study, told Live Science in an email.

The study authors extracted two "nearly complete" adenovirus genomes from the baby teeth, providing a unique but very small sample of viruses upon which to base their analyses, Calvignac-Spencer said. Analyzing younger adenoviruses, dating a few thousand years old, could help the team validate their estimate of when HAdV-Cs first emerged, he noted.

That said, ancient adenovirus samples don't crop up every day.

The baby teeth used in the study came from a remarkable archaeological site in northeastern Siberia called Yana "Rhinoceros Horn Site" (RHS), where an arrow foreshaft made of woolly rhinoceros horn was once found, according to a 2004 report in the journal Science.

The archeological site, located about 300 miles (480 kilometers) north of the Arctic Circle, provides some of the earliest direct evidence of humans living in the high Arctic, NBC News reported. Archaeologists have found stone tools, ivory weapons and the bones of butchered mammoths, bison and bears at the site. The only human remains discovered at Yana RHS are three fragmented baby teeth, which came from two different children who shed them when they were between 10 and 12 years old, according to a 2019 report in the journal Nature.

Viruses can enter teeth via the bloodstream and remain preserved in the tough tissue for many thousands of years, said first author Sofie Nielsen, who was a doctoral student at the University of Copenhagen at the time of the study. And unlike bones in the body, teeth don't ever regenerate — they retain the same cells over time, so they provide a cumulative record of all the pathogens a person has encountered, she told Live Science.

In this case, the ancient baby teeth supplied a record of early childhood infections, and the frigid Arctic environment likely helped to preserve both the teeth and the viral DNA inside, Nielsen said. To extract the viral DNA, the research team had to completely decimate the tooth tissue.

Even the tough teeth and cold climate could not completely shield the viral DNA from degradation, so the genomes became fragmented over time. To piece the broken genomes back together, the team analyzed each bit of DNA and compared the short genetic sequences with reference genomes from modern-day viruses. They identified the two ancient genomes as HAdV-Cs, one of the seven known species of adenovirus, A through G.

The team found that the ancient genomes shared many similarities with modern-day adenoviruses that were circulating between the 1950s and 2010s. For instance, all the modern HAdV-C viruses share the same genetic "backbone" but show diversity in a few key

genes, including ones that help the viruses avoid detection by the host immune system. These slight differences place the viruses into six distinct subtypes; for example, HAdV-C1 and HAdV-C2 are different subtypes under the HAdV-C umbrella.

The team found that the ancient adenoviruses shared most of their genetic backbone with the modern viruses, and that the two ancient genomes fit neatly into the established "C1" and "C2" subtypes. "The extraordinary thing is that … they are more similar to the modern type two and type one than they are to each other," Nielsen said.

In other words, despite both being 31,600 years old, the two ancient genomes matched modern viruses within their subtype better than they matched one another. This finding hints that the various adenovirus subtypes began diverging from one another many thousands of years ago, long before they made their way into baby teeth of two youngsters in ancient Siberia, according to Nielson and her colleagues.

By again comparing the modern genomes to the ancient ones, the team generated a rough estimate of when HAdV-Cs split from all other adenoviruses. "These dates are very uncertain, because we have so few samples," Nielsen said. "But it seems like they were split at least 700,000 years ago."

This estimate places the origin of HAdV-Cs before the emergence of modern humans, which occurred roughly 300,000 years ago, Live Science previously reported. In their report, the study authors suggest that the migratory patterns and cross-species interactions of our hominin ancestors may have helped shape the evolution of these adenoviruses, but if that happened and how remains highly uncertain.

"We have shown ourselves that other HAdVs — HAdV-Bs and Es — were probably transmitted to the human lineage by gorillas and chimps," Calvignac-Spencer told Live Science, referencing previous research by his own lab. "We found that some of these transmission events probably predated our species but others did not." The discovery of more ancient adenovirus samples would help researchers pinpoint when HAdV-Cs first began infecting our human ancestors, and which species the pathogens passed through on their way to the human lineage, he said.

"We have such a long span of time where we know nothing," Nielsen said. Ideally, future analyses would not only include adenoviruses of many ages but also adenoviruses from many different geographical locations, she noted. "For sure, more data is always better."

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Investigational magnetic device shrinks glioblastoma in first-in-world human test

Shrunk a deadly glioblastoma tumor by more than a third

Houston Methodist Neurological Institute researchers from the department of neurosurgery shrunk a deadly glioblastoma tumor by more than a third using a helmet generating a noninvasive oscillating magnetic field that the patient wore on his head while administering the therapy in his own home. The 53-year-old patient died from an unrelated injury about a month into the treatment, but during that short time, 31% of the tumor mass disappeared. The autopsy of his brain confirmed the rapid response to the treatment.

"Thanks to the courage of this patient and his family, we were able to test and verify the potential effectiveness of the first noninvasive therapy for glioblastoma in the world," said David S. Baskin, M.D., FACS, FAANS, corresponding author and director of the Kenneth R. Peak Center for Brain and Pituitary Tumor Treatment in the Department of Neurosurgery at Houston Methodist. "The family's generous agreement to allow an autopsy after their loved ones' untimely death made an invaluable contribution to the further study and development of this potentially powerful therapy."

In a case study published in *Frontiers in Oncology* Baskin and his colleagues detailed the journey of their pioneering patient who suffered from end-stage recurrent glioblastoma, despite a radical surgical excision, chemoradiotherapy and experimental gene therapy.

Glioblastoma is the deadliest of brain cancers in adults, nearly always fatal, with a life expectancy of a few months to two years. When the patient's glioblastoma recurred in August 2019, Baskin and his team, already working on the OMF treatment in mouse models, received FDA approval for compassionate use treatment of the patient with their newly invented Oncomagnetic Device under an Expanded Access Program (EAP). The protocol also was approved by the Houston Methodist Research Institute Institutional Review Board.

The treatment consisted of intermittent application of an oscillating magnetic field generated by rotating permanent magnets in a specific frequency profile and timing pattern. First administered for two hours under supervision in the Peak Clinic, ensuing treatments were given at home with help from the patient's wife, with increasing treatment times up to a maximum of only six hours per day.

The Oncomagnetic Device looks deceptively simple: three oncoscillators securely attached to a helmet and connected to a microprocessor-based electronic controller operated by a rechargeable battery, an invention by case study co-author Dr. Santosh Helekar. During the patient's five weeks of treatment, the magnetic therapy was well-tolerated and the tumor mass and volume shrunk by nearly a third, with shrinkage appearing to correlate with the treatment dose.

"Imagine treating brain cancer without radiation therapy or chemotherapy," said Baskin. "Our results in the laboratory and with this patient open a new world of non-invasive and nontoxic therapy for brain cancer, with many exciting possibilities for the future."

Co-authored by associate professor of neurosurgery Santosh Helekar, M.D., Ph.D., research professor Martyn A. Sharpe, Ph.D., and biomedical engineer Lisa Nguyen, the case study is entitled "Case Report: End-Stage Recurrent Glioblastoma Treated with a New Noninvasive Non-Contact Oncomagnetic Device." The ongoing research is supported by the Translational Research Initiative of the Houston Methodist Research Institute, Donna and Kenneth Peak, the Kenneth R. Peak Foundation, the John S. Dunn Foundation, the Taub Foundation, the Blanche Green Fund of the Pauline Sterne Wolff Memorial Foundation, the Kelly Kicking Center Foundation, the Gary and Marlee Swarz Foundation, the Methodist Hospital Foundation and the Veralan Foundation.

For more information: The study also can be found at DOI: https://doi.org/10.3389/fonc.2021.708017

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Tiny ancient reptile named after Thor's world-ending nemesis

The near-complete fossil dates to about 310 million years ago.

By Mindy Weisberger - Senior Writer

A long-bodied, sinuous reptile that lived about 310 million years ago has been named for a legendary giant snake in Viking mythology that once battled Thor, the Norse god of thunder.

An artistic representation of the tiny but fierce Joermungandr bolti as it battles a centipede. **(Image credit: Created by Henry Sutherland Sharpe, copyright 2019 Henry Sutherland Sharpe)**

But while the Vikings' mythic "World Serpent," named Jörmungandr, was large enough to wrap his body around the entire Earth, the ancient reptile *Joermungandr bolti* (YOR'-mun-gund BOL'-tee) measures just a couple of inches long.

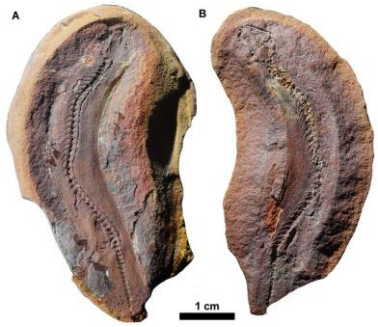
This creature is a microsaur ("small lizard"), an early group of reptiles that were among the first vertebrates (animals with backbones) to evolve on land. *J. bolti* had a slender, elongated body with short limbs and a blunt skull, and the fossil was so well preserved that it retained impressions of specialized scales that

resemble dirt-repelling scales in modern reptiles. Together, these features suggest that the wee microsaur tunneled underground and slithered like a snake, researchers reported in a new study.

The microsaur fossil was in the collection of Chicago's Field Museum, and it came from Mazon Creek in Illinois, where deposits have preserved numerous fossils of complete or near-complete organisms dating to the Carboniferous period (about 359 million to 299 million years ago). Microsaurs represent some of the oldest fossils of amniotes, vertebrates that develop embryos in fluid-filled eggs with multiple membrane layers, according to the University of California Museum of Paleontology in Berkeley.

J. bolti ("bolti" is a nod to the late paleontologist John R. Bolt, an emeritus curator of fossil amphibians and reptiles at the Field Museum) is a microsaur from a group called Recumbirostra, which was around for about 40 million to 50 million years, "from the middle of the Carboniferous to the early Permian [299 million to 251 million years ago]," said lead study author Arjan Mann, a postdoctoral fellow of paleobiology at the Smithsonian National Museum of Natural History in Washington, D.C.

Mann conducted the microsaur research while pursuing a doctoral degree in the Department of Earth Sciences at Carleton University in Ottawa, Canada. He had previously described two microsaur species, naming the genuses *Diabloroter* ("devil digger") and *Infernovenator* ("hell hunter"), according to a 2019 statement.



***Photographs of the fossil J. bolti (FMNH 1309). (a) The part specimen showing the dorsal view; (b) the counterpart specimen showing the ventral view.* (Image credit: Arjan Mann, Ami S. Calthorpe and Hillary C. Maddin)**

Mann told Live Science that most fossils in this microsaur group come from the Permian, so *J. bolti* offered the scientists a rare glimpse of an earlier microsaur. Its body, which measured just 1.9 inches (5 centimeters) from nose to tail tip, was "streamlined, cylindrical and relatively smooth," with stubby limbs and tapered tailbones that hinted its tail was short and rounded, "similar to the morphology of the tails of some modern geckos and some skinks, which use their tails for fat storage," the study authors wrote.

Oval, ridged scales covered the body, and the robust skull had some fused bones, likely to help the microsaur withstand the pressures of digging, Mann said.

"We think this was something like a headfirst burrower; the head would smack into the soil to dig holes like modern reptiles do," Mann said *J. bolti*'s elongated shape would have enabled the microsaur to wriggle and writhe over the ground like a snake, and "its scales appear to have patterns that are similar to what we see in modern fossorial [digging] reptile scales, which may have been used to shed dirt."

If microsaurs are indeed early amniotes, *J. bolti*'s snakelike form (and the elongated body shapes of other microsaurs) offer a new perspective on how quickly animals' bodies diversified once they crawled onto dry land from the ocean. Most early amniotes look like small lizards, and current interpretation of the fossil record suggests that the transition to more diverse forms was slow. However, *J. bolti* and other long-bodied microsaurs suggest otherwise, Mann said.

"This means the evolution of amniotes was an explosive radiation, where as soon as they're on land, they diversify into all these different body forms," Mann said. "That's a much different narrative than what we currently think. We might have had diversity almost on par of what we see today, very quickly."

The findings were published July 21 in the journal Royal Society Open Science.

https://bit.ly/3y6Vswu

Australia's cockatoos are masters of dumpster diving—and now they're learning from each other

Sulphur-crested cockatoos have distinctive yellow crests, calls, and—according to a new study—dumpster-diving skills.

By Cathleen O'Grady

In recent years, some cockatoos living in the Sydney suburbs have figured out how to open household garbage cans, unlocking a food bonanza of sandwiches, fish bones, and fruit. Other cockatoos have picked up on the trick, and the behavior is quickly spreading. What's more, birds in different locations use slightly different methods to open the cans, making this the first time a parrot has been found with local foraging "subcultures," say the authors of the new paper.

A sulphur-crested cockatoo opens the lid of a household garbage can.
Barbara Klump/Max Planck Institute of Animal Behavior

To figure out the extent of the dumpster diving, behavioral ecologist Barbara Klump at the Max Planck Institute of Animal Behavior and her colleagues surveyed citizen scientists in Sydney. Through social media and mailing lists for organizations like the Royal Botanic Garden, they ran two public surveys in 2018 and 2019, asking residents whether they had seen such behavior—and, if so, when and where. More than 1300 people responded. The resulting map was far more accurate than many citizen science efforts because it included negative answers, says Corina Logan, a behavioral ecologist at the Max Planck Institute for Evolutionary Anthropology who wasn't involved in the new work. That "greatly increases the value of the study," she says.

Before 2018, cockatoo dumpster diving had only been reported in three suburbs. By late 2019, it had spread to 44 out of nearly 500 in the survey. And the spread had a clear pattern: It started near those three, original suburbs and trailed off as locations got farther and farther away, the researchers report today in *Science*. That suggests the birds were learning from one another and spreading the behavior through the city, Klump says. In one distant neighborhood, dumpster diving seemed to pop up on its own, suggesting that a new batch of cockatoos had hit on the strategy independently. There are also anecdotal reports of the behavior elsewhere in Australia, Klump says.

To get a clearer picture of what the raven-size cockatoos were doing, the researchers caught and marked 486 birds in some of the garbage can–opening hot spots. After filming 160 successful dives, they noted several common steps: First, a bird lifted the can's lid at the front corner with its bill; then, they held it slightly open while waddling toward the hinges; finally, they flipped up the lid suddenly so that it fell open and yielded its treasure trove of trash.

Individual birds used slightly different techniques: Some held the handle of the can's lid, whereas others just held onto the lid itself. And some held it with both bill and foot, whereas others just used the bill. The farther apart the dives were geographically, the more the birds' techniques differed. "That really means that they socially learn, not just that you *can* open [a garbage can], but how to open it," Klump says. It also suggests local knowledge about dumpster diving is passed along, creating "regional subcultures." Local cultures, or "dialects," have been found in parrot calls, but this is the first time it has been found in parrot foraging. That means cockatoos join a select group of animals, like some primates and whales, that have culture in both communication and food gathering.

The results are exciting—and the number of birds the researchers caught and marked for the study is "astronomical," Logan says: "Studying culture in wild populations is extremely difficult, because you have to track the start and spread of an innovation."

But Claudio Tennie, a cognitive scientist at the University of Tübingen, says the cockatoo culture conclusion is premature. It's a "neat study," he says, that does a good job showing the cockatoos learn from each other. But to show the birds have real cultures—the way humans have cultural differences in things like language or cooking—the researchers would have to clearly identify at least one can-opening sequence that is "locally unique," he says. The researchers found that the sequences broadly differed with distance, but they didn't show that any given technique was restricted to one place. "I like [the paper]," Tennie says. "But it's not the full monty. It's not like human culture—yet."

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Llama 'nanobodies' could hold key to preventing deadly post-transplant infection

Small fragment of a llama antibody is capable of chasing out human cytomegalovirus hiding away from the immune system

Scientists have developed a "nanobody"—a small fragment of a llama antibody—that is capable of chasing out human cytomegalovirus (HCMV) as it hides away from the immune system. This then enables immune cells to seek out and destroy this potentially deadly virus.

Around four out of five people in the UK are thought to be infected with HCMV, and in developing countries this can be as high as 95%. For the majority of people, the virus remains dormant, hidden away inside white blood cells, where it can remain undisturbed and undetected for decades. If the virus reactivates in a healthy individual, it does not usually cause symptoms. However, for people who are immunocompromised—for example, transplant recipients who need to take immunosuppressant drugs to prevent organ rejection—HCMV reactivation can be devastating.

At present, there is no effective vaccine against HCMV, and anti-viral drugs often prove ineffective or have very serious side-effects.

Now, in a study published in *Nature Communications*, researchers at Vrije Universiteit Amsterdam in the Netherlands and at the University of Cambridge have found a way to chase the virus from its hiding place using a special type of antibody known as a nanobody.

Nanobodies were first identified in camels and exist in all camelids—a family of animals that also includes dromedary, llamas and alpacas. Human antibodies consist of two heavy and two light chains of molecules, which together recognize and bind to markers on the surface of a cell or virus known as antigens. For this special class of camelid antibodies, however, only a single fragment of the antibody—often referred to as single domain antibody or nanobody—is sufficient to properly recognize antigens.

Dr. Timo De Groof from Vrije Universiteit Amsterdam, the study's joint first author, said: "As the name suggests, nanobodies are much smaller than regular antibodies, which make them perfectly suited for particular types of antigens and relatively easy to manufacture and adjust. That's why they're being hailed as having the potential to revolutionize antibody therapies."

The first nanobody has been approved and introduced onto the market by biopharmaceutical company Ablynx, while other nanobodies are already in clinical trials for diseases like rheumatoid arthritis and certain cancers. Now, the team in The Netherlands and the UK have developed nanobodies that target a specific virus protein (US28), one of the few elements detectable on the surface of a HCMV latently infected cell and a main driver of this latent state.

Dr. Ian Groves from the Department of Medicine at the University of Cambridge said: "Our team has shown that nanobodies derived from llamas have the potential to outwit human cytomegalovirus. This could be very important as the virus can cause life threating complications in people whose immune systems are not functioning

properly."

In laboratory experiments using blood infected with the virus, the team showed that the nanobody binds to the US28 protein and interrupts the signals established through the protein that help keep the virus in its dormant state. Once this control is broken, the local immune cells are able to 'see' that the cell is infected, enabling the host's immune cells to hunt down and kill the virus, purging the latent reservoir and clearing the blood of the virus.

Dr. Elizabeth Elder, joint first author, who carried out her work while at the University of Cambridge, said: "The beauty of this approach is that it reactivates the virus just enough to make it visible to the immune system, but not enough for it to do what a virus normally does—replicating and spreading. The virus is forced to put its head above the parapet where it can then be killed by the immune system."

Professor Martine Smit, also from from the Vrije Universiteit Amsterdam, added: "We believe our approach could lead to a much-needed new type of treatment for reducing—and potentially even preventing—CMV infectious in patients eligible for organ and stem cell transplants."

More information: *Timo W. M. De Groof et al, Targeting the latent human cytomegalovirus reservoir for T-cell-mediated killing with virus-specific nanobodies, Nature Communications (2021). DOI: 10.1038/s41467-021-24608-5*

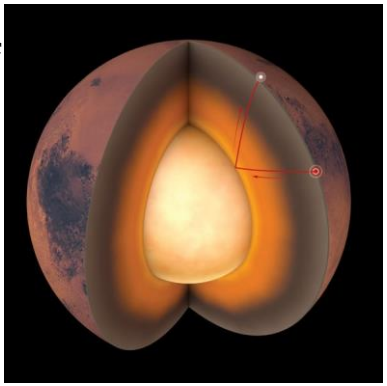
https://bit.ly/3zxaDj1

InSight Lander Makes Best-Yet Maps of Martian Depths

The NASA mission used seismic waves from marsquakes to perform a core-to-crust survey of the planet's subsurface

By Jonathan O'Callaghan

What lurks within the Red Planet? Although only a tenth as massive as Earth, Mars looks to have once been habitable like our own world, leading scientists to wonder whether such similarity cuts to the cores of both planets. In its innards, is Mars still a shrunken mirror of Earth, or is the interplanetary resemblance only crust-deep?



Tantalizing hints have been gleaned from gravitational data provided by past missions. But now the interior of Mars has been revealed as never before, thanks to unprecedented measurements from NASA's InSight lander.

In this illustration of Mars's interior, seismic waves (red lines) propagating from a "marsquake" (red dot) travel through the subsurface to reflect off the planet's iron-nickel core, eventually reaching NASA's InSight lander (white dot). The strength and timing of the waves reveals otherwise hidden details of the planet's interior. **Credit: Chris Bickel Science**

Shortly after reaching the Martian surface in late 2018, InSight has been monitoring seismic waves rippling through the planet and using the echoing reflections of these "marsquakes" to map the subsurface. Only Earth and its moon have previously been subjected to such deep scrutiny. The results show a world both like and unlike our own and offer a thrilling second data point in a vast universe of rocky orbs. "InSight is kind of like the first telescope looking into the interior of the planet," says Michael Meyer, lead scientist of NASA's Mars Exploration Program at the agency's headquarters.

InSight (Interior Exploration Using Seismic Investigations, Geodesy and Heat Transport) is not your typical Mars mission. Whereas others, such as the recently landed Perseverance, were sent to scientifically rich destinations that may have once supported life, InSight's landing zone in Elysium Planitia was decidedly mundane, described by some as a "parking lot." Flat and smooth—nearly featureless save for scattered rocks and impact craters—the site was the perfect place for the stationary lander to study the Martian

interior. The Seismic Experiment for Interior Structure (SEIS) instrument, provided by France's space agency and place gently on the surface by InSight's robotic arm in December 2018, was encased in a domed shield, allowing it to detect waves moving through Mars without interference from wind or dust storms. storms. SEIS "can see motions on the order of atomic-sized vibrations," says Andrew Lazarewicz of the Massachusetts Institute of Technology, who took part in a 1976 attempt to detect seismic waves with a seismometer on NASA's Viking 2 lander.

In a series of papers published today in the journal *Science*, researchers describe how they used this instrument to trace seismic waves caused by dozens of detected marsquakes through the Martian interior. These events were possibly caused by meteorites hitting the planet's surface or even by the stirrings of magma (some were localized to nearby Cerberus Fossae, a geologic formation displaying signs of recent volcanic activity). At less than magnitude 4 on the moment magnitude scale, all of these quakes were so small that they would be barely noticeable on Earth. But SEIS registered them clearly, allowing researchers to track their reverberations through the interior of Mars, all the way down to its core, revealing what was going on inside.

Simon Stähler of the Institute of Geophysics at the Swiss Federal Institute of Technology Zurich and his colleagues measured the waves' reflections off the core to calculate its size and bulk composition. They found that it is likely 1,830 kilometers in radius, several hundred kilometers larger than predicted. And the strength of the reflected waves suggested they were bouncing off a core mostly composed of molten iron and nickel. The size of the core was a "surprise," Stähler says. "People were assuming it must be on the order of 1,500 or 1,600 kilometers," based on the fact that, kilogram for kilogram, Mars is a bit less dense than Earth, and the core would be expected to be mostly iron and nickel, which is heavier than rock. Instead the results show that the ratio of Mars's core radius to its planetary radius is similar to that of Earth—which counterintuitively means the relatively low-density Martian core must be enriched with other elements, such as sulfur and oxygen, that are comparatively less abundant in our planet's core. Why Mars's core would have a different composition than ours is unclear. "If you assume that Mars was made from the same building blocks as Earth, then it is not so easy to explain," Stähler says.

Moving outward, Amir Khan of the Institute of Geophysics and his colleagues used the seismic waves to probe Mars's mantle, the region between the planet's core and surface crust. Although Earth has an insulating liquid lower mantle layer that sits above its core, there is no such feature on our neighboring world. "That lower mantle does not exist on Mars," Khan says. Instead, above the core, the lower mantle of Mars resembles the upper mantle of Earth, which then gives way to a higher layer, colder and more brittle, called the lithosphere. Mars's lithosphere, the study shows, is about 500 kilometers in thickness, compared with Earth's approximately 250-kilometer-thick lithosphere. Such a thick lithosphere, Khan says, could be why Mars lacks plate tectonics today. This unearthly configuration of subsurface layers could also explain how the Red Planet lost its heat because, unlike Earth, it lacks an insulating liquid mantle layer above its core.

At the surface, Brigitte Knapmeyer-Endrun of the University of Cologne in Germany and her colleagues measured the thickness of the Martian crust. They found two possibilities for the crust under InSight: One interpretation of the data suggests a two-layer crust like that of Earth with a thickness of 20 kilometers. The other hints at the presence of three layers totaling 39 kilometers in thickness. For the planet as a whole, the researchers estimate a crustal thickness of up to 72 kilometers, several dozens of kilometers thinner than predicted. If accurate, that estimate could be an

important window into the fundamental differences between how Earth and Mars first formed. “Most of the crust is really old and is from really early on the planet, whereas on Earth, we have a lot of recycling going on due to plate tectonics,” Knapmeyer-Endrun says. The results as a whole reveal intriguing differences between Earth and Mars. “What they’ve done with this single instrument is remarkable,” Lazarewicz says. Despite being rocky worlds that arose in relatively close proximity to the sun, these two planets may not have formed in the same way. They could have, say, coalesced from different mixes of materials that circulated in the disk of gas and dust that surrounded the young sun. Additionally, if InSight manages to seismically probe Mars’s inner core during its mission, that could help settle the long-standing mystery of how the planet lost its protective magnetic field, an event that is thought to have occurred perhaps four billion years ago and that may have allowed solar winds to sweep away much of the world’s atmosphere.

It was not until 1889 that we made our first measurements of seismic waves passing through Earth’s mantle, getting a glimpse at our own world’s interior. Now, more than a century later, we have our first comparative measurements for another planet in the universe, although these may be but a teaser of what is yet to come as scientists delve deeper into InSight’s data. “Now that we know how large the core is, and we know more about the crust and mantle, we can reinterpret the events we’ve detected so far in light of the interior model we have now,” Stähler says.

https://nyti.ms/2VqGea0

Outbreaks of Untreatable, Drug-Resistant Fungus Spread in 2 Cities

For the first time, the C.D.C. identified several cases of Candida auris that were resistant to all drugs, in two health facilities in Texas and a long-term care center in Washington, D.C.

By Andrew Jacobs

A deadly, hard-to-treat fungal infection that has been spreading through nursing homes and hospitals across the United States is becoming even more dangerous, according to researchers, who for the first time have identified several cases in which the fungus, Candida auris, was completely impervious to all existing medication.

The finding, released Thursday by the Centers for Disease Control and Prevention, is an alarming development in the evolution of C. auris, a tenacious yeast infection discovered in Japan in 2009 that has since spread across much of the world.

Federal health officials say the bug has spread even more widely during the coronavirus pandemic, with overwhelmed hospitals and nursing homes struggling to keep up with the surveillance and control measures needed to contain local outbreaks.

In the new report, the C.D.C. said, five of more than 120 cases of C. auris were resistant to treatment.

The C.D.C. did not identify the facilities where the novel infections took place, but health officials said there was no evident link between the outbreaks, which occurred in Texas at a hospital and a long-term care facility that share patients, and at a single long-term care center in Washington, D.C. The outbreaks took place between January and April.

Nearly a third of the infected patients died within 30 days, according to the C.D.C., but because they were already gravely ill, officials said it was unclear whether their deaths were caused by the fungus.

Over the past eight years, the C.D.C. has identified more than 2,000 Americans colonized with C. auris — meaning the fungus was detected on their skin — with most cases concentrated in New York, New Jersey, Illinois and California. Between 5 and 10 percent of those colonized with the pathogen go on to develop more serious bloodstream infections.

Once it gains a foothold, the fungus is difficult to eliminate from health care facilities, clinging to cleaning carts, intravenous poles and other medical equipment. While relatively harmless to those in good health, the yeast infection can be deadly to seriously ill hospital patients, residents of long-term care facilities and others with weakened immune systems.

"If you wanted to conjure up a nightmare scenario for a drug-resistant pathogen, this would be it," said Dr. Cornelius J. Clancy, an infectious diseases doctor at the VA Pittsburgh Health Care System. "An untreatable fungus infection would pose a grave threat to the immunocompromised, transplant recipients and critically ill patients in the I.C.U."

While C. auris has long been notoriously hard to treat, researchers for the first time identified five patients in Texas and Washington, D.C., whose infections did not respond to any of the three major classes of antifungal medication. So-called panresistance had been previously reported in three patients in New York who were being treated for C. auris, but health officials said the newly reported panresistant infections occurred in patients who had never received antifungal drugs, said Dr. Meghan Lyman, a medical officer at the C.D.C. who specializes in fungal diseases.

"The concerning thing is that the patients at risk are no longer the small population of people who have infections and are already being treated with these medications," she said.

Infectious disease specialists say the coronavirus pandemic has probably accelerated the spread of the fungus. The shortages of personal protective equipment that hobbled health care workers during the early months of the pandemic, they say, increased opportunities for the fungus's transmission, especially among the thousands of Covid-19 patients who ended up on invasive mechanical ventilation.

The chaos of recent months also did not help. "Infection control efforts at most heath care systems are stretched thin in the best of times, but with so many Covid patients, resources that might have gone to infection control were diverted elsewhere," Dr. Clancy said.

For many health experts, the emergence of a panresistant C. auris is a sobering reminder about the threats posed by antimicrobial resistance, from superbugs like MRSA to antibiotic-resistant salmonella. Such infections sicken 2.8 million Americans a year and kill 35,000, according to the C.D.C.

Dr. Michael S. Phillips, chief epidemiologist at NYU/Langone Health, said health systems across the country were struggling to contain the spread of such pathogens. The problem, he said, was especially acute in big cities like New York, where seriously ill patients shuttle between nursing homes with lax infection control and top-notch medical centers that often draw patients from across a wider region.

"We need to do a better job at surveillance and infection control, especially in places where we put patients in group settings," he said. "Candida auris is something we should be concerned about, but we can't lose sight of the bigger picture because there are a lot of other drug-resistant bugs out there we should be worried about."

https://bit.ly/3i4hpaf

Why do some people get severe COVID-19? The nose may know

People who develop severe COVID-19 have markedly blunted antiviral responses in the nasopharynx

The body's first encounter with SARS-CoV-2, the virus behind COVID-19, happens in the nose and throat, or nasopharynx. A new study in the journal *Cell* suggests that the first responses in this battleground help determine who will develop severe disease and who will get through with mild or no illness.

Building on work published last year identifying SARS-CoV-2-susceptible cells, a team of collaborators at Boston Children's

Hospital, MIT, and the University of Mississippi Medical Center comprehensively mapped SARS-CoV-2 infection in the nasopharynx. They obtained samples from the nasal swabs of 35 adults with COVID-19 from April to September 2020, ranging from mildly symptomatic to critically ill. They also got swabs from 17 control subjects and six patients who were intubated but did not have COVID-19.

"Why some people get more sick than others has been one of the most puzzling aspects of this virus from the beginning," says José Ordovás-Montañés, PhD, of Boston Children's, co-senior investigator on the study with Bruce Horwitz, MD, PhD of Boston Children's, Alex K. Shalek, PhD, of MIT and Sarah Glover, DO, of the University of Mississippi. "Many studies looking for risk predictors have looked for signatures in the blood, but blood may not really be the right place to look."

COVID-19's first battlefield: the nasopharynx

To get a detailed picture of what happens in the nasopharynx, the researchers sequenced the RNA in each cell, one cell at a time. (For a sense of all the work this entailed, each patient swab yielded an average of 562 cells.) The RNA data enabled the team to pinpoint which cells were present, which contained RNA originating from the virus -- an indication of infection -- and which genes the cells were turning on and off in response.

It soon became clear that the epithelial cells lining the nose and throat undergo major changes in the presence of SARS-CoV-2. The cells diversified in type overall. There was an increase in mucus-producing secretory and goblet cells. At the same time, there was a striking loss of mature ciliated cells, which sweep the airways, together with an increase in immature ciliated cells (which were perhaps trying to compensate).

The team found SARS-CoV-2 RNA in a a diverse range of cell types, including immature ciliated cells and specific subtypes of secretory cells, goblet cells, and squamous cells. The infected cells, as compared to the uninfected "bystander" cells, had more genes turned on that are involved in a productive response to infection.

A failed early immune response

- The key finding came when the team compared nasopharyngeal swabs from people with different severity of COVID-19 illness:

In people with mild or moderate COVID-19, epithelial cells showed increased activation of genes involved with antiviral responses -- especially genes stimulated by type I interferon, a very early alarm that rallies the broader immune system.

- In people who developed severe COVID-19, requiring mechanical ventilation, antiviral responses were markedly blunted. In particular, their epithelial cells had a muted response to interferon, despite harboring high amounts of virus. At the same time, their swabs had increased numbers of macrophages and other immune cells that boost inflammatory responses.

"Everyone with severe COVID-19 had a blunted interferon response early on in their epithelial cells, and were never able to ramp up a defense," says Ordovás-Montañés. "Having the right amount of interferon at the right time could be at the crux of dealing with SARS-CoV-2 and other viruses."

Boosting interferon responses in the nose?

As a next step, the researchers plan to investigate what is causing the muted interferon response in the nasopharynx, which evidence suggests may also occur with the new SARS-CoV-2 variants. They will also explore the possibility of augmenting the interferon response in people with early COVID-19 infections, perhaps with a nasal spray or drops.

"It's likely that, regardless of the reason, people with a muted interferon response will be susceptible to future infections beyond COVID-19," Ordovás-Montañés says. "The question is, 'How do you make these cells more responsive?'"

Other recent COVID-19 research at Boston Children's Hospital

Carly Ziegler, Vincent Miao, Andrew Navia, and Joshua Bromley of MIT and Harvard; Anna Owings of the University of Mississippi; and Ying Tang of Boston Children's Hospital were co-first authors on the paper. Funders include the Chan Zuckerberg Initiative DAF, the National Institutes of Health, the New York Stem Cell Foundation, the Richard and Susan Smith Family Foundation, the AGA Research Foundation, the Food Allergy Science Initiative, The Leona M. and Harry B. Helmsley Charitable Trust, the Crohn's and Colitis Foundation, the Bill and Melinda Gates Foundation, and the Ragon Institute of MGH, MIT and Harvard.

https://bit.ly/2VgvQ20

Tomatoes have a kind of nervous system that warns about attacks

Tomatoes that are being eaten by insects use electrical signals to send an alert to the rest of the plant, similar to the way our nervous systems warn of damage.

By Clare Wilson

The messages seem to help the plant muster defences such as releasing hydrogen peroxide, a reactive chemical that combats microbial infections of damaged tissues, a study has found.

Human nervous systems use specialised cells called neurons to send electrical signals between different parts of the body. Plants lack neurons, but they do have long, thin tubes called xylem and phloem for moving sap between their roots, leaves and fruit. Charged ions flowing in and out of these tubes can propagate electrical signals around different parts of the plant in a similar way to neurons, although much less is known about the process in plants than in animals.

Previous work found that leaves that are physically damaged send electrical signals to other leaves. In a new study, Gabriela Niemeyer Reissig at the Federal University of Pelotas in Brazil and her colleagues investigated if this could happen with fruit.

They studied small cherry tomato plants (tomatoes are a fruit, botanically speaking) by placing them inside Faraday cages, which block external electric fields, and confined caterpillars of the moth *Helicoverpa armigera* on the surface of fruit within plastic bags.

Electrodes placed in the fruit stalks showed that the patterns of electrical activity changed during and after the caterpillars started eating. They also varied depending on whether the fruits were ripe or green. "The electrical activity of the fruit is constantly changing every second," says Niemeyer Reissig. "We can find a [distinct] pattern in the electrical activity when an insect attacks."

There was also a rise in levels of hydrogen peroxide produced by untouched fruit and leaves all over an attacked plant. "This is probably to avoid microbial infections of damaged plant tissue or as a strategy to cause cell death in the affected region, preventing the spread of pathogens," says Niemeyer Reissig.

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