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There's a Link Between Air Pollution And Irreversible Vision Loss, Study Reveals

Study finds a link between fine particle air pollution and macular degeneration

Clare Watson

Air pollution could cloud your vision in later life, according to a large study that found a link between fine particle air pollution and macular degeneration, an age-related eye disease that can lead to irreversible blindness.

The findings serve as a clear reminder of the many ways that air pollution can be harmful to our health, even though it's still early days for this research.

"Our findings add to the growing evidence of the damaging effects of ambient air pollution, even in the setting of relative low exposure of ambient air pollution," the study authors write in their paper.

Air pollution is a global problem many can't escape, with the World Health Organisation (WHO) estimating over 90 per cent of the world's population lives in places where air quality levels exceed the limits set for pollutants that pose health risks.

The biggest public health concerns about poor air quality circle around pollutants such as particulate matter (dust, soot, and more), ground-level ozone, nitrogen dioxide, sulfur dioxide and other gases, which are emitted from motor vehicles, heavy industry, and wood fires. Fine particles, called $PM_{2.5}$ for short, are especially concerning. These microscopic particles less than 2.5 micrometres in size can penetrate deep into the lungs and enter the bloodstream, causing inflammation around the body.

Repeated exposure to pollutants like these can irritate people's eyes and throat, cause breathing difficulties. Furthermore, ambient air pollution accounts for 43 percent of deaths from chronic obstructive pulmonary disease, and for over a quarter of all deaths from lung cancer, heart disease, or stroke.

In this study, the focus was on age-related macular degeneration (AMD), a condition where a person's vision worsens with age, leading to increased vision loss and potentially even blindness.

The disease is linked to leaky blood vessels in the back of the eye and small blobs of fat and protein that build up on the macula, the part of the eye at the centre of the retina. Genetics and being a smoker are amongst the main risk factors for this condition.

For their analysis, the researchers pulled data on thousands of people enrolled in the UK Biobank and estimated the annual air pollution levels around their homes using other publicly available datasets. From 2006 onwards, almost 116,000 people were asked to report if their doctor diagnosed them with macular degeneration.

Of that larger group, 52,062 people also had their eyesight examined and retinal thickness measured, as an indicator of any changes to their eye health.

What the study found is that people who were exposed to higher levels of fine particle air pollution had higher rates of self-reported AMD. Exposure to other pollutants, including nitrogen dioxide but not coarse particulate matter, was also associated with changes in retina thickness, detected on imaging.

But don't be swayed by the big numbers alone. Only a tiny fraction of people were actually diagnosed with AMD during the study – and remember, while this observational study can bring our attention to trends and patterns observed across a population, it can't establish a cause.

In other words, researchers do what they can in population-wide studies like these to account for other factors, such as lifestyle, that influence disease risk but suffice to say, trying to untangle the precise health impacts of exposure to air pollution in a world where everything is interconnected is not always clear cut.

The researchers suggest that air pollution may affect the eye in a roundabout way through inflammation and oxidative stress, two defence mechanisms where the body is fighting against foreign material and trying to detoxify chemical species, respectively. But more research will be required to examine that plausible link.

It's not the first time though that air pollution has been linked to eye disease. A 2019 study examining the global burden of glaucoma found higher average levels of fine particulates were associated with more cases of glaucoma, which affects the optic nerve.

"The good news is that ambient air pollution can be controlled and the diseases it causes prevented," writes Philip Landrigan, a public health physician and epidemiologist from Icahn School of Medicine at Mount Sinai, New York, who was not involved in the study.

Enforcing air quality standards and reducing emissions from coal-fired power plants – by transitioning to clean fuels and ultimately to renewable energy sources – would both be effective strategies for reducing air pollution.

We saw how quickly the skies cleared in the first few months of the coronavirus pandemic, which grounded air traffic and pulled cars off the road as people stayed at home. Although such drastic changes weren't ultimately sustainable, the momentary relief from the air pollution that usually blankets cities has shown us what's possible.

"Cities and countries will need to switch to non-polluting energy sources, encourage active commuting, enhance their transportation networks, [and] redesign industrial processes to eliminate waste," writes Landrigan. "These changes will not be easy. They will need to overcome strong opposition by powerful vested interests. But, fortunately, the technical, institutional, and policy tools needed to control air pollution are already at hand."

In the meantime, more research will be needed to build the evidence around the long-term risks that air pollution poses to eye health. The research was published in the *British Journal of Ophthalmology*.

https://bit.ly/3attn9o

Novel Theory Explains Possible Origin of Dinosaur-Killing Chicxulub Impactor

New theory that could explain the origin and journey of the Chicxulub impactor

At the end of the Cretaceous period, about 66 million years ago, a 10-km impactor crashed into Earth near the site of the small town of Chicxulub in what is now Mexico. The impact unleashed an incredible amount of climate-changing gases into the atmosphere, triggering a chain of events that led to the extinction of non-avian dinosaurs and 75% of life on the planet. In a new paper published in the journal *Scientific Reports*, Harvard University astrophysicists Amir Siraj and Professor Avi Loeb put forth a new theory that could explain the origin and journey of the Chicxulub impactor.

A popular theory on the origin of the Chicxulub impactor claims that the object originated from the main belt, which is an asteroid population between the orbit of Jupiter and Mars.

Evidence found at the Chicxulub crater suggests the rock was composed of carbonaceous chondrite. However, carbonaceous chondrites are rare amongst main-belt asteroids, but possibly widespread amongst long-period comets, providing additional support to the cometary impact hypothesis.

Using statistical analysis and gravitational simulations, Siraj and Professor Loeb calculate that a significant fraction of long-period comets originating from the Oort cloud, an icy sphere of debris at the edge of the Solar System, can be bumped off-course by Jupiter’s gravitational field during orbit.

“The Solar System acts as a kind of pinball machine. Jupiter, the most massive planet, kicks incoming long-period comets into orbits that bring them very close to the Sun,” Siraj said.

During close passage to the Sun, the comets — nicknamed sungrazers — can experience powerful tidal forces that break apart pieces of the rock and ultimately, produce cometary shrapnel.

"In a sungrazing event, the portion of the comet closer to the sun feels a stronger gravitational pull than the part that is further, resulting in a tidal force across the object," Siraj said.

"You can get what's called a tidal disruption event, in which a large comet breaks up into many smaller pieces. And crucially, on the journey back to the Oort cloud, there's an enhanced probability that one of these fragments hit the Earth."

The new calculations increase the chances of long-period comets impacting Earth by a factor of about 10, and show that about 20% of long-period comets become sungrazers.

This rate is consistent with the age of Chicxulub, providing a satisfactory explanation for its origin and other impactors like it.

"Our paper provides a basis for explaining the occurrence of this event," Professor Loeb said. "We are suggesting that, in fact, if you break up an object as it comes close to the Sun, it could give rise to the appropriate event rate and also the kind of impact that killed the dinosaurs."

A. Siraj & A. Loeb. 2021. Breakup of a long-period comet as the origin of the dinosaur extinction. Sci Rep 11, 3803; doi: 10.1038/s41598-021-82320-2

http://nyti.ms/2ZmDDd5

Scientists Are Trying to Spot New Viruses Before They Cause Pandemics

Scientists want to build a weather system for viruses. It would require a big financial investment, plus buy-in from doctors, hospitals and blood banks.

By Veronique Greenwood

Back in the summer, Dr. Michael Mina made a deal with a cold storage company. With many of its restaurant clients closed down, the firm had freezers to spare. And Dr. Mina, an epidemiologist at the Harvard T.H. Chan School of Public Health, had a half-million vials of plasma from human blood coming to his lab from across the country, samples dating back to the carefree days of January 2020.

The vials, now in three hulking freezers outside Dr. Mina's lab, are at the center of a pilot project for what he and his collaborators call the Global Immunological Observatory. They envision an immense surveillance system that can check blood from all over the world for the presence of antibodies to hundreds of viruses at once. That way, when the next pandemic washes over us, scientists will have detailed, real-time information on how many people have been infected by the virus and how their bodies responded.

It might even offer some early notice, like a tornado warning. Although this monitoring system will not be able to detect new viruses or variants directly, it could show when large numbers of people start acquiring immunity to a particular kind of virus.

The human immune system keeps a record of pathogens it has met before, in the form of antibodies that fight against them and then stick around for life. By testing for these antibodies, scientists can get a snapshot of which flu viruses you have had, what that rhinovirus was that breezed through you last fall, even whether you had a respiratory syncytial virus as a child. Even if an infection never made you sick, it would still be picked up by this diagnostic method, called serological testing. "We're all like little recorders," keeping track of viruses without realizing it, Dr. Mina said.

Spotting Patterns

This type of readout from the immune system is different from a test that looks for an active viral infection. The immune system starts to produce antibodies one to two weeks after an infection begins, so serology is retrospective, looking back at what you have caught. Also, closely related viruses may produce similar responses, provoking antibodies that bind to the same kinds of viral proteins.

That means carefully designed assays are needed to distinguish between different coronaviruses, for example.

But serology uncovers things that virus testing does not, said Derek Cummings, an epidemiologist at the University of Florida. With a large database of samples and clinical details, scientists can begin to see patterns emerge in how the immune system responds in someone with no symptoms compared to someone struggling to clear the virus. Serology can also reveal before an outbreak starts whether a population has robust immunity to a given virus, or if it is dangerously low. "You want to understand what has happened in a population, and how prepared that population is for future attacks of a particular pathogen," Dr. Cummings said.

The approach could also detect events in the viral ecosystem that otherwise go unnoticed, Dr. Cummings said. For example, the 2015 Zika outbreak was detected by doctors in Brazil who noticed a cluster of babies with abnormally small heads, born seven to nine months after their mothers were infected. "A serological observatory could conceivably have picked this up before then," he said.

Serological surveys are often small and difficult to set up, since they require drawing blood from volunteers. But for several years Dr. Mina and his colleagues have been discussing the idea of a large and automated surveillance system using leftover samples from routine lab tests.

"Had we had it set up in 2019, then when this virus hit the U.S., we would have had ready access to data that would have allowed us to see it circulating in New York City, for example, without doing anything different," Dr. Mina said.

Although the observatory would not have been able to identify the new coronavirus, it would have revealed an unusually high number of infections from the coronavirus family, which includes those that cause common colds. It might also have shown that the new coronavirus was interacting with patients' immune systems in unexpected ways, resulting in telltale markers in the blood. That would have been a signal to start genetic sequencing of patient samples, to identify the culprit, and might have provided grounds to shut down the city earlier, Dr. Mina said. (Similarly, serology would not be able to spot the emergency of a new virus variant, like the contagious coronavirus variants that were discovered in South Africa and England before spreading elsewhere. For that, researchers must rely on standard genomic sequencing of virus test samples.)

A Powerful Investment

The observatory would require agreements with hospitals, blood banks and other sources of blood, as well as a system for acquiring consent from patients and donors. It also faces the problem of financing, noted Alex Greninger, a virologist at the University of Washington. Health insurance companies would be unlikely to foot the bill, since serology tests are usually not used by doctors to treat people.

Dr. Mina estimated that the observatory would cost about $100 million to get off the ground. He pointed out that, according to his calculations, the federal government has allocated more than twice that much to diagnostics company Ellume to produce enough rapid Covid tests to cover the American demand for only a handful of days. A pathogen observatory, he said, is like a weather forecasting system that draws on vast numbers of buoys and sensors around the globe, passively reporting on events where and when they arise. These systems have been funded by government grants and are widely valued.

The predictive power of serology is worth the investment, said Jessica Metcalf, an epidemiologist at Princeton and one of the observatory team members. A few years ago, she and her collaborators found in a smaller survey that immunity to measles

was ominously low in Madagascar. Indeed, in 2018 an outbreak took hold, killing more than 10,000 children.

Now, the half-million plasma samples in Dr. Mina's freezers, collected by the plasma donation company Octopharma from sites across the country last year, are starting to undergo serological tests focused on the new coronavirus, funded by a $2 million grant from Open Philanthropy. Testing had to wait for the researchers to set up a new robotic testing facility and process the samples, but now they are working through their first batches.

The team hopes to use this data to show how the virus flowed into the United States, week by week, and how immunity to Covid has grown and changed. They also hope it will spark interest in using serology to illuminate the movement of many more viruses.

"The big idea is to show the world that you don't have to spend huge dollars to do this kind of work," Dr. Mina said. "We should have this happening all the time."

http://bit.ly/2NAcn8A

Keeping schools open without masks or quarantines doubled Swedish teachers' COVID-19 risk

Keeping schools open with only minimal precautions doubled teachers' risk of being diagnosed with coronavirus

By Gretchen Vogel

A careful analysis of health data from Sweden suggests keeping schools open with only minimal precautions in the spring roughly doubled teachers' risk of being diagnosed with the pandemic coronavirus. Their partners faced a 29% higher risk of becoming infected than partners of teachers who shifted to teaching online. Parents of children in school were 17% more likely to be diagnosed with COVID-19 than those whose children were in remote learning. Whether the harms of school closures outweigh the risks of virus transmission in classrooms and hallways has been the subject of intense debate around the world. Outbreaks have demonstrated that the virus can spread via schools to the wider community at least occasionally, and some data suggest teachers have higher than average risk of infection. However, it has been difficult to separate school-based transmission from other confounding factors, especially because schools have tended to open or close in concert with other restrictions lifting or tightening.

Coming out the same week as new guidelines for opening schools from the U.S. Centers for Disease Control and Prevention, the new study will help policymakers better understand and weigh the risks and benefits. "It's just great to see such a carefully done study," says Anita Cicero, an expert in pandemic response policy at the Johns Hopkins University Bloomberg School of Public Health. "We've been starved for studies" that quantify the impact of open or closed schools on wider community transmission.

In March 2020, schools around the world closed as governments tried to keep SARS-CoV-2 in check. But children in Sweden through ninth grade continued to attend class, while 10th through 12th graders shifted to remote learning. Economists Jonas Vlachos, Helena Svaleryd, and Edvin Hertegård at Uppsala University took advantage of this natural experiment and Sweden's detailed health care data.

They compared infection rates of parents whose youngest child was in ninth grade with those whose youngest was in 10th grade. They also compared infection rates in teachers who continued to teach in person at lower secondary schools (grades seven to nine) with those of teachers at upper secondary schools (grades 10 to 12), who taught remotely. Finally, they compared infection rates in the spouses of teachers in the two types of schools. They describe their results in a paper posted on 12 February in the *Proceedings of the National Academy of Sciences*.

The authors took steps to make sure their groups were as comparable as possible. For example, they excluded families with

health care workers from the study because they had more exposure to the virus and were tested more frequently. Sweden's coronavirus testing was very limited in the spring, swabbing only people with moderate to severe symptoms. Although this missed many cases, Vlachos says, it was actually an advantage for their analysis. As testing increased in the summer and fall, testing rates started to correlate more with income, which would have skewed the findings. (So few children and teens were tested that the researchers couldn't draw conclusions about their infection rates.)

Swedish schools instituted only relatively mild precautions against infection in the spring. Health authorities encouraged pupils and teachers to wash or disinfect their hands regularly, keep their distance when possible, and stay home when ill. But neither teachers nor students wore masks, and close contacts of confirmed cases were not quarantined.

The impact on teachers was significant, the authors say, and the results underscore the need to prioritize educators in COVID-19 vaccination schedules. Whereas teachers at upper secondary schools had an average infection risk among 124 occupations in Sweden, the researchers found, lower secondary teachers ranked seventh. (Primary school teachers had a somewhat lower, but still above average, risk.)

Among the country's 39,000 teachers in lower secondary schools, 79 were hospitalized with COVID-19 between March and June 2020, and one died. Shifting these schools to online learning would have prevented perhaps 33 of those severe cases, the authors estimate.

Adding masks would likely have reduced the risks to both teachers and families, says Danny Benjamin, a pediatrician at Duke University who has studied the spread of the pandemic coronavirus in North Carolina schools. But the Swedish study shows that "even if schools do not require masking, risk to families of in-person schooling is low," he says.

Vlachos agrees that more interventions would reduce risk further. "Our estimates are likely an upper bound," he says.

The authors calculated that keeping lower secondary schools open likely led to 500 additional detected cases in the spring among the 450,000 parents with kids in lower secondary school and 38 additional cases among teachers' partners. (Because testing was so limited, the real number of additional infections was likely much higher, the authors note.)

"The results for parents provide perhaps the best evidence of how school closure impacts virus transmission in society," says Douglas Almond, an economist at Columbia University. By comparing families with ninth graders and 10th graders, the team was able to compare families with teenagers whose social behavior and viral risk were similar, he says. "This is where their natural experiment really shines." The ability to link teachers to their spouses through the health registries "is also quite elegant," says Jonas Björk, an epidemiologist at Lund University.

"It is to be expected that opening schools can increase COVID-19 infections, but knowing that does not really inform policy," Almond says. "One needs to know *how much* infections increase due to school reopening. This is the best paper I know of that quantifies this effect."

More comparisons of schools with different policies regarding masks, distancing, and quarantines would be helpful, Cicero says. Using the Swedish health registry, the researchers could even take the analysis a step further and look at risk to parents of teachers, Björk says, which would help estimate the impact on a more vulnerable age group.

The emergence of more transmissible variants of SARS-CoV-2 means mask wearing and other interventions to prevent school transmission are even more important, Benjamin says. Cicero

agrees. “That is the next step” for research, too, she says: funding studies on the impact of the variants, and which interventions can keep risks at schools as low as possible.

***Correction, 16 February, 2:35 a.m.:** This story has been corrected to say the study could be extended to parents of teachers, not grandparents of students.*

http://bit.ly/3pzPMq4

The Colossal Weight of Cities Is Making Them Sink, Even as Sea Levels Are Rising

Cities are slowly sinking under the weight of their own development

David Nield

Cities don't just have sea level rises to worry about – they're also slowly sinking under the weight of their own development, according to new research, which emphasises the importance of factoring subsidence into models of climate change risk.

Geophysicist Tom Parsons, from the United States Geological Survey (USGS) agency, looked at San Francisco as a case study of how large urban developments could be affecting and depressing the actual surface of the Earth.

By his calculations, San Francisco might have sunk as much as 80 millimetres (3.1 inches) as the city has grown over time. Considering the Bay Area is under threat from as much as 300 mm (11.8 inches) of sea level rise by 2050, the extra variation added by slow subsidence is significant enough to be concerning.

"As global populations move disproportionately toward the coasts, this additional subsidence in combination with expected sea level rise may exacerbate risk associated with inundation," writes Parsons in his paper.

Taking into account an inventory of all the buildings in the city and their contents, the study calculated the weight of the San Francisco Bay Area (population: 7.75 million) as being around 1.6 trillion kilograms – about 3.5 trillion pounds, or roughly 8.7 million Boeing 747s.

That could be enough to both bend the actual lithosphere on which the urban centre sits, and perhaps more significantly, to change the relative levels of fault blocks – the floating chunks of rock that make up Earth's surface.

In fact the 80 mm of slip is likely to be a conservative estimate, as the weight calculations didn't include things outside buildings – including transport infrastructure, vehicles, or people. The same sort of sinking is likely in other parts of the world, though it partially depends on the local geology.

"The specific results found for the San Francisco Bay Area are likely to apply to any major urban centre, though with varying importance," writes Parsons.

"Anthropogenic loading effects at tectonically active continental margins are likely greater than more stable continental interiors where the lithosphere tends to be thicker and more rigid."

There are plenty of other causes of subsidence to think about too, including tectonic plate shifting and the groundwater pumping necessary to support a growing population – something we've seen cause significant city sinking in other parts of the world.

While this current study only looked at San Francisco and the Bay Area, and made some broad assumptions in terms of modelling, the findings are notable enough to make city weight another consideration when scientists are figuring out how geography might change over time, and which areas are under threat as the sea level gets higher.

There's still plenty of detail to dig into as well, particularly in cities already under threat from subsidence. The compaction of sediment and aquifer systems under San Francisco International Airport on the coast – the heaviest building in the city – has already been calculated as causing 4 mm (0.16 inches) of sinking each year.

"It should be possible to improve on the methods presented here by

using satellite or air photos to make more detailed analyses in likely flood zones," writes Parsons.

"Such detailed analyses might also yield better insights about changes to subsurface porosity changes and resultant fluid flow."

The research has been published in *AGU Advances*.

https://bit.ly/37Ln8w7

Sooty Layers in Stalagmites Record Human Activity in Caves

Scientists analyzing cave formations in Turkey find layers of soot and charcoal in stalagmites, revealing that humans—and their fires—occupied caves thousands of years ago.

By Katherine Kornei

Caves have long been used as places of shelter, burial, and ritual. Now, researchers have analyzed stalagmites from two caves in southwestern Turkey and found that they contain layers of soot and charcoal, presumably from human-set fires. By precisely dating the stalagmite layers bracketing this black carbon, the scientists estimated that people were exploring these caves thousands of years ago. These results reveal how geophysical data can complement archaeological records, the team concluded.

The Allure of Caves

To many ancient cultures, the dark passageways of caves represented a metaphorical connection to another world. Even today, with the advent of powerful flashlights that slice through darkness, caves are still alluring—the National Speleological Society, a nonprofit organization devoted to cave exploration, counts more than 7,000 members. "They're special places," said Koray Koç, a paleoclimatologist at Akdeniz University in Antalya, Turkey.

In 2015, Koç and his colleagues headed underground to explore several caves in southwestern Turkey. Spelunking is always an adventure, said Koç, and these trips were no exception. In one cave, the team had to shimmy though an extremely narrow passageway barely wider than a person, and they found human and animal remains in addition to pieces of pottery.

Natural Record Keepers

Koç and his collaborators observed many stalagmites and stalactites. Because speleothems like these grow slowly over time, they're record keepers of past environmental conditions: Scientists have used them to reconstruct droughts and climate variability, among other changes. Koç and his colleagues collected 16 stalagmites, the shortest about the length of a pinkie finger and the longest topping a meter.

Back in the laboratory, the scientists split the stalagmites lengthwise to reveal their interior layers. They were astonished to find that 14 of the stalagmites were shot through with black layers of soot and charcoal up to a millimeter thick and easily visible to the naked eye. That discovery changed the direction of the investigation, said Koç.

The researchers had initially been planning to use the stalagmites to reconstruct the ancient climate in the region. "Our main purpose was to collect clean and suitable samples for paleoclimate research," said Koç. But now the hunt was on to better understand these layers.

Koç and his colleagues focused on three stalagmites from Tabak Cave and Kocain Cave with particularly well defined black layers. These layers reveal a human presence in these caves, the researchers suggest.

Evidence of Fires

The black layers in the speleothems are the result of people carrying torches or setting fires in the caves, Koç and his collaborators say. Combustion releases particles of black charcoal that hitch a ride on air currents, and in a cave, some of these particles are bound to end up sticking to growing stalagmites. (The same effect can be seen today on the stone surfaces of old buildings exposed to pollution.)

The researchers estimated the ages of the speleothems' normal layers using uranium-thorium dating. By tabulating the ages of layers adjacent to each band of soot and charcoal, they estimated when the black carbon was deposited and therefore when humans were exploring these caves.

A Summer Refuge?

Koç and his colleagues found three layers of soot and charcoal in the stalagmites from Tabak Cave. They dated the layers to roughly 6,700, 7,100, and 7,400 years before present (i.e., before 1950 CE), with an uncertainty of about 200 years. That's surprisingly early, said Koç, but it makes sense that people were inhabiting these caves. Turkey is notoriously hot in June, July, and August, so maybe these caves functioned as a refuge from the heat, he said. "People might have used these caves as a shelter during the summer."

It's unlikely that these layers of black carbon are due to nonanthropogenic triggers like far-away wildfires, the researchers suggest. That's because the ventilation in Tabak Cave is poor—airborne particles circulating aboveground probably wouldn't have traveled far into the cave. (The stalagmites the researchers analyzed were tens of meters—and several narrow passageways—beyond the entrance.) Furthermore, archaeological artifacts like pottery sherds found in Tabak Cave confirm a human presence deep underground that probably needed a source of light.

The stalagmite from Kocain Cave exhibited a wider spread in the ages of its five soot and charcoal layers: 470, 810, 1,500, 1,700, and 2,800 years before present. It's possible that some of these layers derive from aboveground fires, the researchers acknowledge, because of Kocain Cave's wide, open entrance and lack of narrow passageways.

These results are an important demonstration of the value of geophysical data, said Koç. The ability to precisely age date a speleothem has the potential to be a boon to archaeology, he said. "In archaeological studies, the trickiest part is getting robust ages."

Breaking Down Barriers

Ségolène Vandevelde, an archaeologist who studies speleothems at the University of Paris 1 – Pantheon-Sorbonne, agrees. This work breaks down barriers between geological and archaeological approaches to science, said Vandevelde, who is not involved in the research. "Speleothems are often used as environmental and paleoclimate archives. Here, [scientists] use them as an archaeological record." These results were published last year in the *Journal of Archaeological Science*.

There's a lot more information that can be mined from these speleothems, said Vandevelde. "It'd be really interesting to synchronize all the different sequences of the Tabak Cave speleothems to reconstruct a complete chronology of human occupation in the cave."

Citation: *Kornei, K. (2021), Sooty layers in stalagmites record human activity in caves, Eos, 102, https://doi.org/10.1029/2021EO154717. Published on 16 February 2021.*

http://bit.ly/3k5Wra0

Small 'window of opportunity' for best recovery after stroke

An international study has shown, for the first time, that the capacity of the human brain to recover and rewire itself peaks around two weeks after a stroke and diminishes over time.

The finding, published today in the *Neurorehabilitation and Neural Repair* journal, is the result of a study in London and Adelaide that followed the recovery of 60 stroke patients up to one year after their stroke.

Lead author Dr Brenton Hordacre, from the University of South Australia, says the multi-site study showed conclusive evidence that the brain only has a small window of opportunity to more easily repair itself after stroke.

"Earlier animal studies suggested this was the case, but this is the

first time we have conclusively demonstrated this phenomenon exists in humans," Dr Hordacre says.

The researchers scanned the brains of stroke survivors as they recovered over 12 months. They found that in the initial days following an ischemic stroke (caused by a blocked artery to the brain), the brain has a greater capacity to modify its neural connections and its plasticity is increased.

"It is during this early period after stroke that any physiotherapy is going to be most effective because the brain is more responsive to treatment. "Earlier experiments with rats showed that within five days of an ischemic stroke they were able to repair damaged limbs and neural connections more easily than if therapy was delayed until 30 days post stroke."

The researchers used continuous transcranial magnetic stimulation (cTBS) to repetitively activate different hemispheres of the motor cortex to measure brain plasticity.

The Adelaide laboratory tested the stroke damaged motor cortex, which is the main area that controls movement. The London laboratory tested the non-stroke damaged hemisphere which is also important to help recovery. "Our assessments showed that plasticity was strongest around two weeks after stroke in the non-damaged motor cortex. Contrary to what we expected, there was no change in the damaged hemisphere in response to cTBS."

Dr Hordacre says the findings confirm the importance of initiating therapy as soon as possible after a stroke.

Current evidence indicates that less than eight minutes of daily therapy is dedicated to upper limb recovery within the first four weeks of a stroke. "Delivering more treatment within this brief window is needed to help people recover after stroke.

"The next step is to identify techniques which prolong or even re-open a period of increased brain plasticity, so we can maximise recovery," Dr Hordacre says.

Notes to Editors

The paper, "Evidence for a Window of Enhanced Plasticity in the Human Motor Cortex following Ischemic Stroke" is available at:
https://journals.sagepub.com/doi/full/10.1177/1545968321992330
Researchers from the following institutions were involved in the study: University of South Australia; University College London (UCL); University of Adelaide; Hospital Universitario Ramón y Cajal and Hospital Ruber Internacional in Madrid; Queen Mary University, London; the Royal London Hospital; National Hospital for Neurology and Neurosurgery, London; Murdoch University, WA; Royal Adelaide Hospital; and the Physio Clinic, Adelaide.

http://bit.ly/2MbuJMQ

COVID-19 infection rates high in pregnant women

This population should be considered at a high risk and be included in Phase 1B vaccination schedules, the authors say.

The COVID-19 infection rate among pregnant women was estimated to be 70% higher than in similarly aged adults in Washington state, according to a new study published today in *American Journal of Obstetrics and Gynecology*. Other key findings include:

The study also showed that the number of COVID-19 infections in pregnant patients from nearly all communities of color in Washington was high. There was a twofold to fourfold higher prevalence of pregnant patients with COVID-19 infections from communities of color than expected based on the race-ethnicity distribution of pregnant women in Washington in 2018.

A high number of pregnant women with COVID-19 received their medical care in a language other than English. This indicates that public health outreach to enhance vaccination rates in these communities is crucial.

"Our data indicates that pregnant people did not avoid the pandemic as we hoped that they would, and communities of color bore the greatest burden," said Dr. Kristina Adams Waldorf, an ob-gyn with the University of Washington School of Medicine and the report's senior author. "We were disheartened to see the higher infection

rates in communities of color as well as in patients with limited English proficiency."

COVID-19 vaccine allocation is based priority lists set by each state's department of health, which can vary. In some states, pregnancy is considered a high-risk health condition for COVID-19 vaccine allocation in Phase 1B. Texas, New Hampshire, New Mexico and Alaska are among the states that prioritize pregnant women for COVID-19 vaccines in schedule Phase 1B.

"The vaccine distribution plans vary quite a bit, state-by-state, and pregnant women are written out of the allocation prioritization in about half of U.S. States. Many states are not even linking their COVID-19 vaccine allocation plans with the high-risk medical conditions listed by the CDC - which include pregnancy, Adams Waldorf said.

"The higher infection rates in pregnant patients, coupled with an elevated risk for severe illness and maternal mortality due to COVID-19, suggests that pregnancy should be considered a high-risk health condition for COVID-19 vaccine allocation in Phase 1B all across the United States," she added. "The time to act is now."

She said this study is unique in the United States because it is the first to address the question of infection rates in pregnancy in a large population that represents the majority of pregnancies in the state. The data can inform vaccine policy and guide public health workers and physicians in trying to mitigate COVID-19 in vulnerable populations.

The multisite study included 35 hospitals and clinics that compose the Washington State COVID-19 in Pregnancy Collaborative led by Adams Waldorf and Erica Lokken, an epidemiologist at the UW School of Public Health. The group identified 240 pregnant women who acquired COVID-19 from March through June 2020. This number represents all such known cases at the collaborating sites, which account for 61% of births in the state each year.

"Higher infection rates in pregnant patients may be due to the overrepresentation of women in many professions and industries considered essential during the COVID-19 pandemic - including healthcare, education, service sectors," said Lokken. Pregnant women may also have larger households, children in daycare or playgroups, and be caregivers within an extended family, she added.

This study data fills critical gaps and provides an important estimate of regional COVID-19 infection rates in the pregnant population, Waldorf said. The Centers for Disease Control and Prevention's estimated infection rates may not be representative, she said.

"COVID-19 case reports are missing pregnancy status in up to 65% of reports for women of reproductive age. As a result, the number of pregnant patients infected with COVID-19 was likely underrepresented in national numbers," the authors concluded.

"When the data is woefully incomplete for specific groups, like pregnant women, it is easy to assume that they haven't been impacted by the pandemic. This was not the case," said Adams Waldorf.

Pregnant healthcare workers have received the COVID-19 vaccine, and Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, has reported no "red flags" in preliminary data about post-vaccination well-being of this population.

Adams Waldorf urges pregnant women to discuss the risks and benefits of COVID-19 vaccination with their prenatal care provider. More ob-gyns have begun recommending that pregnant women take the vaccine.

"We want to use information from this study to be more prepared for the next pandemic and to not brush pregnant women to the side. They need to have a seat at the table when it comes to vaccine trials and vaccine allocation," Adams Waldorf said.

http://nyti.ms/3az2a5e

Potential for New Coronaviruses May Be Greater Than Known

Researchers calculated the likelihood of different viruses recombining in the same animal to make new disease-causing pathogens.

By James Gorman

As the coronavirus continues to evolve, the scientific and public health focus has been on new variants in which a few mutations make the virus more infectious, or even, it may be, more deadly.

These changes in the virus are all what scientists call point mutations, the substitution of one tiny bit of genetic code for another. Coronaviruses, as a group, are not known to mutate rapidly, but the pandemic caused by the virus SARS-CoV-2 means that millions and millions of people are infected by billions and billions of viral particles, offering countless chances for change.

There is, however, another more significant way that coronaviruses change. Individual viral particles exchange larger sections of genetic material, with another virus. If two different kinds of coronavirus inhabit the same cell, the result could be not a new variant, but a new species.

Three University of Liverpool researchers writing in the journal Nature Communications predicted, based on a computer analysis, that such events are far more likely than previously thought, and recommended monitoring of target species to watch for possible emergence of new coronavirus diseases.

The work pointed in some directions where scientists are already alert. They identified the lesser Asiatic yellow bat and the greater and intermediate horseshoe bats as animals where recombination would be more likely to occur. But their analysis also pointed to animals that scientists have been less focused on, such as the common pig, as a creature that should be monitored.

Marcus S. C. Blagrove, a virologist who wrote the report along with Maya Wardeh, who specializes in computer analysis of animal disease spread, and Matthew Bayliss, a veterinary epidemiologist, said that coronaviruses were known for “swapping large chunks all over the place.”

Emergence of new diseases through this process is not common because an animal needs to be infected with two different kinds of coronaviruses at the same time.

Jeremy Luban, a virologist at the University of Massachusetts, said such a double infection with two kinds of viruses replicating in one cell had yet to be documented in humans. But just such a recombination is how SARS seems to have emerged, and researchers think SARS-CoV-2 may also be the result of two viruses combining.

Dr. Luban said he thought that “this kind of work is extremely important” because it could come up with surprising insights that experiments and field work can follow up on.

The group of researchers at Liverpool used a kind of computer analysis called machine learning to look at a number of different data points, including the genetic structure of coronaviruses and mammalian species as well as their behavioral similarity and geographic proximity to come up with predictions of which animals were most likely to harbor the most numbers of coronaviruses.

They predict that 40 times as many mammal species can be infected with four or more different kinds of coronaviruses than are now known, and that up to 126 species of mammals may be susceptible to infection by SARS-CoV-2.

As a reality check, they pointed out that their analyses correctly predicted some known associations of animals and viruses. The modeling highlighted the palm civets, the animal from which SARS seemed to have spilled over to humans as a potential hot spot for coronavirus evolution.

Over all, they warned that the possibility of recombination resulting in the emergence of some new dangerous coronavirus is highly underestimated.

http://bit.ly/2OO4Nrj

CT scans of Egyptian mummy reveal new details about the death of a pivotal pharaoh

New interpretations based on medical imaging suggest Seqenenre-Taa-II was executed by multiple attackers and embalmers had skillfully concealed some head wounds

Modern medical technology is helping scholars tell a more nuanced story about the fate of an ancient king whose violent death indirectly led to the reunification of Egypt in the 16th century BC. The research was published in *Frontiers in Medicine*.

Dr Sahar Saleem placing the mummy in the CT scanner **Sahar Saleem**

Pharaoh Seqenenre-Taa-II, the Brave, briefly ruled over Southern Egypt during the country's occupation by the Hyksos, a foriegn dynasty that held power across the kingdom for about a century (c. 1650-1550 BCE). In his attempt to oust the Hyskos, Seqenenre-Taa-II was killed. Scholars have debated the exact nature of the pharaoh's death since his mummy was first discovered and studied in the 1880s.

These and subsequent examinations -- including an X-ray study in the 1960s -- noted the dead king had suffered several severe head injuries but no other wounds to his body. The prevailing theory, based on the evidence, was that the king had been captured in battle and then executed afterward, possibly by the Hyksos king himself. Others have suggested he was murdered in his sleep by a palace conspiracy.

In addition, the poor condition of the mummy suggested the embalming had been done hastily, away from the royal mummification workshop.

But computed tomography (CT) scans of the mummified remains of Seqenenre revealed new details about his head injuries, including previously undetected lesions that embalmers had skillfully concealed.

The authors of the new paper offer a novel interpretation of the events before and after the king's death based on the computer-processed X-ray images: Seqenenre had indeed been captured on the battlefield, but his hands had been tied behind his back, preventing him from defending against the attack.

"This suggests that Seqenenre was really on the front line with his soldiers risking his life to liberate Egypt," said lead author Dr. Sahar Saleem, a professor of radiology at Cairo University who specialises in paleoradiology.

This investigative technique employs medical imaging technologies to non-invasively study a cross section of archaeological remains, including bodies. It can help determine age at death, sex and even how the person died.

For example, the CT scans, combined with other evidence, suggest the execution had been carried out by multiple attackers, which the scientists confirmed by studying five different Hyksos weapons that matched the king's wounds.

"In a normal execution on a bound prisoner, it could be assumed that only one assailant strikes, possibly from different angles but not with different weapons," Saleem explained. "Seqenenre's death was rather a ceremonial execution."

The CT study also determined that Seqenenre was about 40 when he died, based on the detailed morphology revealed in the images, providing the most precise estimate to date.

Saleem and co-author Zahi Hawass, an archaeologist and former

Egyptian minister of antiquities, have pioneered the use of CT scans to study the New Kingdom pharaohs and warriors, including well-known names such as Hatshepsut, Tutankhamun, Ramesses III, Thutmose III and Rameses II.

Yet Seqenenre, based on the available evidence, appears to be the only one among this illustrious group to have been on the frontline of the battlefield.

In addition, the CT study revealed important details about the mummification of Seqenenre's body. For instance, the embalmers used a sophisticated method to hide the king's head wounds under a layer of embalming material that functioned similarly to the fillers used in modern plastic surgery. This would imply that mummification took place in a real mummification laboratory rather than in a poorly equipped place, as previously interpreted.

Saleem said the CT scan study provides important new details about a pivotal point in Egypt's long history.

"Seqenenre's death motivated his successors to continue the fight to unify Egypt and start the New Kingdom," she said.

https://go.nature.com/2Zz5vLc

Million-year-old mammoth genomes shatter record for oldest ancient DNA

Permafrost-preserved teeth, up to 1.6 million years old, identify a new kind of mammoth in Siberia.

The million-year-old genome is here. Mammoth teeth preserved in eastern Siberian permafrost have produced the oldest ancient DNA on record, pushing the technology close to — but perhaps not past — its limits.

Ancient DNA retrieved from different mammoth species is illuminating a complex evolutionary picture. **Beth Zaiken/Centre for Palaeogenetics**

Genomic DNA extracted from a trio of tooth specimens excavated in the 1970s has identified a new kind of mammoth that gave rise to a later North American species. The findings were published in *Nature* on 17 February[1].

“I love the paper. I’ve been waiting for that paper for, what, eight years now,” says Ludovic Orlando, an ancient-DNA specialist at the Centre for Anthropobiology and Genomics of Toulouse in France, who co-led a 2013 effort that sequenced the previous oldest ancient DNA — a genome from a 560,000-to-780,000-year-old horse leg bone[2]. “I’m pleased to lose this record, because it was a heavy one,” he says.

Researchers had suspected that ancient DNA could survive beyond one million years, if the right sample could be found. Once an organism dies, its chromosomes shatter into pieces that get shorter over time.

Eventually, the DNA strands become so small that — even if they can be extracted — they lose their information content.

Orlando’s team found that fragments as short as 25 DNA letters in their horse bone, from the Canadian Yukon Territory, could still be interpreted.

They estimated that million-year-old remains preserved in the constant cold of permafrost — which slows DNA fragmentation — should also contain DNA fragments of that length. “My only doubt: does such a sample exist?” Orlando says.

Decadal dream

Love Dalén, an evolutionary geneticist at the Swedish Museum of Natural History (SMNH) in Stockholm, had been dallying with the idea of sequencing very old mammoth remains since he first encountered a collection of them, in 2007.

The samples his team sequenced, one from an early woolly mammoth (*Mammuthus primigenius*) and two assigned to a precursor known as steppe mammoths (*Mammuthus trogontherii*),

had been excavated by the Russian palaeontologist Andrei Sher.

Dalén hoped that DNA from the samples could capture the evolution of woolly mammoths and other species in action, but he was sceptical because of previous bad experiences with much younger remains found in permafrost. “It’s not like everything found in the permafrost always works. The vast majority of samples have crap DNA,” he says.

And indeed, two of the three mammoth molars from Sher’s excavations, retrieved from sediments more than than one million years old, contained so little DNA that Dalén says he would have discarded them had they been younger.

But thanks to advances in sequencing technology and bioinformatics, his team managed to obtain 49 million base pairs of nuclear DNA from the oldest sample, found near a village called Krestovka, and 884 million base pairs from another tooth, called Adycha.

Analysis of the DNA suggested that the Krestovka sample was 1.65 million years old, and the Adycha sample around 1.3 million (see ‘Ancient genomes’). The third sample, a 600,000-year-old woolly mammoth tooth dubbed Chukochya, produced nearly 3.7 billion base pairs of DNA, more than the length of its 3.1-billion-base-pair genome.

From their shape, the two oldest teeth looked like they belonged to steppe mammoths, a European species that researchers think predated woolly mammoths and Columbian mammoths (*Mammuthus columbi*), a North American species. But their genomes painted a more complicated picture. The Adycha specimen was part of the lineage that gave rise to woolly mammoths, but the Krestovka specimen clearly was not.

Dalén’s team found that it belonged to an entirely new lineage. “We can’t say it’s a different species, but it sure looks like it,” he says. Although the Krestovka sample is from Russia, he suspects the lineage became isolated from other steppe mammoths in North America. The team found that Columbian mammoths trace half their ancestry to the Krestovka mammoth lineage, and the other half to woolly mammoths. Dalén estimates that the two lineages mixed more than 420,000 years ago.

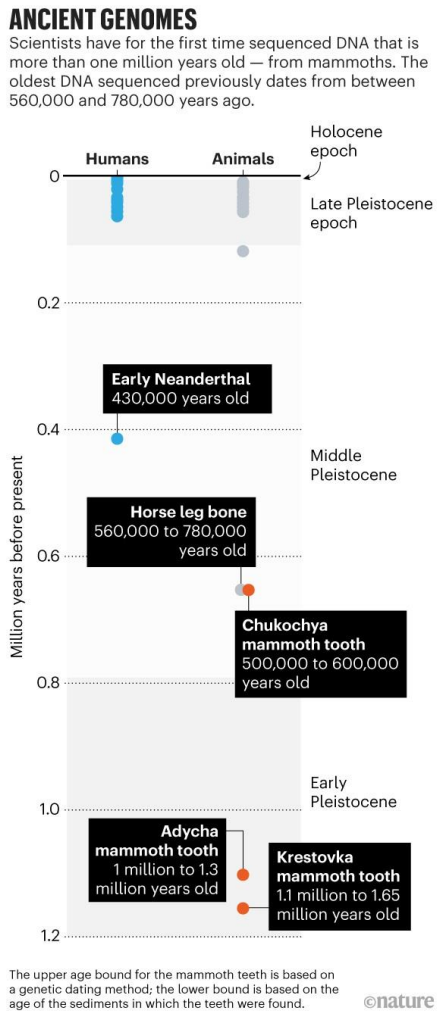
The idea that new species can form through mixing — and not just splitting from a single parent species — is gaining currency among evolutionary biologists. But this is the first evidence for ‘hybrid speciation’ from ancient DNA, says Orlando.

“This is amazing.”

Hendrik Poinar, an ancient-DNA specialist at McMaster University in Hamilton, Canada, says different mammoth species probably routinely hybridized when glacial expansion brought them together. His team has found evidence that later woolly and Columbian mammoths occasionally interbred.

The future of ancient DNA

Even though researchers have long been expecting a million-year-old genome, crossing that threshold is important, says Viviane Slon, a palaeogeneticist at Tel Aviv University in Israel. “There’s a difference between what we think is possible and actually showing it.”



Source: David Diez-del-Molino

Tom van der Valk, a bioinformatician at the University of Uppsala in Sweden who led the mammoth-tooth work with evolutionary biologists Patrícia Pečnerová and David Díez-del-Molino at the SMNH, hopes that it will encourage other labs. “It is a symbolic barrier that I hope can inspire and motivate other groups that have ideas about really deep-time sequencing.”

By crossing the million-year threshold, ancient-DNA researchers might be able to access the early histories of other mammals big and small, says Dalén. Very old permafrost samples of musk oxen, moose and lemmings are now on his lab’s radar.

The mammoth DNA does not represent the oldest biomolecular information from the fossil record. In 2016, researchers reported protein sequences from 3.8-million-year-old ostrich eggshells from Tanzania[3], and in 2019 another team decoded proteins from a 1.77-million-year-old rhinoceros tooth from Georgia[4].

Protein sequences tend to be much less informative about an organism’s ancestry than DNA. But protein molecules are much hardier, so researchers can use them to glean insights from very old fossils found in places with no permafrost. The ostrich and rhino samples both come from archaeological sites famous for hominin remains.

The chances of finding million-year-old remains of ancient human relatives in the permafrost are very low, researchers say. But Dalén thinks that the right environment, such as a deep cave, could yield samples that old. Early Neanderthal remains from a Spanish cave dated to 430,000 years ago represent the oldest DNA from an ancient human relative discovered so far[5].

“Finding a hominin in the sort of ideal context for preservation as permafrost would be would be a dream,” says Slon.

As for the likely age limit of ancient DNA, Dalén says that’s easy to determine: “2.6 million years. That’s the limit of the permafrost. Before that, it was too warm.”

doi: https://doi.org/10.1038/d41586-021-00436-x

Read the related News & Views article: ‘A mammoth step back in genomic time’

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https://go.nature.com/2NK9DWq

Impervious to cold? A gene helps people to ward off the chills

A mutation that is common in northern Europe is less so in Africa.

A genetic variation that increases muscle tone also makes people more tolerant of cold conditions, according to a study of volunteers dunked for long stretches in chilly water.

More than 1.5 billion people globally have two non-functional versions of the gene *ACTN3*, which encodes a muscle protein. The non-functional gene is more common in the colder climates of central and northern Europe than in Africa.

To find out why, Håkan Westerblad at the Karolinska Institute in Stockholm, Marius Brazaitis at the Lithuanian Sports University in Kanaus and their colleagues recruited 27 men who had functional *ACTN3* and 15 who did not. Participants were immersed in water at 14˚C in 20-minute bursts until their body temperature had fallen below 35.5 ˚C, or they had spent a total of 120 minutes in the cold water.

The authors found that 69% of the participants with non-functional *ACTN3* could maintain their body temperature above 35.5˚C, compared with only 30% of those with the functional variant. Those lacking functional *ACTN3* — and the protein it encodes — seemed to preserve heat not by shivering but by tensing their muscles, temporarily increasing muscle tone. *Am. J. Hum. Gen.* (2021)

http://bit.ly/37tHdXh

Immune system protects children from severe COVID-19

Children are protected from severe COVID-19 because their innate immune system is quick to attack the virus, a new study has found.

The research led by the Murdoch Children's Research Institute (MCRI) and published in *Nature Communications*, found that specialised cells in a child's immune system rapidly target the new coronavirus (SARS-CoV-2). MCRI's Dr Melanie Neeland said the reasons why children have mild COVID-19 disease compared to adults, and the immune mechanisms underpinning this protection, were unknown until this study.

"Children are less likely to become infected with the virus and up to a third are asymptomatic, which is strikingly different to the higher prevalence and severity observed in children for most other respiratory viruses," she said. "Understanding the underlying age-related differences in the severity of COVID-19 will provide important insights and opportunities for prevention and treatment, both for COVID-19 and possible future pandemics."

The study involved an analysis of blood samples from 48 children and 70 adults across 28 Melbourne households infected with, or exposed to, the new coronavirus. Immune responses were monitored during the acute phase of infection and up to two months afterwards.

Francesca Orsini and Alessandro Bartesaghi took part in the study along with their two daughters, Beatrice and Camilla, after all tested positive to COVID-19.

Both daughters, aged six and two, only had a mild runny nose but Francesca and Alessandro had extreme fatigue, headaches, muscle pain and loss of appetite and sense of taste. It took Francesca and Alessandro at least a fortnight to fully recover.

Dr Neeland said the study showed that children with COVID-19 have a more robust innate immune response to the virus compared to adults. "Coronavirus infection in children was characterised by activation of neutrophils, the specialised white blood cell that helps heal damaged tissues and resolves infections, and a reduction in first-responder immune cells such as monocytes, dendritic cells and natural killer cells from the blood," she said. "This suggests these infection-fighting immune cells are migrating to infection sites, quickly clearing the virus before it has a chance to really take hold."

"This shows that the innate immune system, our first line of defence against germs, is crucial to prevent severe COVID-19 in children. Importantly, this immune reaction was not replicated among adults in the study."

But Dr Neeland said children and adults who were exposed to, but tested negative for the coronavirus also had altered immune responses. "Both kids and adults had increased neutrophil numbers, out to seven weeks after exposure to the virus, which could have provided a level of protection from disease," she said.

The study confirms previous MCRI research that found three children in a Melbourne family developed a similar immune response after prolonged exposure to the coronavirus from their parents.

The research stated although the children had been infected with the coronavirus, they were able to mount an immune response which was highly effective in stopping the virus from replicating, meaning they never returned a positive test.

Researchers from the University of Melbourne and The Royal Children's Hospital also contributed to the study.

Publication: Melanie R. Neeland, Samantha Bannister, Vanessa Clifford, Kate Dohle, Kim Mulholland, Philip Sutton, Nigel Curtis, Andrew C. Steer, David P. Burgner, Nigel W. Crawford, Shidan Tosif and Richard Saffery. 'Innate cell profiles during the acute and convalescent phase of SARS-CoV-2 infection in children,' Nature Communications. DOI: 10.1038/s41467-021-21414-x

http://bit.ly/37sqHHh

Setting hospital prices would save more than increasing competition or price transparency

But price regulations face the greatest political obstacles

Among strategies to curb hospital prices among the commercially insured population in the U.S., direct price regulations such as setting rates are likely to achieve greater savings than other approaches like increasing competition or improving price transparency, according to a new RAND Corporation study.

But price regulations face the greatest political obstacles and historically have been strongly opposed by medical providers, according to the report.

Setting prices for all commercial health care payers could reduce hospital spending by $61.9 billion to $236.6 billion annually if the rates were set as high as 150% to as low as 100% of the amounts paid by the federal Medicare program, a change that would cut overall national health spending by 1.7% to 6.5%, according to the analysis.

Researchers estimate that improving health care price transparency could reduce U.S. spending by $8.7 billion to $26.6 billion per year. Meanwhile, increasing competition by decreasing hospital market concentration could reduce hospital spending by $6.2 billion to $68.9 billion annually, depending on the magnitude of the change and how sensitive hospital prices are to market concentration.

"Improving markets through increased price transparency and competition could help reduce prices, but would not reduce hospital spending to the extent that aggressively regulating prices could," said Jodi Liu, the study's lead author and a policy researcher at RAND, a nonprofit research organization. "Direct price regulation could have the largest impact on hospital spending, but this approach faces the biggest political challenges."

Spending on hospital services is the largest health spending category in the United States, accounting for one-third of national health expenses.

Private insurers such as employers and insurance companies cover about 40% of hospital spending. Compared with public payers, private insurers pay higher prices to hospitals and those costs have risen faster over time.

The RAND study analyzes the impact of three policy options -- regulating hospital prices, improving price transparency and increasing competition among hospitals -- on hospital spending by employer-sponsored and individual market plans and their enrollees. Using nationwide data from the federal Hospital Cost Report Information System, researchers explored key considerations for each strategy and estimated the potential impact on hospital prices and spending.

The report provides a menu of policy scenarios to help policymakers understand how key design choices or stakeholder responses might affect the impact of a given policy.

For example, the effectiveness of price transparency initiatives would depend on details such as whether patients would use price transparency tools to choose lower-cost providers. RAND researchers modeled both patient-driven scenarios, in which patients use price information to seek lower prices, and employer-driven scenarios, in which employers use price information to create health plans that steer patients toward lower-cost hospitals.

For rate-setting scenarios, researchers changed average commercial plan prices to an amount relative to Medicare prices for a given hospital. Prices were pegged to multiples of the Medicare price, as well as blended rates in between commercial and Medicare prices (such as using 25% of the Medicare rate and 75% of the commercial rate).

Researchers modeled competition scenarios by reducing hospital market concentration in hospital referral regions, computing a price

reduction with respect to the change in market concentration.

However, researchers concluded that given how concentrated today's hospital markets are, policymakers would need to radically restructure hospital markets beyond what the study modeled for prices to approach competitive levels.

"Regulating commercial hospital prices is a direct way to create significant reductions in spending, but doing so could potentially lead to hospital closures, erode quality, and face daunting political hurdles," said study co-author Christopher Whaley, a RAND policy researcher. "As policymakers consider options for reducing hospital prices paid by private health plans, they will need to weigh the potential impact of different policies on hospital revenues and the quality of care, and they will also need to take into account the political and administrative feasibility of each option."

Support for the study was provided by Arnold Ventures.

The study, "Impact of Policy Options for Reducing Hospital Prices Paid by Private Health Plans," is available at http://www.rand.org. Other authors of the report are Zachary M. Levinson and Nabeel Shariq Qureshi.

http://bit.ly/2ZyGFv5

Déjà brew? Another shot for lovers of coffee

Long black, espresso, or latte, whatever your coffee preference, drink too much and you could be in hot water, especially when it comes to heart health.

In a world first genetic study, researchers from the Australian Centre for Precision Health at the University of South Australia found that that long-term, heavy coffee consumption - six or more cups a day - can increase the amount of lipids (fats) in your blood to significantly heighten your risk of cardiovascular disease (CVD).

Long-term, heavy coffee consumption can heighten your risk of cardiovascular disease. **Pixabay / Ermal Tahiri**

Importantly, this correlation is both positive and dose-dependent, meaning that the more coffee you drink, the greater the risk of CVD.

It's a bitter pill, especially for lovers of coffee, but according to UniSA researcher, Professor Elina Hyppönen, it's one we must swallow if we want keep our hearts healthy.

"There's certainly a lot of scientific debate about the pros and cons of coffee, but while it may seem like we're going over old ground, it's essential to fully understand how one of the world's most widely consumed drinks can impact our health," Prof Hyppönen says.

"In this study we looked at genetic and phenotypic associations between coffee intake and plasma lipid profiles - the cholesterols and fats in your blood - finding causal evidence that habitual coffee consumption contributes to an adverse lipid profile which can increase your risk of heart disease.

"High levels of blood lipids are a known risk factor for heart disease, and interestingly, as coffee beans contain a very potent cholesterol-elevating compound (cafestol), it was valuable to examine them together.

"Cafestol is mainly present in unfiltered brews, such as French press, Turkish and Greek coffees, but it's also in espressos, which is the base for most barista-made coffees, including lattes and cappuccinos.

"There is no, or very little cafestol in filtered and instant coffee, so with respect to effects on lipids, those are good coffee choices.

"The implications of this study are potentially broad-reaching. In my opinion it is especially important for people with high cholesterol or who are worried about getting heart disease to carefully choose what type of coffee they drink.

"Importantly, the coffee-lipid association is dose-dependent - the more you drink unfiltered coffee the more it raises your blood lipids, putting you at greater risk of heart disease."

Globally, an estimated 3 billion cups of coffee are consumed every day. Cardiovascular diseases are the number one cause of death globally, taking an estimated 17.9 million lives each year.

The study used data from 362,571 UK Biobank participants, aged 37-73 years, using a triangulation of phenotypic and genetic approaches to conduct comprehensive analyses.

While the jury still may be out on the health impacts of coffee, Prof Hyppönen says it is always wise to choose filtered coffee when possible and be wary of overindulging, especially when it comes to a stimulant such as coffee.

"With coffee being close to the heart for many people, it's always going to be a controversial subject," Prof Hyppönen says.

"Our research shows, excess coffee is clearly not good for cardiovascular health, which certainly has implications for those already at risk.

"Of course, unless we know otherwise, the well-worn adage usually fares well - everything in moderation - when it comes to health, this is generally good advice."

http://bit.ly/3dxyQhA

Fuel for earliest life forms: Organic molecules found in 3.5 billion-year-old rocks

Solutions from archaic hydrothermal vents contained essential components that formed a basis for the earliest life

A research team including the geobiologist Dr. Helge Missbach from the University of Cologne has detected organic molecules and gases trapped in 3.5 billion-year-old rocks. A widely accepted hypothesis says that the earliest life forms used small organic molecules as building materials and energy sources. However, the existence of such components in early habitats on Earth was as yet unproven. The current study, published in the journal '*Nature Communications*', now shows that solutions from archaic hydrothermal vents contained essential components that formed a basis for the earliest life on our planet.

Specifically, the scientists examined about 3.5 billion-year-old barites from the Dresser Formation in Western Australia. The barite thus dates from a time when early life developed on Earth. 'In the field, the barites are directly associated with fossilized microbial mats, and they smell like rotten eggs when freshly scratched. Thus, we suspected that they contained organic material that might have served as nutrients for early microbial life,' said Dr. Helge Missbach of the Institute of Geology and Mineralogy and lead author of the study.

In the fluid inclusions, the team identified organic compounds such as acetic acid and methanethiol, in addition to gases such as carbon dioxide and hydrogen sulfide. These compounds may have been important substrates for metabolic processes of early microbial life. Furthermore, they are discussed as putative key agents in the origin of life on Earth. 'The immediate connection between primordial molecules emerging from the subsurface and the microbial organisms - 3.5 billion years ago - somehow surprised us. This finding contributes decisively to our understanding of the still unclear earliest evolutionary history of life on Earth,' Missbach concluded.

http://nyti.ms/3uixUDl

A Hitchhiker's Guide to an Ancient Geomagnetic Disruption

A shift in Earth's poles 42,000 years ago may have drastically altered the planet's climate, scientists have found — and they're naming the period after the author Douglas Adams.

By Alanna Mitchell

About 42,000 years ago, Earth was beset with oddness. Its magnetic field collapsed. Ice sheets surged across North America, Australasia and the Andes. Wind belts shifted across the Pacific and Southern Oceans. Prolonged drought hit Australia; that continent's biggest

mammals went extinct. Humans took to caves to make ochre-color art. Neanderthals died off for good.

Through it all, one giant kauri tree stood tall — until, after nearly two millenniums, it died and fell in a swamp, where the chemical records embedded in its flesh were immaculately preserved. That tree, unearthed a few years ago near Ngawha Springs in northern New Zealand, finally allowed researchers to fit a tight timeline to what before had seemed like an intriguing but only vaguely correlated series of events.

***An ancient kauri tree, unearthed near Ngawha Springs in New Zealand, bore witness to a lengthy disintegration of the planet's magnetic field, a period known as the Laschamp excursion.*...Nelson Parker**

What if, the researchers posited, the crash of the magnetic field spawned the climatic changes of that era? And to think that the Ngawha kauri tree had borne witness to the whole thing.

"It must have seemed like the end of days," said Chris S.M. Turney, a geoscientist at the University of New South Wales in Sydney, Australia, and part of a large team that described the findings in a study published Thursday in Science. "And this tree lived through all that. Which is incredible, really."

By comparing tree-ring age data and radioactive carbon concentrations from that kauri tree and three others of similar vintage to recent dating information derived from two stalagmites in the Hulu caves in China, Dr. Turney and his 32 co-authors were able to pinpoint when the tree lived and died. That gave them what they call a "calibration curve," allowing them to convert radiocarbon dating from that period into calendar years.

Scientists across disciplines said the kauri data were a dazzling addition to the radiocarbon canon and were long awaited.

"For a radiocarbon person, the kauri records are just amazing," said Luke C. Skinner, a paleoclimatologist at the University of Cambridge, who was not involved in the study. He said the fossil kauri trees were the main way for scientists to get at radiocarbon information from so long ago.

The tree lived through a lengthy disintegration of the magnetic field, a period known as the Laschamp excursion, when the magnetic poles attempted unsuccessfully to switch places. As a result, Dr. Turney and his co-authors were able to use the new data to describe more precisely when that excursion happened and trace what else was going on, including the bizarre climate and extinctions.

"It was suddenly, gosh, these things actually are happening simultaneously around the world, all at the same time," Dr. Turney said. "It was just an extraordinary revelation."

That discovery unlocked a multipronged thought experiment. Earth's magnetic field, which is constantly being generated deep within the planet's molten outer core, protects against dangerous galactic and solar rays. Were all those peculiar climatic, biological and archaeological phenomena 42,000 years ago linked to the wasted magnetic field? Had its collapse altered the course of life on Earth? And what about other disturbances of the magnetic field, including that time 780,000 years ago when the magnetic poles actually did switch places?

Scientists have been trying to find answers to these questions since the fact of magnetic pole reversals was established several decades ago. Consequently, this latest endeavor has drawn immense scrutiny.

"It's pretty brave," said Catherine G. Constable, a geophysicist at the Scripps Institution of Oceanography in San Diego, who was not involved in the study.

Using cutting-edge global climate model simulations that allowed for chemistry interactions, Dr. Turney and his colleagues used the

timeline generated by the kauri tree to try to find out what the climate was like during the excursion.

The data revealed "modest but significant changes in atmospheric chemistry and climate," according to the paper. Among them: a slightly depleted ozone layer; slightly increased ultraviolet radiation, particularly near the Equator; a jump in tissue-damaging ionizing radiation; and auroras as close to the Equator as the 40th Parallels of latitude, which would run through the middle of the continental United States in the Northern Hemisphere and through the bottom tip of Australia in the south.

Adding a period of low sun activity, known as grand solar minima, into the mix produced more dramatic effects. A peculiar, century-long series of deposits of beryllium-10 isotopes has been identified in ice cores from Greenland, dating from the Laschamp excursion 42,000 years ago. Such isotopes are created when cosmic rays batter the upper atmosphere; in the geological record they indicate times when Earth experienced a diminished magnetic field and, sometimes, solar changes.

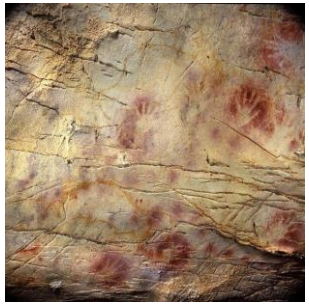
In the more extreme computer scenario, with solar effects factored in, ultraviolet radiation rose by 10 to 15 percent from the norm and ozone declined by about the same amount. Those effects cascaded through the climate system, Dr. Turney said:

"It was basically like a perfect storm," he said.

The simulations suggest that the weakened magnetic field caused some of the climatic changes of 42,000 years ago, and that those changes may have had wider impacts: prompting the extinction of many large mammals in Australia, hastening the end of the Neanderthals, and perhaps giving rise to cave art as humans hid for long periods to avoid skin-damaging ultraviolet rays, the authors proposed.

In fact, the effects were so striking that the researchers have given a new name to the years leading up to the middle of the Laschamp excursion. They call it the Adams Transitional Geomagnetic Event.

"The Adams Event appears to represent a major climatic, environmental and archaeological boundary that has previously gone unrecognized," the team writes, concluding, "Overall, these findings raise important questions about the evolutionary impacts of geomagnetic reversals and excursions throughout the deeper geologic record."



***Hand prints of red ochre in a cave in Spain, believed to be roughly 42,000 years old....*Paul Pettitt, Gobierno de Cantabria**

The new name is a homage to the British humorist Douglas Adams, author of "The Hitchhiker's Guide to the Galaxy" and the book and radio series "Last Chance to See," about extinction. It is also a nod to Mr. Adams's famous line that "the answer to life, the universe and everything" is 42 — which Dr. Turney said reminded him of the timing of the magnetic episode 42,000 years ago.

"It just seems uncanny," he said, laughing. "How did he know?"

The interpretation is destined to create controversy. Some scientists who read the paper expressed admiration for the breathtaking linkages across disciplines.

"One of the strengths of the paper, just from the perspective of its scholarly work, not necessarily the analytical science that it does, is just the degree to which it stitches together all of these disparate sources of information to make its case," said Jason E. Smerdon, a climate scientist at the Lamont-Doherty Earth Observatory of Columbia University in New York, who was not involved in the study. He called it a "tour de force."

Likewise, James E.T. Channell, an emeritus professor of geophysics at the University of Florida, who was not involved in the study but was a peer reviewer, said that scholars had been

stymied for half a century by the question of whether a waning magnetic field affects life. The paper opens up new avenues of research.

“If we knew enough about the timing of excursions, then perhaps we could relook at the problem,” he said.

But other scientists said the sweeping analysis left them wondering whether there were other explanations for some of the phenomena during the Laschamp excursion.

“It’s opening a can of worms rather than resolving a set of questions,” Dr. Skinner said.

Like several others interviewed, he worried whether the Adams Event nomenclature would lead to confusion in the scientific literature, and whether it was necessary. But he praised the paper for stimulating discussion.

“I’m certainly more excited about this topic today than I was yesterday,” he said.

http://bit.ly/3kbc9AP

Lab-grown 'mini-bile ducts' used to repair human livers in regenerative medicine first

First time the technique has been used on human organs

Scientists have used a technique to grow bile duct organoids - often referred to as 'mini-organs' - in the lab and shown that these can be used to repair damaged human livers. This is the first time that the technique has been used on human organs.

The research paves the way for cell therapies to treat liver disease - in other words, growing 'mini-bile ducts' in the lab as replacement parts that can be used to restore a patient's own liver to health - or to repair damaged organ donor livers, so that they can still be used for transplantation.

Bile ducts act as the liver's waste disposal system, and malfunctioning bile ducts are behind a third of adult and 70 per cent of children's liver transplantations, with no alternative treatments. There is currently a shortage of liver donors: according to the NHS, the average waiting time for a liver transplant in the UK is 135 days for adults and 73 days for children. This means that only a limited number of patients can benefit from this therapy.

Approaches to increase organ availability or provide an alternative to whole organ transplantation are urgently needed. Cell-based therapies could provide an advantageous alternative. However, the development of these new therapies is often impaired and delayed by the lack of an appropriate model to test their safety and efficacy in humans before embarking in clinical trials.

Now, in a study published today in *Science*, scientists at the University of Cambridge have developed a new approach that takes advantage of a recent 'perfusion system' that can be used to maintain donated organs outside the body. Using this technology, they demonstrated for the first time that it is possible to transplant biliary cells grown in the lab known as cholangiocytes into damaged human livers to repair them. As proof-of-principle for their method, they repaired livers deemed unsuitable for transplantation due to bile duct damage. This approach could be applied to a diversity of organs and diseases to accelerate the clinical application of cell-based therapy.

"Given the chronic shortage of donor organs, it's important to look at ways of repairing damaged organs, or even provide alternatives to organ transplantation," said Dr Fotios Sampaziotis from the Wellcome-MRC Cambridge Stem Cell Institute. "We've been using organoids for several years now to understand biology and disease or their regeneration capacity in small animals, but we have always hoped to be able to use them to repair human damaged tissue. Ours is the first study to show, in principle, that this should be possible."

Bile duct diseases affect only certain ducts while sparing others. This is important because in disease, the ducts in need of repair are often fully destroyed and cholangiocytes may be harvested

successfully only from spared ducts.

Using the techniques of single-cell RNA sequencing and organoid culture, the researchers discovered that, although duct cells differ, biliary cells from the gallbladder, which is usually spared by the disease, could be converted to the cells of the bile ducts usually destroyed in disease (intrahepatic ducts) and vice versa using a component of bile known as bile acid. This means that the patient's own cells from disease-spared areas could be used to repair destroyed ducts.

To test this hypothesis, the researchers grew gallbladder cells as organoids in the lab. Organoids are clusters of cells that can grow and proliferate in culture, taking on a 3D structure that has the same tissue architecture, function and gene expression and genetic functions as the part of the organ being studied. They then grafted these gallbladder organoids into mice and found that they were indeed able to repair damaged ducts, opening up avenues for regenerative medicine applications in the context of diseases affecting the biliary system.

The team used the technique on human donor livers taking advantage of the perfusion system used by researchers based at Addenbrooke's Hospital, part of Cambridge University Hospitals NHS Foundation. They injected the gallbladder organoids into the human liver and showed for the first time that the transplanted organoids repaired the organ's ducts and restored their function. This study therefore confirmed that their cell-based therapy could be used to repair damaged livers.

Professor Ludovic Vallier from the Wellcome-MRC Cambridge Stem Cell Institute, joint senior author, said: "This is the first time that we've been able to show that a human liver can be enhanced or repaired using cells grown in the lab. We have further work to do to test the safety and viability of this approach, but hope we will be able to transfer this into the clinic in the coming years."

Although the researchers anticipate this approach being used to repair a patient's own liver, they believe it may also offer a potential way of repairing damaged donor livers, making them suitable for transplant.

Mr Kourosh Saeb-Parsy from the Department of Surgery at the University of Cambridge, joint senior author, added: "This is an important step towards allowing us to use organs previously deemed unsuitable for transplantation. In future, it could help reduce the pressure on the transplant waiting list."

The research was supported by the European Research Council, the National Institute for Health Research and the Academy of Medical Sciences.

Reference

Sampaziotis, F et al. Cholangiocyte organoids can repair bile ducts after transplantation in human liver. Science; 19 Feb 2021

http://bit.ly/2Me62PQ

'Classic triad' of symptoms misses positive COVID-19 cases, study finds

Extending the symptoms that trigger a PCR test for COVID-19 could help detect around a third more cases of the disease.

New research led by researchers at King's College London and published in the *Journal of Infection* suggests that restricting testing to the 'classic triad' of cough, fever and loss of smell which is required for eligibility for a PCR test through the NHS may have missed cases. ***Extending the list to include fatigue, sore throat, headache and diarrhoea would have detected 96% of symptomatic cases***.

A team of researchers at King's College London and the Coalition for Epidemic Preparedness Innovations (CEPI) analysed data from more than 122,000 UK adult users of the ZOE COVID Symptom Study app. These users reported experiencing any potential COVID-19 symptoms, and 1,202 of those reported a positive PCR test within a week of first feeling ill.

While PCR swab testing is the most reliable way to tell whether

someone is infected with the SARS-CoV-2 coronavirus that causes COVID-19, the analysis suggests the limited list of three does not catch all positive cases of COVID-19.

Testing people with any of the three 'classic' symptoms would have spotted 69% of symptomatic cases, with 46 people testing negative for every person testing positive. However, testing people with any of seven key symptoms - cough, fever, anosmia, fatigue, headache, sore throat and diarrhoea - in the first three days of illness would have detected 96% of symptomatic cases. In this case, for every person with the disease identified, 95 would test negative.

Researchers also found users of the Symptom Study App were more likely to select headache and diarrhoea within the first three days of symptoms, and fever during the first seven days, which reflects different timings of symptoms in the disease course. Data from the ZOE app shows that 31% of people who are ill with COVID-19 don't have any of the triad of symptoms in the early stages of the disease when most infectious.

The researchers applied a multi-objective evolutionary algorithm (MOEA) to generate a set of optimal symptom combinations, each characterised by a good trade-off between specificity and sensitivity. MOEA starts generating a population of random symptom combinations and then evolves that population towards better combinations ending with a set of optimal symptom combinations. The choice of the optimal combination to use depends on the testing capacity.

Cough or dyspnoea (shortness of breath) were reported by 46% of individuals positive for COVID-19 within the first three days of symptom onset. When users reported fever, the sensitivity increased to 60%, while logging anosmia/ageusia increased sensitivity to 69%. When headache and fatigue was added the proportion of COVID-19 cases increased to 92% but the tests per case doubled.

The findings may be valuable in situations where there is a limited testing capacity. Researchers suggest a range of optimal symptom combinations that could be used in vaccine efficacy trials or in public health settings, when assessing financial and logistical resources.

Professor Sebastien Ourselin from King's College London said: ""The identification of this combination of symptoms through the COVID Symptom Study app is another prime demonstration of the value of big data analytics and mobile health technology to support the management of this pandemic. Daily self-reported symptoms from a mobile application at the scale of an entire country has offered a new perspective for public health research and response towards the rapid spread of infectious diseases such as COVID-19."

Dr Claire Steves, Reader at King's College London, said: "There are many symptoms which occur in acute COVID, including some like fatigue and headache which are also common in other conditions. Depending on the testing available, different symptom combinations can be used to be as sensitive or specific as possible. We hope these models are of use in a range of settings - from vaccine trials to detecting and treating COVID outbreaks going forward."

Professor Tim Spector from King's College London said: "We've known since the beginning that just focusing testing on the classic triad of cough, fever and anosmia misses a significant proportion of positive cases. We identified anosmia as a symptom back in May and our work led to the government adding it to the list, it is now clear that we need to add more. By inviting any users who log any new symptoms to get a test, we confirmed that there are many more symptoms of COVID-19. This is especially important with new variants that may cause different symptoms. For us, the message for the public is clear: if you're feeling newly unwell, it could be COVID and you should get a test."

Dr Jakob Cramer, Head of Clinical Development, at the Coalition

for Epidemic Preparedness Innovations, said: "Accurate diagnosis of COVID-19 cases is crucial when assessing the efficacy of COVID-19 vaccine candidates in large-scale studies, especially since the signs and symptoms associated with the disease are extensive and overlap with other common viral infections. The findings of this study provide important insights that will help optimise the choice of triggering symptoms for diagnostic work-up in COVID-19 vaccine-efficacy trials. We hope the findings of this study will not only aid CEPI's COVID-19 vaccine-development partners but also the wider R&D community."

http://bit.ly/3aE2sIf

The long-standing myth of sea monsters has a dark explanation

Mythical sea serpents were probably marine animals tangled in fishing gear

Ashley Marranzino

Stories of sea serpents and other ocean-dwelling monsters are long-standing myths. Now, in research published in the journal Fish and Fisheries, one scientist has uncovered the culprit behind historical sea serpent sightings in the British Isles.

After parsing through over 200 reports of sea-serpent sightings made between 1809-2000, Robert France from Dalhousie University concluded that accounts of a “many-humped” monster lurking near the water’s surface in the British Isles were actually early sightings of marine animals entangled in fishing gear.

France scoured sightings published in historical newspapers, scientific journals, natural history books, cryptozoology texts, and even legally sworn testimonials. While sightings varied substantially, there were some common threads: The sea-serpent body stretched for tens of meters in length (up to 100m), formed many coils or humps at the surface, and frequently had hair or whiskers. Many reports suggested the serpents were capable of moving rapidly or reported them thrashing at the surface of the water.

But France argues these descriptions conflict with all known (living and extinct) marine animals and can be more easily explained when considering the possibility of a marine animal pulling lines of rope and buoys behind them.

Today, the synthetic materials that impart strength and durability to fishing gear weave a tight cocoon around unfortunate animals tangled within their grasp. But before the advent of these materials, fishing gear was made of natural products that would have allowed for animals to move more freely while attached to fishing gear. Instead of succumbing to more instantaneous deaths we associate with entanglements today, animals may have simply carried their entrapment devices around with them until the natural materials eventually degraded.

Beyond solving an age-old mystery that has enchanted sea-goers, France points to a more insidious narrative: marine entanglements have long been a pervasive problem, plaguing the oceans far longer than scientists expected.

http://wb.md/3sqMeIz

Tales From Geriatric Practice: Hard to Swallow

Desperation Leads to Inspiration

Mark E. Williams, MD

My 87-year-old patient was a former amateur boxer who'd achieved some notoriety in his youth. As an adult, he had spent decades working for the US Foreign Service. He was 6'4", 240 lb, and muscular, but not the least bit obese. He had red hair, freckles, a boyish face, and a warm, avuncular manner. He enjoyed telling stories of international travel to exotic places.

My patient's wife was a very talented artist who drew numerous portraits of their family. They had lost a daughter under suspicious circumstances, and while the death was ruled accidental, the

emotional scars were always near the surface.

Most of the wife's portraits were of the daughter who had passed away; the images captured the young woman's natural beauty, sweet smile, and youthful innocence. The couple had another daughter who was a gifted artist as well. She was able to weave her grief into stunning works of art and had several art shows in prestigious museums and high-end art galleries.

A Different, More Gradual Loss

When my patient developed significant dementia, he and his wife moved into a lifecare community. Initially his dementia was manageable, but as it progressed, he became more and more disoriented and disruptive, and required nursing home care.

While my patient lost the ability to verbally communicate, he could engage you with his eyes. If you looked familiar to him, he would chuckle and laugh as if he were recognizing an old friend.

Dinner and a Trip to the ED

Things were stable until one December evening when my patient choked on a piece of pork chop. His esophageal obstruction was below his airway. The staff could not perform the Heimlich maneuver on him because of his extreme restlessness and threatening manner. He was sent to the emergency department (ED) in severe distress. The hope was that a gastroenterologist could use an endoscope to push down the impacted piece of meat.

Despite prior communication with the ED, he was superficially evaluated and kept overnight. He was sent back to the facility in the same state that he left in, with the justification that his code status was "do not resuscitate." The gastroenterologist was not inclined to take any further action.

A Patient Whose Eyes Said, 'Do Something'

I saw my patient shortly after he returned from the ED. His wife told me she was frustrated that no one seemed to listen to her. Nothing had been done except to draw blood and document the obstruction on her husband's chest x-ray.

My patient was in significant distress when I examined him. His eyes had a pleading look that said, "Please do something." He could not pass anything through his esophagus, and he kept coughing and aspirating his oral secretions. Something needed to be done before his complete esophageal obstruction resulted in aspiration pneumonia. But what?

Desperation Leads to Inspiration

Desperate moments like this sometimes spark a moment of clarity. I asked one of the floor nurses to go to the kitchen and find some meat tenderizer. Perhaps we could dissolve the meat. We mixed a slurry of the powder in water and asked the patient to sip it slowly. He seemed to know that we were trying to help. I went back on the floor to see another patient.

Twenty minutes later, the nurse called me to his room. I learned that my patient had let out a tremendous belch and the obstruction had passed. He was now smiling broadly and his breathing was not as labored. He grabbed my hand, shook it, and gave me a bear hug that nearly took my breath away.

A small miracle had just happened.

Upon Reflection...

A subsequent literature review revealed that my insight was not unique. Meat tenderizer has been used for esophageal meat impactions. It is risky because the chemicals in the tenderizer can also dissolve parts of the esophagus and increase the risk for esophageal perforation.

Not long after the choking incident, I received a stunning (museum quality) piece of artwork from my patient's daughter with an inscription of her gratitude. The wife continued to paint, but her subject changed: She began doing portraits of her husband.

And my patient? He went on to live another year without any further episodes of choking or swallowing difficulty.

http://bit.ly/3pLoj4Q

Asthmatics no higher risk dying from COVID, review of studies on 587,000 people shows

Review of 57 studies shows people with asthma had a 14% lower risk of getting COVID-19 and were significantly less likely to be hospitalized with the virus

A new study looking at how COVID-19 affects people with asthma provides reassurance that having the condition doesn't increase the risk of severe illness or death from the virus.

George Institute for Global Health researchers in Australia analysed data from 57 studies with an overall sample size of 587,280. Almost 350,000 people in the pool had been infected with COVID-19 from Asia, Europe, and North and South America and found they had similar proportions of asthma to the general population.

The results, published in the peer-reviewed *Journal of Asthma*, show that just over seven in every 100 people who tested positive for COVID-19 also had asthma, compared to just over eight in 100 in the general population having the condition. They also showed that people with asthma had a 14 percent lower risk of acquiring COVID-19 and were significantly less likely to be hospitalized with the virus.

There was no apparent difference in the risk of death from COVID-19 in people with asthma compared to those without.

Head of The Institute's Respiratory Program, co-author Professor Christine Jenkins said that while the reasons for these findings weren't clear, there were some possible explanations - such as some inhalers perhaps limiting the virus' ability to attach to the lungs.

"Chemical receptors in the lungs that the virus binds to are less active in people with a particular type of asthma and some studies suggest that inhaled corticosteroids - commonly used to treat asthma - can reduce their activity even further," she said.

"Also, initial uncertainty about the impact of asthma on COVID-19 may have caused anxiety among patients and caregivers leading them to be more vigilant about preventing infection."

Lead author Dr Anthony Sunjaya added that while this study provides some reassurance about the risks of exposure to COVID-19 in people with asthma, doctors and researchers were still learning about the effects of the virus.

"While we showed that people with asthma do not seem to have a higher risk of infection with COVID-19 compared to those without asthma and have similar outcomes, we need further research to better understand how the virus affects those with asthma," he said.

When the COVID-19 pandemic first spread across the world concerns were raised that people with asthma might be at a higher risk of becoming infected, or of becoming sicker or even dying.

Previous findings have shown that people with chronic respiratory conditions like asthma were reported to be at greater risk during the Middle East Respiratory Syndrome (MERS) outbreak, caused by a virus with a similar structure.

"Respiratory infections like those caused by coronaviruses can exacerbate asthma symptoms and corticosteroid treatment may increase susceptibility to COVID-19 infection and its severity," Dr Sunjaya said.

However this study using the best evidence available on the risk of infection, severe illness - requiring admission to ICU and/or ventilator use - and death from COVID-19 in people with asthma finds "no significant difference" of people with asthma being at higher risk.

Funded by Asthma Australia, the review included analysis of 45 hospital-based studies, six studies in the community and six with mixed setting. 22 of the studies were carried out in North America, 19 Asia, 14 Europe, and two in South America. Four of the studies only included children, making up 211 of the participants.

The average age of the participants was roughly 52; while 52.5%

were males, 11.75% were current smokers and 16.2% were former. 54% had some form of comorbidities, 21% had diabetes and approximately 8% had chronic obstructive pulmonary disease.

Thirty-six studies were peer-reviewed publications; another 17 were preprints, 3 were government reports and 1 an open dataset.

The paper's findings also show increasing age is strongly associated with an increased risk of acquiring COVID-19 among asthmatics and explained 70% of the in-between study variance in the analysis. "This is an expected finding and in line with other COVID-19 studies showing age as one of the most important predictors for vulnerability to COVID-19 and prognosis," the authors add.

This review has "rigorously adhered to the guidelines of performing systematic reviews", limitations, however are that this is the synthesis of primarily observational studies, with a short duration of follow-up, mainly self-reported asthma and variable reporting of outcomes which may introduce bias in the pooled effect.

http://bit.ly/3ka0UZr

Study reveals how a longevity gene protects brain stem cells from stress

A gene linked to unusually long lifespans in humans protects brain stem cells from the harmful effects of stress, according to a new study by Weill Cornell Medicine investigators.

Studies of humans who live longer than 100 years have shown that many share an unusual version of a gene called Forkhead box protein O3 (FOXO3). That discovery led Dr. Jihye Paik, associate professor of pathology and laboratory medicine at Weill Cornell Medicine, and her colleagues to investigate how this gene contributes to brain health during aging.

In 2018, Dr. Paik and her team showed that mice who lack the FOXO3 gene in their brain are unable to cope with stressful conditions in the brain, which leads to the progressive death of brain cells. Their new study, published Jan. 28 in *Nature Communications*, reveals that FOXO3 preserves the brain's ability to regenerate by preventing stem cells from dividing until the environment will support the new cells' survival.

"Stem cells produce new brain cells, which are essential for learning and memory throughout our adult lives," said Dr. Paik, who is also a member of the Sandra and Edward Meyer Cancer Center at Weill Cornell Medicine. "If stem cells divide without control, they get depleted. The FOXO3 gene appears to do its job by stopping the stem cells from dividing until after the stress has passed."

Many challenges like inflammation, radiation or a lack of adequate nutrients can stress the brain. But Dr. Paik and her colleagues looked specifically what happens when brain stem cells are exposed to oxidative stress, which occurs when harmful types of oxygen build up in the body.

"We learned that the FOXO3 protein is directly modified by oxidative stress," she said. This modification sends the protein into the nucleus of the stem cell where it turns on stress response genes.

The resulting stress response leads to the depletion of a nutrient called s-adenosylmethionine (SAM). This nutrient is needed to help a protein called lamin form a protective envelope around the DNA in the nucleus of the stem cell.

"Without SAM, lamin can't form this strong barrier and DNA starts leaking out," she said.

The cell mistakes this DNA for a virus infection, which triggers an immune response called the type-I interferon response. This causes the stem cell to go dormant and stop producing new neurons.

"This response is actually very good for the stem cells because the outside environment is not ideal for newly born neurons," Dr. Paik explained. "If new cells were made in such stressful conditions they would be killed. It's better for stem cells to remain dormant and wait until the stress is gone to produce neurons."

The study may help explain why certain versions of the FOXO3 are linked to extraordinarily long and healthy lives--they may help people keep a good reserve of brain stem cells. It may also help explain why regular exercise, which boosts FOXO3 helps preserve mental sharpness. But Dr. Paik cautioned it is too early to know whether this new information could be used to create new therapies for brain diseases.

"It could be a double-edged sword," Dr. Paik explained. "Over activating FOXO3 could be very harmful. We don't want to keep this on all the time."

To better understand the processes involved, she and her colleagues will continue to study how FOXO3 is regulated and whether briefly turning it on or off would be beneficial for health.

http://wb.md/3duEYqJ

How to Spot a Fake N95

Recognizing phony N95s can be easy using a few simple steps

Christina Bennett

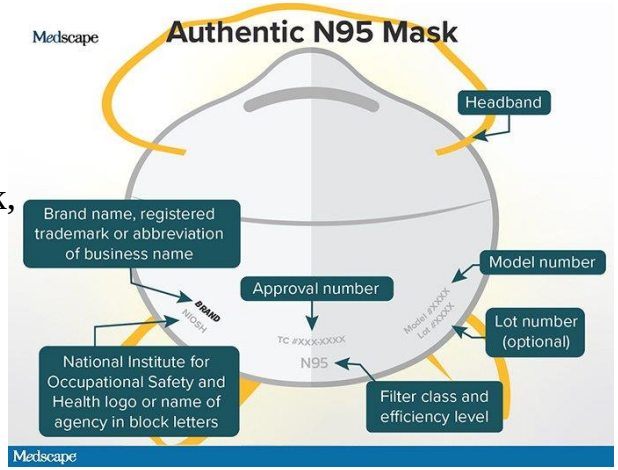
Counterfeit N95 face masks are on the rise and according to the Centers for Disease Control and Prevention, there is no guarantee they provide the same protection as masks approved by the National Institute for Occupational Safety and Health (NIOSH), the agency in the United States that regulates filtering facepiece respirators.

But recognizing phony N95s can be easy using a few simple steps.

Authentic N95 masks have an approval number, which is preceded by the letters TC, as well as a labeled model number and possibly a lot number.

Reliable masks have information about the filter class (as designated by the letters N, P, or R) and the filter efficiency (as indicated by the numbers 95, 99, or 100). An N95 mask has N for the filter class and 95 for the filter efficiency, meaning it can filter 95% or more of certain sized particles.

Valid masks also feature the NIOSH logo or the name of the agency in block letters and the brand name, registered trademark, or abbreviated name of the business holding approval for the mask. It will also have headbands, not ear loops, to secure the mask to the user's face.



A clear sign of a counterfeit mask is the presence of an FDA logo or mention of a Food and Drug Administration approval or registration; the FDA does not regulate face masks, only NIOSH does. And NIOSH does not approve face masks for children — so if there is any mention of child safety, that's another sign of a bogus mask.

http://bit.ly/3dzCW8T

Pfizer vaccine doesn't need ultra-cold storage after all, company says

The pharma giant and partner BioNTech have asked FDA to revise the vaccine's label.

Beth Mole

In a bit of good news, Pfizer and BioNTech announced today that their highly effective COVID-19 vaccine does not require ultra-cold storage conditions after all and can be kept stable at standard freezer temperatures for two weeks.

The companies have submitted data to the US Food and Drug Administration demonstrating the warmer stability in a bid for regulatory approval to relax storage requirements and labeling for the vaccine.

If the FDA greenlights the change, the warmer storage conditions

could dramatically ease vaccine distribution, allowing doses to be sent to non-specialized vaccine administration sites. The change would also make it much easier to distribute the vaccine to low-income countries.

“We have been continuously performing stability studies to support the production of the vaccine at commercial scale, with the goal of making the vaccine as accessible as possible for healthcare providers and people across the US and around the world,” Pfizer CEO Albert Bourla said in a statement. “If approved, this new storage option would offer pharmacies and vaccination centers greater flexibility in how they manage their vaccine supply.”

Balmy future

Currently, the vaccine is labeled as requiring storage between -80°C and -60°C (-112°F to -76°F) for up to six months. But it can also be refrigerated for up to five days at standard refrigerator temperature (2ºC and 8ºC (36ºF and 46ºF)). The ultra-cold requirement cooled enthusiasm for the vaccine when the FDA first granted it emergency authorization for use. Only specialized facilities, such as hospitals and research labs, tend to have freezers equipped to maintain such cold temperatures, raising concerns about how easy it would be to get the vaccine into people’s arms.

Prior to the vaccine’s rollout, Pfizer and BioNTech tried to ease those anxieties, emphasizing their expertise and existing cold-chain infrastructure. The two companies developed specially designed, temperature-controlled thermal shippers filled with dry ice to maintain a temperature of -70°C ± 10°C. The containers included GPS-enabled thermal sensors to track the location and temperature of each vaccine shipment as they made their way to distribution sites. Vaccine doses could be kept in the thermal containers for up to 30 days if the dry ice was refilled every five days.

If approved, the new storage conditions would allow the vaccine to be kept at a mere -25°C to -15°C (-13°F to 5°F)—a temperature range any standard freezer can handle—for up to two weeks. And the vaccine doses can then be kept at standard refrigerator temperatures of 2ºC to 8ºC for five days on top of that.

The companies report that as they continue testing the limits of the vaccine, they expect the expiration dates could be extended as well.

https://wb.md/3dDWnqD

FDA: COVID-19 Not Transmitted by Food or Packaging

There is no evidence you can catch coronavirus through food or food packaging, the FDA and other government agencies said Thursday.

Ralph Ellis

Since the pandemic began more than a year ago, the CDC and other health agencies have said they're pretty certain the virus is not transmitted through food or food packages. The latest statement reconfirmed that idea.

"After more than a year since the coronavirus disease 2019 (COVID-19) outbreak was declared a global health emergency, the U.S. Department of Agriculture, the U.S. Food and Drug Administration and the U.S. Centers for Disease Control and Prevention continue to underscore that there is no credible evidence of food or food packaging associated with or as a likely source of viral transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus causing COVID-19," said the statement attributed to Janet Woodcock, MD, acting commissioner of food and drugs at the U.S. Food and Drug Administration.

The statement noted that COVID-19 is a respiratory illness spread person to person. Some researchers found small amounts of virus particles on food or food packaging, but infection usually requires a much higher number of particles, the statement said.

The statement said there's an "international consensus" that the chances of infection from touching food packaging or eating food is

extremely low, such as the recent opinion from the International Commission on Microbiological Specifications for Foods.

"Based on the scientific information that continues to be made available over the course of the pandemic, the USDA and FDA continue to be confident in the safety of the food available to American consumers and exported to international customers," the statement said.

Sources:

FDA. "COVID-19 Update: USDA, FDA Underscore Current Epidemiologic and Scientific Information Indicating No Transmission of COVID-19 Through Food or Food Packaging."

CDC. "Food and Coronavirus Disease 2019 (COVID-19)."

ICMF. "ICMSF Opinion on SARS-CoV-2 and its relationship to food safety."

http://bit.ly/3bnGN66

Why a dazed deer in Tennessee had hair growing from its eyeballs

A whitetail deer was found stumbling through the streets of Farragut, Tennessee, with thick hair growing out of both of its eyeballs.

By Nicoletta Lanese - Staff Writer

The hair protruded from discs of flesh covering both the buck's cornea — the transparent part of the eye that covers the iris and pupil. The bizarre condition, called corneal dermoids, has been documented in just one other whitetail in the state of Tennessee, according to Quality Whitetails magazine, the journal of the National Deer Association.

(Image credit: National Deer Association)

A dermoid, by definition, is a type of benign tumor made of tissues that usually appear in other parts of the body; in this case, skin tissue complete with hair follicles cropped up in the deer's cornea.

The hairy-eyed deer "maybe could tell day from dark, but I wouldn't think it would be able to see where it was going," Sterling Daniels, a wildlife biologist at the Tennessee Wildlife Resources Agency (TWRA), told Quality Whitetails. "I'd compare it to covering your eyes with a washcloth. You could tell day from night, but that's about it."

The same deer tested positive for epizootic hemorrhagic disease (EHD), which can cause fever, severe tissue swelling and loss of fear of humans, according to the Cornell Wildlife Health Lab. This may explain why the disoriented animal wandered into a suburban street in late August 2020 and seemed unaware of the people nearby, Quality Whitetails reported. However, the illness does not explain why the deer's eyes sprouted tufts of hair.

The hairy skin patches likely formed early in the animal's development, while it was still in the womb, Dr. Nicole Nemeth, an associate professor in the Department of Pathology at the Southeastern Cooperative Wildlife Disease Study unit (SCWDS) of the University of Georgia vet school, told Quality Whitetails. Rather than successfully developing into a clear cornea, the tissue instead formed skin and hair follicles, obscuring the growing deer's eyes. Beneath the thick hair, the deer's eyes contained all the expected anatomy.

Despite being born with corneal dermoids, the buck had lived to be more than a year old and even grew its first set of antlers before catching EHD, which has no treatment, Quality Whitetails reported. Since the deer survived so long, Nemeth said that the dermoids probably "developed gradually," allowing the animal to adapt to its decreasing field of vision over time.

"How fast [dermoids] develop over time probably isn't well known and may vary case to case," Nemeth told Quality Whitetails.

Humans can develop dermoids in their eyes, too, causing hair to grow on their eyeballs, Live Science previously reported. The

condition is rare, so an eye doctor may only see one or two cases in their entire career. Not all these dermoids cover the center of the cornea, as in the deer's case; some dermoids form at the intersection of the cornea and the white part of the eye, called the sclera.

In this case, the condition can cause blurred vision but doesn't usually cause extreme sight problems, Live Science reported. The dermoids may be removed for cosmetic reasons, but their removal typically doesn't improve patients' eyesight.

(You can read more about the case of the hairy-eyed deer at Quality Whitetails magazine.)

http://bit.ly/37SMOXJ

Fujifilm to restart trial of Avigan to treat COVID-19, report says

Fujifilm Holdings Corp will restart a clinical trial in Japan of its antiviral drug Avigan for the treatment of COVID-19, the Nikkei newspaper reported on Sunday.

Domestic approval of the drug was delayed after a health ministry panel said in December that trial data was inconclusive. The new study will involve about 270 patients and Fujifilm will aim to seek approval again in October, Nikkei said. Representatives from Fujifilm did not immediately respond to a request for comment.

***Japan has approved Avigan as an emergency flu medicine. But concerns remain, as the drug has been shown to cause birth defects in animal studies.* | REUTERS**

Japan has approved Avigan, known generically as favipiravir, as an emergency flu medicine. But concerns remain, as the drug has been shown to cause birth defects in animal studies and its effectiveness against COVID-19 has proven difficult to demonstrate.

Japan's government has called on Fujifilm to triple national stockpiles of the drug, which has been approved for COVID-19 treatment in Russia, India and Indonesia.

http://nyti.ms/3sjPyEX

People Who Have Had Covid Should Get Single Vaccine Dose, Studies Suggest

New studies show that one shot of a vaccine can greatly amplify antibody levels in those who have recovered from the coronavirus.

By Apoorva Mandavilli

Nearly 30 million people in the United States — and probably many others whose illnesses were never diagnosed — have been infected with the coronavirus so far. Should these people still be vaccinated?

Two new studies answer that question with an emphatic yes.

In fact, the research suggests that for these people just one dose of the vaccine is enough to turbocharge their antibodies and destroy the coronavirus — and even some more infectious variants.

The results of these new studies are consistent with the findings of two others published over the past few weeks. Taken together, the research suggests that people who have had Covid-19 should be immunized — but a single dose of the vaccine may be enough.

"I think it's a really strong rationale for why people who were previously infected with Covid should be getting the vaccine," said Jennifer Gommerman, an immunologist at the University of Toronto who was not involved in the new research.

A person's immune response to a natural infection is highly variable. Most people make copious amounts of antibodies that persist for many months. But some people who had mild symptoms or no symptoms of Covid-19 produce few antibodies, which quickly fall to undetectable levels.

The vaccines "even the playing field," Dr. Gommerman said, so that anyone who has recovered from Covid-19 produces enough antibodies to protect against the virus.

The latest study, which has not yet been published in a scientific journal, analyzed blood samples from people who have had Covid-

19. The findings suggested that their immune systems would have trouble fending off B.1.351, the coronavirus variant first identified in South Africa.

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But one shot of either the Pfizer-BioNTech or Moderna vaccine significantly changed the picture: It amplified the amount of antibodies in their blood by a thousandfold — "a massive, massive boost," said Andrew T. McGuire, an immunologist at the Fred Hutchinson Cancer Research Center in Seattle, who led the study.

Flush with antibodies, samples from all of the participants could neutralize not only B.1.351, but also the coronavirus that caused the SARS epidemic in 2003.

In fact, the antibodies seemed to perform better than those in people who had not had Covid and had received two doses of a vaccine. Multiple studies have suggested that the Pfizer-BioNTech and Moderna vaccines are about five times less effective against the variant.

The researchers obtained blood samples from 10 volunteers in the Seattle Covid Cohort Study who were vaccinated months after contracting the coronavirus. Seven of the participants received the Pfizer-BioNTech vaccine and three received the Moderna vaccine.

Blood taken about two to three weeks after vaccination showed a significant jump in the amounts of antibodies compared with the samples collected before vaccination. The researchers don't yet know how long the increased amount of antibodies will persist, but "hopefully, they'll last a long time," Dr. McGuire said.

Is this helpful?

The researchers also saw increases in immune cells that remember and fight the virus, Dr. McGuire said. "It looks pretty clear that we're boosting their pre-existing immunity," he said.

In another new study, researchers at New York University found that a second dose of the vaccine did not add much benefit at all for people who have had Covid-19 — a phenomenon that has also been observed with vaccines for other viruses.

In that study, most people had been infected with the coronavirus eight or nine months earlier, but saw their antibodies increase by a hundredfold to a thousandfold when given the first dose of a vaccine. After the second dose, however, the antibody levels did not increase any further.

"It's a real testament to the strength of the immunologic memory that they get a single dose and have a huge increase," said Dr. Mark J. Mulligan, director of the N.Y.U. Langone Vaccine Center and the study's lead author.

In some parts of the world, including the United States, a significant minority of the population has already been infected, Dr. Mulligan noted. "They definitely should be vaccinated," he said.

It's unclear whether the thousandfold spike in antibody levels recorded in the lab will occur in real-life settings. Still, the research shows that a single shot is enough to increase the levels of antibodies significantly, said Florian Krammer, an immunologist at the Icahn School of Medicine at Mount Sinai in New York.

Dr. Krammer led another of the new studies, which showed that people who have had Covid-19 and received one dose of a vaccine experienced more severe side effects from the inoculation and had more antibodies compared with those who had not been infected before.

"If you put all four papers together, that's providing pretty good information about people who already had an infection only needing one vaccination," Dr. Krammer said.

He and other researchers are trying to persuade scientists at the Centers for Disease Control and Prevention to recommend only one dose for those who have recovered from Covid-19.

Ideally, those people should be monitored after the first shot in case

their antibody levels plummet after some weeks or months, said Dennis R. Burton, an immunologist at the Scripps Research Institute in La Jolla, Calif.

The fact that the supercharged antibodies observed in the new study can fight the 2003 SARS virus suggests that a single dose of the vaccine may have prompted the volunteers' bodies to produce "broadly neutralizing antibodies" — immune molecules capable of attacking a broad range of related viruses, Dr. Burton said.

He and other scientists have for decades investigated whether broadly neutralizing antibodies can tackle multiple versions of H.I.V. at once. H.I.V. mutates faster than any other virus and quickly evades most antibodies.

The new coronavirus mutates much more slowly, but there are now multiple variants of the virus that seem to have evolved to be more contagious or to thwart the immune system. The new study may provide clues on how to make a single vaccine that stimulates the production of broadly neutralizing antibodies that can destroy all variants of the coronavirus, Dr. Burton said.

Without such a vaccine, scientists will need to tweak the vaccines every time the virus changes significantly. "You're stuck in a kind of Whac-a-Mole approach," he said. It will probably take many months if not longer to develop and test that sort of vaccine against the coronavirus, but "that's the longer-term way to approach this virus."