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Simple diagnostic tool predicts individual risk of Alzheimer's

Algorithm combines data from a blood test and brief memory tests to accurately predict who will develop Alzheimer's

Researchers at Lund University in Sweden have developed an algorithm that combines data from a simple blood test and brief memory tests, to predict with great accuracy who will develop Alzheimer's disease in the future. The findings are published in *Nature Medicine*.

Approximately 20-30% of patients with Alzheimer's disease are wrongly diagnosed within specialist healthcare, and diagnostic work-up is even more difficult in primary care. Accuracy can be significantly improved by measuring the proteins tau and beta-amyloid via a spinal fluid sample, or PET scan. However, those methods are expensive and only available at a relatively few specialized memory clinics worldwide. Early and accurate diagnosis of AD is becoming even more important, as new drugs that slow down the progression of the disease will hopefully soon become available.

A research group led by Professor Oskar Hansson at Lund University have now shown that a combination of relatively easily acccessible tests can be used for early and reliable diagnosis of Alzheimer's disease. The study examined 340 patients with mild memory impairment in the Swedish BioFINDER Study, and the results were confirmed in a North American study of 543 people.

A combination of a simple blood test (measuring a variant of the tau protein and a risk gene for Alzheimer's) and three brief cognitive tests that only take 10 minutes to complete, predicted with over 90% certainty which patients would develop Alzheimer's dementia within four years. This simple prognostic algorithm was significantly more accurate than the clinical predictions by the dementia experts who examined the patients, but did not have access to expensive spinal fluid testing or PET scans, said Oskar Hansson.

"Our algorithm is based on a blood analysis of phosphylated tau and a risk gene for Alzheimer's, combined with testing of memory and executive function. We have now developed a prototype online tool to estimate the individual risk of a person with mild memory complaints developing Alzheimer's dementia within four years", explains Sebastian Palmqvist, first author of the study and associate professor at Lund University.

One clear advantage of the algorithm is that it has been developed for use in clinics without access to advanced diagnostic instruments. In the future, the algorithm might therefore make a major difference in the diagnosis of Alzheimer's within primary healthcare.

"The algorithm has currently only been tested on patients who have been examined in memory clinics. Our hope is that it will also be validated for use in primary healthcare as well as in developing countries with limited resources", says Sebastian Palmqvist.

Simple diagnostic tools for Alzheimer's could also improve the development of drugs, as it is difficult to recruit the suitable study partcipants for drug trials in a time- and cost-effective manner.

"The algorithm will enable us to recruit people with Alzheimer's at an early stage, which is when new drugs have a better chance of slowing the course of the disease", concludes Professor Oskar Hansson.

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

Injection of light-sensitive proteins restores blind man's vision

The first successful clinical test of a technique called optogenetics has allowed a person to see for the first time in decades, with the help of image-enhancing goggles.

Sara Reardon

After 40 years of blindness, a 58-year-old man can once again see images and moving objects[1], thanks to an injection of light-sensitive proteins into his retina.

The study, published on 24 May in *Nature Medicine*, is the first successful clinical application a optogenetics, in which flashes of light are used to control gene expression and neuron firing. The technique is widely used in laboratories to probe neural circuitry and is being investigated as a potential treatment for pain, blindness and brain disorders.

The clinical trial, run by the company GenSight Biologics, based in Paris, enrolls people with retinitis pigmentosa (RP): a degenerative disease that kills off the eye's photoreceptor cells, which are the first step in the visual pathway. In a healthy retina, photoreceptors detect light and send electrical signals to retinal ganglion cells (RGCs), which then transmit the signal to the brain. GenSight's optogenetic therapy skips the damaged photoreceptor cells entirely by using a virus to deliver light-sensitive bacterial proteins into the RGCs, allowing them to detect images directly.

The researchers injected the virus into the eye of a man with RP, then waited four months for protein production by the RGCs to stabilize before testing his vision. José-Alain Sahel, an ophthalmologist at the University of Pittsburgh Medical Center in Pennsylvania and leader of the study, says that one of the challenges was regulating the amount and type of light entering the eye, because a healthy retina uses a variety of cells and light-sensitive proteins to see a wide range of light. "No protein can replicate what the system can do," he says. So the researchers engineered a set of goggles that captured the visual information around the man and optimized it for detection by the bacterial proteins.

Using a camera, the goggles analyse changes in contrast and brightness and convert them in real time into what Sahel describes as a 'starry sky' of amber-coloured dots. When the light from these dots enters a person's eye, it activates the proteins and causes the RGCs to send a signal to the brain, which then resolves these patterns into an image.

The trial participant had to train with the goggles for several months before his brain adjusted to interpret the dots correctly. "He was like an experimentalist, a scientist trying to understand what he was seeing and make sense of it," Sahel says. Eventually, he was able to make out high-contrast images, including objects on a table and the white stripes in a crosswalk. When the researchers recorded his brain activity, they found that his visual cortex reacted to the image in the same way as it would have if he had normal sight.

The man still can't see without the goggles, but Sahel says that he wears them for several hours per day and that his vision has continued to improve in the two years since his injection. Six other people were injected with the same light-sensitive proteins last year, but the COVID-19 pandemic delayed their training with the goggles. Sahel expects to have their results within about a year.

Safe and permanent

"It's a big step for the field," says John Flannery, a neurobiologist at the University of California, Berkeley. "The most important thing is that it seems to be safe and permanent, which is really encouraging." Because the retina contains around 100 times more photoreceptors than do RGCs, the resolution of images detected by RGCs will never be as good as natural vision. But Flannery says it is exciting that the brain can interpret images accurately.

Others say that more research is needed. "It's interesting, but it's an *N* of 1," says Sheila Nirenberg, a neuroscientist at Weill Cornell Medical College in New York City. She says she looks forward to seeing whether the other people in the trial, including some who were injected with higher doses of the protein, have similar results.

GenSight is one of several companies developing optogenetics as a

treatment for RP and other disorders of the retina. In March, Nirenberg's company Bionic Sight announced that four of the five people with RP it had treated with a similar optogenetic therapy and a virtual-reality headset had recovered some level of vision, although the full trial results have not yet been published. And Swiss pharma giant Novartis is developing a therapy based on a different protein that is so light sensitive that goggles might not be needed. That therapy has not yet entered clinical trials.

Karl Deisseroth, a neuroscientist at Stanford University in California who co-developed optogenetics as a lab technique, says the study is important because it is the first time that the technique's effects have been shown in people. "It will be interesting to try this with more light-sensitive opsins" that might not require goggles, he says. But he expects optogenetics to be most useful as a research tool that leads to therapies, rather than a therapy itself. "What we hope to see even more of is optogenetics-guided human and clinical studies," he says.

doi: https://doi.org/10.1038/d41586-021-01421-0

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https://go.nature.com/3c43OvX

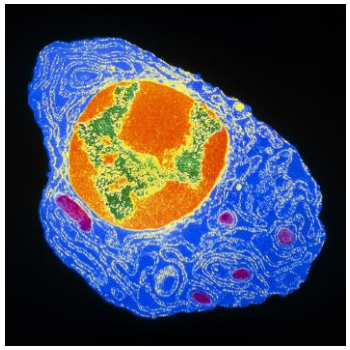
Had COVID? You'll probably make antibodies for a lifetime

People who recover from mild COVID-19 have bone-marrow cells that can churn out antibodies for decades, although viral variants could dampen some of the protection they offer.

Ewen Callaway

Many people who have been infected with SARS-CoV-2 will probably make antibodies against the virus for most of their lives. So suggest researchers who have identified long-lived antibody-producing cells in the bone marrow of people who have recovered from COVID-19[1].

The study provides evidence that immunity triggered by SARS-CoV-2 infection will be extraordinarily long-lasting. Adding to the good news, "the implications are that vaccines will have the same durable effect", says Menno van Zelm, an immunologist at Monash University in Melbourne, Australia. Antibodies — proteins that can recognize and help to inactivate viral particles — are a key immune defence. After a new infection, short-lived cells called plasmablasts are an early source of antibodies.



A bone-marrow plasma cell (artificially coloured). Such cells, which produce antibodies, linger for months in the bodies of people who have recovered from COVID-19. **Credit: Dr Gopal Murti/Science Photo Library**

But these cells recede soon after a virus is cleared from the body, and other, longer-lasting cells make antibodies: memory B cells patrol the blood for reinfection, while bone marrow plasma cells (BMPCs) hide away in bones, trickling out antibodies for decades.

"A plasma cell is our life history, in terms of the pathogens we've been exposed to," says Ali Ellebedy, a B-cell immunologist at Washington University in St. Louis, Missouri, who led the study, published in *Nature* on 24 May.

Researchers presumed that SARS-CoV-2 infection would trigger the development of BMPCs — nearly all viral infections do — but there have been signs that severe COVID-19 might disrupt the cells' formation[2]. Some early COVID-19 immunity studies also stoked worries, when they found that antibody levels plunged not long after recovery[3].

Ellebedy's team tracked antibody production in 77 people who had recovered from mostly mild cases of COVID-19. As expected, SARS-CoV-2 antibodies plummeted in the four months after infection. But this decline slowed, and up to 11 months after

infection, the researchers could still detect antibodies that recognized the SARS-CoV-2 spike protein.

To identify the source of the antibodies, Ellebedy's team collected memory B cells and bone marrow from a subset of participants. Seven months after developing symptoms, most of these participants still had memory B cells that recognized SARS-CoV-2. In 15 of the 18 bone-marrow samples, the scientists found ultra-low but detectable populations of BMPCs whose formation had been triggered by the individuals' coronavirus infections 7–8 months before. Levels of these cells were stable in all five people who gave another bone-marrow sample several months later.

"This is a very important observation," given claims of dwindling SARS-CoV-2 antibodies, says Rafi Ahmed, an immunologist at Emory University in Atlanta, Georgia, whose team co-discovered the cells in the late 1990s. What's not clear is what antibody levels will look like in the long term and whether they offer any protection, Ahmed adds. "We're early in the game. We're not looking at five years, ten years after infection."

Ellebedy's team has observed early signs that Pfizer's mRNA vaccine should trigger the production of the same cells[4]. But the persistence of antibody production, whether elicited by vaccination or by infection, does not ensure long-lasting immunity to COVID-19. The ability of some emerging SARS-CoV-2 variants to blunt the protective effects of antibodies means that additional immunizations may be needed to restore levels, says Ellebedy. "My presumption is, we will need a booster."

doi: https://doi.org/10.1038/d41586-021-01442-9

Updates & Corrections

Correction 27 May 2021*: An earlier version of this article gave the wrong number of bone-marrow samples. This has now been corrected.*

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https://bit.ly/34vq04E

Scientists discover a new feature that distinguishes modern humans from Neanderthals

Mutation did not occur in Neanderthals, so it affected metabolism in brain tissues and contributed to modern humans evolving as a separate species

Skoltech scientists and their colleagues from Germany and the United States have analyzed the metabolomes of humans, chimpanzees, and macaques in muscle, kidney, and three different brain regions. The team discovered that the modern human genome undergoes mutation which makes the adenylosuccinate lyase enzyme less stable, leading to a decrease in purine synthesis. This mutation did not occur in Neanderthals, so the scientists believe that it affected metabolism in brain tissues and thereby strongly contributed to modern humans evolving into a separate species. The research was published in the journal *eLife*.

The predecessors of modern humans split from their closest evolutionary relatives, Neanderthals and Denisovans, about 600,000 years ago, while the evolutionary divergence between our ancestors and those of modern chimpanzees dates as far back as 6.5 million years ago. Evolutionary biologists are after the particular genetic features that distinguish modern humans from their ancestors and may give a clue as to why humans are what they are.

Researchers from the Skoltech Center for Neurobiology and Brain Restoration (CNBR) led by Professor Philipp Khaitovich and their colleagues from the Max Planck Institutes in Leipzig, Dresden and Cologne and the University of Denver studied metabolic differences in the brain, kidney and muscle of humans, chimpanzees, and macaques.

The research supervisor was a renowned evolutionary biologist, Professor Svante Pääbo, who earlier on had discovered the Denisovan and led the Neanderthal Genome Project.

The team looked at an interesting human mutation that leads to amino acid substitution in adenylosuccinate lyase, an enzyme involved in the synthesis of purine inside DNA. This substitution reduces the enzyme's activity and stability, which results in a lower concentration of purines in the human brain. The team showed that the new mutation is typical for humans only and does not appear in other primates or Neanderthals. The researchers proved that this mutation is indeed the reason for the metabolic peculiarities in humans by introducing it into the mouse genome. The mice subjected to mutation produced fewer purines, whereas an ancestral gene, when introduced into human cells, led to apparent metabolic changes.

"Although a powerful tool for scientists, the decoded human genome, unfortunately, cannot account for all the phenotypic differences between humans. The study of the metabolic composition of tissues can give clues about why functional changes occur in humans. I am delighted that we have succeeded in predicting the metabolic characteristics of modern humans and validated our hypotheses on mouse and cell models, even though we did not have 'live Neanderthals' to work on," says lead author and Skoltech Ph.D. student Vita Stepanova.

More information: *Vita Stepanova et al, Reduced purine biosynthesis in humans after their divergence from Neandertals, eLife (2021).* *DOI: 10.7554/eLife.58741*

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Efficacy of Chinese vaccines is “not high”—officials back 3rd dose

Protection wanes by 6 months; experts call for high-risk people to get 3rd dose.

Beth Mole

Officials in Beijing are reportedly planning to roll out third doses of China’s COVID-19 vaccines. These shots have long been dogged by doubts of their efficacy.

According to a report by The Washington Post, health experts in China say that protection from the vaccines may not last after six months and that people who are at high risk of COVID-19 should get a third dose. Now, state-run media outlets suggest Beijing is on board with the suggestion and is preparing to offer the third doses.

Last week, both the United Arab Emirates and Bahrain said they would offer third doses of China’s Sinopharm vaccine to try to boost protection. UAE is offering the extra shots to anyone who was vaccinated six or more months ago. Bahrain is offering third doses to high-risk groups.

***Enlarge** / A vial and boxes of the Sinopharm Group Co Ltd. COVID-19 vaccine.* **Getty | Bloomberg**

Sinopharm’s COVID-19 vaccine as well as China’s Sinovac vaccine are made with whole, inactivated coronavirus SARS-CoV-2. Inactivated virus vaccines have the advantage of being relatively easy to make. But, they come with the potential drawback of providing weaker protection than more targeted vaccine approaches, such as the mRNA-based vaccines (Pfizer-BioNTech and Moderna), which take aim at just one particular key element of the virus: the spike protein.

Efficacy problems

Sinopharm has reported a 79 percent efficacy rate for its inactivated vaccine, but it has not released the full data supporting that estimate. Sinovac’s vaccine may have an efficacy rate as low as 50 percent, according to trial data out of Brazil.

Last month, the head of the Chinese Center for Disease Control and

Prevention, George Gao, seemed to acknowledge the problem, saying that the efficacy of China's vaccines is "not high."

Gao, speaking at a conference in Chengdu, said that Beijing was "formally considering" possibilities to "solve the problem that the efficacy of the existing vaccines is not high." Those possibilities included altering individual doses or increasing the number of doses people receive.

The comments were quickly censored on Chinese social media, the Post reported at the time. The Post also noted that state-run media called reports of Gao's statements "hyped up."

Though experts have raised questions about the efficacy of China's vaccines since their data-less release, the need for boosters isn't necessarily avoidable. Speaking in a series of public interviews last week, top US infectious disease expert Anthony Fauci noted that immunity to common coronaviruses isn't long-term. He predicted that people given the highly efficacious mRNA vaccines may still need a booster "within a year or so." Pfizer CEO Albert Bourla largely agreed with Fauci, saying boosters may be needed somewhere between eight to 12 months, though the data is still unclear on the exact timing.

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Weird Discovery Shows 'Supertasters' Could Be Better at Fighting Off SARS-CoV-2

If you are extremely sensitive to bitter flavors, you may be more resistant to SARS-CoV-2 - at least, that seems to be the implication from a newly published study.

Michelle Starr

According to data from nearly 2,000 patients in Baton Rouge, Louisiana, people with the 'supertaster' variant of a taste receptor gene made up a disproportionately small percentage of those testing positive for COVID-19.

This finding not only furthers a link between the gene variant and reduced susceptibility to upper respiratory tract infections, but could help doctors better assess the risk and outcomes of COVID-19.

"We set out to identify an association between T2R genotype with phenotype and outcomes after infection with COVID-19," the researchers wrote in their paper.

"We present our findings as an area that warrants further scientific study to potentially create a safe, cost-effective, accurate, and easily scalable screening tool that has the potential to stratify patients into groups and assess the risk of infection with SARS-CoV-2 and the expected clinical course of the disease."

The idea arose when a team of medical doctors led by Henry Barnham of Sinus and Nasal Specialists of Louisiana set out to investigate one of the hallmark symptoms of COVID-19 - the subjective loss of taste and smell. They gave a taste test to 100 patients who had tested positive for the virus, and, curiously, found that none of them was a supertaster.

Obviously, they decided this warranted more investigation, and between 1 July and 30 September 2020, they expanded their research to 1,935 patients at their tertiary outpatient clinical practice and inpatient hospital.

These patients were given the same taste test - strips of litmus paper treated with phenylthiocarbamide, thiourea, or sodium benzoate. The first two substances can taste either extremely bitter or like nothing at all, and sodium benzoate can taste sweet, salty, sour, bitter or - again - like nothing.

Together, the three taste tests helped to determine whether the patient likely had the supertaster variant of a bitter taste receptor gene called TAS2R38. Patients were then categorized in three groups - of the 1,935 participants, 508 (26.3 percent) were supertasters, 917 (47.4 percent) were tasters, and 510 (26.4 percent) were nontasters, people with a lower-than-average taste perception.

From the group, a total of 266 patients tested positive for SARS-CoV-2 in a polymerase chain reaction (PCR) test - currently the gold standard for COVID-19 diagnosis.

The distribution of those 266 patients did not match the distribution of the entire 1,935-participant group. Just 104 COVID-19 patients (39.1 percent) were from the taster group. The nontaster group was startlingly disproportionately represented; although they only constituted 26.4 percent of the entire group, they made up 55.3 percent of the COVID-19 group, with 147 of the 266 patients falling into this category.

Finally, supertasters made up just 5.6 percent of those infected by SARS-CoV-2, at 15 patients.

Taste sensitivity was linked to the severity of the disease, too - 55 of the 266 positive patients had to be hospitalized; and 47 of those were classified as nontasters. It's also important to note that none of the patients reported loss of taste as a symptom (although roughly half did experience loss of smell).

The doctors think this may have something to do with the way activation of bitter taste receptor genes can trigger an immune response, mainly the calcium-ion-driven production of nitric oxide, a compound that can damage invading microbes. These calcium ions can also trigger certain respiratory cells to release antimicrobial compounds.

The study does have some limitations. The supertasters were identified phenotypically, that is, based on observable traits. Future work could genetically confirm the taste sensitivities of the patients. In addition, given that SARS-CoV-2 is a new virus, there's a lot we don't know about how it behaves in different populations.

However, the discovery does suggest a fascinating new avenue for investigating and assessing patient risk and outcome, as well as how the disease operates.

"Bitter taste receptors appear to play a crucial role in the innate immunity against upper respiratory tract pathogens," the researchers wrote in their paper.

"This finding carries potential global implications for our understanding of SARS-CoV-2, in addition to yearly infections with additional viruses, including influenza."

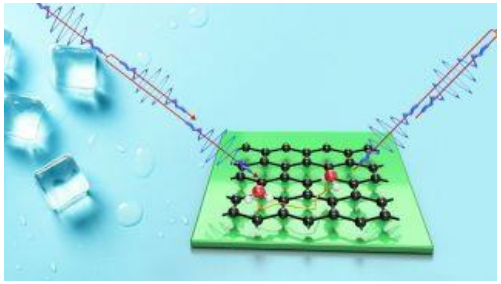
The research has been published in *JAMA Network Open*.

https://bit.ly/2RUwLUj

New study turns our understanding of ice upside down

You actually need some extra heat to freeze water into ice.

By Nicoletta Lanese - Staff Writer



As water freezes into ice, free-wheeling water molecules suddenly stop moving and begin forming ice crystals with their neighbors — but ironically, they need a bit of heat to do so, scientists recently discovered.

Scientists used beams of helium atoms (blue lines) to study the movement of water molcules (red and white balls) during ice formation. **(Image credit: Anton Tamtögl of Graz University of Technology)**

Yes, you read that right: You actually need some extra heat to freeze water into ice. That's according to a new study, published Tuesday (May 25) in the journal Nature Communications, which zoomed in on the movement of individual water molecules deposited on a frigid graphene surface. The research team used a technique called helium spin-echo, first developed at the University of Cambridge, which involves firing a beam of helium atoms at the water molecules, and then tracking how those helium atoms scatter once they ram into the forming ice.

The technique works similarly to radar detectors that use radio waves to determine how quickly a car is zipping down the highway, said first author Anton Tamtögl, a postdoctoral researcher at the

Institute of Experimental Physics at Graz University of Technology in Austria. "This is more like a radar trap for molecules, on an atomic scale," he told Live Science.

The method not only enabled the researchers to collect data from each teensy atom in their experiments, but also helped them record the earliest stage of ice formation, known as "nucleation," when water molecules first begin to coalesce into ice. Nucleation takes place at mind-boggling speeds — within a fraction of a billionth of a second — and as a result, many studies of ice formation focus on the period of time just after nucleation, when patches of ice have already formed and begin to merge into a kind of thick film, Tamtögl said.

For instance, studies that rely on conventional microscopes can't capture what occurs at the start of nucleation, because the instruments aren't capable of snapping images fast enough to keep up with the speedy water molecules, he said. Scientists sometimes slow down this molecular movement by applying liquid nitrogen to their experiments, lowering the temperature to around minus 418 degrees Fahrenheit (minus 250 degrees Celsius), but if you want to observe ice freezing at warmer temperatures, "then you need to use this spin-echo," Tamtögl said. In their own experiments, the team cooled the graphene surface to between minus 279 F and minus 225 F (minus 173 C to minus 143 C).

But when the team applied helium spin-echo to water molecules deposited on the graphene, they discovered something counterintuitive.

"What came as a surprise to us is this signature we had from the repulsive interaction — from the water molecules 'not liking each other,'" Tamtögl said. Essentially, as the team put water down upon the graphene surface, the molecules appeared to repel each other at first, maintaining a degree of distance.

"They had to kind of overcome this barrier before they could form the islands" of ice upon the graphene surface, he said. To better understand the nature of this repulsive force, and how the molecules overcame it, the team generated computational models to map out the interactions of the water molecules in different configurations.

These models revealed that, upon being placed on cold graphene, the water molecules all orient in the same direction, with their two hydrogen atoms pointed down; the hydrogen atoms in a water molecule stick off from the central oxygen atom like two mouse ears. These water molecules somewhat cluster together on the surface of the graphene, but due to their orientation, a few molecules' worth of empty space still persists between them.

To bond into ice crystals, the molecules must scooch a tiny bit closer to one another and break out of their uniform orientation. "That's what forms this barrier, where it will cost energy" to nucleate, Tamtögl said.

By adding more energy to the system in the form of heat, the team found they could nudge the water molecules toward each other and allow them to reorient and nucleate, finally forming ice. Adding more water molecules to the system also helped overcome the energy barrier, as the system became more and more crowded and molecules cozied up to one another, Tamtögl said.

All these interactions take place on incredibly short timescales, so this brief struggle to overcome the energy barrier passes in a flash.

Tamtögl and his colleagues plan to study whether ice nucleation unfolds similarly on different surfaces. For instance, so-called "white graphene," also known as hexagonal boron nitride, shares a similar structure to normal graphene but forms stronger bonds with water molecules, so nucleation may unfold more slowly on that type of surface, he said.

More broadly, learning exactly how ice forms would be useful in many scientific applications. For instance, with fine-grain

knowledge of ice formation, scientists could potentially improve technologies meant to prevent aeronautical equipment, wind turbines and communication towers from icing over, the authors wrote in their paper. Ice appears on cosmic dust grains and in Earth's atmosphere, and of course in glaciers; so unpacking the nitty-gritty physics of ice could have far-reaching relevancy in research.

"Water is such a ubiquitous molecule, right? But it appears there's still so much we don't understand in detail, even though it's a simple molecule," Tamtögl said. "There's still much more to be learned."

https://bit.ly/3yLTr9Y

Greenland's Melting Glaciers Are Polluting Coasts With Shocking Amounts of Mercury

Greenland's melting ice sheet is unleashing an astonishing amount of mercury into the nation's rivers and fjords.

Carly Cassella

Downstream of three glaciers in the southwest, researchers have found coastal ecosystems are swimming in high concentrations of the heavy metal, which can build up in the food web to toxic levels.

The quantity of mercury observed in three glacial rivers and three fjords in Greenland was among the worst in recorded history. In fact, researchers say the concentrations here are only matched by the polluted waterways of Industrial China, which overall produces about one-third of the world's mercury pollution.

As Greenland's glaciers continue to melt in line with our worst-case scenarios, experts are worried even more trapped mercury (Hg) could one day be released into the environment.

"This large, unaccounted for and climatically sensitive Hg source has not been considered in current global Hg budgets and Hg management strategies, but it should be assessed urgently given the human and economic implications of elevated Hg exposure," the authors of the new study warn.

Mercury is a natural and widespread element, released by wildfires, volcanic eruptions, and erosion. Yet in the past 150 years, industrial activity has been actively pumping even more of this pollutant into the atmosphere.

As the metal gradually drifts down from above, the element is passed from one organism to another, gradually concentrating in the food chain. People and animals in the Arctic are more likely to ingest toxic levels of mercury from their food and water, possibly because global circulation carries these heavy metals to the north.

In addition, increasing amounts of mercury also fall onto glaciers, snow, and ice, which can then run off into local waterways or rise into the atmosphere.

Previous studies have shown moderate mercury concentrations in run-off from melting glaciers, but the concentrations found in Greenland are two orders of magnitude higher than what scientists have found in other Arctic rivers.

"We didn't expect there would be anywhere near that amount of mercury in the glacial water there," says climate scientist Rob Spencer from Florida State University (FSU).

"Naturally, we have hypotheses as to what is leading to these high mercury concentrations, but these findings have raised a whole host of questions that we don't have the answers to yet."

Given the sheer amount of mercury discovered and the lack of major industry in the region, researchers think these high concentrations are probably not from industrial sources.

Instead, they might be coming from eroding rock underneath Greenland's ice sheet, which is naturally mercury-rich and is growing ever more exposed to the elements with climate change.

If the hunch is right, Greenland may very well be a neglected hotspot of natural mercury emissions, which have been trapped in ice for millennia. Even if we curb industrial mercury emissions tomorrow, the rapid melting of all this ice could sabotage human

efforts to reduce pollution from this heavy metal to safe levels.

Already, experts think Greenland's ice sheet has reached a tipping point, with much of its ice doomed to melt. As glaciers disappear, revealing the bedrock underneath, preliminary research indicates atmospheric mercury could also increase.

"All the efforts to manage mercury thus far have come from the idea that the increasing concentrations we have been seeing across the Earth system come primarily from direct anthropogenic activity, like industry," explains environmental biogeochemist Jon Hawkings from FSU and the German Research Centre for Geosciences.

"But mercury coming from climatically sensitive environments like glaciers could be a source that is much more difficult to manage."

Given that Greenland is a major exporter of seafood, and the region is home to precious marine ecosystems, we'd best find out what's going on. *The study was published in Nature Geoscience.*

https://bit.ly/3fO7oLG

Humans Could Live up to 150 Years, New Research Suggests

A study counts blood cells and footsteps to predict a hard limit to our longevity

By Emily Willingham

The chorus of the theme song for the movie *Fame,* performed by actress Irene Cara, includes the line "I'm gonna live forever." Cara was, of course, singing about the posthumous longevity that fame can confer. But a literal expression of this hubris resonates in some corners of the world—especially in the technology industry. In Silicon Valley, immortality is sometimes elevated to the status of a corporeal goal. Plenty of big names in big tech have sunk funding into ventures to solve the problem of death as if it were just an upgrade to your smartphone's operating system.

Yet what if death simply cannot be hacked and longevity will always have a ceiling, no matter what we do? Researchers have now taken on the question of how long we can live if, by some combination of serendipity and genetics, we do not die from cancer, heart disease or getting hit by a bus. They report that when omitting things that usually kill us, our body's capacity to restore equilibrium to its myriad structural and metabolic systems after disruptions still fades with time.

And even if we make it through life with few stressors, this incremental decline sets the maximum life span for humans at somewhere between 120 and 150 years. In the end, if the obvious hazards do not take our lives, this fundamental loss of resilience will do so, the researchers conclude in findings published on May 25 in Nature Communications.

Jeanne Calment enjoys her daily cigarette and glass of red wine on the occasion of her 117th birthday. In 1997, she died at the age of 122 and still holds the record for being the person with the longest lifespan. **Jean-Pierre Fizet Getty Images**

"They are asking the question of 'What's the longest life that could be lived by a human complex system if everything else went really well, and it's in a stressor-free environment?'" says Heather Whitson, director of the Duke University Center for the Study of Aging and Human Development, who was not involved in the paper. The team's results point to an underlying "pace of aging" that sets the limits on lifespan, she says.

For the study, Timothy Pyrkov, a researcher at a Singapore-based company called Gero, and his colleagues looked at this "pace of aging" in three large cohorts in the U.S., the U.K. and Russia. To evaluate deviations from stable health, they assessed changes in blood cell counts and the daily number of steps taken and analyzed them by age groups.

For both blood cell and step counts, the pattern was the same: as age increased, some factor beyond disease drove a predictable and incremental decline in the body's ability to return blood cells or gait to a stable level after a disruption. When Pyrkov and his colleagues in Moscow and Buffalo, N.Y., used this predictable pace of decline to determine when resilience would disappear entirely, leading to death, they found a range of 120 to 150 years. (In 1997 Jeanne Calment, the oldest person on record to have ever lived, died in France at the age of 122.)

The researchers also found that with age, the body's response to insults could increasingly range far from a stable normal, requiring more time for recovery. Whitson says that this result makes sense: A healthy young person can produce a rapid physiological response to adjust to fluctuations and restore a personal norm. But in an older person, she says, "everything is just a little bit dampened, a little slower to respond, and you can get overshoots," such as when an illness brings on big swings in blood pressure.

Measurements such as blood pressure and blood cell counts have a known healthy range, however, Whitson points out, whereas step counts are highly personal. The fact that Pyrkov and his colleagues chose a variable that is so different from blood counts and still discovered the same decline over time may suggest a real pace-of-aging factor in play across different domains.

Study co-author Peter Fedichev, who trained as a physicist and co-founded Gero, says that although most biologists would view blood cell counts and step counts as "pretty different," the fact that both sources "paint exactly the same future" suggests that this pace-of-aging component is real.

The authors pointed to social factors that reflect the findings. "We observed a steep turn at about the age of 35 to 40 years that was quite surprising," Pyrkov says. For example, he notes, this period is often a time when an athlete's sports career ends, "an indication that something in physiology may really be changing at this age."

The desire to unlock the secrets of immortality has likely been around as long as humans' awareness of death. But a long life span is not the same as a long health span, says S. Jay Olshansky, a professor of epidemiology and biostatistics at the University of Illinois at Chicago, who was not involved in the work. "The focus shouldn't be on living longer but on living healthier longer," he says.

"Death is not the only thing that matters," Whitson says. "Other things, like quality of life, start mattering more and more as people experience the loss of them." The death modeled in this study, she says, "is the ultimate lingering death. And the question is: Can we extend life without also extending the proportion of time that people go through a frail state?"

The researchers' "final conclusion is interesting to see," says Olshansky. He characterizes it as "Hey, guess what? Treating diseases in the long run is not going to have the effect that you might want it to have. These fundamental biological processes of aging are going to continue."

The idea of slowing down the aging process has drawn attention, not just from Silicon Valley types who dream about uploading their memories to computers but also from a cadre of researchers who view such interventions as a means to "compress morbidity"—to diminish illness and infirmity at the end of life to extend health span. The question of whether this will have any impact on the fundamental upper limits identified in the *Nature Communications* paper remains highly speculative. But some studies are being launched—testing the diabetes drug metformin, for example—with the goal of attenuating hallmark indicators of aging.

In this same vein, Fedichev and his team are not discouraged by their estimates of maximum human life span. His view is that their research marks the beginning of a longer journey. "Measuring

something is the first step before producing an intervention," Fedichev says. As he puts it, the next steps, now that the team has measured this independent pace of aging, will be to find ways to "intercept the loss of resilience."

https://bit.ly/3p3CEun

New Measurements Reveal The Full Danger of The World's Largest Volcano

An earthquake of magnitude 6 could trigger an eruption

David Nield

Active for at least the last 700,000 years, and dominating the landscape of Hawaii, Mauna Loa is the largest shield volcano on Earth (above water, at least) – and new data have revealed more about what might be enough to set off future eruptions.

Looking at shifts in the ground tracked by GPS and satellite data, researchers have been able to model the flow of magma on the inside of the volcano, as well as figuring out what would and wouldn't be likely to trigger the next major eruption from Mauna Loa.

In the 'would be likely' column: a sizable earthquake. That conclusion is based on measurements of magma influx that have happened since 2014, directed by the topographic stress of the surrounding rock.

"An earthquake of magnitude 6 or greater would relieve the stress imparted by the influx of magma along a sub-horizontal fault under the western flank of the volcano," says Bhuvan Varugu, a geologist at the Rosenstiel School of Marine and Atmospheric Science at the University of Miami.

"This earthquake could trigger an eruption."

The scientists determined that 0.11 square kilometers (about 0.04 square miles) of new magma flowed into a new spot in the volcano chamber between 2014 and 2020, changing direction according to the pressures being placed on it.

These kinds of magma body changes haven't been measured before. Together with surface lava flows and ground shifts along the fault the volcano is sitting on, magma intrusions change the shape of the volcano – and the likelihood of it erupting.

Volcanologists already know that flank activity and eruptions are closely related at Mauna Loa, which means that changes in these flanks caused by magma injections can make a substantial difference in terms of how the volcano behaves.

"An earthquake could be a game changer," says marine geologist Falk Amelung, from the University of Miami.

"It would release gases from the magma comparable to shaking a soda bottle, generating additional pressure and buoyancy, sufficient to break the rock above the magma."

According to the data, Mauna Loa is already under a "pretty heavy" topographic load. Further magma intrusions will increase the likelihood of an earthquake and an eruption, but it might not necessarily be needed: a lack of recent movement under the volcano's western flank makes the researchers think this is where an earthquake might be due.

Recent eruptions emphasize just how important an early warning could be: in 1950, lava from a Mauna Loa eruption reached the coast in just three hours. The 1950 eruption and another major one in 1984 were both preceded by substantial earthquakes.

Predicting the timings of eruptions is an incredibly complex task, with a lot of variables and estimates involved – but careful magma mapping strategies like the one in this new study can provide invaluable data for future modeling.

"It is a fascinating problem," says Amelung.

"We can explain how and why the magma body changed during the past six years. We will continue observing and this will eventually lead to better models to forecast the next eruption site."

The research has been published in *Scientific Reports*.

https://bit.ly/3fSCfqF

Immediate Skin-to-Skin Touch Could Save The Lives of Many Preterm Babies, Study Shows

When a baby is born prematurely, immediate skin-to-skin contact could save their lives.

Carly Cassella

Instead of placing low-weight newborns in an incubator, new research suggests they should be nestled up close to their mother's chest, or that of a close caregiver's, and fed exclusively on breast milk. This approach, dubbed kangaroo care, has proved to be one of the best and safest ways to treat preterm infants with low birth weights, resulting in fewer infections, higher rates of breastfeeding, and better weight gain in studies.

Despite the growing number of benefits, the practice has not been widely adopted. Currently, the World Health Organization recommends continuous kangaroo care for all preterm infants, but only after they are taken away and declared clinically stable in the neonatal intensive care unit (NICU).

A randomized controlled trial in five hospitals now suggests the WHO's recommendation separates babies and their mothers too soon. Instead, hospitals should implement a mother-infant care unit with beds and chairs so that hospital staff can look after new parents and babies at the same time.

The study was conducted among 3,211 low-weight infants in Ghana, India, Malawi, Nigeria, and Tanzania, who were either assigned immediate kangaroo care in a specially arranged "Mother-NICU" or were separated from the parents for conventional care, with brief moments of touch allowed after the first 24 hours.

In the first three days, infants who received immediate skin-to-skin contact were held for roughly 17 hours a day in the Mother-NICU. Meanwhile, those infants placed in incubators or radiant warmers received only 1.5 hours of intermittent daily contact.

Compared to conventional neonatal care, those infants who received immediate touch from their parents were 25 percent less likely to die in the first month of life.

Continuously held newborns were also less likely to develop hypothermia and bacterial blood poisoning, possibly because these infants had greater exposure to their mother's protective microbiome, were more likely to receive early breast milk, and were handled by fewer people.

Avoiding separation stress between the mother and the infant might also have contributed to greater health outcomes. Touch between a baby and its mother has been shown to stabilize the newborn's heart rate, calm its breathing, and decrease its crying.

"Keeping the mother and baby together right from birth, with zero separation, will revolutionize the way neonatal intensive care is practiced for babies born early or small," argues Rajiv Bahl, the Head of Maternal and Newborn Health Research and Development at WHO.

"This study illustrates that kangaroo mother care has the potential to save many more lives if it is started immediately after birth, a finding with relevance for countries of all income levels."

Today, over 96 percent of all infants with a low birth weight are born in developing countries, and these children are particularly vulnerable to infectious disease, developmental delays, and death.

Conventional neonatal care is expensive and requires great skill and logistical support, which many countries with lower incomes cannot afford. Kangaroo care, on the other hand, is a safe and effective alternative much easier to implement. The findings support a recent meta-analysis that found kangaroo care after clinical stabilization results in 40 percent lower infant mortality.

Yet, many premature babies don't make it to that stage. Studies reveal nearly 50 percent of neonatal deaths in a number of Asian and African nations occur within 24 hours of delivery, and 80

percent occur in the first week of life, which means many lives are being lost before kangaroo care can be initiated.

"The idea of giving skin-to-skin contact immediately after delivery to very small, unstable babies has encountered quite strong resistance, but about 75 percent of deaths occur before the infant has been judged sufficiently stable," explains Nils Bergman from the Karolinska Institutet in Sweden.

If low-weight infants receive immediate kangaroo care, the authors of the new study estimate it could save 150,000 underweight newborns each year. WHO is currently in the process of reviewing its guidance on kangaroo care. The study was published in *NEJM*.

https://bit.ly/3wII6Wq

Archaeology: Prehistoric violence at Jebel Sahaba may not have been single event

Reanalysis of prehistoric cemetery suggests hunter-fisher-gatherers engaged in repeated, smaller conflicts

Reanalysis of the prehistoric cemetery Jebel Sahaba (Sudan), one of the earliest sites showing human warfare (13,400 years ago), suggests that hunter-fisher-gatherers engaged in repeated, smaller conflicts. The findings are published in Scientific Reports. Healed trauma on the skeletons found in the cemetery indicates that individuals fought and survived several violent assaults, rather than fighting in one fatal event as previously thought.

Isabelle Crevecoeur and colleagues reanalysed the skeletal remains of 61 individuals, who were originally excavated in the 1960s, using newly available microscopy techniques. The authors identified 106 previously undocumented lesions and traumas, and were able to distinguish between projectile injuries (from arrows or spears), trauma (from close combat), and traces associated to natural decay. They found 41 individuals (67%) buried in Jebel Sahaba had at least one type of healed or unhealed injury. In the 41 individuals with injuries, 92% had evidence of these being caused by projectiles and close combat trauma, suggesting interpersonal acts of violence.

The authors suggest that the number of healed wounds matches sporadic and recurrent acts of violence, which were not always lethal, between Nile valley groups at the end of the Late Pleistocene (126,000 to 11,700 years ago). They speculate these may have been repeated skirmishes or raids between different groups. At least half of the injuries were identified as puncture wounds, caused by projectiles like spears and arrows, which supports the authors' theory that these injuries happened when groups attacked from a distance, rather than during domestic conflicts.

Article details:

New insights on interpersonal violence in the Late Pleistocene based on the Nile valley cemetery of Jebel Sahaba DOI: 10.1038/s41598-021-89386-y

https://bit.ly/3vBv2lw

Oldest gold artifact in southwest Germany found

Gold spiral may have been used as a hair ornament.

By Owen Jarus - Live Science Contributor

Archaeologists have uncovered the 3,800 year-old burial of a woman who was around 20 years old when she died in what is now Tübingen, Germany. Inside her tomb, archaeologists found just one grave good — a spiral gold wire that may have been used as a hair ornament.

This gold artifact, which may have been used as a hair ornament, was found buried with a woman who died around 3,800 years ago. **(Image credit: Yvonne Mühleis, LAD Esslingen)**

It's considered the oldest gold artifact found in southwest Germany. "The gold contains about 20% silver, less than 2% copper, and has traces of platinum and tin. This composition points to a natural gold alloy typical of gold washed from rivers," a chemical composition that suggests it came from the Carnon River area in Cornwall,

England, the researchers said in a statement.

"Precious metal finds from this period are very rare in southwestern Germany," the researchers said in the statement. "The gold find from the Tübingen district [is] evidence that western cultural groups [such as from Britain and France] gained increasing influence over central Europe in the first half of the second millennium [B.C.]," researchers said.

The woman was buried in a fetal position facing south, not far from a prehistoric hilltop settlement where other graves have been found.

The researchers found no evidence of any injuries or disease, so they have no idea what she died from, Raiko Krauss, a professor in the Institute of Prehistory and Medieval Archaeology at the University of Tübingen, told Live Science. Krauss and Jörg Bofinger, a conservator with the Baden-Württemberg State Office for Cultural Heritage Management, led the excavation of the grave.

The fact that the artifact is made of gold suggests that the woman may have had a high social status, the researchers said. They ran radiocarbon dating on the woman's remains, finding she died some time between 1850 B.C. and 1700 B.C. At that time, writing had not yet spread to southwest Germany so there are no written records that could help to identify who she might have been.

The grave was excavated in autumn 2020 and the team's findings were published May 21 in the journal Praehistorische Zeitschrift.

https://bit.ly/2TkfQuC

'Limnic eruption': DR Congo's volcano nightmare

Rare, potentially catastrophic risk when volcanic activity combined with a deep lake can spew out lethal, suffocating gas

Orders on Thursday to evacuate Goma, a city lying in the shadow of DR Congo's Mount Nyiragongo volcano, have shed light on a rare but potentially catastrophic risk—a "limnic eruption," when volcanic activity combined with a deep lake can spew out lethal, suffocating gas.

The phenomenon first came to the world's attention in August 1984, when 37 people mysteriously died at Lake Monoun in western Cameroon.

Scientists found that dissolved carbon dioxide (CO_2) gas in the depths of the lake had erupted, creating invisible clouds at the surface that were borne by winds into homes and fields, snuffing out life.

Eruption: Mount Nyiragongo and Lake Kivu last Saturday.

Two years later, more than 1,700 people and thousands of cattle died in Lake Nyos, also in Cameroon, strengthening the belief that earthquakes and volcanic activity can trigger these unusual events.

More than 600,000 people live in Goma, although the region's population is around two million, in addition to more than 90,000 people who live across the border in the Rwandan city of Gisenyi.

Both cities lie on the northeastern shore of Lake Kivu, which is dominated by Nyiragongo, a strato-volcano nearly 3,500 metres (11,500 feet) high that straddles the East African Rift tectonic divide.

The much-feared volcano roared back into life on Saturday, spewing two rivers of lava over the next day that have claimed 32 lives and left around 20,000 homeless.

This was followed by hundreds of aftershocks, some of them the equivalent of small earthquakes, that have collapsed or destroyed several buildings, ripped cracks in the ground and terrified the population.

Map of DR Congo locating the Mount Nyiragongo volcano.

Disaster scenario

The evacuation order comes on the heels of a warning by the Goma Volcano Observatory (OVG), which monitors the pulse of Nyiragongo and the Nyamuragira volcano, 13 kilometres (nine miles) away. In a technical note seen by AFP, the OVG said it saw worrying signs of activity by Nyiragongo that pointed to three potential outcomes.

In the first two scenarios, Nyiragongo would erupt again, sending renewed lava flows southwards towards Goma and Gisenyi, destroying buildings in their path before reaching Lake Kivu.

In both cases, the quantity of lava likely to enter the lake would not be enough to raise its deep-water temperature by at least one degrees Celsius (1.8 degrees Fahrenheit)—a key condition for a limnic eruption. But in the worst-case scenario, lava flows from Nyiragongo would combine with volcanic activity under the floor of the lake.

This activity could take the form of a "fissural or phreato-magmatic eruption under the lake and/or a large earthquake of 6.5 or 7 magnitude," the OVG said.

In this scenario, "a limnic eruption would take place and dissolved gas in the lake's deep water would rise to the surface, especially CO2, asphyxiating all living beings around Lake Kivu on the Congolese and Rwandan side." "There would be thousands of deaths," the OVG said, spelling out the need for resources to carry out an "urgent exploration" of Lake Kivu.

Volcanic region

The OVG also cautioned against the use of rainwater for drinking or washing food, given the ashfall from the volcano. Six volcanoes dot the Goma region, dominated by Nyiragongo, which is 3,470 metres (11,400 feet) high, and Nyamuragira, 3,058 metres.

Nyiragongo last erupted on January 17, 2002, killing more than 100 people and covering almost all of the eastern part of Goma with lava, including half of the airport's landing strip.

Its deadliest eruption was in 1977, when more than 600 people died. Nyamuragira is also highly active, with its last major eruption a decade ago.

https://bit.ly/2RZqVAZ

Diabetes vaccine shows promise for some patients in early trial

In patients with type 1 diabetes, the body's immune system attacks the beta cells in the pancreas that produce insulin.

By Yasemin Saplakoglu - Staff Writer

In a small, early study, a vaccine for type 1 diabetes helped preserve the body's natural production of insulin, at least in a subset of newly diagnosed patients.

In patients with type 1 diabetes, the body's immune system attacks the beta cells in the pancreas that produce insulin, a hormone that's necessary for cells to absorb glucose from the bloodstream. These patients need lifelong insulin injections to stay alive.

And because so many hidden factors inside the body can affect how much insulin a person needs, people who are insulin-dependent often have high and low blood sugar. High blood sugar, or hyperglycemia, damages the organs over the long term, while low blood sugar, or hypoglycemia, can lead to seizures or death in the short term.

In the current study, the researchers wanted to test whether a vaccine might be able to stop or slow the destruction of these insulin-producing beta cells.

"Studies have shown that even an extremely small production of insulin in the body is highly beneficial for patient health," lead author Dr. Johnny Ludvigsson, a senior professor in the Department of Biomedical and Clinical Sciences at Linköping University in Sweden, said in a statement. "People with diabetes who produce a certain amount of insulin naturally do not develop low blood sugar levels, hypoglycemia, so easily."

Ludvigsson and his team developed a vaccine made from glutamic acid decarboxylase (GAD), a protein anchored to the surface of beta cells that many people with type 1 diabetes form antibodies against. (The treatment is called GAD-alum).

People with certain versions of immune system genes, known as human leukocyte antigen (HLA) genes, are at higher risk of developing type 1 diabetes. Several HLA types increase the risk of the autoimmune disorder, but one genetic variant, known as "HLA-DR3-DQ2," exposes a form of the GAD protein (GAD65) to the immune system on the surface of beta cells, according to the statement. This triggers the immune system to produce antibodies against the protein and target the beta cells for destruction.

The researchers wanted to see if a vaccine that exposed the body to more GAD would help the immune system better tolerate the body's natural GAD65 and thus stop attacking the insulin-producing cells.

For the phase 2 clinical study, the researchers recruited 109 patients between the ages of 12 and 24 who had been diagnosed with type 1 diabetes within the past six months. About half of the patients carried the HLA-DR3-DQ2 gene variant.

The researchers divided the participants into two groups: Half of the participants, assigned randomly, were given three shots of the vaccine into their lymph nodes, each one month apart, and the other half were given a placebo.

The researchers analyzed how much natural insulin the participants produced at the start of the study and after 15 months. They also analyzed changes to long-term blood sugar levels and how much supplementary insulin they needed to take daily.

As a whole, there was no difference in the treatment and placebo groups. But the subset of patients who had the HLA-DR3-DQ2 variant did not lose insulin production as quickly as other patients did.

"Treatment with GAD-alum seems to be a promising, simple and safe way to preserve insulin production in around half of patients with type 1 diabetes, the ones who have the right type of HLA," Ludvigsson said. "This is why we are looking forward to carrying out larger studies, and we hope these will lead to a drug that can change the progress of type 1 diabetes."

The study, published online May 21 in the journal Diabetes Care, was funded by the pharmaceutical company Diamyd Medical AB, which was also involved in planning and collecting data in the trial, the Swedish Child Diabetes Foundation and the Swedish Diabetes Foundation.

https://bit.ly/3cmJIxp

Waking just one hour earlier cuts depression risk by double digits

Waking up just one hour earlier could reduce a person's risk of major depression by 23%, suggests a sweeping new genetic study published May 26 in the journal JAMA Psychiatry.

The study of 840,000 people, by researchers at University of Colorado Boulder and the Broad Institute of MIT and Harvard, represents some of the strongest evidence yet that chronotype--a person's propensity to sleep at a certain time --influences depression risk. It's also among the first studies to quantify just how much, or little, change is required to influence mental health.

As people emerge, post-pandemic, from working and attending school remotely-- a trend that has led many to shift to a later sleep schedule--the findings could have important implications.

"We have known for some time that there is a relationship between sleep timing and mood, but a question we often hear from clinicians is: How much earlier do we need to shift people to see a benefit?" said senior author Celine Vetter, assistant professor of integrative physiology at CU Boulder. "We found that even one-hour earlier sleep timing is associated with significantly lower risk of depression."

Previous observational studies have shown that night owls are as much as twice as likely to suffer from depression as early risers, regardless of how long they sleep. But because mood disorders themselves can disrupt sleep patterns, researchers have had a hard time deciphering what causes what.

Other studies have had small sample sizes, relied on questionnaires from a single time point, or didn't account for environmental factors which can influence both sleep timing and mood, potentially confounding results.

In 2018, Vetter published a large, long term study of 32,000 nurses showing that "early risers" were up to 27% less likely to develop depression over the course of four years, but that begged the question: What does it mean to be an early riser?

To get a clearer sense of whether shifting sleep time earlier is truly protective, and how much shift is required, lead author Iyas Daghlas, M.D., turned to data from the DNA testing company 23 and Me and the biomedical database UK Biobank. Daghlas then used a method called "Mendelian randomization" that leverages genetic associations to help decipher cause and effect.

"Our genetics are set at birth so some of the biases that affect other kinds of epidemiological research tend not to affect genetic studies," said Daghlas, who graduated in May from Harvard Medical School.

More than 340 common genetic variants, including variants in the so-called "clock gene" PER2, are known to influence a person's chronotype, and genetics collectively explains 12-42% of our sleep timing preference.

The researchers assessed deidentified genetic data on these variants from up to 850,000 individuals, including data from 85,000 who had worn wearable sleep trackers for 7 days and 250,000 who had filled out sleep-preference questionnaires. This gave them a more granular picture, down to the hour, of how variants in genes influence when we sleep and wake up.

In the largest of these samples, about a third of surveyed subjects self-identified as morning larks, 9% were night owls and the rest were in the middle. Overall, the average sleep mid-point was 3 a.m., meaning they went to bed at 11 p.m. and got up at 6 a.m.

With this information in hand, the researchers turned to a different sample which included genetic information along with anonymized medical and prescription records and surveys about diagnoses of major depressive disorder.

Using novel statistical techniques, they asked: Do those with genetic variants which predispose them to be early risers also have lower risk of depression?

The answer is a firm yes.

Each one-hour earlier sleep midpoint (halfway between bedtime and wake time) corresponded with a 23% lower risk of major depressive disorder.

This suggests that if someone who normally goes to bed at 1 a.m. goes to bed at midnight instead and sleeps the same duration, they could cut their risk by 23%; if they go to bed at 11 p.m., they could cut it by about 40%.

It's unclear from the study whether those who are already early risers could benefit from getting up even earlier. But for those in the intermediate range or evening range, shifting to an earlier bedtime would likely be helpful.

What could explain this effect?

Some research suggests that getting greater light exposure during the day, which early-risers tend to get, results in a cascade of hormonal impacts that can influence mood.

Others note that having a biological clock, or circadian rhythm, that trends differently than most peoples' can in itself be depressing.

"We live in a society that is designed for morning people, and evening people often feel as if they are in a constant state of

misalignment with that societal clock," said Daghlas.

He stresses that a large randomized clinical trial is necessary to determine definitively whether going to bed early can reduce depression. "But this study definitely shifts the weight of evidence toward supporting a causal effect of sleep timing on depression."

For those wanting to shift themselves to an earlier sleep schedule, Vetter offers this advice:

"Keep your days bright and your nights dark," she says. "Have your morning coffee on the porch. Walk or ride your bike to work if you can, and dim those electronics in the evening."

https://bit.ly/3i7vjbQ

Surprise Discovery in The Human Spleen Could 'Redefine' What We Know About Malaria

Scientists thought that the spleen is where malaria parasites go to die.

Clare Watson

Now, a team of researchers has discovered "a surprisingly large" amount of live *Plasmodium* parasites hiding out in the spleens of people with chronic malaria infections. The discovery adds a new dimension to the multistep life cycle of mosquito-borne malaria parasites, some of which can lay dormant in the liver before bursting out into the bloodstream to multiply and spread.

It also helps to explain why chronic cases of malaria fly under the radar on blood tests but then suddenly relapse, and also how some malaria parasites have adapted to survive.

"Our findings redefine the malaria life-cycle," says Steven Kho, an infectious disease researcher at the Menzies School of Health Research in Darwin, Australia.

"Chronic malaria should be considered predominantly an infection of the spleen, with just a small proportion circulating in the blood."

In two papers, Kho and his colleagues report discovering two of the five species of *Plasmodium* parasites known to cause malaria in humans – *P. falciparum* and *P. vivax* – lurking in the spleens of people living in Papua, Indonesia, where malaria is endemic and chronic cases are common.

Although *P. falciparum* is the deadliest form of malaria parasite, *P. vivax* poses a greater challenge to disease eradication; the latter is spread more widely across the globe and causes recurring infections, effectively hiding without easy detection in-between bouts.

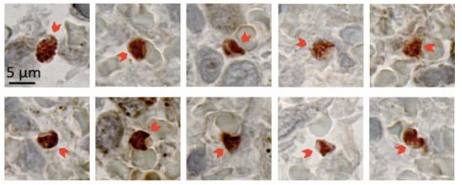
Cases of chronic *P. vivax* malaria, which can still be fatal, are also on the rise as disease control activities hone in on *P. falciparum*, a sign of how this horrid disease keeps thwarting our best efforts.

"The recent drive to rid the world of malaria has brought *P. vivax* to the fore," explains parasitologist Georges Snounou in a different paper from 2018, "with the recognition that relapses pose a serious obstacle to its eradication."

Of the new work, the first study - led by Kho - describes a group of 15 adults who showed no symptoms of malaria and had their spleens surgically removed for other medical reasons.

Using microscopes and cell staining to expose the parasites in blood samples and spleen tissue, the researchers found most of these people had bulk *Plasmodium* parasites in their spleen.

In an extension of this first study, expanding the total number of volunteers out to 22, the researchers again identified significant numbers of parasites in spleens, in spite of patients presenting no symptoms of malaria.



Red cells infected with P. vivax in the spleen. **(Kho et al. 2021)**

The spleen has the job of filtering our blood to remove old, damaged, or infected red blood cells. The levels of *P. vivax* that had accumulated in these people's spleens were in some cases hundreds, even thousands of times higher than what was found circulating in the bloodstream.

This was way more than you'd expect to see if the parasites were only replicating in red blood cells that the spleen strained out of circulation, the researchers calculated. So, the findings suggest that the spleen is a previously unrecognized reservoir where *Plasmodium* parasites can hang out and replicate.

"Accumulation of parasites in the spleen was found with both major *Plasmodium* species causing malaria, but was particularly apparent in *P. vivax*, where over 98 percent of all the parasites in the body were hiding in the spleen," Kho explains.

What's more, a couple of people had such low levels of malaria parasites in their blood it was undetectable, yet their spleens were packed full of parasite-infected cells. This has researchers worried, but with so few examples to date, larger studies are really needed to further validate the findings.

"This is another factor limiting the success of malaria elimination programs relying on mass testing of blood and only treating those with detectable infection," says infectious disease physician Nick Anstey, noting how this could hamper surveillance and eradication efforts.

But why *P. vivax* accumulates so intensely in the spleen, well – that's still an unknown. The researchers have a hunch though: the spleen stockpiles a lot of young red blood cells called reticulocytes, which are the only type of red cells that *P. vivax* can infect.

"This makes the spleen a highly favorable location in which the vivax malaria parasites can multiply," Anstey says.

This may also reinvigorate research into malaria treatments and vaccine candidates that attack different stages of the *Plasmodium* life cycle, now that we know the spleen is a crucial part of the puzzle for *P. vivax* infections.

Both are sorely needed for this disease which infects around 250 million people each year in the Asia-Pacific region alone, and for *P. vivax* which has been long overlooked in research.

The studies were published in the *New England Journal of Medicine* and *PLOS Medicine*.

https://bit.ly/3uBaQPp

'Magic' jar holding dismembered chicken used as a curse in ancient Athens

Finding reveals new evidence for how people tried to use "magic" in the city.

By Owen Jarus - Live Science Contributor

A 2,300-year-old ceramic jar filled with the bones of a dismembered chicken was likely part of an ancient curse to paralyze and kill 55 people in ancient Athens, archaeologists say. The finding reveals new evidence for how people tried to use "magic" in the city.

They discovered the jar, along with a coin, beneath the floor of the Agora's Classical Commercial Building, which was used by ancient craftspeople. "The pot contained the dismembered head and lower limbs of a young chicken," Jessica Lamont, a classics professor at Yale University, wrote in an article published in the journal Hesperia.

At the time, around 300 B.C., the people who made the curse also gouged a large iron nail through the vessel.

"All exterior surfaces of the [jar] were originally covered with text; it once carried over 55 inscribed names, dozens of which now survive only as scattered, floating letters or faint stylus strokes" Lamont wrote, noting that the Greek writing contains words that may mean "we bind." The nail and chicken parts likely played a role in the curse. Nails are commonly found with ancient curses and "had an inhibiting force and symbolically immobilized or restrained the faculties of [the curse's] victims," Lamont wrote.

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The chicken was no older than 7 months when it was killed, and the people who created the curse may have wanted to transfer "the

chick's helplessness and inability to protect itself" to the people whose names are inscribed on the jar, Lamont wrote. The presence of the chicken's head and lower legs in the jar suggests that "by twisting off and piercing the head and lower legs of the chicken, the curse composers sought to incapacitate the use of those same body parts in their victims," Lamont wrote.

"The ritual assemblage belongs to the realm of Athenian binding curses and aimed to 'bind' or inhibit the physical and cognitive faculties of the named individuals," Lamont wrote. The jar was placed near several burned pyres that contained animal remains — something that may have enhanced the curse's power, according to Lamont.

Inside the curse jar, archaeologists found iron nail, coin and bones of a chicken. **(Image credit: Athenian Agora excavations)**

Why was the curse created?

The style of the handwriting on the jar suggests that at least two individuals wrote the names on the jar, Lamont said. "It was certainly composed by people/persons with good knowledge of how to cast a powerful curse," Lamont told Live Science in an email. Why they went to the trouble of creating such an elaborate curse is not certain, but it may have been related to a legal case.

"The sheer number of names makes an impending lawsuit the most likely scenario," Lamont wrote, noting that "curse composers might cite all imaginable opponents in their maledictions, including the witnesses, families and supporters of the opposition." Trials were common at the time in Athens and galvanized a lot of the public, according to Lamont.

The jar's location — a building used by craftspeople — suggests that the lawsuit may have involved a workplace dispute. "The curse could have been created by craftspersons working in the industrial building itself, perhaps in the lead-up to a trial concerning an inter-workplace conflict," Lamont wrote.

Another possibility is that the curse is related to the strife in Athens around 2,300 years ago. After Alexander the Great died in 323 B.C., his empire collapsed and his generals and officials fought for power. Historical records show that several factions fought for control of Athens at the time. It was "a period plagued by war, siege and shifting political alliances," Lamont wrote.

The curse jar was excavated in 2006 and was recently analyzed and deciphered by Lamont. Excavation of the jar was overseen by Marcie Handler, who was a doctoral student in classics at the University of Cincinnati at the time.

https://bbc.in/3uztuqU

Covid-19: UK in early stages of third wave - scientist

There are signs the UK is in the early stages of a third wave of coronavirus infections, a scientist advising the government has said.

By Katie Wright

Prof Ravi Gupta, from the University of Cambridge, said although new cases were "relatively low" the Indian variant had caused "exponential growth". He said ending Covid restrictions in England on 21 June should be postponed.

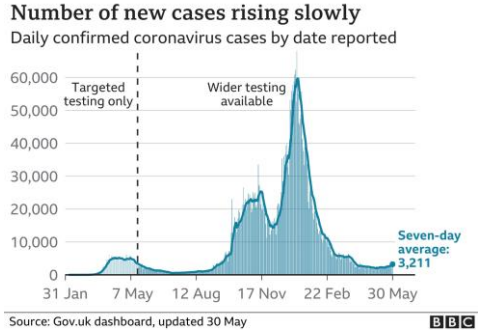
Environment Secretary George Eustice said the government could not rule out a delay to the planned lockdown easing. On Sunday, the UK reported more than 3,000 new Covid infections for a fifth successive day.

Prior to this, the UK had not surpassed that number since 12 April.

Asked on BBC Radio 4's Today programme whether the UK was already in a third wave of infections, Prof Gupta said: "Yes, there has been exponential growth in the number of the new cases and at least three-quarters of them are the new (Indian) variant.

"Of course the numbers of cases are relatively low at the moment - all waves start with low numbers of cases that grumble in the background and then become explosive, so the key here is that what we are seeing here is the signs of an early wave."

However, he said the number of people who have been vaccinated in the UK meant this wave would probably take longer to emerge than previous ones. "There may be a false sense of security for some time, and that's our concern."



Prof Gupta - a member of the New and Emerging Respiratory Virus Threats Advisory Group (Nervtag) - said ending restrictions in June should be delayed "by a few weeks whilst we gather more intelligence".

"If you look at the costs and benefits of getting it wrong, I think it is heavily in favour of delay, so I think that's the key thing," he added.

The final stage of the government's roadmap for lifting lockdown, which would see all legal limits on social contact removed, is due no earlier than 21 June.

However, Mr Eustice told the BBC the government had to take things "one step at a time". "We can't rule anything out. We know this has been a difficult pandemic, a dynamic situation. We have to make that judgment a couple of weeks before. "It will only be by then that we will see the impact of the latest easement we made on 17 May." A final decision on whether restrictions will be lifted will be reached on 14 June.

The Indian variant - known as B.1.617.2 - is thought to spread more quickly than the Kent variant, which was responsible for the surge in cases in the UK over the winter.

In some areas of England - including in Bolton, Blackburn, and Sefton in north-west England and Bedford, Chelmsford and Canterbury in the South East - the Indian variant is causing the majority of infections.

Dr Helen Wall, senior responsible officer for the vaccine programme in Bolton, said the rise in cases in the town was slowing but there was no room for complacency. She told BBC Breakfast: "It's only been a few days of the rates slowing down so we really are keen to keep pushing forwards and get the rates down further."

The seven-day rate in Bolton currently stands at 386.7 cases per 100,000, down from 452.8 on 21 May.

She said many of the areas with the highest increases had very young populations, and getting more of those vaccinated will help tackle the rise. "I think the age of (vaccine) eligibility going down every few days has really helped, and will really help us, if we can get those people through the doors to be vaccinated asap," she said.

In England, people aged over 30 are able to book to get the vaccine.

https://bit.ly/2TvN0aX

The Age of Autonomous Killer Robots May Already Be Here

Likely the first recorded death carried out by an autonomous killer robot

Alyse Stanley

A “lethal” weaponized drone “hunted down” and “remotely engaged” human targets without its handlers’ say-so during a conflict in Libya last year, according to a United Nations report first covered by New Scientist this week. Whether there were any casualties remains unclear, but if confirmed, it would likely be the first recorded death carried out by an autonomous killer robot.

In March 2020, a Kargu-2 attack quadcopter, which the agency called a “lethal autonomous weapon system,” targeted retreating soldiers and convoys led by Libyan National Army’s Khalifa Haftar during a civil conflict with Libyan government forces.

“The lethal autonomous weapons systems were programmed to attack targets without requiring data connectivity between the operator and the munition: in effect, a true ‘fire, forget and find’ capability,” the UN Security Council’s Panel of Experts on Libya wrote in the report.

It remains unconfirmed whether any soldiers were killed in the attack, although the UN experts imply as much. The drone, which can be directed to self-destruct on impact, was “highly effective” during the conflict in question when used in combination with unmanned combat aerial vehicles, according to the panel. The battle resulted in “significant casualties,” it continued, noting that Haftar’s forces had virtually no defense against remote aerial attacks.

The Kargu-2 is a so-called loitering drone that uses machine learning algorithms and real-time image processing to autonomously track and engage targets. According to Turkish weapons manufacturer STM, it’s specifically designed for asymmetric warfare and anti-terrorist operations and has two operating modes, autonomous and manual. Several can also be linked together to create a swarm of kamikaze drones.

Zachary Kallenborn, a research affiliate with the Unconventional Weapons and Technology Division of the National Consortium for the Study of Terrorism and Responses to Terrorism, said this incident could mark a terrifying turning point in global warfare. Writing for the Bulletin of the Atomic Scientists, he called the Kargu-2's deployment “a new chapter in autonomous weapons, one in which they are used to fight and kill human beings based on artificial intelligence.”

Meaning you can add “flying killer robots” to your list of plausible fears that science fiction predicted.

Several human rights watchdogs and non-governmental organizations have petitioned for a global ban on lethal autonomous weapons systems. However, a coalition of UN members, including the U.S., has fiercely argued that preemptive legal regulations aren’t necessary given our current technology’s limitations, effectively stalling any progress on the issue.