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CRP Test Pinpoints Which COVID Patients Should Get Steroids

C-reactive protein (CRP) test can help physicians decide which patients are likely to benefit from dexamethasone and other steroids

Marcia Frellick

Patients hospitalized with COVID-19 who have high levels of inflammation may benefit significantly from dexamethasone and other steroids, researchers say. They warn, however, that patients with low levels of inflammation could face a significantly higher risk for severe outcomes with steroid use.

Lead author Marla Keller, MD, vice chair for research in the Department of Medicine at the Albert Einstein College of Medicine and the Montefiore system, New York City, and colleagues also found that a C-reactive protein (CRP) test can help physicians decide which patients are likely to benefit. They published their findings online July 22 in *Journal of Hospital Medicine*.

In patients with high levels of inflammation — at least 20 mg/dL — steroid treatment was associated with a 77% reduction in the risk of needing mechanical ventilation or dying (odds ratio [OR], 0.23).

Importantly, treating with steroids when CRP levels were less than 10 mg/dL was associated with an almost threefold increased risk of going on mechanical ventilation or dying (OR, 2.64).

"The laboratory test could potentially be very helpful," Keller *told Medscape Medical News*.

Paper Builds on Randomized RECOVERY Findings

The work builds on findings of the large, randomized, open-label RECOVERY (Randomised Evaluation of COVid-19 thERapY) trial in the United Kingdom. That study, with more than 6000 patients, found that dexamethasone, compared with standard of care, reduced deaths by about a third in ventilated patients and by about one fifth among people who needed oxygen therapy but were not on a ventilator. The New York study confirmed findings of the RECOVERY trial but also that the benefits were true for steroids beyond dexamethasone.

Keller's team treated one group of 140 patients with steroids within 48 hours of hospital admission and compared results with a control group of 1666 similar patients who did not receive steroids. Most who received steroids got prednisone; some received dexamethasone and methylprednisolone.

Keller said their work led to developing a protocol for deciding who should get steroids that has changed practice throughout the Montefiore Health System.

"Opportunity to Save Many Lives"

She also said the results may have large implications for public health: "The RECOVERY trial and our study show that steroids reduce mortality," she said, adding that that knowledge and having a widely available indicator for when to administer the steroids gives "the opportunity to save many lives."

She acknowledged, however, that theirs is a single-institution study and more research must be done to narrow down which patients will benefit or be harmed most. They didn't look at, for instance, how quickly CRP levels fall after steroid use.

Keller also emphasized that the findings should in no way promote use of steroids in the outpatient setting for treating COVID-19.

Many physicians remain hesitant to use steroids because with other viruses such as Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and influenza "there were studies that showed that steroids could delay clearing the virus," she said. Others are concerned about their potential to increase glucose or secondary bacterial or fungal infections.

An added benefit of the New York study is that 37.5% of patients studied were Black and 36% were Hispanic, groups that have been

especially hard hit by COVID-19 but often underrepresented in research, Keller continued.

Randy Cron, MD, PhD, professor of medicine and pediatrics at University of Alabama at Birmingham (UAB), who is actively involved in COVID-19 research, told *Medscape Medical News* that UAB is among the institutions that have changed their thinking and moved toward promoting steroid use for certain hospitalized patients with COVID-19.

He said it's important to remember the New York report doesn't have the strength of a randomized trial, though it aligns with the findings of the RECOVERY trial.

But the findings about the CRP test may help clinicians make decisions for patients in the emergency room or admitted to the hospital with COVID-19 about whether to give steroids, he said.

The test is inexpensive, widely available, has a fast turnaround, and most patients with a fever entering the hospital would be getting it anyway, he noted.

Cron explained that what often kills patients with COVID-19 are the cytokine storms rather than the disease itself; the virus is what's triggering the cytokine storm. Ideally, there would be treatment for both. However, "At this point we don't have great antiviral therapy — remdesivir helps a little bit but it's not a home run," he noted.

The timing for giving steroids is also very important, he said.

"You don't necessarily want to give it really early on when the virus is going nuts because that's when giving immunosuppression, like a corticosteroid, is going to make it harder to keep the virus under control," he continued. "But at the point where you're sick enough to be hospitalized with the coronavirus, that may be where you want to intervene to dampen down the immune system if it's up, and the C-reactive protein may be a marker of that."

He said the move toward steroid use for patients with COVID-19 strengthened as hospitals globally began to be overrun.

"Clinicians were tired of watching people die in front of them," he said. "People outside of clinical trials were using (steroids) in desperation and reporting, eventually, that they worked."

He explained there is still considerable hesitation to use steroids from conservative physicians who won't be convinced without more clinical trials.

On the other hand, he said, after the RECOVERY trial "some centers have completely flipped so that now everyone gets steroids and I'm not sure that's right either."

Ideally, there would be time for multiple randomized trials to help find the best solution. "This isn't like we're exploring a new medicine for a chronic condition to see if it works better than something else. Hundreds of thousands of people have died and we don't necessarily have the time to wait for all these randomized trials. It's a tough question," he said.

Sobi provided study drugs for some COVID-19 trials at the University of Alabama at Birmingham. The study authors have disclosed no relevant financial relationships. Cron reported being a consultant for, receiving support from, or being on the advisory board for Novartis, Sobi, and Sironax.

J Hosp Med. Published online July 22, 2020. Full text

https://bit.ly/39GzzZC

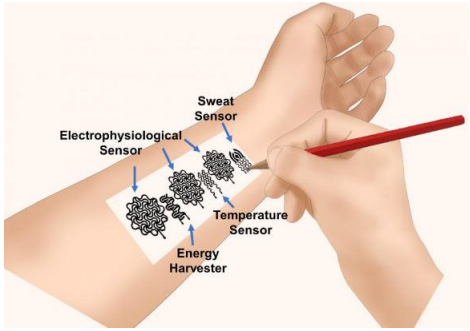
Researchers Use Pencil to Draw Bioelectronic Devices on Human Skin

Combination of pencils and paper could be used to create on-skin bioelectronic devices that might be used to monitor personal health.

Scientists from the University of Missouri, the University of Illinois and Yale University have demonstrated that a combination of pencils and paper could be used to create on-skin bioelectronic devices that might be used to monitor personal health. They've fabricated and evaluated a rich variety of pencil-paper-based bioelectronic devices, ranging from biophysical sensors and sweat

biochemical sensors to thermal stimulators, ambient humidity energy harvesters, and transdermal drug-delivery systems.

"Many existing commercial on-skin biomedical devices often contain two major components — a biomedical tracking component and a surrounding flexible material, such as plastic, to provide a supportive structure for the component to maintain an on-skin connection with a person's body," said senior author Dr. Zheng Yan, a researcher in the Department of Biomedical, Biological & Chemical Engineering and the Department of Mechanical & Aerospace Engineering at the University of Missouri.



Conceptual illustrations of drawing on-skin electronics on paper using a 9B sketching pencil. **Image credit: Xu et al, doi: 10.1073/pnas.2008422117.**

"The conventional approach for developing an on-skin biomedical electronic device is usually complex and often expensive to produce." "In contrast, our approach is low-cost and very simple. We can make a similar device using widely available pencils and paper."

In the study, Dr. Yan and colleagues discovered that pencils containing more than 90% graphite are able to conduct a high amount of energy created from the friction between paper and pencil caused by drawing or writing. Specifically, they found pencils with 93% graphite were the best for creating a variety of on-skin bioelectronic devices drawn on commercial office copy paper.

"A biocompatible spray-on adhesive could also be applied to the paper to help it stick better to a person's skin," Dr. Yan said.

The discovery could have broad future applications in home-based, personalized health care, education and remote scientific research.

The team's next step would be to further develop and test the use of the biomedical components, including electrophysiological, temperature and biochemical sensors. "For example, if a person has a sleep issue, we could draw a biomedical device that could help monitor that person's sleep levels," Dr. Yan said.

"Or in the classroom, a teacher could engage students by incorporating the creation of a wearable device using pencils and paper into a lesson plan." "Furthermore, this low-cost, easily customizable approach could allow scientists to conduct research at home, such as during a pandemic."

"An additional benefit to our approach is that paper can decompose in about a week, compared to many commercial devices that contain components that are not easily broken down."

The team's paper was published in the *Proceedings of the National Academy of Sciences*.

Yadong Xu et al. Pencil-paper on-skin electronics. PNAS, published online July 13, 2020; doi: 10.1073/pnas.2008422117

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Life in the pits: Scientists identify the key enzyme behind BO

Scientists have discovered a unique enzyme responsible for the pungent characteristic smell we call body odour or BO.

Scientists have discovered a unique enzyme responsible for the pungent characteristic smell we call body odour or BO.

Researchers from the University of York have previously shown that only a few bacteria in your armpit are the real culprits behind BO. Now the same team, in collaboration with Unilever scientists, has gone a step further to discover a unique "BO enzyme" found only within these bacteria and responsible for the characteristic armpit odour.

This new research highlights how particular bacteria have evolved a specialised enzyme to produce some of the key molecules we recognise as BO.

Co-first author Dr Michelle Rudden from the group of Prof. Gavin Thomas in the University of York's Department of Biology, said: "Solving the structure of this 'BO enzyme' has allowed us to pinpoint the molecular step inside certain bacteria that makes the odour molecules. This is a key advancement in understanding how body odour works, and will enable the development of targeted inhibitors that stop BO production at source without disrupting the armpit microbiome."

Your armpit hosts a diverse community of bacteria that is part of your natural skin microbiome. This research highlights Staphylococcus hominis as one of the main microbes behind body odour.

Furthermore, the researchers say that this "BO enzyme" was present in S. hominis long before the emergence of Homo sapiens as a species, suggesting that body odour existed prior to the evolution of modern humans, and may have had an important role in societal communication among ancestral primates.

This research represents an important discovery for Unilever R&D, made possible by its long-standing academic-industry collaboration with the University of York. Unilever co-author Dr Gordon James said: "This research was a real eye-opener. It was fascinating to discover that a key odour-forming enzyme exists in only a select few armpit bacteria - and evolved there tens of millions of years ago."

'The molecular basis of thioalcohol production in human body odour' is published in the journal Scientific Reports: https://www.nature.com/articles/s41598-020-68860-z

The research was funded by the UK Biotechnology and Biological Sciences Research Council (BBSRC) through a LINK scheme awarded to Professor Gavin Thomas in collaboration with Dr Gordon James of Unilever R&D.

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Flu, pneumonia vaccinations tied to lower risk of Alzheimer's dementia

Flu and pneumonia vaccinations are associated with reduced risk of Alzheimer's disease

Chicago -- Three research studies reported at AAIC 2020 suggest:

At least one flu vaccination was associated with a 17% reduction in Alzheimer's incidence. More frequent flu vaccination was associated with another 13% reduction in Alzheimer's incidence.

Vaccination against pneumonia between ages 65 and 75 reduced Alzheimer's risk by up to 40% depending on individual genes.

Individuals with dementia have a higher risk of dying (6-fold) after infections than those without dementia (3-fold).

"With the COVID-19 pandemic, vaccines are at the forefront of public health discussions. It is important to explore their benefit in not only protecting against viral or bacterial infection but also improving long-term health outcomes," said Maria C. Carrillo, Ph.D., Alzheimer's Association chief science officer.

"It may turn out to be as simple as if you're taking care of your health in this way -- getting vaccinated -- you're also taking care of yourself in other ways, and these things add up to lower risk of Alzheimer's and other dementias," Carrillo said. "This research, while early, calls for further studies in large, diverse clinical trials to inform whether vaccinations as a public health strategy decrease our risk for developing dementia as we age."

Seasonal Flu Vaccine May Reduce Incidence of Alzheimer's Dementia

Previous research has suggested vaccinations may have a protective factor against cognitive decline, but there have been no large, comprehensive studies focused on the influenza (flu) vaccine and Alzheimer's disease risk, specifically. To address this gap, Albert Amran, a medical student at McGovern Medical School at The

University of Texas Health Science Center at Houston, and team, investigated a large American health record dataset (n=9,066).

Amran and team found having one flu vaccination was associated with a lower prevalence of Alzheimer's (odds ratio 0.83, p<0.0001), and among vaccinated patients receiving the flu vaccine more frequently was associated with an even lower prevalence of Alzheimer's (odds ratio 0.87, p=0.0342). Thus, people that consistently got their annual flu shot had a lower risk of Alzheimer's. This translated to an almost 6% reduced risk of Alzheimer's disease for patients between the ages of 75-84 for 16 years.

The researchers found the protective association between the flu vaccine and the risk of Alzheimer's was strongest for those who received their first vaccine at a younger age -- for example, the people who received their first documented flu shot at age 60 benefitted more than those who received their first flu shot at age 70.

"Our study suggests that regular use of a very accessible and relatively cheap intervention -- the flu shot -- may significantly reduce risk of Alzheimer's dementia," Amran said. "More research is needed to explore the biological mechanism for this effect -- why and how it works in the body -- which is important as we explore effective preventive therapies for Alzheimer's."

Pneumonia Vaccine May Reduce Alzheimer's Risk Later in Life

Repurposing of existing vaccines may be a promising approach to Alzheimer's disease prevention. Svetlana Ukraintseva, Ph.D., Associate Research Professor in the Biodemography of Aging Research Unit (BARU) at Duke University Social Science Research Institute, and team, investigated associations between pneumococcal vaccination, with and without an accompanying seasonal flu shot, and the risk of Alzheimer's disease among 5,146 participants age 65+ from the Cardiovascular Health Study. The team also took into account a known genetic risk factor for Alzheimer's -- the rs2075650 G allele in the TOMM40 gene.

The researchers found that pneumococcal vaccination between ages 65-75 reduced risk of developing Alzheimer's by 25-30% after adjusting for sex, race, birth cohort, education, smoking, and number of G alleles. The largest reduction in the risk of Alzheimer's (up to 40%) was observed among people vaccinated against pneumonia who were non-carriers of the risk gene. Total number of vaccinations against pneumonia and the flu between ages 65 and 75 was also associated with a lower risk of Alzheimer's; however, the effect was not evident for the flu shot alone.

"Vaccinations against pneumonia before age 75 may reduce Alzheimer's risk later in life, depending on individual genotype," Ukraintseva said. "These data suggest that pneumococcal vaccine may be a promising candidate for personalized Alzheimer's prevention, particularly in non-carriers of certain risk genes."

Infection Substantially Increases Mortality in People with Dementia

People living with dementia commonly experience other health conditions including viral, bacterial, and other infections. There is a growing trend in research to investigate whether infections might be worsening, more life-threatening or possibly causing dementia.

Janet Janbek, a Ph.D. student at the Danish Dementia Research Centre, Rigshospitalet and the University of Copenhagen in Denmark, and team, used data from national health registries to investigate mortality in Danish residents over age 65 (n=1,496,436) who had visited the hospital with an infection. They found that people with both dementia and such hospital visits died at a 6.5 times higher rate compared with people who had neither. Study participants with either dementia alone or infection-related contacts

alone had a threefold increased rate. The rate of mortality was highest within the first 30 days following the hospital visit.

The researchers also found that for people living with dementia the mortality rates remained elevated for 10 years after the initial infection-related hospital visit, and mortality rates from all infections (including major infections like sepsis to minor ear infections) were higher compared with people without dementia or without an infection-related hospital visit.

"Our study supports the need to investigate these relations even further; to find out why infections are linked to higher mortality in people with dementia, specifically which risk factors and biological mechanisms are involved. This will help advance our understanding of the role of infections in dementia," said Janbek.

"Our study suggests that the health care system -- as well as relatives of people with dementia -- should have increased awareness of people with dementia who get infections, so they get the medical care they need. People with dementia require more specialized treatment even when their hospital visits are not directly due to their dementia but to what might appear to be an unrelated infection," Janbek added.

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Offshore wind power now so cheap it could pay money back to consumers

Most recently approved offshore wind projects will most likely operate with 'negative subsidies'

The latest round of offshore wind farms to be built in the UK could reduce household energy bills by producing electricity very cheaply.

Renewable energy projects, including onshore and offshore wind and solar farms, have so far been subsidised by government support schemes. This has led to some to complain that clean energy is pushing up bills.

However, the most recently approved offshore wind projects will most likely operate with 'negative subsidies' - paying money back to the government. The money will go towards reducing household energy bills as the offshore wind farms start producing power in the mid-2020s.

This is the conclusion of an analysis by an international team led by Imperial College London researchers published today in *Nature Energy*.

Lead researcher Dr Malte Jansen, from the Centre for Environmental Policy at Imperial, said: "Offshore wind power will soon be so cheap to produce that it will undercut fossil-fuelled power stations and may be the cheapest form of energy for the UK. Energy subsidies used to push up energy bills, but within a few years cheap renewable energy will see them brought down for the first time. This is an astonishing development."

Negative subsidies

The analysis for five countries in Europe, including the UK, focused on a series of government auctions for offshore wind farms between February 2015 and September 2019.

Companies that want to build wind farms bid in the auctions by stating the price at which they will sell the energy they produce to the government.

These are known as 'contracts for difference' or CfDs. If a company's bid is higher than the wholesale electricity price on the UK market once the wind farm is up and running, then the company will receive a subsidy from the government to top up the price.

However, if the stated price is less than the wholesale price, then the company will pay the government back the difference. This payback is then passed through to consumer's energy bills, reducing the amount that homes and businesses will pay for electricity.

The UK's September 2019 auction made the headlines as winning companies said they could build new offshore wind farms for around £40 per megawatt hour (MWh) of power. This was a new record set by these wind farms with bids 30 percent lower than just two years earlier.

While this was an impressive reduction, researchers could only speculate whether this meant offshore wind had become subsidy free or even subsidy negative, because that depends on how future wholesale electricity prices evolve.

The team analysed likely future electricity price trends and found that contracted price is very likely to be below the UK wholesale price over the lifetime that these wind farms would produce electricity, from the mid-2020s onwards.

The team say that these wind farms are likely to be built and run with these costs, since financing is now accessible at lower costs for such projects, owing to trust in the now mature technology.

A cheap tool for decarbonisation

The researchers analysed similar offshore wind auctions held by governments of five European countries. They found that Germany and the Netherlands have seen some zero-subsidy offshore wind farms winning auctions, but that the UK projects are likely to be the world's first negative-subsidy offshore wind farms.

Dr Iain Staffell, from the Centre for Environmental Policy at Imperial, said: "The price of offshore wind power has plummeted in only a matter of a decade, surprising many in the field.

The UK auctions in September 2019 gave prices that were around one-third lower than those of the last round in 2017, and two-thirds lower than we saw in 2015.

"This amazing progress has been made possible by new technology, economies of scale and efficient supply chains around the North Sea, but also by a decade of concerted policymaking designed to reduce the risk for investing in offshore wind, which has made financing these huge billion-pound projects much cheaper.

"These new wind farms set the stage for the rapid expansion needed to meet the government's target of producing 30 percent of the UK's energy needs from offshore wind by 2030. Offshore wind will be pivotal in helping the UK, and more broadly the world, to reach net-zero carbon emissions with the added bonus of reducing consumers' energy bills."

Mega turbines and hydrogen fuels

One reason the price of offshore wind has fallen so rapidly is technology development, in particular the ability to build larger wind turbines further out at sea. Larger turbines can harness more wind energy and have access to more consistent wind speeds at higher altitudes.

The biggest wind turbines under construction have rotor diameters of 220 metres - twice the diameter of the London Eye. At the same time, wind farms are getting larger; the newest wind farm at Dogger Bank has the same installed capacity as Hinkley Point C and is expected to produce about two-thirds of its annual electricity.

The success of UK offshore windfarms, which are now primarily built in the Dogger Bank region of the North Sea, also means the UK has considerable skills and expertise than can be exported around the world.

The researchers also say this success means even more ambitious projects may now be attempted at offshore wind farms, such as producing hydrogen fuels using the wind power on site, out at sea. Hydrogen fuels could be another key technology in helping decarbonise the UK, by replacing petrol used in transportation and natural gas used for heating homes.

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Study: A plunge in incoming sunlight may have triggered 'snowball earths'

Findings also suggest exoplanets lying within habitable zones may be susceptible to ice ages

Written by Jennifer Chu, MIT News Office

At least twice in Earth's history, nearly the entire planet was encased in a sheet of snow and ice. These dramatic "Snowball Earth" events occurred in quick succession, somewhere around 700 million years ago, and evidence suggests that the consecutive global ice ages set the stage for the subsequent explosion of complex, multicellular life on Earth.

Scientists have considered multiple scenarios for what may have tipped the planet into each ice age. While no single driving process has been identified, it's assumed that whatever triggered the temporary freeze-overs must have done so in a way that pushed the planet past a critical threshold, such as reducing incoming sunlight or atmospheric carbon dioxide to levels low enough to set off a global expansion of ice.

But MIT scientists now say that Snowball Earths were likely the product of "rate-induced glaciations." That is, they found the Earth can be tipped into a global ice age when the level of solar radiation it receives changes quickly over a geologically short period of time. The amount of solar radiation doesn't have to drop to a particular threshold point; as long as the decrease in incoming sunlight occurs faster than a critical rate, a temporary glaciation, or Snowball Earth, will follow.

These findings, published in the *Proceedings of the Royal Society A*, suggest that whatever triggered the Earth's ice ages most likely involved processes that quickly reduced the amount of solar radiation coming to the surface, such as widespread volcanic eruptions or biologically induced cloud formation that could have significantly blocked out the sun's rays.

The findings may also apply to the search for life on other planets. Researchers have been keen on finding exoplanets within the habitable zone -- a distance from their star that would be within a temperature range that could support life. The new study suggests that these planets, like Earth, could also ice over temporarily if their climate changes abruptly. Even if they lie within a habitable zone, Earth-like planets may be more susceptible to global ice ages than previously thought.

"You could have a planet that stays well within the classical habitable zone, but if incoming sunlight changes too fast, you could get a Snowball Earth," says lead author Constantin Arnscheidt, a graduate student in MIT's Department of Earth, Atmospheric and Planetary Sciences (EAPS). "What this highlights is the notion that there's so much more nuance in the concept of habitability."

Arnscheidt has co-authored the paper with Daniel Rothman, EAPS professor of geophysics, and co-founder and co-director of the Lorenz Center.

A runaway snowball

Regardless of the particular processes that triggered past glaciations, scientists generally agree that Snowball Earths arose from a "runaway" effect involving an ice-albedo feedback: As incoming sunlight is reduced, ice expands from the poles to the equator. As more ice covers the globe, the planet becomes more reflective, or higher in albedo, which further cools the surface for more ice to expand. Eventually, if the ice reaches a certain extent, this becomes a runaway process, resulting in a global glaciation.

Global ice ages on Earth are temporary in nature, due to the planet's carbon cycle. When the planet is not covered in ice, levels of carbon dioxide in the atmosphere are somewhat controlled by the weathering of rocks and minerals. When the planet is covered in ice,

weathering is vastly reduced, so that carbon dioxide builds up in the atmosphere, creating a greenhouse effect that eventually thaws the planet out of its ice age.

Scientists generally agree that the formation of Snowball Earths has something to do with the balance between incoming sunlight, the ice-albedo feedback, and the global carbon cycle.

"There are lots of ideas for what caused these global glaciations, but they all really boil down to some implicit modification of solar radiation coming in," Arnscheidt says. "But generally it's been studied in the context of crossing a threshold."

He and Rothman had previously studied other periods in Earth's history where the speed, or rate at which certain changes in climate occurred had a role in triggering events, such as past mass extinctions.

"In the course of this exercise, we realized there was an immediate way to make a serious point by applying such ideas of rate-induced tipping, to Snowball Earth and habitability," Rothman says.

"Be wary of speed"

The researchers developed a simple mathematical model of the Earth's climate system that includes equations to represent relations between incoming and outgoing solar radiation, the surface temperature of the Earth, the concentration of carbon dioxide in the atmosphere, and the effects of weathering in taking up and storing atmospheric carbon dioxide. The researchers were able to tune each of these parameters to observe which conditions generated a Snowball Earth.

Ultimately, they found that a planet was more likely to freeze over if incoming solar radiation decreased quickly, at a rate that was faster than a critical rate, rather than to a critical threshold, or particular level of sunlight. There is some uncertainty in exactly what that critical rate would be, as the model is a simplified representation of the Earth's climate. Nevertheless, Arnscheidt estimates that the Earth would have to experience about a 2 percent drop in incoming sunlight over a period of about 10,000 years to tip into a global ice age.

"It's reasonable to assume past glaciations were induced by geologically quick changes to solar radiation," Arnscheidt says.

The particular mechanisms that may have quickly darkened the skies over tens of thousands of years is still up for debate. One possibility is that widespread volcanoes may have spewed aerosols into the atmosphere, blocking incoming sunlight around the world. Another is that primitive algae may have evolved mechanisms that facilitated the formation of light-reflecting clouds. The results from this new study suggest scientists may consider processes such as these, that quickly reduce incoming solar radiation, as more likely triggers for Earth's ice ages.

"Even though humanity will not trigger a snowball glaciation on our current climate trajectory, the existence of such a 'rate-induced tipping point' at the global scale may still remain a cause for concern," Arnscheidt points out. "For example, it teaches us that we should be wary of the speed at which we are modifying Earth's climate, not just the magnitude of the change. There could be other such rate-induced tipping points that might be triggered by anthropogenic warming. Identifying these and constraining their critical rates is a worthwhile goal for further research."

This research was funded, in part, by the MIT Lorenz Center.

https://nyti.ms/3jVB8rn

These Microbes May Have Survived 100 Million Years Beneath the Seafloor

Rescued from their cold, cramped and nutrient-poor homes, the bacteria awoke in the lab and grew.

By Katherine J. Wu

The South Pacific Gyre is an aquatic nowhere. It’s the spot in the sea that’s farther from land than any other, so devoid of nutrients,

life and even continental dust that it's considered "the deadest spot in the ocean," said Steven D'Hondt, a geomicrobiologist at the University of Rhode Island.

Yet some 20,000 feet beneath the surface of this watery desert, microscopic creatures have not only found a way to eke out a living — they've also managed to weather the inhospitality for many millions of years.

In a paper published Tuesday in Nature Communications, Dr. D'Hondt and his colleagues describe the remarkable revival of a small population of microbes that may have spent the past 101.5 million years ensconced in a slumber under sediments deep below the gyre — only to be roused awake in the lab.

If confirmed, these microbes could be among the oldest living organisms ever found. Spawned during a time when the non-avian dinosaurs still stalked the Earth, these hibernating cells might have rested as the continents creaked into their modern configuration, the globe's first grasses emerged and our great ape lineage took its first steps toward walking upright.

Such longevity is unlikely, even mathematically impossible within the constraints of some models, said Yuki Morono, a microbiologist at the Japan Agency for Marine-Earth Science and Technology, or Jamstec, and an author of the study: "No theoretical microbiology can explain it. But we found it."

Other scientists have unearthed snoozing microbes from harsh environments beneath the seafloor in the past. Crushed by miles of water and mud and starved of food, sunlight and warmth, cells must adapt or perish. Those that adapt can sometimes avoid death by simply teetering on the verge of it.

Scientists think that microbes will grind their metabolism to a near halt so they can make do with the meager motes of food in their environment. Some in the field refer to this strategy as "the slow lane of life," said Nagissa Mahmoudi, a geomicrobiologist at McGill University who wasn't involved in the study. "They're not really thriving. They're just hanging on."

But the relative rarity of such cells has made it tough to determine just how long such states of quasi-suspended animation can actually last.

So a team led by Fumio Inagaki, also of Jamstec, set sail into the southern Pacific Ocean in the fall of 2010 and drilled deep into its sediments. Over eons, mud settles in layers like a chronological stack of pancakes, with the newest additions closest to the seafloor; the oldest, some 250 feet under the ocean bottom, had been laid down about 101.5 million years before.

Even Dr. Morono was skeptical of finding life in the most ancient parts of the mucky, nutrient-poor cores the team extracted. Down there, bits of clay are crammed so tightly together that the spaces between them can't even accommodate the full width of a bacterial cell. "You are packed into the sediment and cannot move," he said. "I cannot even imagine such a harsh environment as a human."

But as he continued to sample backward in time, it became clear that there were microbes all the way down.

The work wasn't easy. To avoid discombobulating the fragile cells too much, Dr. Morono tried to replicate their home environment as best he could. That meant spending up to 10 hours a day working in a room chilled to below 50 degrees Fahrenheit, bundled from head to toe, as he plied the bugs with bits of chemically labeled food.

Dr. Morono expected that after thousands, if not millions, of years stuck in the mud, the microbes would be slow to rise. But within just a few days, some of the groggy germs had started to divide. For nearly two years, the researchers watched their specimens grow; 557 days later, many communities of the teeny troopers were still chugging along.

The microbes' newfound vivacity hints that for millions of years, they were "just kind of waiting for conditions to improve," said

Virginia Edgcomb, a geomicrobiologist at Woods Hole Oceanographic Institution who wasn't involved in the study.

It's hard to determine the age of individual cells, Dr. Edgcomb added. Some may be as old as the sediments they once sat in; others may be the progeny of these ancients. Given how spare the microbes' diets probably were, Dr. D'Hondt suspects that reproduction was probably rare. That makes it all the more remarkable that, even after spending millions of years just barely ticking along, the cells were game to "sit up and party on," he said.

Even older microbes could still be in yet-untested seafloor sediments, which can be up to 200 million years in age. Future-minded scientists could find these stalwart specimens useful — including those involved in the search for extraterrestrial life.

"This opens up a whole Pandora's box for where we could find life elsewhere in the universe," Dr. Mahmoudi said. "It seems everywhere we've gone, we've found life."

https://bit.ly/39LMo4M

First Meta-Analysis Confirms Link Between Lithium in Drinking Water And Suicide Rates

Lithium could have a measurable effect on our lives

Signe Dean

Lithium - the lightest of all solid elements - doesn't just power rechargeable batteries. Traces of lithium permeate virtually every rock on our planet, and are found in our food and water supply. According to a new analysis, this invisible presence could have a measurable effect on our lives.

For decades, lithium has been an often life-saving medication for people with mood disorders, most notably bipolar, with a proven ability to stabilise moods and reduce the risk of suicide in these highly vulnerable patients.

The doses used in psychiatry are relatively high - at least 200 milligrams per day, and side-effects have to be carefully monitored. But some research has indicated that even microdoses of the element, just 400 micrograms daily, can produce an improvement in mood (there are 1,000 micrograms in a milligram).

Since the 1990s, scientists have wondered whether the naturally occurring lithium in drinking water supplies across the world could produce effects at the level of the entire population - lower suicide rates, decreased violence, even less dementia.

Over the years, a slew of observational or ecological studies have hinted at an association between higher levels of lithium in the public water supply, and lower rates of suicide mortality in the local population.

Now, a team of researchers in the UK has produced the first-ever meta-analysis of such studies, confirming this link. We don't know why this might be the case, but it's a curious path to tread.

"It is promising that higher levels of trace lithium in drinking water may exert an anti-suicidal effect and have the potential to improve community mental health," says lead author of the review, epidemiologist Anjum Memon from Brighton and Sussex Medical School.

The team thoroughly searched the literature, ending up with 15 studies they used in a qualitative synthesis, narrowed down further for a meta-analysis of nine studies.

In total, their analysis comprised data from 1,286 localities across Japan, Austria, the US, England, Greece, Italy, and Lithuania. The mean lithium levels found in the drinking water samples ranged from just 3.8 micrograms per litre (µg/L) to 46.3 µg/L, with a few communities peaking above 80 µg/L.

An extensive crunch of the numbers revealed that higher lithium levels naturally occurring in drinking water were indeed linked with lower levels of suicide mortality in the area - what's known as an inverse association.

Of course, as with any complex analysis of the available literature, the results come with important caveats. The team emphasises that ecological studies are conducted to generate hypotheses - rather than being an answer, they're basically just posing the question.

"They are subject to confounding as information on potential confounder(s) may not be available and associations at the population level do not necessarily represent associations at the individual level (ecological fallacy)", they write.

Details on social classes, the prevalence of mental disorders in a population, and even how much people move around can all affect the observational results, not to even mention the fact we also get lithium from our food - and that impact has not been investigated.

"Furthermore, bottled drinking water (processed/treated or natural mineral water from springs) often has a much higher lithium content than tap water – the association between exposure to lithium via bottled water and suicide has not been studied," the team notes.

In light of their findings, the researchers do recommend randomised community trials of supplementing the water supply with lithium, as "a possible means of testing the hypothesis", along with research into food sources of lithium.

Scientists are still working to paint the full picture of how lithium even works, why it can have such a beneficial effect on one's mood levels, and whether the anti-suicidal effects of the element are entirely separate.

Of course, to some this will inevitably sound as the beginnings of a government conspiracy. But there are plenty of experts willing to urge caution before we start any supplementation trials, and plenty of data left to gather.

And if we don't ask the questions, we can't expect an answer.

The review was published in *The British Journal of Psychiatry*.

https://bit.ly/30q7BRp

Mounting poisonings, blindness, deaths as toxic hand sanitizers flood market

The FDA is "extremely concerned" by the growing risks of toxic sanitizers.

Beth Mole

The Food and Drug Administration is renewing warnings this week of dangerous hand sanitizers as it continues to find products that contain toxic methanol—a poisonous alcohol that can cause systemic effects, blindness, and death.

The agency's growing "do-not-use list" of dangerous sanitizers now includes 87 products (See the full list here). And with the mounting tally, the FDA also says there are rising reports from state health departments and poison control centers of injuries and deaths.

"We remain extremely concerned about the potential serious risks of alcohol-based hand sanitizers containing methanol," said FDA Commissioner Stephen M. Hahn in a statement.

Good hand hygiene, which includes using hand sanitizers when hand-washing isn't possible, is an important public health practice, especially amid the pandemic. But, Dr. Hahn said, "consumers must also be vigilant about which hand sanitizers they use, and for their health and safety we urge consumers to immediately stop using all hand sanitizers on the FDA's list of dangerous hand sanitizer products."

Examples of some of the products on the list:

The agency reported that its ongoing testing has found sanitizers containing methanol at levels ranging from 1 percent to 80 percent. No amount of methanol is acceptable, the agency notes. The alcohol, which is metabolized to formaldehyde then to formic acid in the body, can cause systemic toxic effects if ingested, inhaled, or absorbed through the skin. Ingesting just two tablespoons can be

fatal to small children, who may be tempted to drink sanitizers within reach. Smaller amounts can lead to permanent blindness.

States continue to report increasing numbers of harms from the products, which can cause nausea, vomiting, headache, blurred vision, permanent blindness, seizures, coma, permanent damage to the nervous system, cardiac effects, and death. In one case, investigators linked a death to Blumen Hand Sanitizer, distributed by 4e North America and manufactured by 4E Global in Mexico. The company has recently expanded a recall of its products, the FDA notes.

Alerts over toxic hand sanitizer first appeared in late June, when the FDA identified nine offending products all from one manufacturer in Mexico. In an update earlier this month, the FDA said it had identified five additional brands of methanol-containing sanitizers.

The FDA has sent companies warning letters, pushed for recalls, and placed products on import alerts. For consumers, the agency recommends avoiding *all* products from any of the manufacturers on the list. If you find you have one of those products, stop using it immediately, dispose of it in a hazardous waste container (do not flush it down the drain), seek medical attention promptly if necessary, and report the case to the FDA.

https://bit.ly/3hSRqzj

Put down that cup of earl gray tea!

Antioxidant-rich foods like black tea, chocolate and berries may increase risk for certain cancers, new Hebrew University research finds

It is a fact that has long baffled doctors: Cancer in the small intestine is quite rare, whereas colorectal cancer, a neighboring though much smaller organ, is one of the leading causes of cancer death for men and women. What is it about the colon that seems to "attract" cancer?

To answer this question, Professor Yinon Ben-Neriah at Hebrew University of Jerusalem (HU)'s Lautenberg Center for Immunology and Cancer Research and his team led by Dr. Eliran Kadosh, found that cancer mutations are not necessarily bad actors, in and of themselves. In fact, in certain micro-environments like the gut, these mutations can actually help the body to fight cancer, not spread it. However, if the gut microbiome produces high levels of metabolites, like those found in certain bacteria and antioxidant rich foods like black tea and hot cocoa, then it acts as a particularly hospitable environment to mutated genes and will accelerate the growth of bowel cancers. Their breakthrough findings were published today in *Nature* magazine.

Ben-Neriah and his team kept gut microbiomes in mind as they took a closer look at gastrointestinal cancers, and may have found the reason why only 2% of cancers take root in the small intestine, whereas a whopping 98% of cancers take place in the colon. One major difference between these two organs is their levels of gut bacteria: small intestines contain few, whereas colons contain multitudes. "Scientists are beginning to pay more and more attention to the role gut microbiomes play in our health: both their positive effects and, in this case, their sometimes pernicious role in aiding and abetting disease," explained Ben-Neriah.

A little background. TP53 is a gene found in every cell. It produces a protein called p53 which acts as the cell's barrier, suppressing genetic mutations in the cell. However, when p53 becomes damaged, it no longer protects the cell. Quite the opposite, it drives the cancer, helping tumors spread and grow.

To test their theory that gut flora was at play, the researchers introduced mutated p53 ("cancer-driving") proteins into the gut. Amazingly, the small intestine reacted by converting the mutated p53 cancer driver back to normal p53, turning into "super-suppressors" that were better at suppressing cancer growth than

healthy p53 proteins. However, when mutated p53 was introduced into the colon, they did no switcheroo but stayed true to their driving-cancer nature and promoted the cancerous spread. "We were riveted by what we saw," recalls Ben-Neriah. "The gut bacteria had a Jekyll and Hyde effect on the mutated p53 proteins. In the small bowel they totally switched course and attacked the cancerous cells, whereas in the colon they promoted the cancerous growth."

To further test their theory that gut flora was a major factor as to why mutated p53 were acting as tumor blockers in the small bowel but tumor accelerants in the colon, the scientists administered antibiotics to kill off the colon's gut flora. Once they did, the mutated p53 was not able to go on its cancer spree.

What's in this flora that makes colon cancer spread so quickly? A close analysis identified the culprit: gut flora that produces metabolites, aka "antioxidants", which are found in high concentrations in foods such as black tea, hot chocolate, nuts and berries. Tellingly, when the scientists fed mice an antioxidant-rich diet, their gut flora accelerated p53's cancer-driver mode. This finding is of particular concern to those patients with a family history of colorectal cancer.

"Scientifically speaking, this is new territory. We were astonished to see the extent to which microbiomes affect cancer mutations--in some cases, entirely changing their nature," shared Ben-Neriah. Looking towards the future, those at high-risk of colorectal cancer may want to screen their gut-flora more frequently and think twice about the foods they digest, antioxidant and otherwise.

https://bit.ly/39QXtBC

Alaskan seismometers record the northern lights

It's possible to match the striking display of lights with seismic signals

Aaron Lojewski, who leads aurora sightseeing tours in Alaska, was lucky enough to photograph a "eruption" of brilliant pink light in the night skies one night in February.

The same perturbations of the Earth's magnetic field that lit up the sky for Lojewski's camera were also captured by seismometers on the ground, a team of researchers reports in the journal *Seismological Research Letters*. By comparing data collected by all-sky cameras, magnetometers, and seismometers during three aurora events in 2019, University of Alaska Fairbanks seismologist Carl Tape and colleagues show that it's possible to match the striking display of lights with seismic signals, to observe the same phenomenon in different ways.

Aurora near Poker Flats, Alaska. **Aaron Lojewski, Fairbanks Aurora Tours**

Researchers have known for a while that seismometers are sensitive to magnetic fluctuations--and have worked hard to find ways to shield their instruments against magnetic influence or to remove these unwanted signals from their seismic data. But the aurora study offers an example of how seismometers could be paired with other instruments to study these fluctuations.

"It can be hard to be definitive that these seismometer recordings are originating from the same influence as what's going on 120 kilometers up in the sky," Tape said. "It helps to have a simultaneous view of the sky, to given you more confidence about what you're seeing from the signals at ground level."

The aurora borealis, or northern lights, occurs when solar winds--plasma ejected from the Sun's surface--meet the protective magnetic field that surrounds the Earth. The collision of particles produces colorful lights in the sky and creates fluctuations in the

magnetic field that are sometimes called solar or space "storms." Magnetometers deployed on the Earth's surface are the primary instrument used to detect these fluctuations, which can significantly impact electrical grids, GPS systems and other crucial infrastructure. The aurora is commonly visible in wintertime in high-latitude regions such as Alaska.

The seismometers in the study are part of the USArray Transportable Array, a network of temporary seismometers placed across North America as part of the EarthScope project. The array in Alaska and western Canada was completed in the fall of 2017. The aurora paper is one of several included in an upcoming SRL focus section about EarthScope in Alaska and Canada.

These temporary seismic stations are not shielded from magnetic fields, unlike more permanent stations that are often cloaked in mu-metal, a nickel-iron alloy that directs magnetic fields around the instrument's sensors. As a result, "I was blown away by how well you can record magnetic storms across the array," said U.S. Geological Survey seismologist Adam Ringler, a co-author on the SRL paper.

Last month, Ringler and his colleagues published a paper demonstrating how the array's 200-plus seismometers in Alaska can be used to record space weather, potentially augmenting the 13 magnetometers in operation in the state.

Along with the all-sky camera data, seismic array data can help make sense of the strong variations in the magnetic field that occur in a magnetic east-west direction, adding a second dimension to typical north-south directional studies of the aurora and other magnetic storms, Tape and colleagues suggest.

The researchers noted in their paper that the link between the aurora borealis and magnetic perturbations was first discovered in Sweden in 1741, and that a seismometer in Germany detected an atmosphere-generated magnetic event for the first time during a strong solar storm in 1994.

"People have been making these connections for 250 years," Tape said. "This shows that we can still make discoveries, in this case with seismometers, to understand the aurora."

https://bit.ly/2DpHTRu

The Lancet Infectious Diseases: Study reveals where first cases of COVID-19 outside China may have originated based on case travel histories

Of the first confirmed COVID-19 case in each affected country outside mainland China, almost two thirds had travel links to Italy, China, or Iran

- ***Of the first confirmed COVID-19 case in each affected country outside mainland China, almost two thirds had travel links to Italy, China, or Iran.***
- ***Study suggests 1 in 4 of these first cases originated in Italy, and 1 in 5 in China.***
- ***Many small clusters of household transmission were reported among early cases, but clusters in occupational and community settings tended to be larger--supporting the role of physical distancing to slow the spread of COVID-19.***

Web-based surveillance of the global spread of SARS-CoV-2 (the virus that causes COVID-19) during the first 11 weeks of the outbreak (Dec 31, 2019, to March 10, 2020), reveals that three-quarters (75/99) of affected countries outside mainland China reported their first COVID-19 case in people who had recently travelled to an affected country--with almost two-thirds of these first cases linked to travel to Italy (27%), China (22%), or Iran (11%), according to new research published in *The Lancet Infectious Diseases* journal.

"Our findings suggest that travel from just a few countries with substantial SARS-CoV-2 transmission may have seeded additional

outbreaks around the world before the characterisation of COVID-19 as a pandemic on March 11, 2020", says Dr Fatimah Dawood from the Centers for Disease Control and Prevention (CDC), USA, who co-led the research.

The study is the first of its kind to use publicly available global case data to describe travel exposure and case cluster characteristics among early COVID-19 cases in different countries. However, the authors caution that given almost all cases in the analysis were reported in middle-income and high-income countries from Asia and Europe (due to late detection in other regions), they were unable to draw a complete picture of COVID-19's early global epidemiology.

In this study, researchers examined publicly available online reports from national ministries of health and other government agency websites, social media feeds, and press releases on a daily basis to identify newly confirmed cases of COVID-19 reported between Dec 31, 2019, and March 10, 2020 (ie, during the prepandemic period, corresponding to weeks 1-11 of the outbreak). Countries with at least one case were classified as affected. Early cases were defined as the first 100 cases reported in each country, and later cases as those after the first 100 cases. The researchers analysed travel history for the first case reported in each country outside mainland China, case characteristics (eg, age, sex, exposure), and cluster frequencies and sizes.

During the first 11 weeks of the COVID-19 outbreak, 32,459 COVID-19 cases were identified from 99 countries and locations outside mainland China (figure 1).

The analysis found that travel history of the first reported case in each affected country varied by world region (figure 3 and infographic). Travel to Italy was linked with half (3/6 cases) of the first-reported cases in Africa, and over a third (36%, 16/45) in Europe and the Americas (38%, 5/13). Travel to mainland China accounted for 83% (10/12) of the first-reported cases in the Western Pacific and over half (57%, 4/7) in Southeast Asia. Seven (44%) first-reported cases in the Eastern Mediterranean region had a history of travel to Iran.

Among 1,200 cases from 68 countries with age or sex information available [2], 874 (73%) were early cases, with an average age of 51 years. Just 3% of cases (25/762 with age information available) occurred in children younger than 18 years. In total, 2% (21/1,200) of early cases occurred in health-care workers.

During the prepandemic period, 101 clusters involving 386 cases were identified in 29 countries (table 3). Household transmission was reported in three-quarters (76/101) of clusters, with an average of 2.6 cases in each cluster. By contrast, the 11 clusters related to community gatherings (ie, tour groups, faith-based groups, and dinner parties; average 14.2 cases per cluster), and the 14 clusters reported in non-health-care occupational settings (average 4.3 cases per cluster), tended to be larger--supporting a possible role for physical distancing in slowing the spread of COVID-19, researchers say.

"Four large clusters in our analysis, and large outbreaks reported elsewhere, have been linked with transmission in faith-based settings, highlighting the need to partner with faith-based organisations when designing and implementing community mitigation efforts", says co-author Dr Philip Ricks from the US CDC. "Six healthcare-associated clusters were also identified, underscoring the need for strict infection prevention and control practices and monitoring health-care workers for signs of illness." [1]

The analysis also highlights the relatively late detection of COVID-19 in Africa, with only 6 out of 46 (13%) countries studied in the region reporting cases by the time WHO characterised the outbreak a pandemic on March 11, 2020. This compares with a third (13/35)

of countries in the Americas and the majority of countries in Europe (45/54, 83%), Eastern Mediterranean (16/23, 70%), and Southeast Asia (7/11, 64%).

"The epidemiology of COVID-19 in low-income countries and in Africa could differ, as reported in previous influenza pandemics, and accurate data from these settings will be needed to assess the full global effect of the COVID-19 pandemic", says Dawood. [1]

The authors note some important limitations of their study, including that the analysis of case characteristics was limited to only 4% (1,200/32,459) of global confirmed cases that had sufficient information about a case's age or sex; and publicly available data varied in completeness, which could have resulted in some case characteristics going undetected. They also note that the first confirmed case in each country might not have been the first true case of infection in some countries, since early case detection efforts varied substantially.

NOTES TO EDITORS

The study received no funding. It was conducted by researchers from Centers for Disease Control and Prevention (CDC), USA.

The labels have been added to this press release as part of a project run by the Academy of Medical Sciences seeking to improve the communication of evidence. For more information, please see: http://www.sciencemediacentre.org/wp-content/uploads/2018/01/AMS-press-release-labelling-system-GUIDANCE.pdf if you have any questions or feedback, please contact The Lancet press office pressoffice@lancet.com

[1] Quotes direct from authors and cannot be found in text of Article.

[2] The 68 countries and locations with cases with information on age and sex were Algeria, Andorra, Argentina, Australia, Austria, Azerbaijan, Bahrain, Bhutan, Brazil, Bulgaria, Cambodia, Cameroon, Canada, Chile, Croatia, Czech Republic, Denmark, Dominican Republic, Egypt, Estonia, Finland, France, Georgia, Germany, Greece, Hong Kong, Iceland, India, Indonesia, Iraq, Ireland, Israel, Italy, Japan, Kuwait, Lebanon, Lithuania, Macau, Malaysia, Mexico, Moldova, Morocco, Nepal, Netherlands, New Zealand, Oman, Peru, Philippines, Poland, Portugal, Romania, San Marino, Senegal, Serbia, Singapore, South Africa, South Korea, Spain, Sri Lanka, Sweden, Switzerland, Taiwan, Thailand, Togo, Tunisia, Ukraine, United Arab Emirates, and Vietnam.

The 31 countries and locations with cases for which no case had information about age or sex were Afghanistan, Armenia, Belarus, Belgium, Bosnia and Herzegovina, Colombia, Costa Rica, Ecuador, Hungary, Iran, Jordan, Latvia, Liechtenstein, Luxembourg, Maldives, Malta, Monaco, Nigeria, North Macedonia, Norway, Pakistan, Palestine, Panama, Paraguay, Qatar, Russia, Saudi Arabia, Slovakia, Slovenia, the UK, and the USA.

Peer-reviewed / Observational study / People

https://bit.ly/30imbrE

'Good' virus for common infection

Antibiotic-resistant diabetic foot ulcer application

Australian researchers have shown how viruses can be used to save lives, developing the potential use of bacteriophages in bandages to treat life-threatening golden staph infections which may not respond to traditional antibiotics.

Targeting multidrug-resistant Staphylococcus aureus ('golden staph') in diabetic foot ulcers, Flinders University microbiology researchers have joined infectious diseases and pharmaceutical partners to show the usefulness of a possible 'phage cocktail' therapy on wound infections.

A phage (or bacteriophage) is a virus capable of infecting a bacterial cell and is capable of being used in a range of medical applications including as a therapy against 'superbugs'.

Bacteriophages (phages, viruses that infect bacteria) represent an alternative or adjunct therapy to antibiotics, with S aureus a common and particularly virulent pathogen often found to be resistant and limited for antimicrobial treatment options.

"Diabetic foot ulcers are very dangerous and when infected can lead to amputation and even death," says Flinders University Associate Professor Peter Speck, who is Secretary of the Australasian Virology Society.

"The next step in our research is to bind phages to a dressing to make a truly antibacterial dressing, with specific activity against golden staph. The technology exists to make such a dressing, with a big advantage being that bound phages remain viable for a year even when stored at room temperature, making this approach ideal for use in hospitals and clinics - even in rural and remote settings."

Co-author on a new paper in *BMC Microbiology*, Flinders PhD Legesse Garedew Kifelew says the results of the sound treatment in mice were very promising.

"This study demonstrates that phage therapy could be a potential alternative in combating antibiotic-resisant bacterial infections," says Mr Kifelew, who works in infectious disease management at the Queen Elizabeth Hospital and has ties to St Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia.

"The phages effectively decreased the bacterial load and significantly improved wound healing in in multi-drug resistant S aureus infection - similar or superior to the currently prescribed antibiotic treatment," he says.

With diabetes on the rise, the global burden of diabetic foot ulcers (DFUs) is also affecting up to 26.1 million people each year, with these ulcers the cause of almost 90% of limb amputations. The five-year mortality rate following foot amputation due to DFUs has been estimated at up to 74%.

Based on 2015 prevalence data from the International Diabetes Federation, it is estimated that foot ulcers develop in 9.1 million to 26.1 million people with diabetes annually worldwide.

In the US, the annual cost of managing DFU infections is estimated at an additional US$9-13 billion over the cost of diabetes itself. In England, it is estimated that the annual cost of managing DFUs exceeds the total cost of breast, prostate and lung cancers combined.

The paper, 'Efficacy of phage cocktail AB-SA01 therapy in diabetic mouse wound infections caused by multidrug-resistant Staphylococcus aureus' (2020) by LG Kifelew, MS Warner, S Morales, L Vaughan, R Woodman, R Fitridge, JG Mitchell and P Speck has been published in BMC Microbiology (Springer Nature).

https://bit.ly/2Pmho23

Headline news: Botox injections may lessen depression

FDA database of drug side effects indicates the benefit may hold up no matter where Botox is injected

Botox, a medication derived from a bacterial toxin, is commonly injected to ease wrinkles, migraines, muscle spasms, excessive sweating and incontinence. Forehead injection of the medication is also currently being tested in clinical trials for its ability to treat depression.

Researchers at Skaggs School of Pharmacy and Pharmaceutical Sciences at University of California San Diego have mined the U.S. Food and Drug Administration (FDA)'s Adverse Effect Reporting System (FAERS) database to see what nearly 40,000 people reported happened to them after treatment with Botox for a variety of reasons.

In the study, published July 30, 2020 in *Scientific Reports*, the team discovered that people who received Botox injections -- at six different sites, not just in the forehead -- reported depression significantly less often than patients undergoing different treatments for the same conditions.

"For years, clinicians have observed that Botox injected for cosmetic reasons seems to ease depression for their patients," said Ruben Abagyan, PhD, professor of pharmacy. "It's been thought that easing severe frown lines in forehead region disrupts a feedback loop that reinforces negative emotions. But we've found here that the mechanism may be more complex, because it doesn't really matter where the Botox is injected."

Abagyan led the study with Tigran Makunts, PharmD, who was a pharmacy student at the time and is now a research fellow at the FDA, and Marc Axel Wollmer, MD, a psychiatrist and researcher in Germany who has led past clinical studies in which Botox was found to alleviate depression.

The FAERS database contains more than 13 million voluntary reports of adverse effects people experienced while taking a medication. Abagyan and team have found they can also use the database to look at *absence* of a health complaint when a person takes a medication, if compared to a control group. In this case, they searched for the absence of depression.

The team focused on nearly 40,000 FAERS reports of people experiencing adverse events after Botox treatment. The reports cover Botox treatment for eight different reasons and injection sites, including forehead, neck, limbs and bladder. Then the team applied a mathematical algorithm to look for statistically significant differences between Botox users and patients who received different treatments for the same conditions.

Here's what they found: Depression was reported 40 to 88 percent less often by Botox-treated patients for six of the eight conditions and injection sites.

"This finding is exciting because it supports a new treatment to affect mood and fight depression, one of the common and dangerous mental illnesses -- and it's based on a very large body of statistical data, rather than limited-scale observations," Makunts said.

To be clear, the data used in this study was not collected for the purpose of exploring the association between Botox use and depression exclusively. In addition, the FAERS data represents only the subset of Botox users who experienced negative side effects. While the team excluded reports in which a person was also taking antidepressants, the use of other prescription and over-the-counter medications could have been underreported in some cases.

The clinical trial underway are directly testing Botox treatment for people with depression, a gold standard approach for gathering insights on the relationship between a medication and a health condition. Since that trial is only testing forehead injection of Botox, Abagyan says additional clinical trials may be necessary to work out the best site and dose to administer the medication specifically for the treatment of depression.

Likewise, more research is needed to determine the mechanism by which Botox acts as an antidepressant, Abagyan says. He and collaborators hypothesize a few possibilities worth investigating: Botox could be transported to the regions of the central nervous systems involved in mood and emotions. Or, since Botox is commonly used to treat chronic conditions that may contribute to depression, its success in relieving the underlying problem may indirectly also relieve depression.

The World Health Organization estimates that more than 264 million worldwide experience depression. Depression is frequently treated with psychotherapy, selective serotonin reuptake inhibitors, dopamine-norepinephrine reuptake inhibitors and/or serotonin-norepinephrine reuptake inhibitors. Yet these approaches are ineffective for nearly one-third of patients. That's why clinicians and researchers are exploring other therapeutic options, including electroconvulsive therapy, transcranial magnetic stimulation, ketamine infusions and, more recently, Botox forehead injections.

Disclosure: Ruben Abagyan is co-founder of Molsoft, LLC and has equity. M. Axel Wollmer has consulted for Allergan pharmaceuticals.

https://bit.ly/3k7rsdr

Could we go on the offensive against emerging diseases?

The COVID-19 pandemic highlights how reacting to diseases may not be good enough.

John Timmer

Viruses like Ebola and the original SARS have highlighted the risks that emerging diseases pose to our modern, highly connected society. While the standard approach of isolating the infected and limiting the spread of the disease worked in those cases, it works slowly enough to make many people nervous. But the global spread of Zika and SARS-CoV-2 shows that these approaches have their limits, leaving us at risk.

Is there anything else we could do? A perspective by Scott Nuismer and James Bull of the University of Idaho suggests we now have the tools to go on the offensive against viruses before they transfer

to humans. The proposal: treat animal hosts of threatening viruses with virus-based vaccines that can spread through wild populations. While there are a lot of details to work out here, the article lays out how we might determine if this could be a viable approach.

Threats and their hosts

There are a huge number of hosts that share virus with our species. These range from familiar threats, like the mammals that carry the rabies virus, to our agricultural species that have spanned flu pandemics, as well as newly emerging dangers, such as hantaviruses and coronaviruses, carried by mice and a variety of species, respectively. While there's no real pattern to the species that transfer viruses to humans, there have been successful efforts to identify the hosts from which viruses originated. Nuismer and Bull highlight the PREDICT program, run by the US Agency for International Development, which identified nearly 1,000 previously uncharacterized viruses before the Trump administration terminated it in March.

Figuring out which of those viruses might pose a threat is not a simple matter. But for the time being, there are a large collection of viruses that we *know* circulate in animals and are a threat to humans, so there's no shortage of potential targets. If we actually get a preemptive approach to work with them, we can start worrying about potential threats.

So how do you stop a virus that's not even infecting us yet? The basic idea is simple: develop a vaccine and give it to the animals that carry the virus. The obvious challenge to this approach is delivering the vaccine to a wild animal population. Not only are these populations often widely dispersed and difficult to access, but many of the animals (such as mice, in the case of hantavirus) have pretty short lifespans.

The solution that Nuismer and Bull consider is to use a virus as the vaccine—specifically, a virus that can spread beyond the population given the initial dose. In other words, the vaccine will make copies of itself and ensure that the unvaccinated population has a chance to receive a dose. This basic idea has been explored using epidemiological models, and it would likely work, but it's only received a single, limited test in an animal population so far.

Options and risks

The epidemiological models indicate that this spread can be fine-tuned based on the infectivity of the virus being used as a vaccine. With a high-enough infectivity, the vaccine should spread throughout any populations of hosts that aren't sufficiently isolated. A weaker virus with a lower infectivity might spread once or twice after the initial inoculation before fizzling out. Depending on how well we know and can manipulate the virus being used as the vaccine, it might be possible to tune its properties to match the size and distribution of a population, as well as the ease with which we can deliver additional doses.

There are two options for doing this. The first would involve starting with the virus that we're trying to vaccinate against and generating a weakened form, often termed "attenuated." This approach has been used for some human vaccines. Unfortunately, there have been a number of instances where a weakened virus has re-evolved virulence while circulating in a population. If this were to happen with a virus that poses a threat to humans, it would be possible for our vaccination efforts to inadvertently expand the pool of animals that could transfer it to us. For that reason, Nuismer and Bull don't consider this a viable option.

Two for one

The alternative is to do one of the things that is being tried with SARS-CoV-2: engineer a gene that encodes a protein from the virus being targeted into an innocuous virus that can spread through the population. Ideally, as the harmless virus infects new animals, the immune response they generate will target both the virus's proteins

and the one engineered into it, thus providing immunity to two viruses.

Engineering a different virus's gene into a virus is the least challenging aspect of this approach. It's completely dependent upon our ability to find or generate harmless viruses that infect the target species. If we do use a naturally occurring virus, then we run the risk of the targeted population having a pre-existing immunity to it. We may need to spend time tuning its infectivity to match our needs as well. And finally, after all that's done, there's a chance that the protein, which is superfluous to the virus, will end up being lost. Of course, if we plan on reintroducing the vaccine regularly, then the loss of the protein won't be a major factor. But for something like Ebola, where new outbreaks seem to originate in remote areas, this may be more of a challenge.

In the end, the authors recommend a set of basic guidelines: use something that is based on a harmless virus, make sure it's species-specific, and make sure that it's engineered to limit its spread once it's put in a wild population.

What to try first

So far, the authors indicate that this method has been tried a grand total of once. A rabbit virus that had naturally evolved into a harmless form was engineered to carry the gene for a protein that would confer immunity to a more dangerous virus that also targeted rabbits. A group of rabbits were inoculated with this virus before being set loose on a small island. After some time to allow the virus to spread, a bunch of other rabbits were tested, and about half of them were found to have been infected. This suggests that the infectivity was high enough that the rabbit population could eventually hit herd immunity from a single release.

Nuismer and Bull think that's a good model for testing the approach using a virus that targets humans. They suggest something like rabies, which has been intensely studied and has a number of known hosts. Again, they think that an island population is a good choice, as it will allow a detailed tracing of the vaccine's spread through the animals. If that works out, we can start considering the method's use in more widely dispersed populations.

So does it make sense to take the offensive and start a pre-emptive vaccination program in animals against viruses that might be a threat to us? The approach recommended here, which involves identifying harmless, species-specific viruses and then engineering them to be vaccines for a dangerous one, involves a significant amount of work. Safety testing in a controlled environment—with involuntary participants like bats—will add considerably to the effort involved. At some point, it's going to become similar to the effort of designing a human vaccine instead.

But...

For something that poses a regular health risk, like rabies, all this effort may be worthwhile. But to just take a currently relevant example, there are a large collection of coronaviruses in bats alone—along with a very large collection of bat species—and bats aren't the only species that has been the source of a coronavirus that's gone on to infect humans. Most of these are probably harmless, and extensive work will be needed to determine which might pose a threat to us. Can we really expect to protect ourselves from everything relevant there?

It's an intriguing idea, and once we have a better grip on the threats posed by emerging viruses, the method may prove to be a useful way of neutralizing them. For now, while we've certainly got the technology to do it, the number of targets that it makes sense to go after is small enough that this doesn't seem likely to be widely useful.

Nature Ecology and Evolution, 2020. DOI: 10.1038/s41559-020-1254-y (About DOIs).

https://wb.md/3i7apGB

P-tau217 Differentiates AD vs Other Neurodegenerative Conditions

A blood test that measures plasma tau phosphorylated at threonine 217 (P-tau217) can accurately distinguish Alzheimer's disease (AD) from other neurodegenerative disorders, new research suggests.

Megan Brooks

Results from a large multinational study showed that the level of P-tau217 in blood collected during life was an accurate predictor of tau brain changes seen in brain tissue after death.

In addition, increasing blood P-tau217 levels can be detected in some individuals up to 20 years before the average age of onset of the early cognitive decline that signals AD, researchers report.

"While there is still more work to be done, this biomarker has the potential to have a transformational impact on research, treatment, prevention, and therapy development, and in the clinical setting," senior author Eric Reiman, MD, executive director of Banner Alzheimer's Institute in Phoenix, Arizona, told *Medscape Medical News*.

The findings were presented at the Alzheimer's Association International Conference (AAIC) 2020, which was held online this year because of the COVID-19 pandemic, and simultaneously published online July 28 in *JAMA*.

Three Cohorts

The international team of researchers evaluated the P-tau217 blood test in 1402 adults from three cohorts.

The first cohort was comprised of 81 individuals in the Arizona (Banner Sun Health Research Institute) Brain Donation program and included clinical, blood, and neuropathological data.

The second cohort included 699 individuals in the Swedish BioFINDER-2 study and provided clinical, brain imaging, CSF, and blood data.

The third cohort was made up of 522 participants from the Columbian autosomal-dominant AD kindred, including 365 *PSEN1 E280A* mutation carriers and 257 mutation noncarriers.

In the Arizona cohort, plasma P-tau217 discriminated neuropathologically defined AD from non-AD (AUC, 0.89; 95% CI, 0.81 - 0.97) with significantly higher accuracy than plasma P-tau181 and neurofilament light chain (NfL) (AUC range, 0.50-0.72; $P < .05$).

In the Swedish BioFINDER-2 cohort, the discriminative accuracy of plasma P-tau217 for clinical AD dementia versus other neurodegenerative diseases was 96% (AUC, 0.96; 95% CI, 0.93 - 0.98).

This was significantly higher than plasma P-tau181, plasma NfL, and MRI measures (AUC range, 0.50-0.81; $P < .001$), but was not significantly different than CSF P-tau217, CSF P-tau181, and tau-PET (AUC range, 0.90-0.99; $P > .15$).

In the Colombian cohort, plasma P-tau217 levels were significantly greater among *PSEN1* mutation carriers than noncarriers starting at around age 25 years, which is 20 years prior to the estimated onset of mild cognitive impairment among mutation carriers.

Additionally, plasma P-tau217 levels correlated with cerebral tau tangles, and discriminated abnormal versus normal tau-PET scans with significantly higher accuracy than plasma P-tau181, plasma NfL, CSF P-tau181, CSF Aβ42:Aβ40 ratio, and MRI measures.

The blood test "opens the possibility of early diagnosis of Alzheimer's before the dementia stage, which is very important for clinical trials evaluating novel therapies that might stop or slow down the disease process," presenting author Oskar Hansson, MD, PhD, Lund University, Sweden, said in a statement.

Further research is now needed to optimize the P-tau217 blood test, validate the findings in unselected and diverse populations, and determine its potential role in the clinic, the investigators note.

Game Changer?

Commenting on the study for *Medscape Medical News*, Howard Fillit, MD, founding executive director and chief science officer of the Alzheimer's Drug Discovery Foundation, noted his enthusiasm for the test.

"This tau blood test will be a real game changer, advancing clinical care and research," said Fillit, who was not involved in the research. "This is a real breakthrough: a simple and accessible blood test that can diagnose Alzheimer's better than the more costly and invasive methods currently available like PET scans and cerebrospinal fluid biomarkers," he said.

The P-tau217 blood test "is like the equivalent of the cholesterol

Because it's a composite time-lapse photo, the image doesn't show what you would see with the naked eye. But it illustrates why many astronomers worry about the threat that satellite constellations like Starlink pose to ground-based astronomy.

Too many satellites could mess with astronomy on Earth

Long-exposure images are a crucial part of studying distant objects in the night sky. Telescopes on Earth watch celestial targets for hours, slowly building up a detailed image that offers astronomers rich data.

But one poorly timed Starlink satellite can ruin that kind of research by creating a long streak across the image and blocking the objects that astronomers want to study.

"In that couple of seconds, a whole 10- or 15-minute exposure is ruined," the astronomer Jonathan McDowell told Business Insider in June.

SpaceX is sharing Starlink's orbital-path data with astronomers so that they can plan their telescope observations around the satellites' movements. Briefly shutting off the camera as the satellite passes overhead can save a long-exposure image.

But Musk's ambitions could make it nearly impossible to avoid the fast-moving satellites. SpaceX has sought government permission to put a total of 42,000 satellites into orbit to form a "megaconstellation" around Earth.

"If they're coming over all the time, then knowing when they're coming over isn't helpful," McDowell said. Even now, he added, sometimes astronomers can't avoid the photobombers.

SpaceX isn't the only company building a massive fleet of satellites. Companies like OneWeb and Amazon have similar ambitions.

"The sky will not be what it has been for millions of years. Thousands of dots will appear and disappear in the night sky," López told Gizmodo. "I personally think that if no action is taken, it will be the end of astronomy as we know it from the surface of the Earth."

Professional astronomers have given similarly dire warnings.

"The night sky is for everybody. It has been scrutinised and used for millennia," Girard said. "We should cherish it and protect it just like our Earth."

test for heart disease, but for Alzheimer's disease," Fillit added.

As reported by *Medscape Medical News,* another study presented at AAIC 2020 compared P-tau217 with P-tau181 to determine which could best identify individuals with AD.

Results showed that although the two biomarkers were similar overall, P-tau217 had a slight edge in terms of accuracy.

The study was funded by the Swedish Research Council, the Knut and Alice Wallenberg Foundation, and the Swedish Alzheimer Foundation. Hansson has reported receiving grants from Roche, Biogen, and Pfizer, and receiving nonfinancial support from GE Healthcare, AVID Radiopharmaceuticals, and Euroimmun. Reiman has received grants from Roche/Roche Diagnostics and received personal fees from Alkahest, Alzheon, Aural Analytics, Denali, Green Valley, MagQ, Takeda/Zinfandel, and United Neuroscience. He is also a cofounder of AlzPath, which aims to further develop P-tau217 and fluid biomarkers; holds a patent owned by Banner Health for a strategy to use biomarkers to

accelerate evaluation of Alzheimer prevention therapies; and is a principal investigator of prevention trials that include research agreements with Genentech/Roche and Novartis/Amgen, PET studies that include research agreements with Avid/Lilly, and several National Institue of Health and Foundation-supported research studies. Fillit has reported no relevant financial relationships.

Alzheimer's Association International Conference (AAIC) 2020. Presented July 28, 2020.

JAMA. Published July 28, 2020. Full text

https://bit.ly/2D8sAwV

Yep, Starlink Totally Photobombed a Beautiful Image of Comet Neowise

Elon Musk's growing constellation of internet satellites has been sending streaks of bright light across night skies around the world.

Morgan Mc-Fall Johnsen, Business Insider

Even the biggest comet to pass Earth in 25 years wasn't spared.

A striking photo showing Comet Neowise behind those streaks of light shows how easily the satellites can upstage observations of distant objects in space.

The satellite project, called Starlink, is Musk's plan to blanket Earth in high-speed satellite internet. The effort has drawn criticism from professional and amateur astronomers, however, because the bright satellites can mar the skies and disrupt telescope observations.

Trail of Starlink satellites in front of Comet Neowise. **(Daniel Lopez)**

That's what happened to the astrophotographer Daniel López on July 21, when he was shooting Comet Neowise before it flies out of view for another 6,800 years. He shared the resulting image on the Facebook page of his photography company, El Cielo de Canarias, saying it was a shame to see the satellites make such a spectacle.

López's photo is a composite of 17 images taken in the span of 30 seconds. Each image was long exposure, meaning it captured the comet over several seconds.

The astronomer Julien Girard shared the picture on Twitter, saying the satellites had "completely photobombed" the comet.

"Two of my pictures the other night were also bombed by a Starlink," Girard said.

López also shared the time-lapse video behind the picture. He added that traces of the satellites were visible in 20 of his images.

Because it's a composite time-lapse photo, the image doesn't show what you would see with the naked eye. But it illustrates why many astronomers worry about the threat that satellite constellations like Starlink pose to ground-based astronomy.

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https://wb.md/30oNEI9

Time to Stop Pressuring Women on Screening Mammography?

Studies from several countries have questioned the value of screening mammograms.

Andrew M. Kaunitz, MD

This transcript has been edited for clarity.

Although recommending screening mammograms continues to represent standard of care, studies from the United States and other countries, including the Netherlands and Norway, have questioned their value.

In the June issue of JAMA Network Open, Australian investigators assessed the relative impacts of screening and adjuvant therapy on breast cancer mortality, using data from 1986 through 2013. In recent decades, screening has increased substantially among Australian women. For cancer screening to be effective, the number of early-stage tumors diagnosed should increase while the incidence of advanced tumors should decrease.

The investigators identified some 75,000 women with invasive breast cancer in the state of Victoria, where women aged 50-69 are offered biennial screening. During this time period, the use of adjuvant tamoxifen and chemotherapy increased substantially, and breast cancer mortality declined considerably. However, during this same time period, the incidence of advanced breast cancer doubled.

These findings parallel those from the United States and Europe, which paradoxically found that the incidence of advanced breast cancer was stable or increased after screening mammography was introduced.

The Australian authors assert that the increased incidence of advanced cancer means that screening mammography is not responsible for declining breast cancer mortality, and that all of the decline can be attributed to greater use of adjuvant therapy. In their conclusion, they state that because screening mammography does not reduce breast cancer mortality, state-sponsored screenings should be discontinued.

Although some will view the findings and recommendations of these Australian authors with skepticism or even hostility, I view their findings as good news. We have improved the treatment of breast cancer so dramatically that it has become difficult to identify the benefits of finding early tumors with screening.

Although it is challenging, given the time constraints of office visits, I try to engage in shared decision-making with my patients regarding when to start, how often to have, and when to stop screening mammography.

Given our evolving understanding regarding the value of screening, it is time to stop pressuring patients who are reluctant or unwilling to undergo screening. Likewise, insurance companies and government agencies should stop using screening mammography as a quality metric.

Thank you for the honor of your time. I am Andrew Kaunitz.

https://nyti.ms/33q4IPS

Aboard the Diamond Princess, a Case Study in Aerosol Transmission

A computer model of the cruise-ship outbreak found that the virus spread most readily in microscopic droplets light enough to linger in the air.

By Benedict Carey and James Glanz

In a year of endless viral outbreaks, the details of the Diamond Princess tragedy seem like ancient history. On Jan. 20, one infected passenger boarded the cruise ship; a month later, more than 700 of the 3,711 passengers and crew members had tested positive, with many falling seriously ill. The invader moved as swiftly and invisibly as the perpetrators on Agatha Christie's Orient Express, leaving doctors and health officials with only fragmentary evidence to sift through.

Ever since, scientists have tried to pin down exactly how the coronavirus spread throughout the ship. And for good reason: The Diamond Princess' outbreak remains perhaps the most valuable case study available of coronavirus transmission — an experiment-in-a-bottle, rich in data, as well as a dark warning for what was to come in much of the world.

The Diamond Princess cruise ship, docked in Yokohama, Japan, in February. More than 700 of the 3,711 people onboard tested positive for the coronavirus. **Behrouz Mehri/Agence France-Presse — Getty Images**

Now, researchers are beginning to use macroscopic tools — computer models, which have revealed patterns in the virus's global spread — to clarify the much smaller-scale questions that currently dominate public discussions of safety: How, exactly, does the virus move through a community, a building or a small group of people? Which modes of transmission should concern us most, and how might we stop them?

In a new report, a research team based at Harvard and the Illinois Institute of Technology has tried to tease out the ways in which the virus passed from person to person in the staterooms, corridors and common areas of the Diamond Princess. It found that the virus spread most readily in microscopic droplets that were light enough to float in the air, for several minutes or much longer.

The new findings add to an escalating debate among doctors, scientists and health officials about the primary routes of coronavirus transmission. Earlier this month, after pressure from more than 200 scientists, the World Health Organization acknowledged that the virus could linger in the air indoors, potentially causing new infections. Previously, it had emphasized only large droplets, as from coughing, and infected surfaces as the primary drivers of transmission. Many clinicians and epidemiologists continue to argue that these routes are central to disease progression.

The new paper has been posted on a preprint server and submitted to a journal; it has not yet been peer-reviewed, but it was shown by Times reporters to nearly a dozen experts in aerosols and infectious disease. The new findings, if confirmed, would have major implications for making indoor spaces safer and choosing among a panoply of personal protective gear.

For example, ventilation systems that "turn over" or replace the air in a room or building as often as possible, preferably drawing on external air to do so, should make indoor spaces healthier. But good ventilation is not enough; the Diamond Princess was well ventilated and the air did not recirculate, the researchers noted. So wearing good-quality masks — standard surgical masks, or cloth masks with multiple layers rather than just one — will most likely be needed as

well, even in well-ventilated spaces where people are keeping their distance.

The computer modeling adds a new dimension of support to an accumulating body of evidence implicating small, airborne droplets in multiple outbreaks, including at a Chinese restaurant, a choir in Washington State, as well as a recent study at a Nebraska hospital to which 13 passengers from the Diamond Princess had been evacuated.

One researcher not involved in the new work, Julian Tang, an honorary associate professor of respiratory sciences at the University of Leicester in the United Kingdom, said the paper was "the first attempt, as far as I know, to formally compare the different routes of coronavirus transmission, especially of short versus long-range aerosols."

He characterized the distances and the kinds of particles involved with a simple analogy from everyday life: "If you can smell what I had for lunch, you're getting my air, and you can be getting virus particles as well."

Another researcher, Linsey Marr, a professor of civil and environmental engineering at Virginia Tech who studies airborne transmission of viruses, had a more vivid description of the finding: the "garlic breath" effect.

"As you're close to someone, you smell that garlic breath," Dr. Marr said. "As you're farther away, you don't smell it."

The "garlic breath" effect would suggest that powerful ventilation in buildings — primarily using outside air, or very well filtered — could reduce the transmission of the virus. The study found that small particles also had some ability to spread it at longer distances, presumably beyond the range of breath odor.

From the start of the pandemic, scientists have grappled with the mechanisms of coronavirus spread. Early on, surface transmission was widely emphasized; larger droplets, which travel on more ballistic trajectories, like a stone through the air, and strike mucus membranes directly, are now favored by a number of researchers.

Other possibilities are candidates as well, said Dr. John Conly, an infectious disease physician and infection control expert with the University of Calgary in Canada who has done consulting with the World Health Organization.

"We're getting surprises all the way along," Dr. Conly said. "This paper I find interesting, but it has a long way to go to be able to get into a line of credibility, in my mind."

Dr. George Rutherford, a professor of epidemiology at the University of California, San Francisco, was equally skeptical. He said that, outside of hospital settings, "large droplets in my mind account for the vast majority of cases. Aerosols transmission — if you really run with that, it creates lots of dissonance. Are there situations where it could occur? Yeah maybe, but it's a tiny amount."

Dr. Tang and other scientists strongly disagree. "If I'm talking to an infectious person for 15 or 20 minutes and inhaling some of their air," Dr. Tang said, "isn't that a much simpler way to explain transmission than touching an infected surface and touching your eyes? When you're talking about an outbreak, like at a restaurant, that latter seems like a torturous way to explain transmission."

In the new analysis, a team led by Parham Azimi, an indoor-air researcher at Harvard's T.H. Chan School of Public Health, studied the outbreak on the Diamond Princess, where physical spaces and infections were well documented. It ran more than 20,000 simulations of how the virus might have spread throughout the ship. Each simulation made a variety of assumptions, about factors like patterns of social interaction — how much time people spent in their cabins, on deck or in the cafeteria, on average — and the amount of time the virus can live on surfaces. Each also factored in varying contributions of smaller, floating droplets, broadly defined

as 10 microns or smaller; and larger droplets, which fall more quickly and infect surfaces or other people, by landing on their eyes, mouth or nose, say.

About 130 of those simulations reproduced, to some extent, what actually happened on the Diamond Princess as the outbreak progressed. By analyzing these most "realistic" scenarios, the research team calculated the most likely contributions of each route of transmission. The researchers concluded that the smaller droplets predominated, and accounted for about 60 percent of new infections over all, both at close range, within a few yards of an infectious person, and at greater distances.

"Many people have argued that airborne transmission is happening, but no one had numbers for it," Dr. Azimi said. "What is the contribution from these small droplets — is it 5 percent, or 90 percent? In this paper, we provide the first real estimates for what that number could be, at least in the case of this cruise ship."

The logic behind such transmission is straightforward, experts said. When a person is speaking, he or she emits a cloud of droplets, the vast majority of which are small enough to remain suspended in the air for a few minutes or longer. Through inhalation, that cloud of small droplets is more likely to reach a mucus membrane than larger ones soaring ballistically.

The smaller droplets are also more likely to penetrate deeply into the respiratory system, down to the lungs. It may take a much smaller viral load — fewer viruses — to cause infection in the lungs than higher up, such as in the throat. This, at least, is the case for other respiratory viruses, like the flu.

Brent Stephens, an engineering professor at the Illinois Institute of Technology in Chicago and a co-author on the paper, said the findings were important in shaping, for example, measures that should be taken as college students return to campus.

The first, he said, should be "really enforcing mask policies." Another, he said, is to recognize that there is a "huge variability in mask quality," and material that actually stops small aerosols when someone is breathing, speaking, coughing or sneezing is crucial. Surgical masks are good, he said, but single-ply fabrics often are not.

As various transmission routes come into clearer focus, they will provide specific guidelines on how to reopen schools, offices, restaurants and other businesses.

"The value of this model is that it allows for recommendations and guidance to be specific to each unique environment," said another co-author, Joseph G. Allen, an expert in indoor air quality and an assistant professor at Harvard's T.H. Chan School of Public Health. Dr. Allen said those environments ranged from restaurants to dentist offices. In each case, he said, there are low-cost solutions that sharply improve ventilation and filtration — most buildings fall well short of optimal levels — and in turn reduce the risks of airborne infection.

"To me, this is an all-in moment," Dr. Allen said. "We need better ventilation and better filtration, across the board, in all our buildings."

https://bit.ly/3ftzr0M

Do Animals Really Anticipate Earthquakes? Sensors Hint They Do

Cows, sheep and dogs increased their activity before tremors, seemingly reacting, in part, to one another

By Nancy Averett

Despite freezing temperatures, scores of snakes slithered out of their hibernation dens in the weeks before a magnitude 7.3 earthquake struck the Chinese city of Haicheng on February 4, 1975. The reptiles' behavior, along with other incidents, helped

persuade authorities to evacuate the city hours before the massive quake.

For centuries, people have described unusual animal behavior just ahead of seismic events: dogs barking incessantly, cows halting their milk, toads leaping from ponds. A few researchers have tried to substantiate a link.

In a 2013 study, Germany scientists videotaped red wood ants that nested along a fault line and found they changed their usual routine before a quake, becoming more active at night and less active during the day. But most such attempts have relied largely on anecdotal evidence and single observations, according to a 2018 *Bulletin of the Seismological Society of America* review that examined 180 previous studies.

***Sensors were attached to cows and other farm animals to monitor their activity prior to earthquakes.* Credit: Max Planck Institute of Animal Behavior**

Now researchers at the Max Planck Institute of Animal Behavior and the University of Konstanz, both in Germany, along with a multinational team of colleagues, say they have managed to precisely measure increased activity in a group of farm animals prior to seismic activity. Though a definitive link has still not been proved, the scientists say their findings are a significant step forward in the search for one. “There are the old tales from Aristotle and Alexander von Humboldt, who saw this behavior,” says study co-author Martin Wikelski, managing director of the Max Planck Institute of Animal Behavior. “But only now can we do continuous biologging of the activities and the nervousness of animals. The technical possibilities are finally there.”

The researchers used highly sensitive instruments that record accelerated movements—up to 48 each second—in any direction. During separate periods totaling about four months in 2016 and 2017, they attached these biologgers and GPS sensors to six cows, five sheep and two dogs living on a farm in an earthquake-prone area of northern Italy. A total of more than 18,000 tremors occurred during the study periods, with more seismic activity during the first one—when a magnitude 6.6 quake and its aftershocks struck the region. The team’s work was published in July in *Ethology*.

Earthquake damage to a house in Italy. Credit: Max Planck Institute of Animal Behavior

The paper’s statistical analysis took the animals’ normal daily movements and interactions into account. It showed their activity significantly increased before magnitude 3.8 or greater earthquakes when they were housed together in a stable—but not when they were out to pasture. Wikelski says this difference could be linked to the increased stress some animals feel in confined spaces. Analyzing the increased movements as a whole, the researchers claim, showed a clear signal of anticipatory behavior hours ahead of tremors. “It’s sort of a system of mutual influence,” Wikelski says. “Initially, the cows kind of freeze in place—until the dogs go crazy. And then the cows actually go even crazier. And then that amplifies the sheep’s behavior, and so on.”

Wikelski says this observation is consistent with collective behavior theory. That idea was pioneered, in part, by his Max Planck colleague Iain Couzin, whose lab has reported finding evidence that mammals, birds, insects and fish share information that collectively improves survival skills, such as navigation and predator avoidance. This “swarm intelligence” can happen within or across species, Wikelski says. For example, “we did a study on Galápagos marine iguanas, and we know that they are actually listening in to mockingbirds’ warnings about the Galápagos hawks,” he adds. “These kinds of systems exist all over the place. We’re just not really tuned in to them yet.”

The researchers say the farm animals appeared to anticipate tremors anywhere from one to 20 hours ahead, reacting earlier when they were closer to the origin and later when they were farther away. This finding, the authors contend, is consistent with a hypothesis that animals somehow sense a signal that diffuses outward. It holds that in the days before an earthquake, shifting tectonic plates squeeze rocks along a fault line. This action causes the rocks to release minerals that expel ions into the air, according to a 2010 study. "The animals then react to this novel sensation," suggested the authors of a 2013 paper.

Wendy Bohon, a geologist at the Incorporated Research Institutions for Seismology in Washington, D.C., who was not involved with the new study, is skeptical of the air ionization idea. Numerous geologists have unsuccessfully tried to find such a precursory signal of impending earthquakes, she notes. Bohon does allow that Wikelski and his co-authors did some "cool things" to explore the possibility of animals predicting earthquakes. But she wonders whether there were instances in which the creatures showed unusual activity and there was no earthquake or did not react before one did occur. "My cat could act crazy before an earthquake," she says. "But my cat also acts crazy if somebody uses the can opener." In order to use the animals as prognosticators, it would be imperative to establish that they exhibited unusual behavior *only* in reaction to upcoming seismic events, Bohon says. "Otherwise," she adds, "it becomes the 'Boy Who Cried Wolf' problem."

Heiko Woith, a geologist at GFZ German Research Center for Geosciences and a co-author of the 2018 review, praised the authors of the new study for measuring more than a single occasion of abnormal behavior. But he says the time frame was still too short. Woith also points out that many studies claiming to show precursory earthquake signals often rely on too little data collection over time, making it impossible to determine whether a measured signal was related to a quake or was simply noise.

Wikelski and his colleagues say their single study could not differentiate all the potential stimuli the animals might react to. But they still argue that it is a good first step toward more controlled studies in the future. The researchers are setting up a new project in Italy, as well as one in Chile and another on Russia's Kamchatka Peninsula. They hope to test many more species to see if those animals display sensitivity to earthquake activity. "We're calling it a biotreasure hunt," Wikelski says.

https://bit.ly/3fufHdz

Extrasolar Planetary Systems Could Have Up to Seven Earth-Like Planets in Their Habitable Zones

Other stars could have as many as seven Earth-like planets in the absence of farther out giant planets, according to a new study led by the University of California, Riverside.

The search for life in outer space is typically focused on the habitable zone, which is the area around a star in which an orbiting planet could have liquid water.

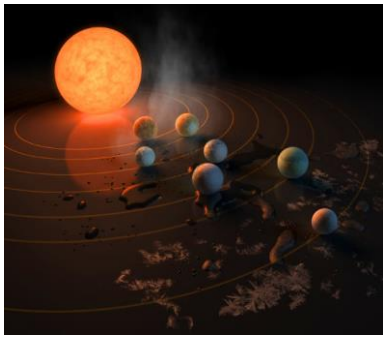
University of California, Riverside astrobiologist Stephen Kane and colleagues had been studying a nearby system called TRAPPIST-1, which has three Earth-like planets in its habitable zone.

"This made me wonder about the maximum number of habitable planets it's possible for a star to have, and why our star only has one. It didn't seem fair!" Dr. Kane said.

In the study, the researchers created a model system in which they simulated planets of various sizes orbiting their stars.

An algorithm accounted for gravitational forces and helped test how the planets interacted with each other over millions of years. They found it is possible for some stars to support as many as seven, and that a star like our Sun could potentially support six planets with liquid water.

"More than seven, and the planets become too close to each other and destabilize each other's orbits," Dr. Kane said. "Why then does our Solar System only have one habitable planet if it is capable of supporting six? It helps if the planets' movement is circular rather than oval or irregular, minimizing any close contact and maintain stable orbits."



This artist's impression displays TRAPPIST-1 and its planets reflected in a surface. **Image credit: NASA / R. Hurt / T. Pyle.**

The scientists suspect Jupiter, which has a mass two-and-a-half times that of all the other planets in the Solar System combined, limited our system's habitability. "It has a big effect on the habitability of our Solar System because it's massive and disturbs other orbits," Dr. Kane said. Only a handful of stars are known to have multiple planets in their habitable zones.

Moving forward, the authors plan to search for additional stars surrounded entirely by smaller planets. They already identified one such star, Beta CVn, which is relatively close by at 27 light-years away. Because it doesn't have a Jupiter-like planet, it will be included as one of the stars checked for multiple habitable zone planets. Future studies will also involve the creation of new models that examine the atmospheric chemistry of habitable zone planets in other star systems.

"Although we know Earth has been habitable for most of its history, many questions remain regarding how these favorable conditions evolved with time, and the specific drivers behind those changes," Dr. Kane said.

"By measuring the properties of exoplanets whose evolutionary pathways may be similar to our own, we gain a preview into the past and future of this planet — and what we must do to main its habitability."

The team's work was published in the *Astronomical Journal*.

Stephen R. Kane et al. 2020. Dynamical Packing in the Habitable Zone: The Case of Beta CVn. AJ 160, 81; doi: 10.3847/1538-3881/ab9ffe

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Humans Might Be So Sickly Because We Evolved to Avoid a Single Devastating Disease

Hundreds of thousands of years ago, our ancestors evolved a simple trick that could have helped thwart a major infectious disease. It probably saved our skins, but the change was far from a perfect solution.

Mike McRae

New research has uncovered evidence that mutations arising between 600,000 and 2 million years ago were part of a complex of adaptations that may have inadvertently made us prone to inflammatory diseases and even other pathogens.

An international team of researchers compared around a thousand human genomes with a few from our extinct cousins, the Neanderthals and Denisovans, to fill in missing details on the evolution of a family of chemicals that coat the human body's cells.

Sialic acids are a diverse group of carbohydrates that blossom like leaves from the tips of proteins covering the surfaces of human cells. This canopy of sugars is typically the first thing you'd bump into if you were the size of a virus or bacterium, so it's no surprise that these chemicals serve as a security badge, identifying friend from foe.

Changes in sialic acid markers can give rise to a number of diseases. But it was one specific change particular to all humans that the researchers here were most keen to gain an understanding of.

Most mammals – including closely related apes – have a compound called N-glycolylneuraminic acid, or Neu5Gc. We've known for

some time that the gene for this version of sialic acid is broken in us, leaving its precursor form, N-acetylneuraminic acid (Neu5Ac), to do its job.

Researchers previously speculated that this mutation was selected for in humans to make it harder for devastating malarial parasites such as *Plasmodium knowlesi* to latch onto red blood cells.

It's a swap that other animals – including a number of birds, bats, and even whales – have also evolved on their own.

Since chimpanzees retain the gene for Neu5Gc, the mutation must have occurred within the past 6 million years or so, sometime after we parted ways from one another.

This window can now be narrowed down even further. This most recent study shows Neanderthals and Denisovans share our variant of sialic acid, meaning the change happened before our branch of the family tree separated roughly 400,000 to 800,000 years ago.

Sialic acid markers are only part of the story, though. To differentiate between cells that belong to us from possible invaders, our immune cells are armed with a scanning chemical called sialic acid-binding immunoglobulin-type lectins. Or Siglecs for short.

When an inspection occurs, if a cell's sialic acid marker isn't up to scratch, it's curtains for that cell. Naturally, any changes to our sialic acid name-tag would imply our system of Siglecs would have needed adjusting as well.

Sure enough, on further investigation the researchers found significant mutations among a cluster of Siglec genes that are common to humans and their ilk, but not great apes.

Not all of these versions are found on immune cells, either. According to the study, some are found on other tissues, such as the brain, placenta, and gut.

This radical rewiring of our immune system is no small thing. If the malaria-hypothesis carries weight, it would have given Neu5Ac humans living in areas prone to the parasitic disease a huge advantage over their Neu5Gc relatives.

But it might have been a big price to pay. A decade ago, researchers from the same team suggested the mutation would have separated our ancestral communities, potentially preventing them from reproducing.

In other words, our species' lineage might have splintered as a result of this complex of immune mutations, possibly occurring with the emergence of *Homo erectus* a little more than 2 million years ago.

But there are other consequences of the change we're still experiencing today.

Siglec expression is linked with conditions such as asthma and Alzheimer's disease, raising the possibility that protection from a devastating disease put us at risk of other conditions.

As for that swap in sialic acid, it might have provided a new opportunity for a slew of other pathogens.

A wide variety of viruses and bacteria gain entry to our cells by grabbing onto the fuzz of sialic acid, many of which infect humans but not apes. Many, such as cholera, smallpox, influenza, and coronaviruses, are far from trivial.

"Most coronaviruses infect cells in two steps – first by recognising abundant sialic acids as binding sites to gain a foothold, and then seeking out the higher affinity protein receptors like ACE2," physician Ajit Varki told *Science* magazine's Ann Gibbons.

Strangely, a human-like elimination of the NeuA5c gene in mice gives them a boost in running ability, and in activating other parts of their immune system. Given the new cognitive and physical talents emerging in humans a couple of million years ago, asthma and cholera might well have been worth the swap.

Evolution gets the job done. But nobody said it was perfect.

This research was published in *Genome Biology and Evolution*.

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Young women with polycystic ovary syndrome have raised risk of heart disease

Women in their 30s and 40s with a common condition affecting how the ovaries work are more likely to get heart disease. Sophia Antipolis - That's the finding of a study published today in the *European Journal of Preventive Cardiology*, a journal of the European Society of Cardiology (ESC).1

"Polycystic ovary syndrome isn't a life sentence - there are many ways to stay heart healthy," said study author Dr. Clare Oliver-Williams of the University of Cambridge, UK. "Small changes add up, like eating more fruits and vegetables and doing more exercise."

It is estimated that 6-20% of women of reproductive age have polycystic ovary syndrome (PCOS).2 Features of the condition include multiple cysts (fluid-filled sacs) on the ovaries, irregular periods, excess body hair or hair loss from the head due to high levels of male hormones, and difficulty becoming pregnant.

Women with PCOS are more likely to be overweight or obese, have diabetes, and have high blood pressure - all risk factors for heart disease and stroke.

This study examined whether this risky profile translates into a greater likelihood of developing cardiovascular disease - and, for the first time, whether that persists across the lifespan. Dr. Oliver-Williams explained: "Some PCOS symptoms are only present during the reproductive years, so it's possible that the raised chance of heart disease might disappear later in life."

The study included 60,574 women receiving treatment to help them get pregnant, such as in vitro fertilisation (IVF), from 1994 to 2015. Of those, 6,149 (10.2%) had PCOS. The researchers used medical records to follow the women for nine years. During that period, 2,925 (4.8%) women developed cardiovascular disease.

Overall, women with PCOS were at 19% higher risk of developing cardiovascular disease than women who did not have PCOS.

When divided into age groups, women with PCOS aged 50 and over did not have a higher risk of developing cardiovascular risk compared to their peers without PCOS.

Women in their 30s and 40s with PCOS were at greater risk of cardiovascular disease compared to those without PCOS. The evidence in those under 30 was less clear; this is likely because there were insufficient women of that age in the dataset to identify the risk.

Dr. Oliver-Williams said: "Heart health appears to be a particular problem for young women with PCOS. This may be because they are more likely to be overweight and have high blood pressure and diabetes compared to their peers. Previous studies have suggested that these differences diminish with age. In other words, as women without PCOS get older, they increasingly become overweight and develop high blood pressure and diabetes. In a negative sense, they catch up to their peers with PCOS."

She encouraged young women with PCOS to stay positive: "PCOS can be a distressing condition. Not just because it can affect fertility. The physical effects can cause anxiety and depression. There's so much pressure on young women to achieve what we're told is the physical ideal. It takes age and time to embrace yourself and getting support from others is a vital step, so reach out if you need it."

"Knowledge is power and being aware of the heart risks means women with PCOS can do something about it," said Dr. Oliver-Williams. "Women with PCOS have been dealt a tough hand but this is about how these women play their cards. There are fantastic PCOS support groups where they can find out what has helped others with PCOS lose weight, get more exercise, and have a healthier diet."

She noted that the study only included Scandinavian women taking fertility treatment and caution is needed when extending the findings to other groups.

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Notes

References

1Oliver-Williams C, Vassard D, Pinborg A, Schmidt L. Risk of cardiovascular disease for women with polycystic ovary syndrome: results from a national Danish registry cohort study. Eur J Prev Cardiol. 2020. doi:10.1177/2047487320939674.

2Jayasena CN, Franks S. The Management of Patients With Polycystic Ovary Syndrome. Nat Rev Endocrinol. 2014;10:624-636.