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A grim warning from Israel: Vaccination blunts, but does not defeat Delta

Over half of Israel's cases are in the fully vaccinated, underscoring the extraordinary transmissibility of the Delta variant

By Meredith Wadman

"Now is a critical time," Israeli Minister of Health Nitzan Horowitz said as the 56-year-old got a COVID-19 booster shot on 13 August, the day his country became the first nation to offer a third dose of vaccine to people as young as age 50. "We're in a race against the pandemic."

His message was meant for his fellow Israelis, but it is a warning to the world. Israel has among the world's highest levels of vaccination for COVID-19, with 78% of those 12 and older fully vaccinated, the vast majority with the Pfizer vaccine. Yet the country is now logging one of the world's highest infection rates, with nearly 650 new cases daily per million people. More than half are in fully vaccinated people, underscoring the extraordinary transmissibility of the Delta variant and stoking concerns that the benefits of vaccination ebb over time.

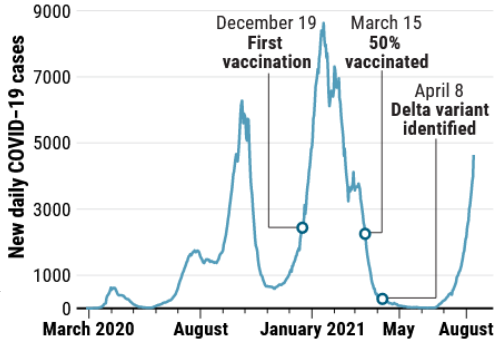
The sheer number of vaccinated Israelis means some breakthrough infections were inevitable, and the unvaccinated are still far more likely to end up in the hospital or die. But Israel's experience is forcing the booster issue onto the radar for other nations, suggesting as it does that even the best vaccinated countries will face a Delta surge.

"This is a very clear warning sign for the rest of world," says Ran Balicer, chief innovation officer at Clalit Health Services (CHS), Israel's largest health maintenance organization (HMO). "If it can happen here, it can probably happen everywhere."

Israel is being closely watched now because it was one of the first countries out of the gate with vaccinations in December 2020 and quickly achieved a degree of population coverage that was the envy of other nations— for a time. The nation of 9.3 million also has a robust public health infrastructure and a population wholly enrolled in HMOs that track them closely, allowing it to produce high-quality, real-world data on how well vaccines are working.

"I watch [Israeli data] very, very closely because it is some of the absolutely best data coming out anywhere in the world," says David O'Connor, a viral sequencing expert at the University of Wisconsin, Madison. "Israel is the model," agrees Eric Topol, a physician-scientist at Scripps Research. "It's pure mRNA [messenger RNA] vaccines. It's out there early. It's got a very high level population [uptake]. It's a working experimental lab for us to learn from."

Israel's HMOs, led by CHS and Maccabi Healthcare Services (MHS), track demographics, comorbidities, and a trove of coronavirus metrics on infections, illnesses, and deaths. "We have rich individual-level data that allows us to provide real-world evidence in near–real time," Balicer says. (The United Kingdom also compiles a wealth of data. But its vaccination campaign ramped up later than Israel's, making its current situation less reflective of what the future may portend; and it has used three different vaccines, making its data harder to parse.)



Israel's sobering setback

Israel, which has led the world in launching vaccinations and in data gathering, is confronting a surge of COVID-19 cases that officials expect to push hospitals to the brink. Nearly 60% of gravely ill patients are fully vaccinated. **K. Franklin/*Science***

Now, the effects of waning immunity may be beginning to show in Israelis vaccinated in early winter; a preprint published last month

by scientists at MHS found that protection from COVID-19 infection during June and July dropped in proportion to the length of time since an individual was vaccinated. People vaccinated in January had a 2.26 times greater risk for a breakthrough infection than those vaccinated in April. (Potential confounders include the fact that the very oldest Israelis, with the weakest immune systems, were vaccinated first.)

At the same time, cases in the country, which were scarcely registering at the start of summer, have been doubling every week to 10 days since then, with the Delta variant responsible for most of them. They have now soared to their highest level since mid-February, with hospitalizations and intensive care unit admissions beginning to follow. How much of the current surge is due to waning immunity versus the power of the Delta variant to spread like wildfire is uncertain.

What is clear is that "breakthrough" cases are not the rare events the term implies. As of 15 August, 514 Israelis were hospitalized with severe or critical COVID-19, a 31% increase from just 4 days earlier. Of the 514, 59% were fully vaccinated. Of the vaccinated, 87% were 60 or older. "There are so many breakthrough infections that they dominate and most of the hospitalized patients are actually vaccinated," says Uri Shalit, a bioinformatician at the Israel Institute of Technology (Technion) who has consulted on COVID-19 for the government. "One of the big stories from Israel [is]: 'Vaccines work, but not well enough.'"

"The most frightening thing to the government and the Ministry of Health is the burden on hospitals," says Dror Mevorach, who cares for COVID-19 patients at Hadassah Hospital Ein Kerem and advises the government. At his hospital, he is lining up anesthesiologists and surgeons to spell his medical staff in case they become overwhelmed by a wave like January's, when COVID-19 patients filled 200 beds. "The staff is exhausted," he says, and he has restarted a weekly support group for them "to avoid some kind of PTSD [post-traumatic stress disorder] effect."

To try to tame the surge, Israel has turned to booster shots, starting on 30 July with people 60 and older and, last Friday, expanding to people 50 and older. As of Monday, nearly 1 million Israelis had received a third dose, according to the Ministry of Health. Global health leaders including Tedros Adhanom Ghebreyesus, director-general of the World Health Organization, have pleaded with developed countries not to administer boosters given that most of the world's population hasn't received even a single dose. The wealthy nations pondering or already administering booster vaccines so far mostly reserve them for special populations such as the immune compromised and health care workers.

Still, studies suggest boosters might have broader value. Researchers have shown that boosting induces a prompt surge in antibodies, which are needed in the nose and throat as a crucial first line of defense against infection. The Israeli government's decision to start boosting those 50 and older was driven by preliminary Ministry of Health data indicating people over age 60 who have received a third dose were half as likely as their twice-vaccinated peers to be hospitalized in recent days, Mevorach says. CHS also reported that out of a sample of more than 4500 patients who received boosters, 88% said any side effects from the third shot were no worse, and sometimes milder, than from the second.

Yet boosters are unlikely to tame a Delta surge on their own, says Dvir Aran, a biomedical data scientist at Technion. In Israel, the current surge is so steep that "even if you get two-thirds of those 60-plus [boosted], it's just gonna give us another week, maybe 2 weeks until our hospitals are flooded." He says it's also critical to vaccinate those who still haven't received their first or second doses, and to return to the masking and social distancing Israel thought it had left behind—but has begun to reinstate.

Aran's message for the United States and other wealthier nations considering boosters is stark: "Do not think that the boosters are the solution."

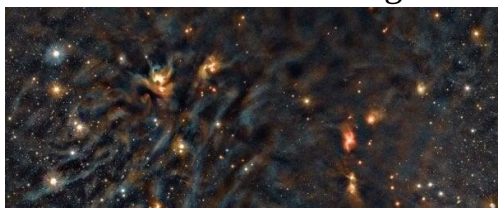
https://bit.ly/2VW2cjq

This Eerie Star Nursery Shows How The Solar System Got Radioactive Elements

A roiling cloud complex, thick with the turbulence of star formation, is yielding up new clues as to the formation of our Solar System.

Michelle Starr

Analysis of gamma rays from the Ophiuchus star-forming complex has given us even more evidence that short-lived radioactive elements in the early Solar System were delivered via the supernova explosions of nearby stars when the Sun was being born. This validates an elemental enrichment model suspected for decades, and gives us valuable insight into the breathtaking life-and-death cycle of stars.



The stellar nursery in near-infrared. **(João Alves/ESO VISIONS)**

"Our Solar System was most likely formed in a giant molecular cloud together with a young stellar cluster, and one or more supernova events from some massive stars in this cluster contaminated the gas which turned into the Sun and its planetary system," said astronomer and astrophysicist Douglas N. C. Lin of the University of California, Santa Cruz.

"Although this scenario has been suggested in the past, the strength of this paper is to use multi-wavelength observations and a sophisticated statistical analysis to deduce a quantitative measurement of the model's likelihood."

Stars are born when a spinning knot of dense gas in a molecular cloud collapses under its own gravity. Material in the cloud flattens out into an accretion disk that feeds into the growing star; once the star has finished forming, the leftover disk forms everything else in the planetary system - so while elemental abundances may vary from body to body, *everything* in a planetary system is made from the same piece of molecular cloud. These molecular clouds are huge, vast complexes that give birth to many stars. These are called stellar nurseries. Our Sun was probably born this way, although it has long since left its birthplace and siblings behind.

Figuring out how the Solar System was born and came to be the way it is, requires detective work by piecing together clues from within the Solar System, and observing others coming into existence.

The Ophiuchus star-forming complex is just 460 light-years away - that's a pretty short distance on relative cosmic scales. And in this complex, astronomers have detected gamma rays emitted by the short-lived radionuclide aluminum-26.

Aluminum-26 has a half-life of 717,000 years. Therefore, any of this isotope that may have been around in the early Solar System - 4.6 billion years ago - would be long gone by now.

In the 1970s, though, scientists found inclusions in pristine meteorites that they concluded were the decay products of short-lived radionuclides, which raised the question: where did they come from? The answer was from nearby supernovae, or the stellar winds from dying Wolf-Rayet stars, but how many sources, where they are, and the penetration rate of aluminum-26 remained unknown.

It's not unusual for stellar nurseries to be bathed by the radiation of supernovae. Such regions produce a variety of stars, including some so massive that they live and die while other stars are still being born.

Using observations across a range of wavelengths, including incredible new infrared images, the researchers noted a stream of aluminum-26 from a nearby star cluster that had hosted such

supernovae to a star-forming region of the Ophiuchus complex.

"The enrichment process we're seeing in Ophiuchus is consistent with what happened during the formation of the Solar System 5 billion years ago," said astrophysicist John Forbes of the Flatiron Institute. "Once we saw this nice example of how the process might happen, we set about trying to model the nearby star cluster that produced the radionuclides we see today in gamma rays."

These models accounted for every massive star that could have existed in the region in the window to produce aluminum-26, the probability of those stars going supernova, and the potential yields of the radionuclides from supernovae as well as stellar winds.

Based on this modelling, the researchers were able to conclude that there is a 59 percent chance that the aluminum-26 is produced by a supernova, and a 68 percent chance that there were multiple sources and more than one supernova.

This suggests that there is a wide range of radionuclide abundances that can be incorporated into a forming planetary system. In turn, this could have implications for the search for habitable systems.

"Many new star systems will be born with aluminum-26 abundances in line with our solar system, but the variation is huge - several orders of magnitude," Forbes said.

"This matters for the early evolution of planetary systems, since aluminum-26 is the main early heating source. More aluminum-26 probably means drier planets."

The research has been published in *Nature Astronomy*.

https://bit.ly/2W2M4Mw

The search for life on Mars expands to studying its moons

JAXA believe the best chance of finding evidence of life on Mars lies on one or both of its moons

by Bob Yirka , Phys.org

A pair of researchers at the Japan Aerospace Exploration Agency (JAXA) has published a perspective piece in the journal *Science* outlining the efforts being conducted this decade to find out if Mars once hosted life. In their article, Ryuki Hyodo and Tomohiro Usui outline the three main efforts that are involved in looking for evidence of life on Mars over the next ten years, and explain why they and others at JAXA believe the best chance of finding evidence of life on Mars lies on one or both of its moons.

As Hyodo and Usui note, NASA is currently conducting a study of the Jezero Crater on the surface of Mars with its Perseverance rover. That work will be part of a later joint effort between NASA and the ESA to collect samples from Mars and bring them back to Earth. Also scheduled is Japan's Martian Moons eXploration (MMX) project, which will involve sending probes to both of Mars' moons and bringing back samples before the decade is out.

Hyodo and Usui note that both of Mars' moons—Phobos and Deimos—are smaller than Earth's moon. They are also much closer to the planet. The researchers note that probes sent to study the surface of Mars will only be able to test a very small part of its surface—imagine, they suggest, a probe touching down in the middle of the Sahara Desert; it would find signs of life, no doubt, but would find only a very small fraction of it. They suggest that a probe on one of Mars' moons might have more luck. They note that prior research has suggested that Mars was once wet. Prior research has also shown that Mars has been struck by many asteroids over the course of millions of years. Some of the larger strikes have led to bits of the surface being blasted into space—one such bit has even been found here on Earth. They suggest that many bits of the planet have been blasted into space, some of which have no doubt made their way to the surface of one or both of its moons. Such bits, they note, would likely represent a large portion of the Martian surface. Because both moons have very nearly sterile environments, material containing proof of life may still be there.

More information: *Ryuki Hyodo et al, Searching for life on Mars and its moons, Science (2021). DOI: 10.1126/science.abj1512*

https://nyti.ms/3k4u4ti

Saturn's Rings Are Like a Seismometer That Reveal the Planet's Core

Convulsions in the planet's interior are picked up in the region known as the C ring, and help scientists understand what lies within.

By Robin George Andrews

Saturn's icy rings are not just aesthetically wondrous marvels. One of them also records a beautiful planetary soundtrack.

The planet's interior, concealed beneath a shroud of mostly hydrogen gas, convulses. This causes shifts in the local gravity field, which pulls at particles in Saturn's expansive C ring and makes them dance. These idiosyncratic prances can take the form of spiral waves, and distinct sets of waves reveal the characteristics of particular features of Saturn's insides.

Put another way, Saturn is an orchestra. Different notes are showing up on the C ring, like those on sheet music. Scientists can read these notes, hear the music and identify the individual instruments and musicians performing — all without ever seeing the orchestra itself.

Using data from the Cassini mission that ended in 2017, scientists have listened to and deconstructed a variety of symphonies in Saturn's C ring over the years. Now, two researchers from the California Institute of Technology — Christopher Mankovich, a planetary scientist, and Jim Fuller, a theoretical astrophysicist — have decoded enough of this music to hear the sounds of one of Saturn's most puzzling features: its core.

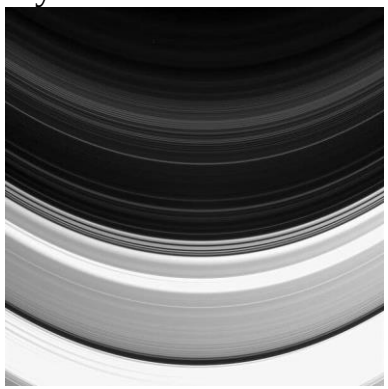
According to their paper, published on Monday in the journal Nature Astronomy, the core is colossal: It makes up 60 percent of the planet's radius and is 55 times the mass of Earth. And unlike the ordered solid clump of metallic, rocky or icy matter found within other worlds, Saturn's core is a pandemonious amalgam of assorted rocks and ices mingling with a fluid metallic form of hydrogen. The findings bring researchers closer to understanding how Saturn — and other gassy behemoths like it, including Jupiter — was born.

"It's a very beautiful story," said Linda Spilker, the project scientist for the Cassini mission at NASA's Jet Propulsion Laboratory, who was not involved with the work.

The geologic viscera of Earth, the moon and (most recently) Mars were mapped out with seismometers, instruments that record the journeys of seismic waves moving through the planet and behaving differently as they traverse through mechanically different layers. Saturn, lacking a solid surface, makes this sort of detective work impossible.

Orbiting spacecraft can roughly map out a gassy planet's internal layer cake structure by detecting subtle changes in gravity. But Saturn's core has such a weak effect on the planet's gravitational field that this trick cannot be used to precisely visualize it.

Fortunately, the shimmying of Saturn's C ring has unveiled what traditional techniques cannot. Over the past three decades, scientists have been observing the ring's strange spiral waves through imagery from both the Voyager missions and Cassini. And they ultimately reasoned that those spirals are being caused by gargantuan oscillations within Saturn.



Saturn's C and D rings. The C rings occupy the bottom half of this image and are brighter than the D rings. **Credit...NASA/JPL-Caltech/Space Science Institute**

"They're just constant quakes that exist everywhere on the planet," Dr. Mankovich said.

It is a technique known as “kronoseismology”: “kronos” being the Greek word for Saturn, and “seismo” pertaining to shakes. In 2019, it was used to solve another puzzle: How long is a day on Saturn? (About 10 and a half Earth-hours.)

Now Saturn’s core has been illuminated. Older models depicted the planet as if it were a distinctly layered cosmic jawbreaker candy. Kronoseismology has revealed the messy truth. The core is made up of not only rock and ice but also fluid metallic hydrogen, which was previously assumed to be a separate layer. There is more rock and ice at its center, and more fluid metallic hydrogen at its outer edges — but, throughout, everything is mixed in a chaotic cocktail. Along with the transitionary change from fluid to gassy hydrogen higher up, this paper paints Saturn as one big fuzzy ball.

Despite the technique’s continued success, scientists still don’t know what is causing the core to oscillate and create those spiral waves in the C ring. Earth resonates like a bell when it is rocked by powerful tectonic temblors. “But Saturn is fluid, so where are the quakes?” asked Mark Marley, a planetary scientist at the University of Arizona and an early trailblazer of kronoseismology who was not involved with the work.

The orchestra’s musicians may finally be known, but the hunt for its elusive conductor continues.

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A Simple Diet Can Send Type 2 Diabetes Into Remission, According to Science

Study results have so far shown a low-carbohydrate diet to be promising

Duane Mellor & Adrian Brown, The Conversation

Until recently, type 2 diabetes has mainly been managed by controlling risk factors – such as high blood pressure, cholesterol and blood sugar (glucose) levels – usually by prescribing drugs.

But this approach doesn't address the underlying causes of type 2 diabetes – such as problems with the hormone insulin no longer effectively controlling blood sugar. While taking drugs can help to manage blood sugar levels, it won't help unpick the biological causes behind type 2 diabetes.

A growing body of research shows that losing weight, either through surgery or dieting, can help address some of the underlying causes of type 2 diabetes. It does this by helping the body control blood sugar levels. This is significant as controlling blood sugar by improving how insulin is made and works is key to bringing type 2 diabetes into remission.

Most of this body of research so far has looked at using meal-replacement shakes to help people with type 2 diabetes, which is why this approach may be prescribed by a doctor.

But, more recently, researchers have begun investigating other diets – such as low-carbohydrate diets – in achieving remission. Although research in this area is still emerging, study results have so far shown a low-carbohydrate diet to be promising.

To better understand which diets are best at helping people achieve type 2 diabetes remission, our recent review looked at over 90 papers describing the effects of various diets on type 2 diabetes.

We found that although the better quality research tended to focus on meal-replacement shakes used in clinical trials, other approaches (such as low-carbohydrate diets) were also shown to work well.

Our review found that meal-replacement diets helped around one in three people successfully achieve remission, while low carbohydrate diets were able to help around one in five people achieve remission. People who lost weight using both of these diets were able to stay in remission for up to two years if they maintained their weight loss. Low calorie and Mediterranean diets were also able to help people achieve remission – but at much lower rates. Only around 5 percent of people on low-calorie diets stayed in remission after one year, while only 15 percent of people on a

Mediterranean diet stayed in remission after a year.

Defining remission

One of the big challenges we faced when writing our review was defining what "remission" is. Knowing how to define it was important so we could understand which diets worked best in helping people achieve remission.

The reason this was difficult is because the definition varies between different expert groups and research studies.

Most define remission as a reduction of blood sugar levels below the range to diagnose diabetes – but some definitions state that this needs to be done without the use of drugs, while others do not. Other definitions say weight (especially fat around the midsection) must be lost to achieve remission.

Another challenge we faced when defining remission was that some reports suggest low-carbohydrate diets can normalize blood sugar levels even without weight loss.

This happens because when we eat carbohydrates, they're broken down into sugars which cause our blood sugar levels to rise. A low-carbohydrate diet means less blood sugar appears in the bloodstream, leading to improved blood sugar control.

For that reason, we initially defined remission using the definition each study used. Then, we compared the numbers of people whose blood sugar levels normalized without drugs for at least six months – which most consider to be true remission.

Mitigation v remission

While low-carbohydrate diets help people achieve remission, there's concern that blood sugar levels could potentially rise again as soon as more carbohydrates are eaten. This is why we suggest in our review that rather than call this remission, it should perhaps be called "mitigation of diabetes", as type 2 diabetes is still present – but the negative effects are being well managed. We think that remission can only be achieved if fat is lost from around the organs. This allows insulin to be made and used effectively again.

But because carbohydrates are also a major energy source in our diet, eating less of these often results in consuming fewer calories – which typically results in weight loss. So if someone is able to maintain a low-carbohydrate diet long term, they will not only reduce blood sugar levels and risk of complications for their diabetes, but may also achieve remission.

Regardless, the evidence that we looked at in our review made clear that there are many ways a person can significantly improve their blood sugar levels through diet – and that this can lead to remission in many cases. The key thing we found with each type of diet is that at least 10-15 kg of body weight needed to be lost to achieve remission.

However, although weight loss seems to be the best predictor of success, it assumes fat loss from the pancreas and liver. It will be important for future studies to compare how these diets work for different ethnic groups, as type 2 diabetes can happen at lower body weights in different ethnic groups, who may have less weight to lose.

Not everyone may be able to achieve remission, but people who are younger (less than 50), male, have had type 2 diabetes for less than six years and lose more weight are more likely to be successful.

This could be because these people are able to reverse the causes of their diabetes, recovering more of the pancreas's ability to make insulin and the liver's ability to use it. But this doesn't mean others won't be successful if they improve their diet and lifestyle, and lose weight. Whether or not a person achieves remission, reducing blood sugar levels is important in managing the negative effects of type 2 diabetes and reducing risk of complications.

But when it comes to choosing a diet, the most important thing is to pick one that suits you – one that you're likely to stick to long term.

Duane Mellor, Lead for Evidence-Based Medicine and Nutrition, Aston Medical School,

Aston University and Dr Adrian Brown, Research Fellow & Lecturer, UCL.

https://wb.md/3yUWdJH

Youngest Kids More Likely to Spread SARS-CoV-2 to Family: Study

Young children are more likely than their older siblings to transmit SARS-CoV-2 in their households

Michele Cohen Marill

Young children are more likely than their older siblings to transmit SARS-CoV-2 in their households, according to an analysis of public health records in Ontario, Canada – a finding that upends the common belief that children play a minimal role in COVID-19 spread.

The study by researchers from Public Health Ontario, published online today in *JAMA Pediatrics*, found that teenagers (14- to 17-year-olds) were more likely than their younger siblings to bring the virus into the household, while infants and toddlers (up to age 3) were about 43% more likely than the older teens to spread it to others in the home.

Children or teens were the source of SARS-CoV-2 in about one in 13 Ontario households between June and December 2020, the study shows. Researchers from Public Health Ontario analyzed health records from 6280 households with a pediatric COVID-19 case and a subset of 1717 households in which a child up to age 17 was the source of transmission in a household. When analyzing the data, researchers controlled for gender differences, month of disease onset, testing delay, and mean family size.

The role of young children in transmission seemed logical to some experts who have been tracking the evolution of the pandemic. "I think what was more surprising was how long the narrative persisted that children weren't transmitting SARS-CoV-2," said Sam Scarpino, PhD, managing director of pathogen surveillance at the Rockefeller Foundation.

Meanwhile, less mask-wearing, the return to school and activities, and the onslaught of the Delta variant have changed the dynamics of spread, said Andrew Pavia, MD, chief of the Division of Pediatric Infectious Diseases at the University of Utah.

"Adolescents and high-school-aged kids have had much, much higher rates of infection in the past," he said. "Now when we look at the rates of school-aged kids, they are the same as high-school-aged kids, and we're seeing more and more in the preschool age groups."

Cases May Be Underestimated

If anything, the study may underestimate the role young children play in spreading COVID in families, since it only included symptomatic cases as the initial source and young children are more likely to be asymptomatic, Pavia said.

The Delta variant heightens the concern; it is more than twice as infectious as previous strains and has spurred a rise in pediatric cases, including some co-infection with other circulating respiratory diseases, such as respiratory syncytial virus (RSV).

The Ontario study covers a period before vaccination and the spread of the Delta variant. "As the number of pediatric cases increases worldwide, the role of children in household transmission will continue to grow," the authors conclude.

Following recommended respiratory hygiene is clearly more difficult with very young children. For example, parents, caregivers, and older siblings aren't going to stay 6 feet away from a sick baby or toddler, noted Susan Coffin, MD, MPH, a pediatric infectious disease physician, and David Rubin, MD, a pediatrician and director of PolicyLab at Children's Hospital of Philadelphia, in an accompanying commentary.

"Cuddling and touching are part and parcel of taking care of a sick young child, and that will obviously come with an increased risk of transmission to parents as well as to older siblings who may be

helping to care for their sick brother or sister," they write.

While parents may wash their hands more frequently when caring for a sick child, they aren't likely to wear a mask, said William Schaffner, MD, an infectious disease specialist at Vanderbilt University, Nashville, Tennessee.

"I imagine some moms even take a sick child into bed with them," he said. "It's probably just the extensive contact one has with a sick, very small child that augments their capacity to transmit this infection."

What Can Be Done

What can be done, then, to reduce the household spread of COVID-19? "The obvious solution to protect a household with a sick young infant or toddler is to make sure that all eligible members of the household are vaccinated," Coffin and Rubin state in their commentary.

The American Academy of Pediatrics recently wrote Janet Woodcock, MD, acting commissioner of the US Food and Drug Administration, asking for the agency to authorize use of SARS-CoV-2 vaccines for children under age 12 "as soon as possible," noting that "the Delta variant has created a new and pressing risk to children and adolescents across this country, as it has also done for unvaccinated adults."

The FDA reportedly asked vaccine makers Pfizer and Moderna to expand the clinical trials of children, which may delay authorization for younger age groups. Pfizer has said it plans to submit a request for emergency use authorization of its vaccine for 5- to 11-year-olds in September or October.

As with adult vaccination, hesitancy is likely to be a barrier. Less than half of parents said they are very or somewhat likely to have their children get a COVID vaccine, according to a national survey conducted by researchers at the University of California, Los Angeles.

The Ontario study provides valuable evidence to support taking steps to protect children from transmission in schools, including mask requirements, frequent testing, and improved ventilation, said Scarpino. "We're not going to be able to control COVID without vaccinating younger individuals," he said.

JAMA Pediatr. Published online August 16, 2021. Study, Commentary

Pavia has consulted for GlaxoSmithKline on non-COVID-related issues. Sarah Buchan, PhD, study author and scientist at Public Health Ontario, reported grants from the Canadian Institutes of Health Research for research on influenza, RSV, and COVID-19, and grants from the Canadian Immunity Task Force for COVID-19 outside the submitted work. Coffin reported grants as a Centers for Disease Control and Prevention co-investigator at a Vaccine and Treatment Evaluation Unit site conducting COVID vaccine trials in children. Scarpino holds unexercised options in ILiAD Biotechnologies, which is focused on the prevention and treatment of pertussis. Schaffner is a consultant for VBI Vaccines.

https://wb.md/3CZt3LJ

'Tainted' Blood: COVID Skeptics Request Blood Transfusions From Unvaccinated Donors

The nation's roiling tensions over vaccination against covid-19 have spilled into an unexpected arena: lifesaving blood transfusions.

JoNel Aleccia

With nearly 60% of the eligible U.S. population fully vaccinated, most of the nation's blood supply is now coming from donors who have been inoculated, experts said. That's led some patients who are skeptical of the shots to demand transfusions only from the unvaccinated, an option blood centers insist is neither medically sound nor operationally feasible.

"We are definitely aware of patients who have refused blood products from vaccinated donors," said Dr. Julie Katz Karp, who directs the blood bank and transfusion medicine program at Thomas Jefferson University Hospitals in Philadelphia.

Emily Osment, an American Red Cross spokesperson, said her organization has fielded questions from clients worried that

vaccinated blood would be "tainted," capable of transmitting components from the covid vaccines. Red Cross officials said they've had to reassure clients that a covid vaccine, which is injected into muscle or the layer of skin below, doesn't circulate in the blood. "While the antibodies that are produced by the stimulated immune system in response to vaccination are found throughout the bloodstream, the actual vaccine components are not," Jessa Merrill, the Red Cross director of biomedical communications, said in an email.

So far, such demands have been rare, industry officials said. Dr. Louis Katz, chief medical officer for ImpactLife, an Iowa-based blood center, said he's heard from "a small handful" of patients asking for blood from unvaccinated donors. And the resounding answer from centers and hospitals, he added, has been "no."

"I know of no one who has acceded to such a request, which would be an operational can of worms for a medically unjustifiable request," Katz wrote in an email.

In practical terms, blood centers have only limited access to donated blood that has not in some way been affected by covid. Based on samples, Katz estimated that as much as 60% to 70% of the blood currently being donated is coming from vaccinated donors. Overall, more than 90% of current donors have either been infected with covid or vaccinated against it, said Dr. Michael Busch, director of the Vitalant Research Institute, who is monitoring antibody levels in samples from the U.S. blood supply.

"Less than 10% of the blood we collect does not have antibodies," Busch noted.

In addition, outside of research studies, blood centers in the U.S. don't retain data noting whether donors have been infected with or vaccinated against covid, and there's no federal requirement that collected blood products be identified in that manner.

"The Food and Drug Administration has determined there's no safety risk, so there's no reason to label the units," said Dr. Claudia Cohn, chief medical officer for AABB, a nonprofit focused on transfusion medicine and cellular therapies.

Indeed, the FDA does not recommend routine screening of blood donors for covid. Respiratory viruses, in general, aren't known to spread by blood transfusion and, worldwide, there have been no reported cases of SARS-CoV-2, the virus that causes the disease, being transmitted via blood. One study identified the risk as "negligible."

All donors are supposed to be healthy when they give blood and answer basic questions about potential risks. Collected units of blood are tested for transmissible infectious diseases before they're distributed to hospitals. But that hasn't quelled concerns for some people skeptical of covid vaccines.

In Bedford, Texas, the father of a boy scheduled for surgery recently asked that his son get blood exclusively from unvaccinated donors, said Dr. Geeta Paranjape, medical director at Carter BloodCare. Separately, a young mother fretted about transfusions from vaccinated donors to her newborn.

Many patients expressing concerns have been influenced by rampant misinformation about vaccines and the blood supply, said Paranjape. "A lot of people think there's some kind of microchip or they're going to be cloned," she said.

Other patients have balked at getting blood from people previously infected with covid, even though federal guidance greenlights donations two weeks after a positive test or the last symptom fades.

Last month, a woman facing a cesarean section for a high-risk pregnancy said she didn't want blood from a donor who had had covid, recalled Cohn with AABB. "I said, 'Listen, the alternative is you don't get the blood and that's what will affect you,'" Cohn said.

Some industry experts were hesitant to discuss the vaccine-free blood requests, for fear it would fuel more such demands. But Cohn

and others said correcting widely spread misinformation outweighed the risk.

Patients are free to refuse transfusions for any reason, industry officials said. But in dire situations — trauma, emergency surgery — saving lives often requires using the available blood. For patients with chronic conditions requiring transfusion, alternative treatments such as medication or certain equipment may not be as efficient or effective.

People who require transfusions also may donate their own blood in advance or request donations from designated friends and family members. But there's no evidence that the blood is safer when patients select donors than that provided by the volunteer blood system, according to the Red Cross.

Earlier in the pandemic, many blood donations were tested to see whether they contained antibodies to the covid virus. The hope was that blood from previously infected people who had recovered from covid could be used to treat those who were very sick with the disease. Tens of thousands of patients were treated with so-called convalescent plasma under a Mayo Clinic-led program and through authorization from the FDA.

But the much-hyped use of convalescent plasma largely fell flat after studies showed no clear-cut benefits for the broad swath of covid patients. (Research continues into the potential benefits of treating narrowly targeted patient groups with high-potency plasma.) Most hospitals stopped testing blood and labeling units with high levels of antibodies this spring, said Busch. "It's really no longer a germane issue because we're not testing anymore," he said. "There's no way we can inform recipients."

Busch stressed that the studies also have shown no harm associated with infusing antibody-containing blood plasma into covid patients.

Past health crises have raised similar concerns about sources of donor blood. In the mid-1980s, recipients scared by the AIDS epidemic didn't want blood donated from cities such as San Francisco with large gay populations, Busch recalled. Even now, some recipients demand not to receive blood from people of certain races or ethnicities.

Such requests, like those for vaccine-free blood, have no medical or scientific basis and are soundly refused, blood center officials said.

The most pressing issue for blood centers remains the ongoing shortage of willing donors. As of the second week of August, the national blood supply was down to two days' worth or less at a third of sites affiliated with America's Blood Centers. That can limit the blood available for trauma victims, surgery patients and others who rely on transfusions to survive.

"If for some reason we didn't want vaccinated people to donate blood, we'd be in a real problem, wouldn't we?" Karp said. "Please believe us when we tell you it's fine."

https://bit.ly/3z0tUJK

Self-screening urine test for depression and other mental illness developed in Japan

Urine for a mental health screening.

Master Blaster

Although progress is being made, mental illness still carries a stigma in Japan, making it harder for many people to seek the help they need. It's especially a problem among the older generation, but when the bulk of the population is elderly, it becomes everyone's problem.

Luckily, one potential solution has arrived in **a test kit developed by Cellspect, a medical equipment supplier in Morioka City, Iwate Prefecture**. From late August, these kits will be made available online and at drugs stores in the six prefectures of the Tohoku region (Akita, Aomori, Fukushima, Iwate, Miyagi, and Yamagata) for between 3,000 and 4,000 yen (US$27-$36) each.

Those who purchase the test must first collect a urine sample and

then submit it either by mail or directly at participating drug stores. The urine will then be analyzed to assess the owner's risk factors for mental illnesses such as depression and the results can be sent directly to their smartphone.

It's important to note that **these tests do not diagnose mental illness but instead gauge a person's potential for developing one.** If a high risk is found, then that person should seek a professional diagnosis to know if they are currently suffering from such an illness or what steps they should take to prevent it in the future.

Urine tests to detect mental illness symptoms themselves are not new and are somewhat controversial as to their effectiveness. However, as a discreet way for people take that first step into examining their own mental health, these self-screen kits could make a significant difference in Japan.

Some readers of the news were also tempted to try one, despite being confused about how it works.

"Why don't they do that with the urine test at my annual physical?"
"I kind of want to try this…"
"Companies should just install these kits directly in their toilets."
"Huh, this could be good."
"They can do that with urine?"
"Isn't it just a test for anti-depressant drugs?"
"Is depression such a thing? I didn't think you could detect mental things with urine, but if a medical supply company can do it, I guess it is possible."

Some of the confusion displayed in the comments show how mental illness is often misunderstood as not even a medical problem, making proper treatment that much more difficult. This uncertainty combined with a sense of embarrassment would often have people resort to self-diagnosing online among all its misinformation.

This new kit gives that same sense of privacy but from a more reliable source that can also help people get on the right track to proper mental health. It may not change the world, but every little bit counts.

https://bit.ly/38353sN

Researchers May Have Discovered the Root Cause of Long COVID Syndrome

Higher measures of blood clotting may help explain the persistent symptoms

New evidence shows that patients with Long COVID syndrome continue to have higher measures of blood clotting, which may help explain their persistent symptoms, such as reduced physical fitness and fatigue.

The study, led by researchers from RCSI University of Medicine and Health Sciences, is published in the *Journal of Thrombosis and Haemostasis*.

Previous work by the same group studied the dangerous clotting observed in patients with severe acute COVID-19. However, far less is known about Long COVID syndrome, where symptoms can last weeks to months after the initial infection has resolved and is estimated to affect millions of people worldwide.

The researchers examined 50 patients with symptoms of Long COVID syndrome to better understand if abnormal blood clotting is involved.

They discovered that clotting markers were significantly elevated in the blood of patients with Long COVID syndrome compared with healthy controls.

These clotting markers were higher in patients who required hospitalization with their initial COVID-19 infection, but they also found that even those who were able to manage their illness at home still had persistently high clotting markers.

The researchers observed that higher clotting was directly related to other symptoms of Long COVID syndrome, such as reduced physical fitness and fatigue.

Even though markers of inflammation had all returned to normal levels, this increased clotting potential was still present in Long

COVID patients.

"Because clotting markers were elevated while inflammation markers had returned to normal, our results suggest that the clotting system may be involved in the root cause of Long COVID syndrome," said Dr. Helen Fogarty, the study's lead author, ICAT Fellow and PhD student at the Irish Centre for Vascular Biology in the RCSI School of Pharmacy and Biomolecular Sciences.

This work was funded by the Welcome Trust, the Health Research Board (HRB) Irish Clinical Academic Training (ICAT) programme as well as the HRB-funded Irish COVID-19 Vasculopathy Study (ICVS).

The work was also supported by a philanthropic grant from the 3M Foundation to RCSI University of Medicine and Health Sciences in support of COVID-19 research.

"Understanding the root cause of a disease is the first step toward developing effective treatments," said Professor James O'Donnell, Director of the Irish Centre for Vascular Biology, RCSI and Consultant Haematologist in the National Coagulation Centre in St James's Hospital, Dublin.

"Millions of people are already dealing with the symptoms of Long COVID syndrome, and more people will develop Long COVID as the infections among the unvaccinated continue to occur. It is imperative that we continue to study this condition and develop effective treatments."

Reference: "Persistent Endotheliopathy in the Pathogenesis of Long COVID Syndrome" by Helen Fogarty, Liam Townsend, Hannah Morrin, Azaz Ahmad, Claire Comerford, Ellie Karampini, Hanna Englert, Mary Byrne, Colm Bergin, Jamie M. O'Sullivan, Ignacio Martin-Loeches, Parthiban Nadarajan, Ciaran Bannan, Patrick W. Mallon, Gerard F. Curley, Roger J.S. Preston, Aisling M. Rehill, Dennis McGonagle, Cliona Ni Cheallaigh, Ross I. Baker, Thomas Renné, Soracha E. Ward, James S. O' Donnell, The Irish COVID-19 Vasculopathy Study (iCVS) investigators, 10 August 2021, Journal of Thrombosis and Haemostasis.

DOI: 10.1111/jth.15490

https://bit.ly/3CXmuJI

With explosive new result, laser-powered fusion effort nears 'ignition'

Single laser shot sparked a fusion explosion that was 70% of the energy of the laser pulse that triggered it

By Daniel Clery

More than a decade ago, the world's most energetic laser started to unleash its blasts on tiny capsules of hydrogen isotopes, with managers promising it would soon demonstrate a route to limitless fusion energy. Now, the National Ignition Facility (NIF) has taken a major leap toward that goal. Last week, a single laser shot sparked a fusion explosion from a peppercorn-size fuel capsule that produced eight times more energy than the facility had ever achieved: 1.35 megajoules (MJ)—roughly the kinetic energy of a car traveling at 160 kilometers per hour. That was also 70% of the energy of the laser pulse that triggered it, making it tantalizingly close to "ignition": a fusion shot producing an excess of energy.

"After many years at 3% of ignition, this is superexciting," says Mark Herrmann, head of the fusion program at Lawrence Livermore National Laboratory, which operates NIF.

NIF's latest shot "proves that a small amount of energy, imploding a small amount of mass, can get fusion. It's a wonderful result for the field," says physicist Michael Campbell, director of the Laboratory for Laser Energetics (LLE) at the University of Rochester.

"It's a remarkable achievement," adds plasma physicist Steven Rose, co-director of the Centre for Inertial Fusion Studies at Imperial College London. "It's made me feel very cheerful. … It feels like a breakthrough."

And it is none too soon, as years of slow progress have raised questions about whether laser-powered fusion has a practical future. Now, according to LLE Chief Scientist Riccardo Betti, researchers

need to ask: “What is the maximum fusion yield you can get out of NIF? That’s the real question.”

Fusion, which powers stars, forces small atomic nuclei to meld together into larger ones, releasing large amounts of energy. Extremely hard to achieve on Earth because of the heat and pressure required to join nuclei, fusion continues to attract scientific and commercial interest because it promises copious energy, with little environmental impact.

Yet among the many approaches being investigated, none has yet generated more energy than was needed to cause the reaction in the first place. Large doughnut-shaped reactors called tokamaks, which use magnetic fields to cage a superhot plasma for long enough to heat nuclei to fusion temperatures, have long been the front-runners to achieve a net energy gain. But the giant $25 billion ITER project in France is not expected to get there for more than another decade, although private fusion companies are promising faster progress.

NIF’s approach, known as inertial confinement fusion, uses a giant laser housed in a facility the size of several U.S. football fields to produce 192 beams that are focused on a target in a brief, powerful pulse—1.9 MJ over about 20 nanoseconds. The aim is to get as much of that energy as possible into the target capsule, a diminutive sphere filled with the hydrogen isotopes deuterium and tritium mounted inside a cylinder of gold the size of a pencil eraser. The gold vaporizes, producing a pulse of x-rays that implodes the capsule, driving the fusion fuel into a tiny ball hot and dense enough to ignite fusion. In theory, if such tiny fusion blasts could be triggered at a rate of about 10 per second, a power plant could harvest energy from the high-speed neutrons produced to generate electricity.

When NIF launched, computer models predicted quick success, but fusion shots in the early years only generated about 1 kilojoule (kJ) each. A long effort to better understand the physics of implosions followed and by last year shots were producing 100 kJ. Key improvements included smoothing out microscopic bumps and pits on the fuel capsule surface, reducing the size of the hole in the capsule used to inject fuel, shrinking the holes in the gold cylinder so less energy escapes, and extending the laser pulse to keep driving the fuel inward for longer. The progress was sorely needed, as NIF’s funder, the National Nuclear Security Administration, was reducing shots devoted to ignition in favor of using its lasers for other experiments simulating the workings of nuclear weapons.

Earlier this year, combining those improvements in various ways, the NIF team produced several shots exceeding 100 kJ, including one of 170 kJ. That result suggested NIF was finally creating a “burning plasma,” in which the fusion reactions themselves provide the heat for more fusion—a runaway reaction that is key to getting higher yields. Then, on 8 August, a shot generated the remarkable 1.35 MJ. “It was a surprise to everyone,” Herrmann says. “This is a whole new regime.”

Exactly which improvements had the greatest impact and what combination will lead to future gains will take a while to unravel, Herrmann says, because several were tweaked at once in the latest shot. “It’s a very nonlinear process. That’s why it’s called ignition: It’s a runaway thing,” he says. But, “This gives us a lot more encouragement that we can go significantly farther.”

Herrmann’s team is a long way from thinking about fusion power plants, however. “Getting fusion in a laboratory is really hard, getting economic fusion power is even harder,” Campbell says. “So, we all have to be patient.” NIF’s main task remains ensuring the United States’ nuclear weapons stockpile is safe and reliable; fusion energy is something of a sideline. But reaching ignition and being able to study and simulate the process will also “open a new window on stewardship,” Herrmann says, because uncontrolled fusion powers nuclear weapons.

Herrmann admits that, when he got a text last week from colleagues saying they'd gotten an "interesting" result from the latest shot, he was worried something might be wrong with the instruments. When that proved not to be the case, "I did open a bottle of champagne."

https://bit.ly/37VmXhd

Stunningly preserved mummy of slave found in Pompeii graveyard

The partially mummified remains of an urbane Pompeii resident have been discovered in a tomb outside the city center erected before the famous eruption that buried the town in ash.

By Stephanie Pappas - Live Science Contributor

According to the inscriptions on the tomb, the deceased was a man named Marcus Venerius Secundio who was in his 60s when he died and was, at one point, enslaved. Later in life, after being freed, Secundio became a well-off priest who conducted rituals in Latin and Greek.

The remains of Marcus Venerius Secundio were preserved in a sealed chamber in a Pompeii cemetery. Though the body is nearly 2,000 years old, close-cropped hair and an ear are still visible on the skull. **(Image credit: Courtesy Archaeological Park of Pompeii/University of Valencia)**

The tomb inscription referring to these Greek rituals is the first direct evidence of Greek performances being held in the Italian city. "That performances in Greek were organised is evidence of the lively and open cultural climate which characterised ancient Pompeii," Gabriel Zuchtriegel, director of the Archaeological Park of Pompeii, said in a statement.

Mummified remains

Secundio's remains rest in a rectangular masonry tomb that was once painted with images of green plants on a blue background; traces of this paint still grace the outside walls of the tomb. The partially mummified body was tucked into a sealed alcove in the tomb with an arched ceiling. Close-cropped hair and an ear are still visible on the skull. Archaeologists also recovered scraps of fabric and two glass bottles called "unguentaria" from Secundio's tomb. Unguentaria are often found in Roman and Greek cemeteries and may have held oils or perfumes for graveside rituals.

The tomb also contained two funerary urns, including a beautiful blue-glass urn belonging to a woman whose name is recorded as Novia Amabilis ("kind wife").

Cremation was the most common method of burial for Pompeiians during the Roman period, according to archaeologists. It's not clear why Secundio's remains weren't cremated. It's also not clear if his body mummified naturally or if it was treated to prevent decomposition.

A beautiful blue glass urn found in the tomb of Marcus Venerius Secundio. The urn likely contains the cremated remains of a woman named Novia Amabilis. **(Image credit: Courtesy Archaeological Park of Pompeii/University of Valencia)**

"We still need to understand whether the partial mummification of the deceased is due to intentional treatment or not," University of Valencia archaeologist Llorenç Alapont said in the statement.

Multilingual city

The tomb is in the Porta Sarno Necropolis, which sits just outside the town walls by the Porta di Nola gate. A number of notables were buried in the necropolis, including city administrator Marcus Obellius Firmus, who lived during the reign of Emperor Nero (between A.D. 54 and 68), according to ArchaeoSpain, a field school that coordinates internships at Pompeii and other sites.

What is known of Marcus Venerius Secundio's life comes from a previously discovered record-keeping tablet belonging to the banker Cecilius Giocondus, as well as the inscription carved in marble on Secundio's tomb. He was a slave at the temple of Venus before his release, after which he joined the priesthood of the imperial cult, dedicated to glorifying the memory of the Roman emperor Augustus, who ruled from 27 B.C. to A.D. 14. As one of these "Augustales," Secundio "gave Greek and Latin 'ludi' for the duration of four days," according to the tomb inscription. "Ludi graeci" were theater performances in Greek, Zuchtriegel said.

"It is the first clear evidence of performances at Pompeii in the Greek language, which had previously been hypothesised on the basis of indirect indicators," he said. These performances indicate that Pompeii in the first century was a multi-lingual, multi-ethnic place where Eastern Mediterranean cultures melded.

https://wb.md/3y1Gnvi

Will Drinking More Water Keep Kidney Disease Away?

Nephrologists have been recommending — increased water intake to keep kidney disease away

Tejas P. Desai, MD

We've all heard the saying, "An apple a day keeps the doctor away." More recently, patients have been asking about — and nephrologists have been recommending — increased water intake to keep kidney disease away.

For years, a growing number of nephrologists and primary care physicians have been recommending drinking more water to either dilute unrecognized nephrotoxins or just bathe the kidneys in a friendly environment. On the surface, this recommendation seems to make sense, but two studies suggest that our zealous pursuit of imbibing more and more water will not give us the kidney protection we're hoping for.

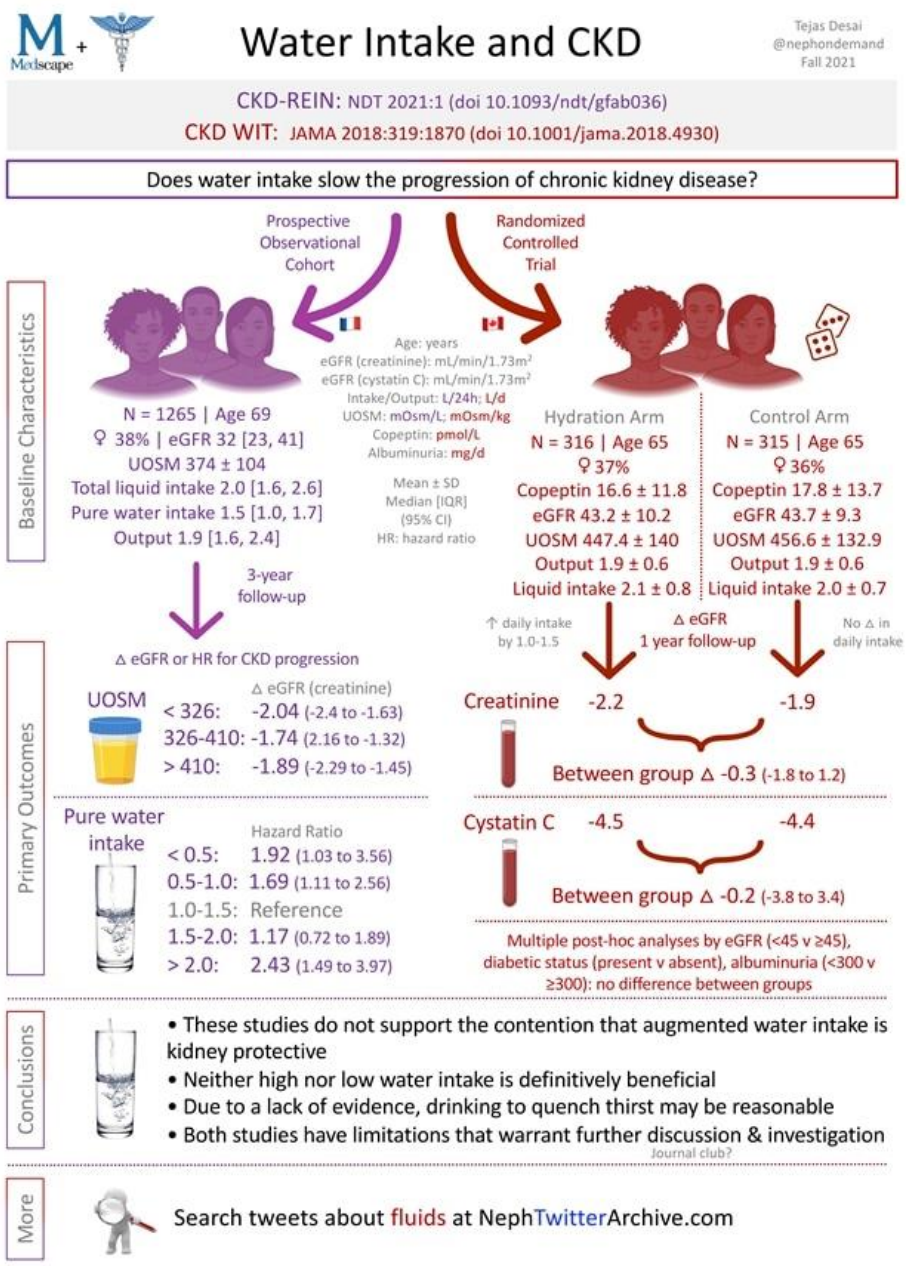

Figure. [Download PDF here]

About 4 years ago, researchers from Canada performed the decently sized but underpowered CKD WIT randomized clinical trial to determine whether increased water intake would slow the rate of kidney decline. Over a 1-year follow-up period, well-matched patients with chronic kidney disease stage 3 or worse were told to increase their daily water intake by 1.0-1.5 L/d vs making no change at all. Using the estimated glomerular filtration rate (eGFR) equation (creatinine-based or cystatin C–based), the extra water consumed in the intervention group did not protect kidney function.

Although a major limitation was a possible lack of adherence to increased water intake (most patients had an increased urine output by only 600 mL/d), CKD WIT was my first scientific exposure to the notion that water wasn't as kidney-protective as once thought.

Nonetheless, organizations remain focused on the renal benefits of increasing water intake. Short clinical studies show that water intake can lower fasting glucose levels or sufficiently restore hemodynamic stability. These are small studies with short follow-up periods, so the true benefits of water intake can't be accurately assessed.

To help resolve this issue, investigators of the CKD-REIN study undertook a 3-year prospective trial of 1265 patients with stage 3 or worse chronic kidney disease to determine which, if any, amount of water intake would reduce decline in kidney function.

Their investigation showed that participants who lowered their urine osmolarity from a baseline of 374 mOsm/L to < 326 mOsm/L had the greatest drop in eGFR (creatinine-based). Individuals who drank the least or most amount of water daily (< 0.5 or > 2.0 L/d, respectively) had the greatest likelihood of experiencing kidney decline (hazard ratio, 1.92 and 2.43, respectively) compared with those who had moderate water intake (1.0-1.5 L/d).

What Should We Tell Patients?

All of this means that we should no longer be focused on the amount of water one drinks. It's still safe to recommend some water intake over none, but drinking excessive amounts of water will not confer any protection.

CKD WIT and CKD-REIN have called into question the belief that we can simply bathe the kidneys with water and all will be well. Just as an apple a day won't actually keep the doctor away, guzzling water won't prevent kidney disease. Moderate water consumption is all we can recommend on the basis of the available science.

https://bit.ly/37U8ySq

Low-Cost, Inflatable Bionic Hand Gives Amputees Real-Time Tactile Control

Prosthetic enables a wide range of daily activities, such as zipping a suitcase, shaking hands, and petting a cat.

By Jennifer Chu, Massachusetts Institute of Technology

For the more than 5 million people in the world who have undergone an upper-limb amputation, prosthetics have come a long way. Beyond traditional mannequin-like appendages, there is a growing number of commercial neuroprosthetics — highly articulated bionic limbs, engineered to sense a user's residual muscle signals and robotically mimic their intended motions.

An MIT-developed inflatable robotic hand gives amputees real-time tactile control. The smart hand is soft and elastic, weighs about half a pound, and costs a fraction of comparable prosthetics. **Credit: Courtesy of the researchers**

But this high-tech dexterity comes at a price. Neuroprosthetics can cost tens of thousands of dollars and are built around metal skeletons, with electrical motors that can be heavy and rigid.

Now engineers at MIT and Shanghai Jiao Tong University have

designed a soft, lightweight, and potentially low-cost neuroprosthetic hand. Amputees who tested the artificial limb performed daily activities, such as zipping a suitcase, pouring a carton of juice, and petting a cat, just as well as — and in some cases better than —those with more rigid neuroprosthetics.

The researchers found the prosthetic, designed with a system for tactile feedback, restored some primitive sensation in a volunteer's residual limb. The new design is also surprisingly durable, quickly recovering after being struck with a hammer or run over with a car.

The smart hand is soft and elastic, and weighs about half a pound. Its components total around $500 — a fraction of the weight and material cost associated with more rigid smart limbs.

"This is not a product yet, but the performance is already similar or superior to existing neuroprosthetics, which we're excited about," says Xuanhe Zhao, professor of mechanical engineering and of civil and environmental engineering at MIT. "There's huge potential to make this soft prosthetic very low cost, for low-income families who have suffered from amputation."

Zhao and his colleagues have published their work today in *Nature Biomedical Engineering*. Co-authors include MIT postdoc Shaoting Lin, along with Guoying Gu, Xiangyang Zhu, and collaborators at Shanghai Jiao Tong University in China.

Big Hero hand

The team's pliable new design bears an uncanny resemblance to a certain inflatable robot in the animated film "Big Hero 6." Like the squishy android, the team's artificial hand is made from soft, stretchy material — in this case, the commercial elastomer EcoFlex. The prosthetic comprises five balloon-like fingers, each embedded with segments of fiber, similar to articulated bones in actual fingers. The bendy digits are connected to a 3-D-printed "palm," shaped like a human hand.

Rather than controlling each finger using mounted electrical motors, as most neuroprosthetics do, the researchers used a simple pneumatic system to precisely inflate fingers and bend them in specific positions. This system, including a small pump and valves, can be worn at the waist, significantly reducing the prosthetic's weight.

Lin developed a computer model to relate a finger's desired position to the corresponding pressure a pump would have to apply to achieve that position. Using this model, the team developed a controller that directs the pneumatic system to inflate the fingers, in positions that mimic five common grasps, including pinching two and three fingers together, making a balled-up fist, and cupping the palm.

The pneumatic system receives signals from EMG sensors — electromyography sensors that measure electrical signals generated by motor neurons to control muscles. The sensors are fitted at the prosthetic's opening, where it attaches to a user's limb. In this arrangement, the sensors can pick up signals from a residual limb, such as when an amputee imagines making a fist.

The team then used an existing algorithm that "decodes" muscle signals and relates them to common grasp types. They used this algorithm to program the controller for their pneumatic system. When an amputee imagines, for instance, holding a wine glass, the sensors pick up the residual muscle signals, which the controller then translates into corresponding pressures. The pump then applies those pressures to inflate each finger and produce the amputee's intended grasp.

Going a step further in their design, the researchers looked to enable tactile feedback — a feature that is not incorporated in most commercial neuroprosthetics. To do this, they stitched to each fingertip a pressure sensor, which when touched or squeezed produces an electrical signal proportional to the sensed pressure. Each sensor is wired to a specific location on an amputee's residual

limb, so the user can "feel" when the prosthetic's thumb is pressed, for example, versus the forefinger.

Good grip

To test the inflatable hand, the researchers enlisted two volunteers, each with upper-limb amputations. Once outfitted with the neuroprosthetic, the volunteers learned to use it by repeatedly contracting the muscles in their arm while imagining making five common grasps.

After completing this 15-minute training, the volunteers were asked to perform a number of standardized tests to demonstrate manual strength and dexterity. These tasks included stacking checkers, turning pages, writing with a pen, lifting heavy balls, and picking up fragile objects like strawberries and bread. They repeated the same tests using a more rigid, commercially available bionic hand and found that the inflatable prosthetic was as good, or even better, at most tasks, compared to its rigid counterpart.

One volunteer was also able to intuitively use the soft prosthetic in daily activities, for instance to eat food like crackers, cake, and apples, and to handle objects and tools, such as laptops, bottles, hammers, and pliers. This volunteer could also safely manipulate the squishy prosthetic, for instance to shake someone's hand, touch a flower, and pet a cat.

In a particularly exciting exercise, the researchers blindfolded the volunteer and found he could discern which prosthetic finger they poked and brushed. He was also able to "feel" bottles of different sizes that were placed in the prosthetic hand, and lifted them in response. The team sees these experiments as a promising sign that amputees can regain a form of sensation and real-time control with the inflatable hand.

The team has filed a patent on the design, through MIT, and is working to improve its sensing and range of motion.

"We now have four grasp types. There can be more," Zhao says. "This design can be improved, with better decoding technology, higher-density myoelectric arrays, and a more compact pump that could be worn on the wrist. We also want to customize the design for mass production, so we can translate soft robotic technology to benefit society."

Reference: "A soft neuroprosthetic hand providing simultaneous myoelectric control and tactile feedback" by Guoying Gu, Ningbin Zhang, Haipeng Xu, Shaoting Lin, Yang Yu, Guohong Chai, Lisen Ge, Houle Yang, Qiwen Shao, Xinjun Sheng, Xiangyang Zhu and Xuanhe Zhao, 16 August 2021, Nature Biomedical Engineering.
DOI: 10.1038/s41551-021-00767-0

https://bit.ly/2WecOte

How To Trigger and Control Liver Regeneration

Dresden and Cambridge researchers identify cell type that regulates liver regeneration with touch.

From the time of Aristotle, it has been known that the human liver has the greatest regenerative capacity of any organ in the body, being able to regrow even from a 70% amputation, which has enabled live-donor transplants. Although the liver regenerates fully upon injury, the mechanisms that regulate how to activate or stop the process and when regeneration is terminated, are still unknown. Researchers at the Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG) in Dresden (Germany), at the Gurdon Institute (Cambridge, UK) and at the University of Cambridge (Biochemistry Department) have now found that a regulatory cell type – mesenchymal cell – can activate or stop liver regeneration. The mesenchymal cells do so by the number of contacts they establish with the regenerating cells (epithelial cells). This study suggests that mistakes in the regeneration process, which can give rise to cancer or chronic liver diseases, are caused by the wrong number of contacts between both populations. The work is described in a paper published in the journal *Cell Stem Cell* on August 2nd, 2021.

The molecular mechanisms by which adult liver cells trigger the

regenerative response remain largely unknown. Approximately 29 million people in Europe suffer from a chronic liver condition such as cirrhosis or liver cancer. They are a major cause of morbidity and mortality with liver diseases accounting for approximately two million deaths per year worldwide. Currently, there is no cure and liver transplants are the only treatment for liver failure. Scientists are therefore exploring new options for how to trigger the regenerative capacity of the liver as an alternative means to restore function.

Development of mini-livers

Researchers at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden together with colleagues at the University of Cambridge's Gurdon Institute study the biological principles of adult liver regeneration. In 2013, Meritxell Huch together with Prof Hans Clevers, developed the first liver organoids – miniature liver tissues generated from mouse liver cells in a dish in the lab. The researchers were even successful in transplanting the organoid into a mouse, where it was able to perform liver functions. In 2015, they successfully transferred this liver organoid technology to grow human liver in a dish from human liver biopsies and in 2017 they developed a similar system from human liver cancer. The Huch lab was located at the University of Cambridge's Gurdon Institute until 2019 and moved then to the MPI-CBG.

A surprising, exciting observation

Two main functional cells of the adult liver are hepatocytes, which perform many of the liver's functions, and ductal cells, which form the network of tiny ducts delivering bile to the intestine. These work in conjunction with other supporting cells, like the blood vessels or the mesenchymal cells. For building liver organoids, in the beginning the researchers only used ductal cells of the bile duct. In order to improve this model and make it more similar to the real liver, doctoral student Lucía Cordero-Espinoza and postdoctoral researcher Anna Dowbaj planned to build a more complex liver organoid that better mimics the cellular interactions and architecture of the adult liver tissue. For that they added liver mesenchyme – a type of regulatory cell of the connective tissue, which support the tubular structure of the bile duct. "We put the mesenchymal cells next to the organoid, made out of the ductal cells, in a petri dish and saw that they were not touching or connecting, as they do in the native tissue" says Anna Dowbaj. The researchers contacted Florian Hollfelder at the University of Cambridge, who knew a method that enables combining the cells in tiny gels that allow them to meet and establish contact. Anna continues: "We were excited to see how our new and more complex organoid was recapitulating the tissue architecture in a dish, so we decided to study how the cells behave and filmed them under a microscope. To our surprise, we saw a totally unexpected behavior: the tissue (organoid) shrunk on touch with the mesenchymal cells but grew in the absence of contacts. This paradoxical behavior was very striking, but could help us explain why the tissue proliferated or stopped to do so during the regeneration process."

Less is more and more is less

In a healthy liver, there is a defined number of contacts between the ductal cells and the mesenchymal cells, which tells the ductal cells not to make more of themselves and just stay as they are. Once the tissue experiences damage, the mesenchymal cells decrease their number of contacts with the ductal cells, so they can multiply to repair the damage.

From their observation, the researchers concluded that rather than the absolute number of both cell types, it is the number of cellular contacts that controls how many cells are being produced to repair damaged tissue. Too many touches by mesenchymal cells means that fewer or no new ductal cells are being produced, and fewer touches means that more cells are being produced. This regulation

is very important because when there is no signal for ductal cells to stop reproducing themselves to repair tissue, there could be over-production, which could lead to cancer.

Meritxell Huch, who oversaw the study, concludes: "This is the first time that we were able to make those contacts visible and we have proven for the first time that they exist. We were able to do this because of our organoid systems. Even though we performed our experiments in a dish, outside of the living body, we think that the same process is taking place in the living organism. We have seen this in fixed points of time during the damage-regenerative process, but so far, we couldn't observe this in the living organism because the technology is not available. While our study focused on the ductal-mesenchymal interactions in the liver, we can imagine that similar mechanisms take place in any other system where cell numbers dynamically change, such as the lung or breast tissue. Of course, in the far future, we would like to create a liver organoid with all cell types. With such an organoid you could test drugs and see if these not only impact the regenerating cells but also their supportive environment. But for that, we need to wait until the technology is available."

Reference: "Dynamic cell contacts between periportal mesenchyme and ductal epithelium act as a rheostat for liver cell proliferation" by Lucía Cordero-Espinoza, Anna M. Dowbaj, Timo N. Kohler, Bernhard Strauss, Olga Sarlidou, German Belenguer, Clare Pacini, Nuno P. Martins, Ross Dobie, John R. Wilson-Kanamori, Richard Butler, Nicole Prior, Palle Serup, Florian Jug, Neil C. Henderson, Florian Hollfelder and Meritxell Huch, 2 August 2021, Cell Stem Cell. DOI: 10.1016/j.stem.2021.07.002

https://nyti.ms/3j2bRxi

This Brain Remained Intact in a 310 Million-Year-Old Fossil

The discovery suggested that horseshoe crab brains haven't changed much and that there are more ways for soft tissues to be preserved in the fossil record.

By Priyanka Runwal

Brain tissue is innately squishy. Unlike bones, shells or teeth, it is rich in fat and rots quickly, seldom making an appearance in the fossil record.

So when Russell Bicknell, an invertebrate paleontologist at the University of New England in Australia, noticed a pop of white near the front of a fossilized horseshoe crab body where the animal's brain would have been, he was surprised. A closer look revealed an exceptional imprint of the brain along with other bits of the creature's nervous system.

The horseshoe crab, about the size of a penny, was unearthed from the Mazon Creek deposit in northeastern Illinois. **Credit...Russell Bicknell**

Unearthed from the Mazon Creek deposit in northeastern Illinois, and dating back 310 million years, it's the first fossilized horseshoe crab brain ever found. Dr. Bicknell and his colleagues reported the find last month in the journal Geology.

"These kinds of fossils are so rare that if you happen to stumble upon one, you'd generally be in shock," he said. "We're talking a needle-in-a-haystack level of wow."

The find helps fill a gap in the evolution of arthropod brains and also shows how little they have changed over hundreds of millions of years.

Soft-tissue preservation requires special conditions. Scientists have found brains encased in fossilized tree resin, better known as amber, that were less than 66 million years old.

They have also found brains preserved as flattened carbon films, sometimes replaced or overlaid by minerals in shale deposits that are more than 500 million years old. Such deposits include corpses of ocean-dwelling arthropods that sank to the seafloor, were rapidly buried in mud and remained shielded from immediate decay in the

low-oxygen environment.

However, the fossilized brain of Euproops danae, which is kept in a collection at the Yale Peabody Museum of Natural History, required a different set of conditions to be preserved.

This arthropod was not a crab, but is closely related to spiders and scorpions. The extinct penny-size horseshoe crab was buried more than 300 million years ago in what was once a shallow, brackish marine basin. Siderite, an iron carbonate mineral, accumulated rapidly around the dead creature's body, forming a mold. With time, as the soft tissue decayed, a white-colored clay mineral called kaolinite filled the void left by the brain. It was this white cast on a dark-gray rock that helped Dr. Bicknell spot the uniquely preserved brain impression.

"This is a completely different mode of brain preservation," said Nicholas Strausfeld, a neuroanatomist at the University of Arizona who was among the first to report a fossilized arthropod brain in 2012 but wasn't involved in this study. "It's remarkable."

The extinct Euproops brain showed a central cavity for the passage of a feeding tube and branching nerves that would connect with the animal's eyes and legs.

A close-up view of the brain, the first fossilized horseshoe crab brain ever found. **Credit...Russell Bicknell**

Dr. Bicknell and his colleagues compared this ancient brain structure with that of Limulus polyphemus, a horseshoe crab species still found along the Atlantic coast, and noticed remarkable similarity. While the horseshoe crabs look somewhat different on the outside, the internal brain architecture hadn't really changed despite being separated by more than 300 million years.

"It's as if a set of motherboards has remained constant over geological time, whereas peripheral circuits have been variously modified," Dr. Strausfeld said.

Although the E. danae fossil has been examined in the past by other researchers for its shape and dimensions, the brain, which is smaller than a rice grain, remained unnoticed. "If you're not looking for that particular feature, then you're not going to see it," Dr. Bicknell said. "You develop a search image in your head."

With the lucky discovery of this well-preserved ancient brain, the researchers hope to find more examples in other fossils from the Mazon Creek deposit.

"If there is one, there have to be more," said Javier Ortega-Hernández, an invertebrate paleontologist at Harvard University's Museum of Comparative Zoology and the study's co-author.

https://go.nature.com/3qfq132

Decades-old SARS virus infection triggers potent response to COVID vaccines

Dramatic antibody production in people infected during the 2002–04 outbreak furthers hopes of a vaccine against many coronaviruses.

Smriti Mallapaty

People who were infected almost two decades ago with the virus that causes severe acute respiratory syndrome (SARS) generate a powerful antibody response after being vaccinated against COVID-19. Their immune systems can fight off multiple SARS-CoV-2 variants, as well as related coronaviruses found in bats and pangolins.

The Singapore-based authors of a small study published today in *The New England Journal of Medicine*[1] say the results offer hope that vaccines can be developed to protect against all new SARS-CoV-2 variants, as well as other coronaviruses that have the potential to cause future pandemics.

The study is a "proof of concept that a pan-coronavirus vaccine in

humans is possible", says David Martinez, a viral immunologist at the University of North Carolina at Chapel Hill. "It's a really unique and cool study, with the caveat that it didn't include many patients."

SARS-CoV-2 belongs to the sarbecovirus group of coronaviruses, which includes the virus that caused SARS (called SARS-CoV), as well as closely related bat and pangolin coronaviruses.

Sarbecoviruses use what are known as spike proteins to bind to ACE2 receptors in the membranes of host cells and enter them. They can jump from animals to humans, as they did before in both the current pandemic and the 2002–04 outbreak of SARS, which spread to 29 countries. "The fact that this has happened twice in the last two decades is strong rationale that this is a group of viruses that we really need to pay attention to," says Martinez.

Neutralizing antibodies

Last year, Linfa Wang, a virologist at Duke–NUS Medical School in Singapore who led the latest study, went looking for people who had survived SARS to see whether they offered any clues about how to develop vaccines and drugs for COVID-19.

He detected 'neutralizing' antibodies in their blood that blocked the original SARS virus from entering cells, but did not affect SARS-CoV-2 — which he found surprising, because the viruses are closely related.

But when Singapore rolled out the Pfizer–BioNTech COVID-19 vaccine this year, Wang decided to interrogate how the SARS infection affected responses to the vaccine. What he discovered was striking. Eight vaccinated study participants, who had recovered from SARS almost two decades ago, produced very high levels of neutralizing antibodies against both viruses, even after just one dose of the vaccine.

They also produced a broad spectrum of neutralizing antibodies against three SARS-CoV-2 variants of concern in the current pandemic — Alpha, Beta and Delta — and five bat and pangolin sarbecoviruses. No such potent and wide-ranging antibody response was observed in blood samples taken from fully vaccinated individuals, even those who had also had COVID-19.

The researchers suggest that such broad protection could arise because the vaccine jogs the immune system's 'memory' of regions of the SARS virus that are also present in SARS-CoV-2, and possibly many other sarbecoviruses.

Coronaviruses found in bats have the potential to cause future pandemics, so the fact that a broad spectrum of neutralizing antibodies is generated that protects against some of them "is encouraging", says Daniel Lingwood, an immunologist at the Ragon Institute of MGH, MIT and Harvard in Boston, Massachusetts. But researchers say it is not clear how long this protection lasts.

A vaccine that is widely effective against sarbecoviruses could be administered to the general population in high-risk areas close to animals that harbour them, limiting the potential spread of these viruses in people, adds Christopher Barnes, a structural biologist at Stanford University in California.

Which part of the virus

Barton Haynes, an immunologist at Duke University School of Medicine in Durham, North Carolina, says the study raises the question of whether a similar response could be generated if people vaccinated against COVID-19 were given a booster shot that targeted the original SARS virus. This might protect them against new variants of SARS-CoV-2 and other sarbecoviruses. Wang says preliminary studies in mice suggest that is possible.

But the latest study doesn't identify exactly which sections of the viruses induce the broad immune response, something that would be needed to develop vaccines. That's the "biggest question", says Martinez. If it is a region of the virus that is present not just in

sarbecoviruses, but in the entire group of coronaviruses, there is potential for creating a vaccine against all of them, he says.

Several research groups have identified specific antibodies that prevent SARS-CoV-2 and other sarbecoviruses from spreading in cells. Others are already working on pan-coronavirus vaccines, and have synthesized components that induce strong protection in monkeys and mice.

Haynes and his colleagues, for example, have developed[2] a protein nanoparticle studded with 24 pieces of a section of the SARS-CoV-2 spike protein called the receptor binding domain, a key target of antibodies. They found that in monkeys, the nanoparticle induced much higher levels of antibodies against SARS-CoV-2 than did the Pfizer vaccine. It also induced cross-reactive antibodies against the original SARS virus and bat and pangolin sarbecoviruses.

Martinez and his colleagues have induced these widely reactive antibodies in mice, using a vaccine made from a combination of spike proteins from different coronaviruses[3]. But Martinez says the latest study suggests that this complex spike chimaera might not be necessary; a similar protective response could be induced simply by the original SARS virus's spike protein.

Wang says he is already working on potential vaccines that target multiple sarbecoviruses, and he now hopes to find additional survivors of the 2002–04 SARS outbreak to conduct a much larger study, including testing their responses to other COVID-19 vaccines.

doi: https://doi.org/10.1038/d41586-021-02260-9

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Physicians Can Be Savvy Online or Become Irrelevant, Says Report

Physicians with a less developed online presence may struggle to reach new patients

Steph Weber

Consumers are increasingly turning to the internet to find and access care, which means physicians with a less developed online presence may struggle to reach new patients, especially Millennials, according to a new report.

The analysis, by customer experience management company Reputation, looked at 348,000 customer reviews across 113,000 physicians and healthcare facilities. Using a proprietary AI-based scoring system, a Reputation Score was calculated by taking "a snapshot of everything customers say about a provider online," including feedback posted to sites like Google and Facebook, the company said in a statement.

The report found that physicians who amassed more online reviews had higher Reputation Scores and greater patient engagement, as indicated by the 540% uptick in conversions on their Google My Business (GMB) listings. Conversion rates were measured by "how often someone clicks on a GMB listing to call a location, visit a website, or get directions to a location," according to the company.

Patients Turning to the Internet for Decision Making

Reputation also surveyed 1000 US adults aged 27-64 to determine how they choose a physician. Conducted in 2020 after the start of the pandemic, 68% of respondents said they went online at some point during the year to find information about a potential healthcare provider, compared with just 22.4% in 2019 and 9% in 2018.

Those in the market for a new primary care physician relied on word-of-mouth recommendations most often (23%). Although just

12.5% preferred to start with a web search, there was a 25% increase in GMB listing engagement from April-December 2020 when compared with January-February 2020, suggesting the listings were used more frequently as a beginning point to initiate contact with a provider.

Four fifths of respondents (82.4%) said whether a physician accepted their insurance was the most important factor guiding their choice of provider, followed by proximity to work or home (75.4%).

Aside from those considerations, "patient ratings/reviews are the single-most important factor influencing Millennials' choice of physicians" at 38.9%, says the company.

Physicians "Woefully Disconnected"

Despite the search for care going digital, as of 2020, most physicians remained "woefully disconnected" from consumer decision-making. Roughly two thirds (65%) of physicians had zero online reviews and are not providing patient experience information — in the form of ratings and reviews, often across multiple platforms — that the public desires. In turn, they risk developing an "unfavorable reputation among Millennials" and may have trouble expanding patient volumes.

Input from peers can have a powerful effect. Half (50.8%) of survey respondents have chosen one physician over another based on reviews and 66.7% deem a 4-star rating as the "minimum acceptable standard" when considering a provider. More than 9% (9.4%) of respondents read at least 20 reviews before making their decision and 38.9% read five to nine reviews.

As for age-related differences, 47.6% of Millennials preferred using Google reviews to evaluate physicians vs 21.5% of Baby Boomers — the latter group most often read reviews on WebMD. And compared with older adults, Millennials are six times more likely to rely on Facebook reviews of healthcare providers.

How to Boost Online Reputation

Faced with a "digital reckoning," says the company, physicians who "request reviews, respond to them and use patient feedback to improve the patient experience" can improve their online reputations and attract a larger share of consumers now utilizing the web for care decisions. This is particularly critical if providers want to engage hard-to-reach Millennials, who are old enough to be shouldering the responsibilities of their own care as well as for their children and aging parents.

A robust online footprint can also help build connections with the Gen Z population (those born after 1997), who were raised with digital technology, are quickly approaching adulthood, and will soon become prominent players in the healthcare system themselves.

Providers who "fail to improve their digital savvy will become irrelevant," says the company, because "the consumer shapes the reputation of the healthcare provider, and that process begins online."

https://bit.ly/3mdYhZM

Scientists reveal how landmark CFC ban gave planet fighting chance against global warming

Without the global CFC ban we would already be facing the reality of a 'scorched earth', according to researchers measuring the impact of the Montreal Protocol.

Their new evidence reveals the planet's critical ability to absorb carbon from the atmosphere could have been massively degraded sending global temperatures soaring if we still used ozone-destroying chemicals such as CFCs.

New modeling by the international team of scientists from the UK, U.S. and New Zealand, published today in *Nature*, paints a dramatic vision of a scorched planet Earth without the Montreal Protocol, what they call the "World Avoided". This study draws a new stark link between two major environmental concerns—the

hole in the ozone layer and global warming.

The research team, led by a Lancaster University scientist, reveals that if ozone-destroying chemicals, which most notoriously include CFCs, had been left unchecked then their continued and increased use would have contributed to global air temperatures rising by an additional 2.5°C by the end of this century.

Their findings, outlined in the paper 'The Montreal Protocol protects the terrestrial carbon sink', show that banning CFCs has protected the climate in two ways—curbing their greenhouse effect and, by protecting the ozone layer, shielding plants from damaging increases in ultraviolet radiation (UV). Critically, this has protected plant's ability to soak up and lock in carbon dioxide from the atmosphere and so prevented a further acceleration of climate change.

The research team developed a new modeling framework, bringing together data on ozone depletion, plant damage by increased UV, the carbon cycle and climate change. Their novel modeling shows an alternative future of a planet where the use of CFCs continued to grow by around three percent a year.

Their modeling reveals:

**** Continued growth in CFCs would have led to a worldwide collapse in the ozone layer by the 2040s.***

**** By 2100 there would have been 60 percent less ozone above the tropics. This depletion above the tropics would have been worse than was ever observed in the hole that formed above the Antarctic.***

**** By 2050 the strength of the UV from the sun in the mid-latitudes, which includes most of Europe including the UK, the United States and central Asia, would be stronger than the present day tropics.***

The depleted ozone layer would have seen the planet, and its vegetation, exposed to far more of the sun's UV.

Plants absorb carbon dioxide (CO_2) through photosynthesis and studies have shown that large increases in UV can restrict plant growth, damaging their tissues, and impairing their ability to undertake photosynthesis. This means the plants absorb less carbon. Less carbon in vegetation also results in less carbon becoming locked into soils, which is what happens to a lot of plant matter after it dies. All of this would have happened on a global scale.

The researchers' models show that in a world without the Montreal Protocol the amount of carbon absorbed by plants, trees and soils dramatically plummets over this century. With less carbon in plants and soils, more of it remains in the atmosphere as CO_2.

Overall, by the end of this century without the Montreal Protocol CFC ban:

**** There would have been 580 billion tons less carbon stored in forests, other vegetation and soils.***

**** There would be an additional 165-215 parts per million of CO_2 in the atmosphere, depending on the future scenario of fossil fuel emissions. Compared to today's 420 parts per million CO_2, this is an additional 40-50%.***

**** The huge amount of additional CO_2 would have contributed to an additional 0.8°C of warming through its greenhouse effect.***

Ozone depleting substances, such as CFCs, are also potent greenhouse gases and previous research has shown that their ban prevented their contribution to global warming through their greenhouse effect. By the end of this century, their greenhouse effect alone would have contributed an additional 1.7°C global warming. This is in addition to the newly quantified 0.8°C warming, coming from the extra CO_2 that would have resulted from damaged vegetation, meaning that temperatures would have risen 2.5°C overall.

Dr. Paul Young, lead author from Lancaster University, said: "Our new modeling tools have allowed us to investigate the scorched Earth that could have resulted without the Montreal Protocol's ban on ozone depleting substances.

"A world where these chemicals increased and continued to strip away at our protective ozone layer would have been catastrophic for human health, but also for vegetation. The increased UV would have massively stunted the ability of plants to soak up carbon from the atmosphere, meaning higher CO_2 levels and more global warming.

"With our research, we can see that the Montreal Protocol's successes extend beyond protecting humanity from increased UV to protecting the ability of plants and trees to absorb CO_2. Although we can hope that we never would have reached the catastrophic world as we simulated, it does remind us of the importance of continuing to protect the ozone layer. Entirely conceivable threats to it still exist, such as from unregulated use of CFCs."

The planet has already seen 1°C warming from pre-industrial temperatures. Even if we had somehow managed to get to net zero CO_2 emissions, the additional 2.5°C rise would take us to a rise of 3.5°C. This is far in excess of the 1.5°C rise above pre-industrial levels that many scientists see as the most global temperatures can rise in order to avoid some of the most damaging effects of climate change.

Dr. Chris Huntingford of the UK Centre for Ecology & Hydrology said: "This analysis reveals a remarkable linkage, via the carbon cycle, between the two global environmental concerns of damage to the ozone layer and global warming."

More information: *The Montreal Protocol protects the terrestrial carbon sink, Nature (2021). DOI: 10.1038/s41586-021-03737-3 , www.nature.com/articles/s41586-021-03737-3*

https://bit.ly/3D3N0kI

What if our history was written in our grammar?

Grammar reflects best the common prehistory of a population and therefore mirrors genetics more than any other cultural feature

Humans have been always on the move, creating a complex history of languages and cultural traditions dispersed over the globe. An international team under UZH's lead has now traced families of related languages over more than 10,000 years by combining data from genetics, linguistics and musicology using novel digital methods. Their findings: grammar reflects best the common prehistory of a population and therefore mirrors genetics more than any other cultural feature.

Since the beginning of their existence, some populations have split up while others have come together, leaving a deep mark on local languages and cultural traditions. Reconstructing this complex history remains a gigantic challenge. Depending on the places of origin, with more than 7000 languages are currently spoken in the world.

This huge range is also found in genetic variation. According to Charles Darwin, genes and culture evolve in a similar way, transmitted from generation to generation with slight variations in each step. "When their evolution no longer corresponds, it is the sign of contact in the history of a population, be it friendly, such as trade, or unfriendly, such as conquests," says Balthasar Bickel, professor at the Department of Comparative Language Science of the University of Zurich.

Northeast Asia as crossroads between Asia and Native America

An international team under UZH's lead has now identified which data reveal the best correlation between genetic and cultural diversity by combining data from genetics, linguistics and musicology using novel digital methods.

The team selected Northeast Asia as a particularly interesting region for this study. "Northeast Asia is the central crossroad in the prehistory of Asia and Native America. Indeed, while their populations are genetically contiguous, the region is culturally and linguistically highly diverse," says Hiromi Matsumae, former postdoctoral researcher at UZH and now professor at Japan's Tokai

University.

Her team at UZH analyzed data spanning 11 language families incuding such as Tungusic, Chukuto-Kamchatkan, Eskimo-Aleut, Yukagir, Ainu, Korean and Japanese. They furthermore obtained new genetic data from speakers of Nivkh, an isolated language spoken on Sakhalin Island in Siberia.

Analogies and differences in genes, language and culture

The researchers compared the genomes of these populations with digital data on their language (grammar rules, sounds, word lists) and their music (structure, style). "Our results suggest that grammar reflects population history more closely than any other cultural data. We found significant correlations between genetics and grammar," explains co-lead author Peter Ranacher of UZH.

Word lists for example differ from each other in their own ways. And since word lists are the core data for reconstructing language families, such reconstructions remain elusive in the region. The researchers concluded that the correspondence between grammar and genetics reflects a complex maze of vertical descent and contact in prehistory.

Grammar as a mirror of cultural and genetic evolution

"It's through a unique collaboration between genetics and geography with modern digital linguistics and musicology that we have been able to take one small step closer to understanding human cultural history," adds last author Bickel.

Further analysis will be needed to understand the complex web of cultural and genetic evolution. But discovering the importance of the grammatical factor is a first step in the right direction.

The study is published in *Science Advances*.

More information: *Exploring correlations in genetic and cultural variation across language families in Northeast Asia, Science Advances, DOI: 10.1126/sciadv.abd9223*

https://go.nature.com/3D66N2V

Delta's rise is fuelled by rampant spread from people who feel fine

People infected with the Delta variant generally do not have COVID-19 symptoms until two days after they start shedding the coronavirus.

Smriti Mallapaty

People infected with the Delta variant of SARS-CoV-2 are more likely to spread the virus before developing symptoms than are people infected with earlier versions, suggests a detailed analysis of an outbreak in Guangdong, China[1].

"It is just tougher to stop," says Benjamin Cowling, an epidemiologist at the University of Hong Kong and a co-author of the study, which was posted on a preprint server on 13 August.

Cowling and his colleagues analysed exhaustive test data from 101 people in Guangdong who were infected with Delta between May and June this year, and data from those individuals' close contacts. They found that, on average, people began having symptoms 5.8 days after infection with Delta — 1.8 days after they first tested positive for viral RNA. That left almost two days for individuals to shed viral RNA before they showed any sign of COVID-19.

A dangerous window

An earlier study[2] and an unpublished analysis by Cowling and others estimate that before Delta emerged, individuals infected with SARS-CoV-2 took an average of 6.3 days to develop symptoms and 5.5 days to test positive for viral RNA, leaving a narrower window of 0.8 days for oblivious viral shedding.

In the latest work, the researchers also found that those infected with Delta had higher concentrations of viral particles, or viral load, in their bodies than did people infected with the original version of SARS-CoV-2. "Somehow the virus is appearing quicker and in higher amounts," says Cowling.

As a result, 74% of infections with Delta took place during the presymptomatic phase — a higher proportion than for previous variants. This high rate "helps explain how this variant has been able to outpace both the wild-type virus and other variants to become the dominant strain worldwide", says Barnaby Young, an infectious-disease clinician at the National Centre for Infectious Diseases in Singapore.

The researchers also calculated Delta's 'basic reproduction number', or R_0, which is the average number of people to whom every infected person will spread the virus in a susceptible population. They estimated that Delta has an R_0 of 6.4, which is much higher than the R_0 of 2–4 estimated for the original version of SARS-CoV-2, says Marm Kilpatrick, an infectious-disease researcher at the University of California, Santa Cruz. "Delta moves a bit faster, but is much more transmissible."

A small number of study participants experienced 'breakthrough infections' with Delta after receiving two doses of an inactivated-virus COVID-19 vaccine. But the vaccine reduced participants' viral loads at the peak of infection.

Vaccinated individuals were also 65% less likely than unvaccinated individuals to infect someone else, although the estimate was based on a very small sample size. This reduction "is significant and reassuring that COVID-19 vaccines remain effective and a vital part of our response to the pandemic", says Young.

The study has not yet been peer reviewed.

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https://bit.ly/3B1f5au

New Research Explains Why Vaccinated People at Low Risk During COVID Delta Variant Surge

Antibodies Elicited by COVID-19 Vaccination Effective Against Delta Variant

Despite causing a surge in infections this summer that has resulted in thousands of hospitalizations and deaths, the delta variant of the virus that causes COVID-19 is not particularly good at evading the antibodies generated by vaccination, according to a study by researchers at Washington University School of Medicine in St. Louis.

The researchers analyzed a panel of antibodies generated by people in response to the Pfizer COVID-19 vaccine and found that delta was unable to evade all but one of the antibodies they tested. Other variants of concern, such as beta, avoided recognition and neutralization by several of the antibodies.

The findings, published Aug. 16 in the journal Immunity, help explain why vaccinated people have largely escaped the worst of the delta surge.

In previous studies, co-senior author Ali Ellebedy, PhD, an associate professor of pathology & immunology, of medicine and of molecular microbiology, had shown that both natural infection and vaccination elicit lasting antibody production. But the length of the antibody response is only one aspect of protection. The breadth matters, too. An ideal antibody response includes a diverse set of antibodies with the flexibility to recognize many slightly different variants of the virus. Breadth confers resilience. Even if a few antibodies lose the ability to recognize a new variant, other antibodies in the arsenal should remain capable of neutralizing it.

"The fact that delta has outcompeted other variants does not mean that it's more resistant to our antibodies compared to other

variants," said co-senior author Jacco Boon, PhD, an associate professor of medicine, of molecular microbiology and of pathology & immunology. "The ability of a variant to spread is the sum of many factors. Resistance to antibodies is just one factor. Another one is how well the variant replicates. A variant that replicates better is likely to spread faster, independent of its ability to evade our immune response. So delta is surging, yes, but there's no evidence that it is better at overcoming vaccine-induced immunity compared to other variants."

To assess the breadth of the antibody response to SARS-CoV-2, the virus that causes COVID-19, Ellebedy and colleagues — including co-first authors Aaron Schmitz, PhD, a research specialist; Jackson S. Turner, PhD, an instructor in pathology & immunology; and Zhuoming Liu, PhD, a staff scientist — extracted antibody-producing cells from three people who had received the Pfizer vaccine. They grew the cells in the laboratory and obtained from them a set of 13 antibodies that target the original strain that began circulating last year. The researchers tested the antibodies against four variants of concern: alpha, beta, gamma and delta. Twelve of the 13 recognized alpha and delta, eight recognized all four variants, and one failed to recognize any of the four variants.

Scientists gauge an antibody's usefulness by its ability to block virus from infecting and killing cells in a dish. So-called neutralizing antibodies that prevent infection are thought to be more powerful than antibodies that recognize the virus but can't block infection, although both neutralizing and non-neutralizing antibodies contribute to defending the body.

The researchers found that five of the 13 antibodies neutralized the original strain. When they tested the neutralizing antibodies against the new variants, all five antibodies neutralized delta, three neutralized alpha and delta, and only one neutralized all four variants.

"In face of vaccination, delta is relatively a wimpy virus," Ellebedy said. "If we had a variant that was more resistant like beta but spread as easily as delta, we'd be in more trouble."

The antibody that neutralized all four variants of concern — as well as three additional variants tested separately — was called 2C08. In animal experiments, 2C08 also protected hamsters from disease caused by every variant tested: the original variant, delta and a mimic of beta.

Some people may have antibodies just as powerful as 2C08 protecting them against SARS-CoV-2 and its many variants, Ellebedy said. Using publicly available databases, the researchers discovered that about 20% of people infected or vaccinated against SARS-CoV-2 create antibodies that recognize the same spot on the virus that is targeted by 2C08. Moreover, very few virus variants (.008%) carry mutations that allow them to escape antibodies targeting that spot.

"This antibody is not unique to the person we got it from," Ellebedy said. "Multiple antibodies targeting this area have been described in the literature; at least one is under development as a COVID-19 therapy. Similar antibodies have been generated by people infected in Italy and people infected in China and people vaccinated in New York. So it's not limited to people of certain backgrounds or ethnicities; it's not generated only by vaccination or by infection. A lot of people make this antibody, which is great because it is very potent and neutralizes every variant we tested."

Reference: "A vaccine-induced public antibody protects against SARS-CoV-2 and emerging variants" by Aaron J. Schmitz, Jackson S. Turner, Zhuoming Liu, Julian Q. Zhou, Ishmael D. Aziati, Rita E. Chen, Astha Joshi, Traci L. Bricker, Tamarand L. Darling, Daniel C. Adelsberg, Clara G. Altomare, Wafaa B. Alsoussi, James Brett Case, Laura A. VanBlargan, Tingting Lei, Mahima Thapa, Fatima Amanat, Trushar Jeevan, Thomas Fabrizio, Jane A. O'Halloran, Pei-Yong Shi, Rachel M. Presti, Richard J. Webby, Florian Krammer, Sean P.J. Whelan, Goran Bajic, Michael S. Diamond, Adrianus C.M. Boon and Ali H. Ellebedy, Accepted, Immunity.
DOI: 10.1016/j.immuni.2021.08.013

https://bit.ly/387dkMp

A Never-Before-Seen System For Burning 'Deep Fat' Has Been Found in Mouse Studies

A series of new experiments on mice have revealed a key process by which the brain and immune system communicate to burn deep stores of visceral fat.

Carly Cassella

It's the first time scientists have identified a neuro-immune pathway directly linked to fat control, and while the findings are limited to mice, the authors are hopeful the system extends to other mammals, like humans, too.

Visceral or 'deep' fat is the yellow matter that envelops the abdominal organs. Like most forms of fat, its presence is crucial to maintain a body's fundamental functions, but if it builds up too much, it can also cause health issues like heart disease and cancer.

Knowing how it accumulates could one day help us tackle obesity and obesity-related illnesses in humans, but the process is really complicated.

In recent years, scientists have begun to suspect the nervous system and the immune system are both working together to control visceral fat. After all, this deep yellow matter not only houses nerve fibers, it also contains immune cells.

Yet communication between the two is hard to pin down.

Previous lab work performed by these researchers found deep fat around the lung is controlled via messages between nerves and immune cells, but when researchers looked at the deep fat around a mouse's ovaries or testes, they found no such communication.

"The neurons and the immune cells were not talking to each other," explains molecular biologist Ana Filipa Cardoso from the Champalimaud Center for the Unknown in Portugal. "So we investigated other candidates in the tissue, finally coming across a rather unexpected 'middleman'."

What was once thought to be a cellular bystander, has now turned out to be a critical mediator. In fact, mesenchymal cells (MSCs) were all but ignored by scientists until fairly recently.

"The widespread view was that they mainly produced the scaffolding of the tissue, over which other cells would 'do the work'. However, scientists have since discovered that MSCs carry out multiple essential active roles," says immunologist Henrique Veiga-Fernandes, also from the Champalimaud Center.

When researchers burned away mesenchymal cells in the deep fat of mice, the nearby immune cells, known as type 2 innate lymphoid cells (ILC2), stopped regulating the growth of the fat.

To trace the nerves that innervate MSCs back to their original source, researchers injected a glowing retrovirus into the mouse nerves. The peripheral messages received by visceral fat ultimately appeared to be coming from discrete areas in the brain stem, midbrain, amygdala, and the hypothalamus.

Given how important the nucleus of the hypothalamus appears to be in regulating the body's metabolism, the authors hypothesize this area of the brain is a 'central hub' for fat control. From here, messages are sent to specific immune cells within deep fat to ensure energy balance throughout the body.

For visceral fat around the lungs, these neural messages seem to go straight to ILC2s. But in the gonads, it looks as though they first need to be 'translated' by MSCs before they can be sent to nearby immune cells that regulate fat metabolism.

"It's as though the neural and immune cells don't speak the same language, and the MSCs serve as an interpreter," says Veiga-Fernandes.

"Taken within the larger context, it does make sense. MSCs effectively make up the tissue's 'ecosystem', and so they are perfectly situated to fine-tune the activity of other cells."

The study is the first clear example of a body-brain circuit that

instructs immune cells to burn fat, according to Veiga-Fernandes, and it has scientists hopeful we can one day mimic the process to control deep fat stores among those with particularly harmful levels. Of course, there's still a lot we don't know about ILC2s and how they control visceral fat, but the fact that we now have an idea where they are getting their messages from is a good starting point.

Going forward, researchers want to know what might be triggering the nucleus of the hypothalamus to send fat-burning messages to parts of the body in the first place. It's also worth exploring why some stores of visceral fat have ILC2s that can be directly innervated by the sympathetic nervous, while others need translators like MSCs.

"The most challenging thing in a project like this one is that you're truly working at the frontier," says Veiga-Fernandes.

"This is not immunology anymore, and it's not neuroscience either. You have to master technology, methods and approaches that are cross-disciplinary or multidisciplinary. Some of them don't even exist, and you have to develop them by scratch. Yet, at the same time, the conceptual challenge is exhilarating; we are truly venturing into the unknown." The study was published in *Nature*.

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Fighting COVID With COVID: Driving the Disease to Extinction With a Defective Version of the SARS-CoV-2 Virus

Researchers design new COVID-19 therapy that uses a defective version of the SARS-CoV-2 virus to drive the disease-causing version to extinction.

What if the COVID-19 virus could be used against itself? Researchers at Penn State have designed a proof-of-concept therapeutic that may be able to do just that. The team designed a synthetic defective SARS-CoV-2 virus that is innocuous but interferes with the real virus' growth, potentially causing the extinction of both the disease-causing virus and the synthetic virus.

"In our experiments, we show that the wild-type [disease-causing] SARS-CoV-2 virus actually enables the replication and spread of our synthetic virus, thereby effectively promoting its own decline," said Marco Archetti, associate professor of biology, Penn State. "A version of this synthetic construct could be used as a self-promoting antiviral therapy for COVID-19."

Archetti explained that when a virus attacks a cell, it attaches to the cell's surface and injects its genetic material into the cell. The cell is then tricked into replicating the virus' genetic material and packaging it into virions, which burst from the cell and go off to infect other cells.

"Defective interfering" (DI) viruses, which are common in nature, contain large deletions in their genomes that often affect their ability to replicate their genetic material and package it into virions. However, DI genomes can perform these functions if the cell they've infected also harbors genetic material from a wild-type virus. In this case, a DI genome can hijack a wild-type genome's replication and packaging machinery. "These defective genomes are like parasites of the wild-type virus," said Archetti, explaining that when a DI genome utilizes a wild-type genome's machinery, it also can impair the wild-type genome growth.

In addition, he said, "given the shorter length of their genomes as a result of the deletions, DI genomes can replicate faster than wild-type genomes in coinfected cells and quickly outcompete the wild-type." Indeed, in their new study, published in the journal *PeerJ*, Archetti and his colleagues found that their synthetic DI genome can replicate three times faster than the wild-type genome, resulting in a reduction of the wild-type viral load by half in 24 hours.

To conduct their study, the researchers engineered short synthetic DI genomes from parts of the wild-type SARS-CoV-2 genome and

introduced them into African green monkey cells that were already infected with the wild-type SARS-CoV-2 virus. Next, they quantified the relative amounts of the DI and WT genomes in the cells over time points, which gave an indication of the amount of interference of the DI genome with the wild-type genome.

The team found that within 24 hours of infection, the DI genome reduced the amount of SARS-CoV-2 by approximately half compared to the amount of wild-type virus in control experiments. They also found that the DI genome increases in quantity 3.3 times as fast as the wild-type virus.

Archetti said that while the 50% reduction in virus load that they observed over 24 hours is not enough for therapeutic purposes, presumably, as the DI genomes increase in frequency in the cell, the decline in the amount of wild-type virus would lead to the demise of both the virus and the DI genome, as the DI genome cannot persist once it has driven the wild-type virus to extinction.

He added that further experiments are needed to verify the potential of SARS-CoV-2 DIs as an antiviral treatment, suggesting that the experiments could be repeated in human lung cell lines, and against some of the newer variants of SARS-CoV-2. Furthermore, he said, an efficient delivery method should be devised. In further work that is still unpublished, the team has now used nanoparticles as a delivery vector and observed that the virus declines by more than 95% in 12 hours.

"With some additional research and fine-tuning, a version of this synthetic DI could be used as a self-sustaining therapeutic for COVID-19," said Archetti.

Reference: "A synthetic defective interfering SARS-CoV-2" by Shun Yao, Anoop Narayanan, Sydney A. Majowicz, Joyce Jose Marco Archetti, 1 July 2021, PeerJ.
DOI: 10.7717/peerj.11686

Other Penn State authors on the paper include Shun Yao, postdoctoral scholar in biology; Anoop Narayanan, associate research professor of biochemistry and molecular biology; Sydney Majowicz, graduate student in molecular, cellular and integrative biosciences; and Joyce Jose, assistant professor of biochemistry and molecular biology.

The Huck Institutes of the Life Sciences at Penn State supported this research.

https://bit.ly/3B4cM6I

Releasing bacteria-infected mosquitoes in Indonesia prevented the spread of dengue

Mosquitos carrying Wolbachia pipientis bacteria don't spread dengue fever

Madeline Barron

Mosquitos are the banes of our existence — they suck our blood, they spread disease, and for that, they suck in general. Some viruses that mosquitoes, such as the dengue viruses, can be debilitating or even lethal. Scientists have previously shown that infecting mosquitoes with the insect-specific bacterium, Wolbachia pipientis, can stop or slow the replication of dengue virus within the bugs. That work raised the question: Can Wolbachia-infected mosquitoes help prevent the spread of dengue?

In a new study published in The New England Journal of Medicine, researchers sought to answer this question by releasing Aedes aegypti mosquitoes (the type that transmits dengue) with or without Wolbachia into geographic clusters throughout Yogyakarta, Indonesia. They found that Wolbachia-infected mosquitoes maintained stable populations in their areas of release over the three-year experiment. Importantly, the incidence of dengue fever was significantly lower among people living in clusters with Wolbachia-positive mosquitos relative to control clusters — 2.3 percent and 9.3 percent, respectively.

This study points to the efficacy of Wolbachia-mediated methods for controlling dengue virus, and potentially other diseases like yellow fever and Zika. Given the Wolbachia method is being deployed in various regions throughout the world, this new work bolsters evidence that bacteria may be the key for keeping mosquito-transmitted viruses in check.

https://bit.ly/3y4vqct

How will Delta evolve? Here's what the theory tells us

The COVID-19 pandemic is a dramatic demonstration of evolution in action.

Hamish McCallum *

Evolutionary theory explains much of what has already happened, predicts what will happen in the future and suggests which management strategies are likely to be the most effective.

For instance, evolution explains why the Delta variant spreads faster than the original Wuhan strain. It explains what we might see with future variants. And it suggests how we might step up public health measures to respond.

But Delta is not the end of the story for SARS-CoV-2, the virus that causes COVID-19. Here's what evolutionary theory tells us happens next.

Remind me again, how do viruses evolve?

Evolution is a result of random mutations (or errors) in the viral genome when it replicates. A few of these random mutations will be good for the virus, conferring some advantage. Copies of these advantageous genes are more likely to survive into the next generation, via the process of natural selection.

New viral strains can also develop via recombination, when viruses acquire genes from other viruses or even from their hosts.

Generally speaking, we can expect evolution to favour virus strains that result in a steeper epidemic curve, producing more cases more quickly, leading to two predictions.

First, the virus should become more transmissible. One infected person will be likely to infect more people; future versions of the virus will have a higher reproductive or R number.

Second, we can also expect evolution will shorten the time it takes between someone becoming infected and infecting others (a shorter "serial interval"). Both these predicted changes are clearly good news for the virus, but not for its host.

Aha, so that explains Delta

This theory explains why Delta is now sweeping the world and replacing the original Wuhan strain.

The original Wuhan strain had an R value of 2-3 but Delta's R value is about 5-6 (some researchers say this figure is even higher). So someone infected with Delta is likely to infect at least twice as many people as the original Wuhan strain.

There's also evidence Delta has a much shorter serial interval compared with the original Wuhan strain.

This may be related to a higher viral load (more copies of the virus) in someone infected with Delta compared with earlier strains. This may allow Delta to transmit sooner after infection.

A higher viral load may also make Delta transmit more easily in the open air and after "fleeting contact".

Do vaccines affect how the virus evolves?

We know COVID-19 vaccines designed to protect against the original Wuhan strain work against Delta but are less effective. Evolutionary theory predicts this; viral variants that can evade vaccines have an evolutionary advantage.

So we can expect an arms race between vaccine developers and the virus, with vaccines trying to play catch up with viral evolution. This is why we're likely to see us having regular booster shots, designed to overcome these new variants, just like we see with flu booster shots.

COVID-19 vaccines reduce your chance of transmitting the virus to others, but they don't totally block transmission. And evolutionary theory gives us a cautionary tale.

There's a trade-off between transmissibility and how sick a person gets (virulence) with most disease-causing microorganisms. This is because you need a certain viral load to be able to transmit.

If vaccines are not 100% effective in blocking transmission, we can

expect a shift in the trade-off towards higher virulence. In other words, a side-effect of the virus being able to transmit from vaccinated people is, over time, the theory predicts it will become more harmful to unvaccinated people.

How about future variants?

In the short term, it's highly likely evolution will continue to "fine tune" the virus:

**** its R value will continue to increase (more people will be infected in one generation)***

**** the serial interval will decrease (people will become infectious sooner)***

**** variants will make vaccines less effective (vaccine evasion).***

But we don't know how far these changes might go and how fast this might happen.

Some scientists think the virus may already be approaching "peak fitness". Nevertheless, it may still have some tricks up its sleeve.

The UK government's Scientific Advisory Group for Emergencies (SAGE) has recently explored scenarios for long-term evolution of the virus.

It says it is almost certain there will be "antigenic drift", accumulation of small mutations leading to the current vaccines becoming less effective, so boosters with modified vaccines will be essential.

It then says more dramatic changes in the virus ("antigenic shift"), which might occur through recombination with other human coronaviruses, is a "realistic possibility". This would require more substantial re-engineering of the vaccines.

SAGE also thinks there is a realistic possibility of a "reverse zoonosis", leading to a virus that may be more pathogenic (harmful) to humans or able to evade existing vaccines. This would be a scenario where SARS-CoV-2 infects animals, before crossing back into humans. We've already seen SARS-CoV-2 infect mink, felines and rodents.

Will the virus become more deadly?

Versions of the virus that make their host very sick (are highly virulent) are generally selected against. This is because people would be more likely to die or be isolated, lowering the chance of the virus transmitting to others.

SAGE thinks this process is unlikely to cause the virus to become less virulent in the short term, but this is a realistic possibility in the long-term. Yet SAGE says there is a realistic possibility more virulent strains might develop via recombination (which other coronaviruses are known to do).

So the answer to this critical question is we really don't know if the virus will become more deadly over time. But we can't expect the virus to magically become harmless.

Will humans evolve to catch up?

Sadly, the answer is "no". Humans do not reproduce fast enough, and accumulate enough favourable mutations quickly enough, for us to stay ahead of the virus.

The virus also does not kill most people it infects. And in countries with well-resourced health-care systems, it doesn't kill many people of reproductive age. So there's no "selection pressure" for humans to mutate favourably to stay ahead of the virus.

What about future pandemics?

Finally, evolutionary theory has a warning about future pandemics.

A gene mutation that allows a virus in an obscure and relatively rare species (such as a bat) to gain access to the most common and widely distributed species of large animal on the planet — humans — will be strongly selected for.

So we can expect future pandemics when animal viruses spill over into humans, just as they have done in the past.

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Blood Thinners Reduce the Need for Mechanical Ventilation in Certain Patients With COVID-19

Giving moderately ill, hospitalized patients with COVID-19 a full dose of a blood thinner improved their chances of leaving the hospital without needing mechanical ventilation.

But this strategy did not yield the same results for patients with COVID-19 who were critically ill and needed intensive care–level support at the time of enrollment.

These are the findings of two new studies published online on August 4, 2021, in *The New England Journal of Medicine*. The studies of moderately ill and critically ill patients incorporated data from three platform trials as part of a global collaboration to identify possible treatments during the height of the pandemic. The trials are Accelerating COVID-19 Therapeutic Interventions and Vaccines-4 (ACTIV-4a): A Multicenter, Adaptive, Randomized Controlled Platform Trial of the Safety and Efficacy of Antithrombotic Strategies in Hospitalized Adults with COVID-19; Antithrombotic Therapy to Ameliorate Complications of COVID-19 (ATTACC); and Randomized, Embedded, Multi-Factorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) Therapeutic Anticoagulation.

Led by researchers from NYU Grossman School of Medicine, the University of Pittsburgh, and global collaborators, ACTIV-4a was launched after researchers observed that patients that died from COVID-19 had blood clots throughout their bodies, including in their smallest blood vessels. Doctors saw antithrombotics—also known as blood thinners or anticoagulants—as potential treatment because they reduce the risk of clotting. But the field did not know whether a full therapeutic dose that is used to treat blood clots or a low dose typically used to prevent blood clots would be most effective.

"Early on in the pandemic we observed substantial prevalence of clotting in hospitalized COVID-19 patients that caused severe complications," says Jeffrey S. Berger MD, ACTIV-4a co-principal investigator, co-first author of the study of moderately ill patients, associate professor of medicine and surgery, and director of the Center for the Prevention of Cardiovascular Disease at NYU Langone Health. "It is remarkable to lead a clinical trial that proves early intervention targeting clotting can improve outcomes and avoid many complications associated with COVID-19."

As part of the research effort, the lead researchers of three platform trials synchronized their study protocols to study the effects of using full and low doses of the anticoagulant heparin in patients hospitalized with COVID-19. Researchers grouped the patients according to whether they had severe or moderate COVID-19 and by their levels of D-dimer, a blood protein that may indicate clotting.

Moderately ill patients hospitalized with COVID-19 were defined as those who did not receive "organ support," including high-dose oxygen therapy, mechanical ventilation, life support, medicines that increase blood pressure, or medicines that change the force of the heart's contraction. Patients hospitalized with COVID-19 who did require such support were defined as severe or critically ill.

In April 2020, the research teams started randomly assigning half of their patients hospitalized with COVID-19 to receive either a low or full dose of heparin for up to 14 days after enrollment. By December 2020, oversight boards stopped enrollment of critically ill patients in the trial when interim results showed that full-dose anticoagulation did not reduce the need for organ support, and may cause harm, in severe and critically ill patients. One month later,

oversight boards also stopped enrollment of moderately ill patients in the trial when interim results indicated that full doses of blood thinners likely did offer a benefit. The trial enrolled 1,098 critically ill and 2,219 moderately ill patients, and researchers measured how long patients were free of organ support, up to 21 days after enrollment in both cohorts.

Among moderately ill patients, the study authors found that there was a 99 percent chance that full-dose heparin increased the probability of survival to hospital discharge with reduced need for organ support compared to those who received low-dose heparin. However, a small number of patients experienced major bleeding, though this happened infrequently. For critically ill patients, full-dose heparin also decreased the number of major thrombotic events, but it did not result in a greater chance of survival to hospital discharge, or a greater number of days free of organ support than did usual-care pharmacologic thromboprophylaxis, say the authors.

"These results are very exciting and lead us to better understand the impact of applying the right therapies at the right time in the course of this challenging disease," says ACTIV-4a study chair Judith S. Hochman, MD, the Harold Snyder Family Professor of Cardiology and senior associate dean for clinical sciences at NYU Grossman School of Medicine and a co-corresponding author of the study of moderately ill patients. "Our results will help clinicians utilize known and easily available medical therapies to better treat moderately ill COVID-19 patients," she says.

ACTIV-4a Antithrombotics Inpatient is conducting further research to test the effects of adding an antiplatelet agent to anticoagulation.

"More work needs to be done to continue to improve outcomes in patients with COVID-19," says Matthew D. Neal, MD, the Roberta G. Simmons Associate Professor of Surgery at the University of Pittsburgh, co-first author of the study of moderately ill patients and co-senior author of the study of critically ill patients. "Given what we know about the type of blood clots in patients with COVID-19, testing antiplatelet agents is a particularly exciting approach."

References:

"Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19" by The ATTACC, ACTIV-4a, and REMAP-CAP Investigators, 4 August 2021, The New England Journal of Medicine.

DOI: 10.1056/NEJMoa2105911

"Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19" by The REMAP-CAP, ACTIV-4a, and ATTACC Investigators, 4 August 2021, The New England Journal of Medicine.

DOI: 10.1056/NEJMoa2103417

The trials are supported by several funding organizations, including the National Institutes of Health (United States), the Canadian Institutes of Health Research, the National Institute for Health Research (UK), the National Health and Medical Research Council (Australia), and the PREPARE and RECOVER consortia (European Union). The ClinicalTrials.gov identifiers for the two published studies are NCT04505774 and NCT04359277.

https://bit.ly/3sD7vQv

Some Rare Diamonds Form Out of The Remains of Once-Living Creatures, New Study Finds

Despite humanity's intense fascination with sparkly pieces of carbon, it seems there is still plenty to learn about how diamonds form deep within our planet.

Jacinta Bowler

New research has discovered that two different types of rare diamonds share a common origin story – the recycling of once-living organisms over 400 kilometers (250 miles) below the surface.

There are three main types of natural diamonds. The first are lithospheric diamonds, which form in the lithospheric layer around 150 to 250 kilometers (93 - 155 miles) below the surface of Earth. These are by far the most common, and probably the type of diamond you'd find on an engagement ring.

Then there are two rarer types - oceanic and super-deep continental diamonds.

Oceanic diamonds are found in oceanic rocks, while deep

continental diamonds are those formed between 300 and 1,000 kilometers (186 and 621 miles) below the surface of Earth.

Just to put that in perspective, we categorize space as 100 kilometers (62 miles) above sea level, the ISS orbits about 400 km (250 miles) above Earth, and humans have never managed to dig deeper than 12.2 km (7.6 miles) into the ground. So, super-deep continental diamonds form... *super* deep in Earth's mantle.

As you would expect, oceanic and super-deep continental diamonds seem pretty different. Because variation in a carbon isotope signature called $\delta^{13}C$ (delta carbon thirteen) can be used to determine whether the carbon has an organic or inorganic origin, past researchers have suggested that oceanic diamonds originally formed from organic carbon that was once within living beings.

Super-deep continental diamonds, on the other hand, have an extremely variable amount of $\delta^{13}C$. It's hard to tell whether they're made of organic carbon or not.

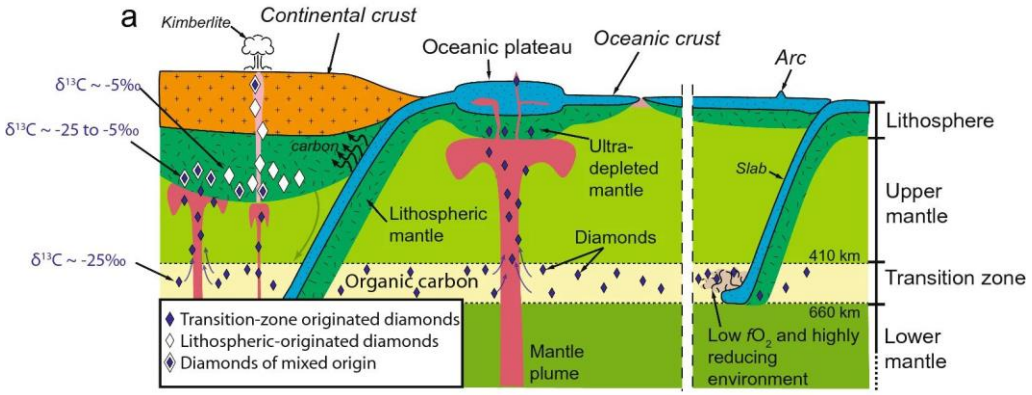
But in this new paper, led by Curtin University geologist Luc Doucet, the team found that the cores of super-deep continental diamonds have a similar $\delta^{13}C$ composition. Surprisingly, this means that, like oceanic diamonds, these gems also contain the remains of once-living creatures.

"Bringing new meaning to the old trash to treasure adage, this research discovered that Earth's engine actually turns organic carbon into diamonds many hundreds of kilometers below the surface," said Doucet.

"Ballooning rocks from Earth's deeper mantle, called mantle plumes, then carry the diamonds back up to Earth's surface via volcanic eruptions for humans to enjoy as sought-after gemstones."

Back in the lithosphere, some of these deep diamonds become cores wrapped in inorganic diamond crusts, whose isotopes match the diamonds from the lithosphere. This explains why their $\delta^{13}C$ composition is so variable.

In recent years, we've learnt a surprising amount about scientists' second favorite form of carbon.



Model for the genesis of three types of diamonds. **(Doucet et al., Sci Rep, 2021)**

Gazing at flawed diamonds can help researchers discover their first moments; the structure of these crystals stays put even under pressure five times higher than Earth's core; in 2019, we even discovered a diamond with a whole another diamond inside.

But this new research isn't the end of the story – not by a long shot. The scientists aren't sure why these deep, rare diamonds found deeper than the lithosphere are using this recycled organic carbon.

"This might have something to do with the physical-chemical environment there", Curtin University geologist Zheng-Xiang Li explained.

"It is not uncommon for a new scientific discovery to raise more questions that require further investigation."

The research has been published in *Scientific Reports*.