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# Water Found in Sunlight and Shadow on the Moon

***Observations by NASA's SOFIA telescope and Lunar Reconnaissance Orbiter reveal signs of water in sun-baked lunar soil, as well as in small, dark craters***

**By Leonard David**

For most of the space age, the moon has been considered a waterless world. In recent years, however, a steady drip-drip of discovery has shown that at least some parts of the moon—such as the large, permanently shadowed craters at its poles—contain significant deposits of water. This week, two new studies published in *Nature Astronomy* turn on the tap a bit more to the prospect of an unexpectedly watery moon.

The timing is good for NASA and other space agencies now planning ambitious human missions of lunar exploration and even settlement. After all, where there is water, there can be life—even if that life still requires space suits and radiation-hardened habitats.

## A Possible Sky-High Signal of Sun-Warmed Water

The first new whiff of lunar water emerged from data gathered by NASA's Stratospheric Observatory for Infrared Astronomy (SOFIA). This modified Boeing 747SP jet provides its 2.7-meter telescope a view above 99 percent of the atmosphere's obscuring water vapor—a unique capability that allows agile observations in infrared without the use of space-based facilities.

In late August 2018 a team led by Casey Honniball, a NASA Postdoctoral Program fellow at the agency's Goddard Space Flight Center and a researcher at the University of Hawaii at Manoa, used infrared instruments onboard SOFIA to study the sunlit lunar surface.

The observations, which spanned a mere 10 minutes, focused on a region at high southern latitudes near the moon's large crater Clavius, and they revealed a strong infrared emission at a wavelength of six microns (μm) from the crater and the surrounding landscape. Warmed by the sun, something on the lunar surface was reemitting the absorbed radiation just as molecular water—plain H2O—would.

"We are unaware of any other material reasonable for the Moon that exhibits a single spectral feature at 6 μm other than H2O," Honniball and her fellow researchers report in their new paper. The authors suggest that the putative water is most likely stored in naturally occurring volcanic glass or sandwiched between microscopic grains of rock dust.

Either scenario could provide shielding from the extreme temperatures and near-vacuum conditions on the moon's surface, allowing the water to persist. As to how it got there in the first place, no one is certain, but the leading explanation is that the water could have formed from free oxygen and hydrogen liberated from lunar rocks by micrometeorite impacts.

Using SOFIA is a new and unique approach for lunar science, Honniball says, but it is not the first time Earth-bound observations have revealed a six-micron emission from the moon. Balloon-borne observations by astronomers G. R. Hunt and J. W. Salisbury showed the spectral feature, she says. But Hunt and Salisbury made no mention of this in their paper on that research, published in 1969. Instead they focused on characterizing minerals on the lunar surface.

"Maybe they just didn't know they made a huge discovery," Honniball speculates.

## A Glass Half-Full

Honniball and her colleagues have already received additional time on SOFIA for follow-up observations. "We hope to map a majority of the moon to characterize the behavior of water," she says. "Does it vary across the lunar surface with lunar time of day and latitude? This will help us understand its sources and where it resides."

And that, in turn, could tell the world just how useful this newfound water might someday prove to be. Extraction will be straightforward if the water exists predominantly on the surfaces of rock grains: one will just need to scoop up lunar soil and subject it to moderate heating. If, however, the water is locked in glass, the material must be melted to release the water for collection—a much more energy-hungry process.

"Currently we do not have a good idea if the water we see with SOFIA is in amounts that make melting the glass worth it," Honniball says. "However, if we find abundances are high enough, this may be a more feasible option than mining water ice in permanently shadowed regions, which are extreme environments and hard to work in."

Jack Schmitt, a geologist who, as a member of the *Apollo 17* crew, remains the only professional scientist to have walked on the moon, says the SOFIA measurement may not be revealing true molecular water but something more fragile and transient.

"The question that I would ask," Schmitt says, "is if the SOFIA data may be related to the possible weak bonding of solar wind hydrogen with oxygen at the surface of grains of silicate glasses and minerals in the regolith rather than being actual molecular water?"

One product of such reactions could be hydroxyl, a molecule just one hydrogen atom short of water. Honniball, however, says the six-micron emission seen by SOFIA is not consistent with hydroxyl. Regardless of what substance is behind SOFIA's signal, Schmitt notes that basic chemistry should allow moisture to be wrung from even bone-dry lunar material.

"Heating of hydrogen-bearing regolith to several hundred degrees would result in some of the hydrogen reacting with oxygen in silicates to produce water almost anywhere on the moon," he says.

**Small Shadows, Immense Possibilities**

Another paper published alongside the SOFIA study in *Nature Astronomy* spotlights an uptick in the distribution of permanently shadowed areas on the moon—sunlight-shy places known as cold traps—in which extremely low temperatures could freeze and sequester water essentially indefinitely, allowing it to accumulate into significant deposits over geologic time.

Scientists have studied such lunar regions for decades for their water-harboring potential, but previous work has focused on large cold traps within huge craters at the moon's poles. In contrast, this latest result extends the range of considered cold trap sizes down to one centimeter in diameter.

Analyzing high-resolution imagery from NASA's Lunar Reconnaissance Orbiter, a team led by University of Colorado Boulder planetary scientist Paul Hayne found that such "micro" cold traps are far more prevalent than the well-studied large ones in the vicinity of the lunar poles. The new accounting raises the total surface area with the capacity to trap water to roughly 40,000 square kilometers—a pan-lunar region that, collectively, would be twice the size of Wales.

"The newly discovered micro cold traps are the most numerous on the moon, thousands of times more abundant than previously mapped cold traps," Hayne says. "If they are all full of ice, this could be a substantial quantity, perhaps more than a billion kilograms of water."

Hayne adds, however, that in situ sampling by robots or astronauts is required to properly assess their actual ice content. "What is really exciting about the micro cold traps is that they are much more accessible, which could enable more efficient extraction and utilization for both science and exploration purposes," he says. Indeed, this proliferation of tiny potential ice reservoirs could be much more accessible to future missions, Hayne says, because they exist in areas where a sunlight-bathed astronaut could comfortably

and safely use a tool to reach into a dangerously cold shadow to dig out any ice.

For now, to further judge the value of micro cold traps, Hayne and his colleagues will use a high-tech camera dubbed the Lunar Compact Infrared Imaging System, which will voyage to the moon on the first south polar lander mission of NASA's Commercial Lunar Payload Services program as early as 2022. The camera will take close-up pictures of micro cold traps for the first time and will measure their temperatures.

**Ground Truthing**

On one hand, SOFIA and micro cold trap studies are welcomed news. Nevertheless, the big picture remains the same, says Ian Crawford, a lunar expert at Birkbeck, University of London.

Clearly, he says, the more easily accessible water there is on the moon, the greater the opportunities for its on-the-spot extraction and use to sustain immediate exploration efforts.

Eventually the development of lunar water as a resource could spark an entire extraterrestrial economy in which the substance would become a lucrative feedstock for rocket fuel and other precious consumables. For now, though, "'ground truth' measurements are urgently required to confirm inferences made on the basis of remote-sensing measurements," Crawford says.

Angel Abbud-Madrid, director of the Colorado School of Mines' Center for Space Resources in Golden, Colo., also flags direct measurements as the most important next step to follow from the new findings. "What is now needed is to touch the lunar surface and gather detailed ground truth," he says.

"Confirmation of not just the existence of water ice but its morphology, concentration, distribution and abundance is a must to proceed with existing exploration and resource-utilization plans."

***https://bit.ly/2JfMVCV***

# Scientists Reveal What May Be the Largest Flying Bird Ever

***Researchers from California and China identified the 50-million-year-old bone of a giant bird that lived in Antarctica***

**By Riley Black**

Imagine an albatross with a hacksaw for a mouth. Set that strange creature about 50 million years in the past and you've got the image of a pelagornithid, a group of ancient avians that included some of the largest flying birds of all time. And now paleontologists have uncovered in that group what may be the largest known flying birds ever, with wingspans of roughly 20 feet.

***A pelagornithid, likely the largest flying bird that ever lived, soared over the open ocean.*** **(Brian Choo)**

The new study documenting the birds, published today in *Scientific Reports,* is the result of a fossil detective story spanning from Antarctica to California. By comparing a pair of polar fossils to the remains of related birds, paleontologists have been able to identify the early history of enormous fliers that were some of the first birds capable of soaring across seas.

During the 1980s, University of California Berkeley paleontologist Peter Kloess says, scientists searching for Antarctic fossils found some delicate bird bones—a jaw and part of a foot from an ancient bird—on Seymour Island. Those bones then made a long journey to California, but their story was only just starting.

The jaw and foot bone were just two of a huge collection kept at the University of California Riverside. In 2003, however, the more than 10,000 fossils of the Riverside collection were transferred to the

University of California Museum of Paleontology at the Berkeley campus, the bird bones among them. And they stood out. “Bony-toothed jaws are rare in the vertebrate record,” senior museum scientist Pat Holroyd says. “When you see one, you remember it and mentally file it away for later.”

The bird jaw, which came from a rock formation laid down over 37 million years ago, looks almost like a woodcutting tool rather than a bone. The jaw has a series of large and small spikes, outgrowths of the beak that have a passing resemblance to teeth. On a living animal, the points would have been covered in keratin and given the bird a sinister saw-toothed smile. That feature immediately identified the jaw as belonging to a pelagornithid, also known as bony-toothed birds that have a very long fossil record.

The oldest pelagornithids evolved about 56 million years ago, and the most recent flew through the skies about two million years ago. Their fossils are found all over the world.

When Kloess visited the University of California Museum of Paleontology to pore over the collections, Holroyd pointed out the bird’s jaw bone. The jaw seemed interesting enough for its rarity, but there was much more to the story. “I started this research project thinking it would be a short descriptive paper on a jaw fragment to add to the knowledge of a cool group of birds,” Kloess says, adding, “I had no idea that it would represent a giant individual.”

Researching the jaw set Kloess and colleagues looking for additional bony-toothed bird bones in the museum collections. The researchers were in luck. In addition to the jaw, the collection included a foot bone—technically called a tarsometatasus—from another Antarctic pelagnornithid. The bone came from another large individual, but its real importance was in its age. A different researcher who previously studied the foot bone labeled it as belonging a rock unit called the Submeseta Formation, which is between 43 and 35 million years old, but by looking over where the fossil was found the researchers reassigned it to a rock layer in the La Meseta Formation, about 50 million years old. This falls within a time called the Eocene, when life had recovered from the asteroid-induced mass extinction and was thriving again. Together, the foot bone and the jaw indicate that large bony-toothed birds thrived in the Antarctic for millions of years.

Paleontologists have found bony-toothed birds from places all over the world, from New Zealand to South Carolina. The newly-described Antarctic fossils, though, are the oldest known and hint that these birds quickly diversified into a range of sizes within six million years of their origin.

By 50 million years ago, there were bony-toothed birds from the size of a modern-day albatross to giants with wingspans twice as wide. The next closet fossil contender is an extinct vulture relative called *Argentavis*, which had a wingspan between 16 and 20 feet. The close competition might be a signal that these birds were pushing the boundaries of flight. Previous studies have calculated that the largest of the bony-toothed birds were near the limit of how big a bird could get and still fly, meaning these birds are the strongest contenders for the largest flying birds to ever soar.

And matched with the new data on the age of the fossils, Kloess says, “we can say that giant pelagornithids appeared earlier than previously known and that Antarctica saw a range of pelagornithid sizes from the early to late Eocene.” Small to large, bony-toothed birds were an important part of ancient Antarctic ecosystems.

Those impressive wings would have allowed the pelagornithids to range far and wide, soaring long distances on outstretched wings. That helps explain why fossils from various species of pelagornithids have been found all over the world during their extended evolutionary tenure. These long-lived and successful birds

likely using their spiky jaws to feed on fish and squid snatched from just beneath the surface.

In the case of the birds described in the new study, the avians lived in an environment that would have seemed strange in some ways and familiar in others. “Eocene Antarctica was much warmer than we see today,” Kloess says, with carpets of ferns and stands of conifers on land that sheltered prehistoric marsupials and even frogs. Some of the other birds might have seemed familiar, though. Ancient relatives of penguins, albatrosses, and falcons have been found from these rocks, with the bony-toothed birds adding to the flock.

Naturally, the existence of these big birds raises the question of whether there might be larger fliers out there, especially because fossils of the ancient seabirds are so rare. “It’s hard to know if we have yet found the largest pelagornithids,” Holroyd says.

***https://bit.ly/3e8MYfn***

## Scientists reveal new clues into how Earth got its oxygen

***Scientists are still trying to understand exactly how—and why—our planet got this beautifully oxygenated atmosphere***

**by Louise Lerner**

Earth’s thin shell of oxygen atmosphere keeps us alive, though we still don’t know exactly how it formed. A new study from the University of Chicago reveals clues in the role that iron had to play. Credit: NASA

For much of Earth's four and a half billion years, the planet was barren and inhospitable; it wasn't until the world acquired its blanket of oxygen that multicellular life could really get going. But scientists are still trying to understand exactly how—and why—our planet got this beautifully oxygenated atmosphere.

"If you think about it, this is the most important change that our planet experienced in its lifetime, and we are still not sure exactly how this happened," said Nicolas Dauphas, the Louis Block Professor of Geophysical Sciences at the University of Chicago. "Any progress you can make toward answering this question is really important."

In a new study published Oct. 23 in *Science*, UChicago graduate student Andy Heard, Dauphas and their colleagues used a pioneering technique to uncover new information about the role of oceanic iron in the rise of Earth's atmosphere. The findings reveal more about Earth's history, and can even shed light on the search for habitable planets in other star systems.

Scientists have painstakingly recreated a timeline of the ancient Earth by analyzing very ancient rocks; the chemical makeup of such rocks changes according to the conditions they formed under.

"The interesting thing about it is that prior to the permanent Great Oxygenation Event that happened 2.4 billion years ago, you see evidence in the timeline for these tantalizing little bursts of oxygen, where it looks like Earth was trying to set the stage for this atmosphere," said Heard, the first author on the paper. "But the existing methods weren't precise enough to tease out the information we needed."

It all comes down to a puzzle.

As bridge engineers and car owners know, if there's water around, oxygen and iron will form rust. "In the early days, the oceans were full of iron, which could have gobbled up any free oxygen that was hanging around," Heard said. Theoretically, the formation of rust should consume any excess oxygen, leaving none to form an atmosphere.

Heard and Dauphas wanted to test a way to explain how oxygen could have accumulated despite this apparent problem: they knew that some of the iron in the oceans was actually combining with sulfur coming out of volcanoes to form pyrite (better known as

fool's gold). That process actually releases oxygen into the atmosphere. The question was which of these processes "wins."

To test this, Heard used state-of-the-art facilities in Dauphas' Origins Lab to develop a rigorous new technique to measure tiny variations in iron isotopes in order to find out which route the iron was taking. Collaborating with world experts at the University of Edinburgh, he also had to flesh out a fuller understanding of how the iron-to-pyrite pathway works. ("In order to make sulfide and run these experiments, you need understanding colleagues, because you make labs smell like rotten eggs," Heard said.) Then, the scientists used the technique to analyze 2.6 to 2.3 billion-year-old rocks from Australia and South Africa.

Their analysis showed that, even in oceans that should have tucked away a lot of oxygen into rust, certain conditions could have fostered the formation of enough pyrite to allow oxygen to escape the water and potentially form an atmosphere.

"It's a complicated problem with many moving parts, but we've been able to solve one part of it," said Dauphas.

"Progress on a problem this enormous is really valuable to the community," Heard said. "Especially as we're starting to look for exoplanets, we really need to understand every detail about how our own earth became habitable."

As telescopes scan the skies for other planets and find thousands, scientists will need to narrow down which to explore further for potential life. By learning more about the way that Earth became habitable, they can look for evidence of similar processes on other planets. "The way I like to think about it is, Earth before the rise of oxygen is the best laboratory we have for understanding exoplanets," said Heard.

***More information:*** *Andy W. Heard et al. Triple iron isotope constraints on the role of ocean iron sinks in early atmospheric oxygenation, Science (2020).* *DOI: 10.1126/science.aaz8821*

*https://bit.ly/3jI76WX*

# Solo stars among the genes

***From maggots' movements to voles' roles, sometimes single genes can have outsize effects on behavior***

**By Emily Underwood**

If you want to annoy a geneticist, talk about a single gene as if it, alone, is responsible for a complex behavior — whom a person is sexually attracted to, say, or whether or not they believe in God. Even for psychiatric diseases that run strongly in families and have a large genetic component, such as depression and schizophrenia, decades of research have shown that there's rarely one lone gene to blame. Instead, our behavioral susceptibilities and strengths lie in many genes with small effects, combined with environments and experiences.

"It's a mistake to buy into the idea that a gene is single-handedly responsible for just about anything," says biologist Joel Levine of the University of Toronto — be it in a human being, a fruit fly or a mouse.

But some genes stand out as powerful regulators of behavior. The following examples, scattered across the animal kingdom, show how tweaking a single gene's activity can lead to profound behavioral changes. People carry versions of some of these genes, so they may even hold lessons for our own species.

## The roaming gene

Marla Sokolowski discovered her life's work early, in an undergraduate biology class. Watching fruit fly maggots wriggling in a petri dish, she noticed that some of the larvae were more active, crawling farther in search of food than their couch-potato-like companions. Sokolowski, now a behavior geneticist at the University of Toronto, dubbed the more active maggots "rovers" and the more sedentary ones "sitters," and went on to demonstrate

that the difference could be traced to a single gene, called *foraging*, or *for*.

The *foraging* gene encodes an enzyme known as a cGMP-dependent protein kinase, or PKG; various forms of it can be found in animals ranging from single-celled paramecia to people. The enzyme's job is to add phosphates to important molecules in cells, boosting or inhibiting different chemical reactions. And the difference between rovers and sitters, it turns out, lies in how active the *foraging* gene is, and thus how much of the enzyme gets made. The more PKG in a maggot's tiny brain, the farther the maggot roams.

Since the gene's discovery, Sokolowski and colleagues have found that activity of *foraging* changes over time as a maggot develops, as well as in response to environmental conditions such as lack of food. "The context matters. So it could be how dense the population is for the larva, how much food is available, how many other friends are around, what the social environment is," says Sokolowski, who coauthored a 2019 article on *forager* in the *Annual Review of Genetics*. The gene also influences a range of other behaviors, such as pain response. When a parasitic wasp inserts its stinger into a fruit fly larva, attempting to lay eggs inside it, for example, rovers respond more vigorously, rolling away from the pain, Sokolowski and colleagues have shown.

Variations of *forager* have been found in many other species, including mice, ants and people. In honeybees, increased *forager* activity levels trigger young nurse bees that care for the queen to leave the hive to become worker bees. In people, a *forager*-like gene called *PRKG1* may influence responses to early life traumas: Two broad scans of variants in the human genome (an approach known as a genome-wide association study, or GWAS) reported that people who had a certain version of *PRKG1* and also experienced childhood trauma were slightly more prone to substance abuse.

Sokolowski suspects that the gene might affect other human behavioral patterns: In a 2019 study, she and her colleagues asked 437 college students to gather virtual berries in a computer game, and found that different *forager* variants were linked to tendencies to either stay put or to boldly explore their surroundings, a pattern similar to the fruit fly rovers and sitters.

**Stay home or play the field?**

With their soft brown fur and plump bodies, prairie voles and meadow voles look pretty similar. But the two species live strikingly different lifestyles: Prairie voles tend to form lifelong bonds with their mates, while meadow voles are more promiscuous, apt to play the field of potential partners.

The difference lies in a gene called *avpr1a*, which encodes a protein that serves as a receptor for the hormone vasopressin. Like its closely related molecular cousin oxytocin, vasopressin plays a vital role in social bonding, attachment and parental care. "When you look at the brains of those two species and ask, where is the receptor for vasopressin, what parts of the brain can vasopressin unlock, it's very different across the two species," says neuroscientist Zoe Donaldson of the University of Colorado.

In 2004, neuroscientist Larry Young and colleagues at Emory University injected a virus carrying the vasopressin receptor gene into a region of meadow vole brains where that gene isn't generally very active. Compared with voles that didn't get the gene, the creatures were much more likely to stick with their first sexual partner than flit from liaison to liaison.

That such a behavioral shift can result simply from changing the distribution of the vasopressin receptor in the brain has important implications for the evolution of mating systems, Donaldson says. Monogamy, for example, is a complex behavior with many

different components: preferring the company of one's partner, sharing the burdens of parenting and being aggressive toward potential competitors. Vasopressin, it turns out, influences each of these components via different brain regions, so changing where *avpr1a* is activated enables mating styles to flexibly adapt as environmental conditions change, Donaldson says.

***Meadow voles (left) are promiscuous, while prairie voles (right) tend to form lifelong bonds. This difference in mating habits has been traced to a single gene. Credits: John M. Coffman (Left) Tom Mchugh (Right) / Science Source***

Even among the famously faithful prairie voles, some males stray, and the vasopressin receptor appears to be involved. In 2015, biologist Steven Phelps of the University of Texas at Austin found that males with fewer vasopressin receptors in a brain region involved in spatial memory tended to wander farther from their own territories — and have sex with more females. Under some conditions, this could be an evolutionary boon: When prairie vole populations are high, the wandering males may sire more offspring because they have more opportunities to be unfaithful. But when vole populations crash, males that stay close to home to defend their mates may have a better chance of passing their genes to the next generation.

Donaldson is now studying the neural circuits responsible for bonding in prairie voles. She hopes that what she finds will offer understanding into human bonding, too, including neurodevelopmental conditions that are marked by social deficits, such as autism and schizophrenia. (Some studies have reported links between these conditions and levels of vasopressin or oxytocin.) She recently found a cluster of neurons that fire only when the voles run to meet their mates, in what may be a sort of neural signature for longing. Maybe, she speculates, the work could help illuminate causes of complicated grief, a severe, prolonged reaction to loss. "Grieving is painful, but it is also terrible for your health," she says. "Is there a way that we can mitigate some of those health impacts?"

**Off with her head**

Disturb a nest of stinging South American red fire ants (*Solenopsis invicta*) and you're likely to end up covered in swollen, painful welts. The insects don't limit their aggression to outsiders: Thanks to variations in a cluster of genes known as the *Gp-9* supergene, the species is split into two groups with radically different social structures. And when they meet up, murder often ensues.

The first group, called monogyne ants, carries two identical copies of *Gp-9*. These ants will accept only one ruler: a large, fat queen that can lay many eggs. The second group, called polygyne ants, has two different variants of the supergene. These ants are willing to follow many different, smaller queens, and even queens from other nests as long as they, too, are polygyne. If the polygyne ants encounter a monogyne queen, they assassinate her.

But how do the ants know if a queen is genetically different from themselves? The *Gp-9* supergene does many things — it regulates a whole suite of social behaviors — and one of them is to produce an odor receptor. That molecule helps ants detect when a queen smells "off" — foreign — or like kin, biologists Michael Krieger and Kenneth Ross of the University of Georgia reported in 2001. More recently, biologist Laurent Keller of the University of Lausanne in Switzerland and colleagues found that it's not just *S. invicta* whose social organization depends on the *Gp-9* supergene. It also affects an entire group of South American fire ants that branched off from other ant species half a million years ago.

It's hard to say for sure why a supergene that causes so much infighting has endured so long, but scientists know that the two social structures provide different advantages, depending on the circumstances. Colonies of *S. invicta* with multiple queens, for example, are often many times as dense as single-queen colonies, and far more difficult to eradicate. Another possibility is that *Gp-9* is what evolutionary biologist and author Richard Dawkins hypothesized as a " greenbeard gene" — a gene that gives some members of a species a distinctive, easily perceptible trait (say, a green beard), which allows others with that same trait to recognize and favor individuals genetically similar to themselves.

If the notion of a single gene overturning society sounds discomfiting, never fear: Thus far, the only other examples of greenbeard genes found in nature are in relatively simple organisms, such as slime molds.

**The original clock gene**

A female *Drosophila melanogaster* fruit fly lays about 100 eggs per day: Within 10 days or so, pale maggots emerge, grow, pupate and then metamorphose into winged insects. In the 1970s, Ron Konopka and Seymour Benzer at Caltech identified three types of mutant fly strains in which the timing of these events was topsy turvy.

In one of the three, flies emerged from their pupal cases earlier in the day than normal, in another, later than normal — and in the third, the flies emerged with no clear daily rhythm. Activity of the hatched flies was similarly perturbed — as though they were living out shorter days, longer days or were blind to daily cycles entirely. The reason: Mutations in a gene that the scientists dubbed *period* had messed up the flies' internal clocks, speeding up, slowing down or completely eliminating the circadian rhythms that control how much they moved around throughout the day.

At the time, the notion that a single gene could affect something as complex as an animal's internal biological clock was "heretical," Levine says. But a small group of researchers dived in to study the *period* gene and, despite facing skepticism from other geneticists, three of them — Jeffrey C. Hall, Michael Rosbash and Michael W. Young — went on to receive the 2017 Nobel Prize in Physiology or Medicine for isolating and cloning the *period* gene and demonstrating that it regulates biological clocks by encoding a protein that builds up in cells at night, and breaks down during the day.

The *period* gene is far from being the only gene underpinning circadian rhythms, notes Levine, who worked as a postdoc in Hall's lab. "Nobody ever believed that *period* was the whole story," he says — including its discoverers who, along with others, found a number of other genes crucial to the workings of the body's internal clocks. But *period's* discovery flung open field of the molecular machinery of clocks to further study, including Levine's own work (also with Drosophila) on how social interaction affects circadian rhythms.

Scientists now know that myriad species, including people, carry versions of the *period* gene. As the first demonstration that altering the function of a single gene could influence complex behaviors, Levine says, "the scope of that original finding was enormous."

***https://wb.md/3oIO3zt***

## COVID-19 Taking a Toll on Med Students, Survey Shows

***Many medical students believe it will affect how they practice medicine long after the pandemic subsides***

**Megan Brooks**

The COVID-19 pandemic has dramatically altered medical students' experience in 2020, and many believe it will affect how they practice medicine long after the pandemic subsides, according

to the more than 2600 US medical students who responded to the the *Medscape Medical Student & Life Education Report 2020*.

As it has for physicians, COVID-19 has weighed heavily on students, with about 1 in 10 reporting that they have personally known a resident, faculty member or medical professional who died from the illness.

Only about half of students (45%) said they are satisfied with how their institutions are handling the pandemic.

Despite pandemic-related hardships, slightly more than half of the students said the pandemic has only reinforced their decisions to become physicians; 38% said it had no effect and just 8% said it weakened their choice to pursue medicine as a career.

**Graduation Concerns**

As for graduating on time, 43% of students are at least moderately concerned that COVID-19 interruptions will delay their graduation, women more so than men (47% vs 36%).

The vast majority (87%) of students said that COVID-19 had at least some negative effect on their experience taking United States Medical Licensing Examination (USMLE) tests.

Despite COVID-19 interruptions, more than half (58%) of medical students said they felt prepared or very prepared for their USMLE test, which is comparable to the 2018 survey.

About 2 in 5 students think COVID-19 interruptions and changes to their education will have at least a moderately negative effect on their ability to practice medicine as they launch their careers, with more women than men feeling this way (46% vs 36%).

About one third of students said COVID-19 has had at least some effect on their choice of specialty while two thirds said it's had no influence.

Not much has changed in terms of the most popular specialities since Medscape's 2018 report on medical student life and education. The top five choices remain family medicine (12%), internal medicine (11%), emergency medicine (11%), pediatrics (10%), and psychiatry (7%).

This year, students overwhelmingly said that personal interest in the field was the biggest factor in their choice. A slightly greater share of women (76% vs 68% of men) cited this reason, while men more often cited lifestyle (20% vs 15%) — similar to the 2018 survey.

Future earnings remain at least moderately important in choosing a speciality for the vast majority of students (84%) with more men than women feeling this way.

For both women and men, the desire to help those in need is the top factor influencing their decision to go to medical school (87% and 85%), followed by feeling a call toward medicine (68% and 63%), interest in science (67% and 78%), and prestige of a medical career (27% and 42%).

Overall, the prestige of a career in medicine has become somewhat less of a factor since 2016, when 37% of students cited it, compared with 33% in 2020.

What are the biggest challenges in medical school? The ability to master the clinical information ranked number one for both men and women. Work-life balance was the next most common concern for men, whereas passing educational requirements and mandatory tests was next for women.

Debt also weighs heavy on medical students. Half of students surveyed are expecting to have more than $200,000 of debt when they finish their education. That's up from 45% 2 years ago.

**Burned Out Already**

Burnout among physicians is nothing new and medical students are not immune to it. In line with 2018, about three quarters of survey respondents said they have felt burned out at least sometimes.

These feelings were more common in women than men (81% vs 68%) and among third- and fourth-year students (80% vs 77%, respectively) compared with first-year students (68%).

"If the burnout begins as early as medical school and then you still have 4 more years of residency where the burnout is supposed to be even higher, that is not a good start," commented Emily Kahoud, a third-year medical student at Rutgers University, in the report. "We don't want students graduating medical school already burned out. That is something everyone should be concerned about."

Most medical students have neither experienced nor witnessed unwanted verbal, physical, or sexual advances from patients, other students or faculty, similar to what was reported in 2018.

However, half of women reported experiencing some kind of bias from faculty, students, or patients during medical school. Gender bias was reported by 40% of women (vs 9% of men) and race/ethnicity bias by 22% of women (vs 15% of men).

Nearly half of students (46%) said they considered leaving medical school at some point, including 49% of women and 41% of men.

More than half (60%) said they have at least sometimes doubted their ability to be a competent practicing physician, women more so than men (64% vs 55%).

***https://bit.ly/37UCD5r***

## A 'genomic Rosetta stone' for discovering the rules of gene regulation

***How DNA is used is as important as what it says.***

**by Lori Dajose**

As early as 1975, biologists discovered that the protein-coding parts of the chimpanzee and human genomes are more than 99 percent identical. Yet, chimpanzees and humans are clearly different in significant ways. Why?

The answer lies in the fact that how DNA is used is as important as what it says. That is, the genes that make up a genome are not always being used; they can be turned on or off or dialed up or down over time, and they interact with one another in complex ways. Some genes encode instructions for producing specific proteins and others encode information about regulating other genes. Now, researchers in the laboratory of Rob Phillips, the Fred and Nancy Morris Professor of Biology and Biophysics, have developed a new tool for determining how various genes in the common bacterium Escherichia coli are regulated. Though E. coli has been used as a model organism in biology and bioengineering for decades, researchers understand the regulatory behavior of only about 35 percent of its genes. The new method from the Phillips laboratory sheds light on how nearly 100 previously uncharacterized genes are regulated and lays the foundation for studying many others.

A paper describing the new technique appears in the journal *eLife*.

Imagine you could read the alphabet and punctuation of some new language, but you could not understand what individual words meant or any of the rules of grammar. You could read a book and recognize each letter you read without having any comprehension of what a sentence or paragraph was saying. This is analogous to the challenge faced by biologists in the modern genomic era: Sequencing an organism's genome is now rapid and straightforward, but actually understanding how each gene is regulated is much more difficult. An understanding of gene regulation is key to understanding health and disease, and is important if we are to one day repurpose cells so they can do things that we have designed them to do.

"We've developed a general tool that researchers could use on nearly any microbial organism," says Phillips. "Our dream is that someone like Victoria Orphan [James Irvine Professor of Environmental Science and Geobiology] could go down to the ocean floor and come back with some never-before-seen bacterium, and we could use our tool on it to determine not only the sequence of its genome but how it is regulated."

In the new method, researchers make systematic perturbations to the genome, and see what happens. Essentially, the equivalent of typographical errors are made in the genome, and the impact of those typos on cellular function is observed. For example, if you replace the letter "k" in the word "walk" with the letter "x" to make "walx," the intent of the original word is still fairly clear. This is not the case if you swap the letter "w" for a "t" to produce "talk." This suggests that the letter "w" carries important information about the meaning of the original word.

In the same way, making changes to a genome using the DNA alphabet allows researchers to figure out which letters are most important for the correct "meaning."

To validate their method, Phillips and colleagues first examined 20 particular E. coli genes that researchers already knew how to turn off and on. Their method correctly characterized these 20 genes. Next, the team moved on to 80 other, less-understood genes to understand how they work as well.

For now, the method has only been used on bacterial cells, but ultimately Phillips envisions being able to examine eukaryotic cells (such as human cells), which are more complex, with a modified version of the method.

"This was a decade-long project supported by the NIH Director's Pioneer Award, and required a sustained hard effort and funding," says Phillips. "This is the kind of project where there are no quick results."

The paper is titled "Deciphering the regulatory genome of Escherichia coli, one hundred promoters at a time."

***More information:*** *William T Ireland et al. Deciphering the regulatory genome of Escherichia coli, one hundred promoters at a time, eLife (2020). DOI: 10.7554/eLife.55308*

***https://wb.md/3e8UWVI***

# Let's Not Get Too Excited About Having a Vaccine Really Soon

***There are some practical reasons for that that don't get enough attention.***

**Arthur L. Caplan, PhD**

Hi. I'm Art Caplan. I'm at the Division of Medical Ethics at New York University's Grossman School of Medicine.

Have you heard enough about vaccines lately? The news about vaccines is everywhere. We have the president hoping and promising that a vaccine will be around soon to work our way out of this pandemic. Other health officials, like Tony Fauci, Dr [Deborah] Birx, and many others think that vaccines are coming — maybe not by the election date, but hopefully soon.

We hear about pressure being put on the FDA to allow for early approval of vaccines. We even have — imagine this — pharmaceutical companies making vaccines, signing pledges that say they're not going to try to get approval for anything until they're convinced that the science holds up for efficacy and safety.

Who would have thought that, at the end of the day, it might be the manufacturers who are holding the line about when to say a vaccine is ready to go? But remember, aside from doing the right thing, their reputation is on the line and so is their liability. I'm sure they want to make sure that the FDA is satisfied and that they're satisfied before anybody gets the vaccine.

Well, despite this vaccine obsession, I don't think vaccines are going to be working our way out of the pandemic anytime soon. There are some practical reasons for that that don't get enough attention. Among the leading vaccine candidates, a couple of them have never actually been used to make a vaccine; they are new platforms that involve RNA. We'll see if they work. They may not.

We can't be sure that the first vaccines out of the box are going to be effective.

Second, [regarding] how effective they're going to be, what if they only gave immunity for 2 months or 3 months and then it faded out? That would not be useful for large percentages of the population. That might be something we would try if you are a frontline nursing home worker or a frontline anesthesiologist having to intubate people on a regular basis. However, a short-duration vaccine is not the answer.

We also have a number of these early vaccines that require extreme refrigeration and are difficult to handle. They require almost liquid nitrogen temperatures. Many places can't store them and many trucks can't move them. There's no guarantee that even if they got approved, that they would be widely available anytime soon because they're very difficult to handle.

A number of these vaccines require two shots, maybe a month apart: a primer and a booster. Although that's okay, it slows down the ability to get the vaccine out.

It's well known that many people, having got a first vaccine, don't come back for the second vaccine. We've seen that with the cervical cancer vaccine for HPV. That has been a three-shot vaccine around the world. Many women and some men who get it fail to appear for the second and third shot. It's hard to get good compliance when you require more than one shot.

Now, some of the vaccines are just one shot and don't require super-refrigeration, but they are behind. They're not moving along as fast in the process as some of these other ones.

From a practical point of view — forgetting the arguments about who should go first and whether we should share vaccine supply with other countries — the reality is that the early contenders have practical limits on manufacturing them in big amounts, moving them around the country, having enough vials and needles to administer them, refrigerating them, and making sure that, if it's a two-dose situation, people come back and get the required second dose.

We also don't know how long they'll last. That could collapse the ability of vaccines to really make a big dent in the pandemic.

I hope we get a vaccine that works. I hope we get one that works at 50% or better. That would really start to build us toward herd immunity. Whether it's the first one that comes out for approval, the third one, or the fifth one remains unknown and unclear.

Even if we do get an approved vaccine, forget about Election Day, forget about the end of the year. We're well into next year before you could have large amounts of vaccine out and available to use in large numbers of Americans, much less people around the world.

Let's hope there's a vaccine. But remember, we're probably stuck with masking, distancing, isolation, handwashing, and behavior change for some time, even after a vaccine gets approved. That's just the practical reality of vaccine manufacturing, vaccine distribution, and the fragility of some of the new forms of vaccines that are being pursued now.

I'm Art Caplan at the Division of Medical Ethics at New York University's Grossman School of Medicine. Thank you for watching.

*Arthur L. Caplan, PhD, is director of the Division of Medical Ethics at New York University Langone Medical Center and School of Medicine. He is the author or editor of 35 books and 750 peer-reviewed articles as well as a frequent commentator in the media on bioethical issues.*

***https://bit.ly/3jHMazd***

## The Epigenetic Secrets Behind Dopamine, Drug Addiction and Depression

***New research links serotonin and dopamine not just to addiction and depression, but to the ability to control genes.***

**R. Douglas Fields**

As I opened my copy of *Science* at home one night, an unfamiliar word in the title of a new study caught my eye: dopaminylation. The term refers to the brain chemical dopamine's ability, in addition to transmitting signals across synapses, to enter a cell's nucleus and control specific genes. As I read the paper, I realized that it completely upends our understanding of genetics and drug addiction. The intense craving for addictive drugs like alcohol and cocaine may be caused by dopamine controlling genes that alter the brain circuitry underlying addiction. Intriguingly, the results also suggest an answer to why drugs that treat major depression must typically be taken for weeks before they're effective. I was shocked by the dramatic discovery, but to really understand it, I first had to unlearn some things.

"Half of what you learned in college is wrong," my biology professor, David Lange, once said. "Problem is, we don't know which half." How right he was. I was taught to scoff at Jean-Baptiste Lamarck and his theory that traits acquired through life experience could be passed on to the next generation. The silly traditional example is the mama giraffe stretching her neck to reach food high in trees, resulting in baby giraffes with extra-long necks. Then biologists discovered we really can inherit traits our parents acquired in life, without any change to the DNA sequence of our genes. It's all thanks to a process called epigenetics — a form of gene expression that can be inherited but isn't actually part of the genetic code. This is where it turns out that brain chemicals like dopamine play a role.

**Quantized**

A regular column in which top researchers explore the process of discovery. This month's columnist, R. Douglas Fields, is a neuroscientist studying the cellular mechanisms of brain development and plasticity.

All genetic information is encoded in the DNA sequence of our genes, and traits are passed on in the random swapping of genes between egg and sperm that sparks a new life. Genetic information and instructions are coded in a sequence of four different molecules (nucleotides abbreviated A, T, G and C) on the long double-helix strand of DNA. The linear code is quite lengthy (about 6 feet long per human cell), so it's stored neatly wound around protein bobbins, similar to how magnetic tape is wound around spools in cassette tapes.

Inherited genes are activated or inactivated to build a unique individual from a fertilized egg, but cells also constantly turn specific genes on and off throughout life to make the proteins cells need to function. When a gene is activated, special proteins latch onto DNA, read the sequence of letters there and make a disposable copy of that sequence in the form of messenger RNA. The messenger RNA then shuttles the genetic instructions to the cell's ribosomes, which decipher the code and make the protein specified by the gene.

But none of that works without access to the DNA. By analogy, if the magnetic tape remains tightly wound, you can't read the information on the cassette. Epigenetics works by unspooling the tape, or not, to control which genetic instructions are carried out. In epigenetic inheritance, the DNA code is not altered, but access to it is.

I was shocked by the dramatic discovery, but to really understand it, I first had to unlearn some things.

This is why cells in our body can be so different even though every cell has identical DNA. If the DNA is not unwound from its various spools — proteins called histones — the cell's machinery can't read the hidden code. So the genes that would make red blood corpuscles, for example, are shut off in cells that become neurons.

How do cells know which genes to read? The histone spool that a specific gene's DNA winds around is marked with a specific chemical tag, like a molecular Post-it note. That marker directs other proteins to "roll the tape" and unwind the relevant DNA from that histone (or not to roll it, depending on the tag).

It's a fascinating process we're still learning more about, but we never expected that a seemingly unrelated brain chemical might also play a role. Neurotransmitters are specialized molecules that transmit signals between neurons. This chemical signaling between neurons is what enables us to think, learn, experience different moods and, when neurotransmitter signaling goes awry, suffer cognitive difficulties or mental illness.

Serotonin and dopamine are famous examples. Both are monoamines, a class of neurotransmitters involved in psychological illnesses such as depression, anxiety disorders and addiction. Serotonin helps regulate mood, and drugs known as selective serotonin reuptake inhibitors are widely prescribed and effective for treating chronic depression. We think they work by increasing the level of serotonin in the brain, which boosts communication between neurons in the neural circuits controlling mood, motivation, anxiety and reward. That makes sense, sure, but it is curious that it usually takes a month or more before the drug relieves depression.

Dopamine, on the other hand, is the neurotransmitter at work in the brain's reward circuits; it produces that "gimme-a-high-five!" spurt of euphoria that erupts when we hit a bingo. Nearly all addictive drugs, like cocaine and alcohol, increase dopamine levels, and the chemically induced dopamine reward leads to further drug cravings. A weakened reward circuitry could be a cause of depression, which would help explain why people with depression may self-medicate by taking illicit drugs that boost dopamine.

In epigenetic inheritance, the DNA code is not altered, but access to it is.

But (as I found out after reading that dopaminylation paper), research last year led by Ian Maze, a neuroscientist at the Icahn School of Medicine at Mount Sinai, showed that serotonin has another function: It can act as one of those molecular Post-it notes. Specifically, it can bind to a type of histone known as H3, which controls the genes responsible for transforming human stem cells (the forerunner of all kinds of cells) into serotonin neurons. When serotonin binds to the histone, the DNA unwinds, turning on the genes that dictate the development of a stem cell into a serotonin neuron, while turning off other genes by keeping their DNA tightly wound. (So stem cells that never see serotonin turn into other types of cells, since the genetic program to transform them into neurons is not activated.)

That finding inspired Maze's team to wonder if dopamine might act in a similar way, regulating the genes involved in drug addiction and withdrawal. In the April *Science* paper that so surprised me, they showed that the same enzyme that attaches serotonin to H3 can also catalyze the attachment of dopamine to H3 — a process, I learned, called dopaminylation.

Together, these results represent a huge change in our understanding of these chemicals. By binding to the H3 histone, serotonin and dopamine can regulate transcription of DNA into RNA and, as a consequence, the synthesis of specific proteins from them. That turns these well-known characters in neuroscience into double agents, acting obviously as neurotransmitters, but also as clandestine masters of epigenetics.

Maze's team naturally began exploring this new relationship. First they examined postmortem brain tissue from cocaine users. They found a decrease in the amount of dopaminylation of H3 in the

cluster of dopamine neurons in a brain region known to be important in addiction: the ventral tegmental area, or VTA.

That turns these well-known characters in neuroscience into double agents.

That's just an intriguing correlation, though, so to find out if cocaine use actually affects dopaminylation of H3 in these neurons, the researchers studied rats before and after they self-administered cocaine for 10 days. Just as in the human cocaine users' brains, dopaminylation of H3 dropped within the neurons in the rats' VTA. The researchers also found a rebound effect one month after withdrawing the rats from cocaine, with much higher dopaminylation of H3 found in these neurons than in control animals. That increase might be important in controlling which genes get turned on or off, rewiring the brain's reward circuitry and causing an intense drug craving during withdrawal.

Ultimately, it looks as though dopaminylation — not just typical dopamine functioning in the brain — may control drug-seeking behavior. Long-term cocaine use modifies neural circuits in the brain's reward pathway, making a steady intake of the drug necessary for the circuits to operate normally. That requires turning specific genes on and off to make the proteins for those changes, and this is an epigenetic mechanism driven by dopamine acting on H3, not a change in DNA sequence.

To test that hypothesis, the researchers genetically modified H3 histones in rats by replacing the amino acid that dopamine attaches to with a different one it doesn't react with. This stops dopaminylation from occurring. Withdrawal from cocaine is associated with changes in the readout of hundreds of genes involved in rewiring neural circuits and altering synaptic connections, but in the rats whose dopaminylation was prevented, these changes were suppressed. Moreover, neural impulse firing in VTA neurons was reduced, and they released less dopamine, showing that these genetic changes were indeed affecting the brain's reward circuit operation. This might account for why people with substance use disorder crave drugs that boost dopamine levels in the brain during withdrawal. Finally, in subsequent tests, the genetically modified rats exhibited much less cocaine-seeking behavior.

It looks as though dopaminylation … may control drug-seeking behavior.

To put it plainly, the discovery that monoamine neurotransmitters control epigenetic regulation of genes is transformative for basic science and medicine. These experiments show that the tagging of H3 by dopamine does indeed underlie drug-seeking behavior, by regulating the neural circuits operating in addiction.

And, equally exciting, the implications likely go well beyond addiction, given the crucial role of dopamine and serotonin signaling in other neurological and psychological illnesses. Indeed, Maze told me that his team's latest research (not yet published) has also found this type of epigenetic marking in the brain tissues of people with major depressive disorder. Perhaps this connection even explains why antidepressant drugs take so long to be effective: If the drugs work by activating this epigenetic process, rather than just supplying the brain's missing serotonin, it can take days or even weeks before these genetic changes become apparent.

Looking ahead, Maze wonders if such epigenetic changes might also occur in response to other addictive drugs, including heroin, alcohol and nicotine. If so, medicines based on this newly discovered epigenetic process could eventually lead to better treatments for many types of addiction and mental illnesses.

In a commentary accompanying the research, Jean-Antoine Girault of Sorbonne University in Paris made a final, intriguing observation. We know that typical neural impulse firing works by causing a ripple effect of dynamic changes in calcium concentration inside

neurons that eventually reach the nucleus. But Girault noted that the enzyme that catalyzes the attachment of dopamine to H3 is also regulated by levels of intracellular calcium. In this way, electrical chatter between neurons is relayed to the nucleus, suggesting that neural activity — driven by a behavior — could attach the dopamine epigenetic marker to genes responsible for drug-seeking behavior. That's how the experiences one has in life can select which genes get read out, and which do not. Lamarck would be proud.

***https://bit.ly/2TF59Qb***

## War songs and lullabies behind origins of music

***Love is not the reason why we sing and create symphonies--at least not the primary reason, according to a new evolutionary theory of the origins of music.***

Vancouver, Wash. - In an article published recently in the journal *Behavioral and Brain Sciences*, a team of anthropologists and psychologists argue more evidence supports music coming from the need for groups to impress allies and foes, and for parents to signal their attention to infants.

The researchers also take issue with other music origin theories including that making music arose out of a need for social bonding, or that it is merely a fancy evolutionary byproduct with no real purpose--"auditory cheesecake" as the cognitive psychologist Steven Pinker once called it.

The sexual-selection theory, however, is perhaps the most entrenched, dating back to Charles Darwin who first suggested that like bird-song, music was developed by humans to attract mates.

"Sex and mating are a part of the story, but music seems to expand far beyond that particular domain," said Ed Hagen, an evolutionary anthropologist with Washington State University and a co-author on the study. "The sexual selection hypothesis doesn't really explain a core feature of music: that it is often performed in groups. It's also listened to and performed by both sexes."

Hagen and his colleagues from Harvard and UCLA point out that if the sexual selection theory were true men would have developed superior music skills and women highly selective listening abilities--yet from simple observations and scientific experiments, both sexes show the similar levels of aptitude in each area.

The researchers also argue against the social bonding theory noting that there are many more efficient ways for groups to bond than the time-consuming process of making music, including talking and sharing a meal. The theory also does not account for the fact that music is often performed for others who take no part in the creation of it.

The audience is the key, the authors say, to understanding the utility of music. Animals often use vocalizations to signal their territory, warn others of intruders and scare others off, and there is evidence that this is a central function of human music as well.

"If we study music in traditional societies, we see it used consistently to form political alliances," said Hagen.

Elaborate musical performances from war dances to military bands and even college marching bands, are often used to show a coalition's strength and impress outsiders. Hagen pointed out that many state visits include a performance by a national orchestra or military band. Studies also show that people can detect how well synchronized musicians are, and connect that higher synchrony to a coalition's strength.

Humans also have another special audience that benefits from the "credible signal" that music provides--babies.

"We need to invest a lot in infants since human babies are born helpless and need all sorts of help from the adults around them," said psychologist Samuel Mehr, director of Harvard's Music Lab. "The parent or caregiver needs a reliable way to signal to the infant

that they are attending to them. But attention is a covert property of the mind. It's hard to determine if someone is actually paying attention to you."

Directed song gives the infant a signal that the adult is paying attention to their needs, Mehr added. When singing, the adults cannot be talking to other people. The music also alerts the baby to the adult's physical location.

"That's information that can't really be faked," he said.

These two audience-focused purposes, coalition building and parent-infant signaling, provide compelling evolutionary reasons for the human development of music, the researchers said -and even makes the null-hypothesis, that music is "auditory cheesecake" and serves no purpose, less convincing.

"I don't think we can completely dismiss the 'auditory cheesecake' hypothesis, but it really doesn't offer a very compelling explanation for the entire package of evidence," said Hagen. "There's a widespread occurrence of similar kinds of vocal signals in many species. Then, there's the fact that we develop musical aptitudes very early in life. Music also appears to be universal. We've found music in every culture that we've studied."

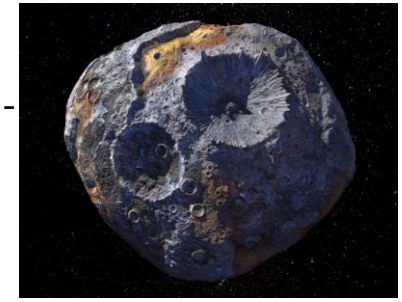
***https://bit.ly/3kZD7v7***

## Hubble Detects Iron and Iron Oxide on Asteroid Psyche

***UV spectrum of the asteroid is best matched with the reflectance spectrum of pure iron***

Astronomers using the Space Telescope Imaging Spectrograph on the NASA/ESA Hubble Space Telescope have observed the main-belt asteroid (16) Psyche, the target object of NASA's Discovery Mission Psyche, at ultraviolet (UV) wavelengths and found that the UV spectrum of the asteroid is best matched with the reflectance spectrum of pure iron; however, small grains of iron may dominate the spectrum even if this metal only comprises up to 10% of the material on the surface.

Psyche, a metal asteroid about 226 km (140 miles) in diameter, is one of the most intriguing targets in the main asteroid belt.



This asteroid orbits the Sun between the orbits of Mars and Jupiter at a distance ranging from 378 to 497 million km (235-309 million miles) from the Sun. The object takes about five Earth years to complete one orbit of the Sun, but only a bit over four hours to rotate once on its axis.

***An artist's concept of the asteroid Psyche, which lies in the main asteroid belt between Mars and Jupiter.*** **Image credit: NASA / JPL-Caltech / ASU.**

Unlike most other asteroids that are rocky or icy bodies, planetary scientists think Psyche is comprised mostly of metallic iron and nickel similar to Earth's core.

They wonder whether this asteroid could be the nickel-iron heart, or exposed core, of an early planet maybe as large as Mars that lost its rocky outer layers through violent collisions billions of years ago.

If so, it would provide a unique look into the Solar System's distant past, when the kind of high-speed protoplanet encounters that created Earth and the other terrestrial planets were common.

"We've seen meteorites that are mostly metal, but Psyche could be unique in that it might be an asteroid that is totally made of iron and nickel," said Dr. Tracy Becker, a planetary scientist at the Southwest Research Institute.

"Earth has a metal core, a mantle and crust. It's possible that as a Psyche protoplanet was forming, it was struck by another object in our Solar System and lost its mantle and crust."

Dr. Becker and her colleagues from the United States and Sweden observed Psyche at two specific points in its rotation to view both

sides of the asteroid completely and delineate as much as possible from observing the surface at UV wavelengths.

"We were able to identify for the first time on any asteroid what we think are iron oxide ultraviolet absorption bands," Dr. Becker said.

"This is an indication that oxidation is happening on the asteroid, which could be a result of the solar wind hitting the surface."

The researchers also observed that the asteroid's surface could be mostly iron, but they noted that the presence of even a small amount of iron could dominate UV observations.

However, while observing Psyche, the asteroid appeared increasingly reflective at deeper UV wavelengths.

"This is something that we need to study further," Dr. Becker said.

"This could be indicative of it being exposed in space for so long. This type of UV brightening is often attributed to space weathering."

The results were published in the *Planetary Science Journal*.

*Tracy M. Becker et al. 2020. HST UV Observations of Asteroid (16) Psyche. Planet. Sci. J 1, 53; doi: 10.3847/PSJ/abb67e*

***https://bit.ly/3jMYP3Y***

## Fungi add flavor to vanilla

***The role that fungi in plants play in the development of the vanilla flavor***

Worldwide, vanilla is the most popular flavor we know. Vanilla is also a popular product in the cosmetic and pharmaceutical industry, where it is used in perfumes and medicines, amongst other things. The only source of vanilla is the vanilla orchid, which is grown in tropical places such as Madagascar, Indonesia and Mexico. Shahnoo Khoyratty conducted Ph.D. research at the Institute of Biology Leiden into the role that fungi in plants play in the development of the vanilla flavor.

**Identical, yet different**

Vanilla plants are not propagated by seed, but by cuttings. As a result, the plants are genetically identical. Nevertheless, the taste of vanilla can differ from plant to plant. According to Khoyratty's promotor Robert Verpoorte, emeritus professor of Pharmacognosy, the taste differences are not only related to the growing conditions of the plants. The fungal endophytes that have nestled in the plant also play a role.

Ph.D. candidate Khoyratty investigated which endophytes can be found on vanilla plants and beans on the island of Réunion near Madagascar. He found that leaves and beans contain different fungal endophytes, with clear differences between the leaves and beans and between individual plants. Plants from different regions also appear to have different endophyte compositions.

**Complex taste**

Khoyratty investigated whether the endophytes influence the formation of the flavors. He isolated and tested different endophytes during an in vitro study in the laboratory. Several endophytes showed to be able to take a step in the biosynthesis of vanilla. The natural vanilla flavor from beans depends on more than 250 different components. Vanillin is the most important substance in terms of quantity. Khoyratty discovered an endophyte that converts ferulic acid—a substance found in the plant—into vanillin. Another fungus was found to convert vanillin into vanillyl alcohol. This substance provides the typical taste of bourbon vanilla, a high-quality type of vanilla.

None of the fungi studied was able to perform the complete biosynthesis of vanilla, but they could do several steps in the process. "To what extent the fungi are involved in the entire biosynthesis is a question that remains open," says Verpoorte. "It could be that the plant supplies ferulic acid and the endophytes do the rest, or it could be a collaboration between the plant and endophytes. There is still a lot of research to be done."

## Vanilla flavor from the industry

The production of vanilla from the vanilla orchid Vanilla planifolia is very labor-intensive and complex; the orchids are pollinated by hand and the beans undergo a lengthy fermentation process after harvest. The demand for vanilla flavor is many times greater than the supply of natural vanilla. The industry uses most of it in cola drinks and ice cream. Vanillin has been chemically produced since the 1920s. In the 1970s, a biotechnological production method was added in which microorganisms produce vanillin based on lignin, a by-product from the paper industry. Ferulic acid from a natural source is also converted into vanillin with the help of micro-organisms. The synthetic vanillin and the vanillin from biotechnology have a less rich taste than the vanilla beans but are much cheaper to produce. Less than 1 percent of the vanilla flavor produced comes from vanilla beans.

***https://bit.ly/2GkTpQ2***

# Alterations in Immune Genes Make Bats Great Viral Hosts

***Bat species use different strategies to dampen immune activation in response to viruses.***

**Abby Olena**

Bats act as reservoirs for lots of viruses—including coronaviruses such as those that cause Middle East respiratory syndrome, severe acute respiratory syndrome, and possibly COVID-19—but they don't often get sick themselves. How they avoid viral illness has been an open question. Researchers reported in *PNAS* yesterday (October 26) that various species of bats have slightly different ways of suppressing inflammation, all centered on changes in genes responsible for triggering innate immune responses.

The authors demonstrate a number of the mechanisms in bats that seem to support their capacity to tolerate viruses that make other mammals really sick, says Cara Brook, a postdoc at the University of California, Berkeley, who was not involved in the work.

"This follows a series of other publications that really highlight a dampened inflammatory response in bats that suggests that they are uniquely resistant and resilient to the consequences of immunopathology . . . and don't experience the kind of autoimmune disease that we often incur against ourselves."

***Cave nectar bats (Eonycteris spelaea)*** **Feng zhu**

In a study published in 2013, Linfa Wang, an immunologist at Duke-NUS Medical School in Singapore, and colleagues compared the genomes of two bat species: the fruit bat (*Pteropus alecto*) and insectivorous bat (*Myotis davidii*). They found that both species had lost a gene called *AIM2*, which in other mammals encodes a protein that senses pathogenic DNA and triggers inflammasomes, protein complexes that activate proinflammatory signals that in turn promote the maturation of cytokines, small signaling proteins that can be released by immune cells and regulate inflammation and immunity.

In the current study, Wang's group followed up on *AIM2* to figure out what affect its loss has on cellular responses to pathogenic DNA. They compared macrophages, the innate immune system's primary effector cells, from mice and fruit bats. The mouse cells, which have a functional gene, make the aggregates of AIM2 and its protein binding partner, which together trigger the inflammasome pathway when cells are exposed to double-stranded DNA. None of this occurred in the fruit bat cells. When the researchers added in a copy of the human version of *AIM2* to fruit bat kidney cells aggregates still formed, but did not activate other inflammasome-related genes, including those that encode the effector enzyme caspase-1, which activates the proinflammatory cytokine IL-1β.

"We hypothesized that further downstream activation of the inflammasome pathway may be affected in bats and decided to investigate these signaling components in an effort to detect any alteration in their function," Wang writes in an email to *The Scientist.*

The researchers determined that the faulty caspase-1 response was due to bat-specific mutations in two sites within the fragment of the enzyme that must be cleaved in order for it to be activated. When they engineered the equivalent human amino acids back into the coding sequence, the bat enzyme worked just as the human protein does. The reverse experiment confirmed these mutations were responsible for the impaired enzyme function. Introducing both bat-specific mutations into the gene for the human protein resulted in a loss of function of human caspase-1.

In contrast, they found, the *Myotis* genus of bats has functional caspase-1, but these animals' genomes instead contain mutations in IL-1β that prevent the cytokine's cleavage and subsequent for cellular secretion. A third species, the cave nectar bat (*Eonycteris spelaea*) had diminished, though not completely suppressed, function of both caspase-1 and IL-1β, resulting from a handful of mutations.

When people "find something about one species of bats, they assume that every bat species does the same thing, and that's not true," says Vikram Misra, a virologist at the University of Saskatchewan who did not participate in the study "What's nice about this paper is that it points to the fact that different species have evolved different mechanisms for achieving the same ends."

"It's very small changes in specific amino acids, where you have one change . . . that can completely change the function of a protein," Karen Mossman, a virologist at McMaster University who did not participate in the work, tells *The Scientist.* In the future, it will be "interesting to really understand how all of these subtle changes in these proteins work collectively to give the bats their immune system," she adds. "It's so similar to the human immune system; the components of the pathways are very similar. And yet, there're these vast, vast changes and differences in how they respond, say, to a viral infection."

Although many species of bats don't seem to get sick from viruses, inflammation in bats does exist, such as when they're exposed to fungal diseases, Misra says. "Even though inflammation because of the viral infection is dampened, there've got to be other pathways that bring out inflammation. That's something that I think we haven't, as a group of bat researchers, addressed completely at this point."

*G. Goh et al., "Complementary regulation of caspase-1 and IL-1β reveals additional mechanisms of dampened inflammation in bats," PNAS, doi:10.1073/pnas.2003352117, 2020.*

**https://wb.md/3oMFbZq**

## Fauci: Early COVID Vaccines Will Prevent Symptoms, Not the Virus

***As people eagerly await new updates about potential coronavirus vaccines, questions still remain about how well they will work and what they will do to stem the pandemic.***

**Carolyn Crist**

Importantly, the initial COVID-19 vaccines will prevent symptoms in those who become infected with the coronavirus rather than kill the virus itself, Anthony Fauci, MD, director of the National Institute for Allergy and Infectious Diseases, said during the Yahoo Finance All Markets Summit on Monday.

"The primary thing you want to do is that if people get infected, prevent them from getting sick, and if you prevent them from getting seriously ill," he said.

Preventing symptoms is a "primary endpoint" in the vaccine development process, Fauci said. Getting rid of the virus altogether is considered a "secondary endpoint."

"What I would settle for, and all of my colleagues would settle for, is the primary endpoint to prevent clinically recognizable disease," he said. "And that's what we hope happens, and if we do, that will go a long way to diffusing this very difficult crisis that we're in."

With reduced severe symptoms, the coronavirus would pose a lower threat as a pandemic. Then scientists could focus on developing a solution that would reach the full goal of preventing initial infection.

Several vaccine candidates are in late-stage clinical trials in the U.S., and safety and efficacy data could be ready for review by the end of the year. That would make initial doses available to frontline workers around the end of 2020 and beginning of 2021 and pave the way for widespread distirubtion several months into 2021.

Mitigation strategies such as wearing face masks, social distancing and avoiding large crowds will be important in preventing the spread of infection for "quite some time," Fauci said.

"Adhering to public health measures now is going to make it easier and more quickly get to where we want to go, which is approaching some form of normality," he said.

***Sources:***

*Yahoo Finance, "Fauci: Early COVID-19 vaccines will only prevent symptoms, not block the virus."*

*Yahoo Finance, "All Markets Summit: Road to Recovery, October 26, 2020."*

***https://bit.ly/3oHI0em***

## Scientists Identify The 5 Symptoms That May Predict a Long-Term Case of Coronavirus

***A spate of preliminary studies are beginning to pinpoint the early signs that a patient won't recover right away.***

**Aria Bendix**

For a select group of coronavirus patients known as "long-haulers", the onset of symptoms is the beginning of an extended battle. Many COVID-19 patients develop weeks- or months-long illnesses that researchers now call "long-COVID".

These individuals are difficult to study, since not all received a proper diagnosis initially due to testing shortages or the abnormal nature of their symptoms. Some may simply not report lingering ailments, making them difficult for researchers to track. But a spate of preliminary studies are beginning to pinpoint the early signs that a patient won't recover right away.

A recent study from King's College London, which is still awaiting peer review, examined more than 4,000 coronavirus patients across Sweden, the UK, and the US by asking them to record their symptoms in an app.

About 20 percent said they still weren't feeling better after four weeks - the threshold at which the researchers mark a case of long-COVID. By eight weeks, around 190 patients reported lingering symptoms. And by 12 weeks, nearly 100 patients said they hadn't recovered yet.

Patients who experienced more than five symptoms during the first week of their illness were significantly more likely to develop long-COVID, the study found. That was true across sex and age groups.

The researchers also identified five symptoms that predicted a case of long-COVID more than others: fatigue, headache, difficulty breathing, a hoarse voice, and muscle or body aches. This could offer clues about targets for future COVID-19 treatments.

"It's important we use the knowledge we have gained from the first wave in the pandemic to reduce the long-term impact of the second," Dr. Claire Steves, the study's senior author, said in a statement. "Thanks to the diligent logging of our contributors so far, this research could already pave the way for preventative and treatment strategies for long-COVID."

Nearly 98 percent of patients with long-COVID in the study reported fatigue, while 91 percent reported a headache.

"We know that fatigue is a huge component, so I'm really glad that their research captured that," Natalie Lambert, an associate professor of medicine at Indiana University who wasn't involved in the study, told Business Insider.

Lambert is also looking at patterns of symptoms among long-COVID patients. All of the roughly 1,500 long-haulers she surveyed in July said they'd experienced fatigue at some point in their illness. Roughly two-thirds said they had experienced muscle or body aches. The same amount said they had difficulty breathing, and around 58 percent said they had developed a headache. The results of the King's College study, Lambert said, square with her observations so far.

**Age, gender, and BMI could also predict long-COVID cases**

By far the strongest predictor of a long-COVID case, according to the King's College study, was age. Around 22 percent of participants ages 70 and older reported long-term symptoms, compared to 10 percent of people ages 18 to 49.

Participants with a higher body mass index (BMI) were also more likely to develop long-COVID.

Though sex wasn't as strong of a predictor of a long-COVID case, women in younger age groups were found to be more likely to suffer this outcome than men. Around 15 percent of women in the study had long-term symptoms compared to nearly 10 percent of men.

That finding is unexpected, since men are on average more vulnerable to severe COVID-19 outcomes than women. Scientists haven't determined exactly why, but studies have shown that women may develop a more robust T-cell reaction or quicker immune response to the virus.

Other scientists have pointed to behavioural factors like men eating less nutritiously than women do, being more likely to smoke cigarettes, or being reticent to wear masks or wash their hands.

One explanation for the surprising trend when it comes to long-lasting cases, however, could simply be that more women than men logged their symptoms into the app in the first place.

"I've had the same experience where many more women who have long-term symptoms took my survey than men by a huge margin," Lambert said. "Is it because more women are experiencing long-term symptoms? Is it because women are more likely to take these surveys and share their health experiences? We won't really know until we get enough data about everybody."

It's important to note, she added, that anyone is vulnerable to long-lasting symptoms. "It can happen to absolutely anybody, no matter how healthy they were beforehand," Lambert said.

**Non-hospitalized patients are still under-studied**

Surveys that ask people to report their own symptoms are imperfect, since people may have trouble remembering each symptom or they might associate it with something other than the virus.

"With COVID, the symptoms are so numerous and wide-reaching that sometimes people don't recognise it as something related to COVID until you ask them about it," Lambert said. "We've found that with things like blurry vision."

But even imperfect data can be useful, she added, since so little is known about the virus' long-term effects.

Most coronavirus studies have focused on hospitalized patients, who may be more likely to develop certain symptoms, like a fever. The King's College London study, for instance, found that fever was a strong predictor of a hospital visit.

But in Lambert's latest survey of roughly 4,000 symptomatic coronavirus patients, only 8 percent of patients reported a fever in the first 10 days of their illness.

To better understand the effects of the virus, Lambert said, more research should track non-hospitalized patients, including people who are asymptomatic.

"On the one hand, it's amazing that scientists and researchers all over the world are finding each other and working on this stuff, but at the same time, we kind of feel like a ragtag team," Lambert said. "These are questions that we really need to answer now."

***https://bit.ly/35RTeEn***

## Scientists discover new organic compounds that could have helped form the first cells

***Many organic compounds polymerise more easily than biological compounds and some even spontaneously form cell-like compartments.***

Chemists studying how life started often focus on how modern biopolymers like peptides and nucleic acids contributed, but modern biopolymers don't form easily without help from living organisms. A possible solution to this paradox is that life started using different components, and many non-biological chemicals were likely abundant in the environment. A new survey conducted by an international team of chemists from the Earth-Life Science Institute (ELSI) at Tokyo Institute of Technology and other institutes from Malaysia, the Czech Republic, the US and India, has found that a diverse set of such compounds easily form polymers under primitive environmental conditions, and some even spontaneously form cell-like structures.

Understanding how life started on Earth is one of the most challenging questions modern science attempts to explain. Scientists presently study modern organisms and try to see what aspects of their biochemistry are universal, and thus were probably present in the organisms from which they descended. The best guess is that life has thrived on Earth for at least 3.5 billion of Earth's 4.5 billion year history since the planet formed, and most scientists would say life likely began before there is good evidence for its existence. Problematically, since Earth's surface is dynamic, the earliest traces of life on Earth have not been preserved in the geological record. However, the earliest evidence for life on Earth tells us little about what the earliest organisms were made of, or what was going on inside their cells. "There is clearly a lot left to learn from prebiotic chemistry about how life may have arisen," says the study's co-author Jim Cleaves.

A hallmark of life is evolution, and the mechanisms of evolution suggest that common traits can suddenly be displaced by rare and novel mutations which allow mutant organisms to survive better and proliferate, often replacing previously common organisms very rapidly. Paleontological, ecological and laboratory evidence suggests this occurs commonly and quickly. One example is an invasive organism like the dandelion, which was introduced to the Americas from Europe and is now a common weed causing lawn-concerned homeowners to spend countless hours of effort and dollars to eradicate. Another less whimsical example is COVID-19, a virus (technically not living, but technically an organism) which was probably confined to a small population of bats for years, but suddenly spread among humans around the world. Organisms which reproduce faster than their competitors, even only slightly faster, quickly send their competitors to what Leon Trotsky termed the "ash heap of history." As most organisms which have ever existed are extinct, co-author Tony Z. Jia suggests that "to understand how modern biology emerged, it is important to study plausible non-biological chemistries or structures not currently present in modern biology which potentially went extinct as life complexified."

This idea of evolutionary replacement is pushed to an extreme when scientists try to understand the origins of life. All modern organisms have a few core commonalities: all life is cellular, life

uses DNA as an information storage molecule, and uses DNA to make ribonucleic RNA as an intermediary way to make proteins. Proteins perform most of the catalysis in modern biochemistry, and they are created using a very nearly universal "code" to make them from RNA. How this code came to be is in itself enigmatic, but these deep questions point to their possibly having been a very murky period in early biological evolution ~ 4 billion years ago during which almost none of the molecular features observed in modern biochemistry were present, and few if any of the ones that were present have been carried forward.

Proteins are linear polymers of amino acids. These floppy strings of polymerised amino acids fold into unique three-dimensional shapes, forming extremely efficient catalysts which foster precise chemical reactions. In principle, many types of polymerised molecules could form similar strings and fold to form similar catalytic shapes, and synthetic chemists have already discovered many examples. "The point of this kind of study is finding functional polymers in plausibly prebiotic systems without the assistance of biology, including grad students," says co-author Irena Mamajanov.

Scientists have found many ways to make biological organic compounds without the intervention of biology, and these mechanisms help explain these compounds' presence in samples like carbonaceous meteorites, which are relics of the early solar system, and which scientists don't think ever hosted life. These primordial meteorite samples also contain many other types of molecules which could have formed complex folded polymers like proteins, which could have helped steer primitive chemistry. Proteins, by virtue of their folding and catalysis mediate much of the complex biochemical evolution observed in living systems. The ELSI team reasoned that alternative polymers could have helped this occur before the coding between DNA and protein evolved. "Perhaps we cannot reverse-engineer the origin of life; it may be more productive to try and build it from scratch, and not necessarily using modern biomolecules. There were large reservoirs of non-biological chemicals that existed on the primeval Earth. How they helped in the formation of life-as-we-know-it is what we are interested in," says co-author Kuhan Chandru.

The ELSI team did something simple yet profound: they took a large set of structurally diverse small organic molecules which could plausibly be made by prebiotic processes and tried to see if they could form polymers when evaporated from dilute solution. To their surprise, they found many of the primitive compounds could, though they also found some of them decomposed rapidly. This simple criterion, whether a compound is able to be dried without decomposing, may have been one of the earliest evolutionary selection pressures for primordial molecules.

The team conducted one further simple test. They took these dried reactions, added water and looked at them under a microscope. To their surprise, some of the products of these reaction formed cell-sized compartments. That simple starting materials containing 10 to 20 atoms can be converted to self-organised cell-like aggregates containing millions of atoms provides startling insight into how simple chemistry may have led to complex chemistry bordering on the kind of complexity associated with living systems, while not using modern biochemicals.

"We didn't test every possible compound, but we tested a lot of possible compounds. The diversity of chemical behaviors we found was surprising, and suggests this kind of small-molecule to functional-aggregate behavior is a common feature of organic chemistry, which may make the origin of life a more common phenomenon than previously thought," concludes co-author Niraja Bapat.

***Reference***

*Kuhan Chandru[1,2*], Tony Z. Jia[3,4], Irena Mamajanov[3], Niraja Bapat[3,5], H. James Cleaves II[3,4,6], Prebiotic oligomerization and self-assembly of structurally diverse xenobiological monomers, Scientific Reports, DOI: 10.1038/s41598-020-74223-5*

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***https://bit.ly/35VvOOD***

# 'Weird' Molecule Detected on Titan Has Never Been Found in Any Atmosphere

***Extremely rare carbon-based molecule that's so reactive, it can only exist on Earth in laboratory conditions***

**Michelle Starr**

Titan, the already pretty weird moon of Saturn, just got a little bit weirder. Astronomers have detected cyclopropenylidene (C3H2) in its atmosphere - an extremely rare carbon-based molecule that's so reactive, it can only exist on Earth in laboratory conditions.

In fact, it's so rare that it has never before been detected in an atmosphere, in the Solar System or elsewhere. The only other place it can remain stable is the cold void of interstellar space. But it may be a building block for more complex organic molecules that could one day lead to life.

"We think of Titan as a real-life laboratory where we can see similar chemistry to that of ancient Earth when life was taking hold here," said astrobiologist Melissa Trainer of NASA's Goddard Space Flight Center, one of the chief scientists set to investigate the moon in the upcoming Dragonfly mission launching in 2027.

"We'll be looking for bigger molecules than C3H2, but we need to know what's happening in the atmosphere to understand the chemical reactions that lead complex organic molecules to form and rain down to the surface."

Cyclopropenylidene – which even NASA researchers describe as a "very weird little molecule" – doesn't tend to last long in atmospheric conditions, because it reacts very quickly and easily with other molecules, forming other compounds.

Once it does so, it's no longer cyclopropenylidene. In interstellar space, any gas or dust is usually very cold, and very diffuse, which means compounds aren't interacting much, and cyclopropenylidene can hang around.

Titan is very different from interstellar space. It's sort of soggy, with hydrocarbon lakes, hydrocarbon clouds, and a predominantly nitrogen atmosphere, with a bit of methane. The atmosphere is four times thicker than Earth's atmosphere (which is also dominated by nitrogen). Under the surface, scientists think there's a huge ocean of salt water.

In 2016, a team led by planetary scientist Conor Nixon of NASA's Goddard Space Flight Centre used the Atacama Large Millimeter/submillimeter Array (ALMA) in Chile to probe the moon's atmosphere, looking for organic molecules.

It was in the tenuous upper atmosphere, high above the surface, where they detected an unknown chemical signature. By comparing it to a database of chemical profiles, the team identified the molecule as cyclopropenylidene. It's likely that the thinness of the atmosphere at that altitude contributes to the molecule's survival, but why it appears on Titan and no other world is a mystery.

"When I realised I was looking at cyclopropenylidene, my first thought was, 'Well, this is really unexpected,'" Nixon said. "Titan is unique in our Solar System. It has proved to be a treasure trove of new molecules."

Cyclopropenylidene is of particular interest because it's what is known as a ring molecule; its three carbon atoms are linked together in a ring (well, a triangle, but the principle is the same). Although cyclopropenylidene itself is not known to play a biological role, the nucleobases of DNA and RNA are based on such molecular rings.

"The cyclic nature of them opens up this extra branch of chemistry that allows you to build these biologically important molecules," said astrobiologist Alexander Thelen of NASA's Goddard Space Flight Centre.

The smaller the molecule, the more potential it has - reactions involving smaller molecules with fewer bonds are expected to happen faster than reactions involving larger, more complicated molecules. That means reactions involving smaller molecules, purely through numbers, are expected to result in a more diverse range of outcomes.

Previously, benzene (C6H6) was thought to be the smallest hydrocarbon ring molecule found in any atmosphere (including Titan's). Cyclopropenylidene has it beat.

Titan is already a hive of organic chemical activity. The nitrogen and methane break up in the sunlight, triggering a cascade of chemical reactions. Whether those reactions could result in life is a question scientists are dying to answer.

"We're trying to figure out if Titan is habitable," said geologist Rosaly Lopes of NASA's Jet Propulsion Laboratory. "So we want to know what compounds from the atmosphere get to the surface, and then, whether that material can get through the ice crust to the ocean below, because we think the ocean is where the habitable conditions are."

Working out which compounds are present in the atmosphere is a very important step in that research process. Cyclopropenylidene may be small, and strange, but this extremely rare molecule could be a key piece of the Titan chemistry puzzle. Now we just have to figure out how it fits in.

The research has been published in *The Astronomical Journal*.

***https://bit.ly/3812hFQ***

## Our Canine Best Friends Were Surprisingly Diverse Already 11,000 Years Ago

***Researchers found that there were already at least five distinct genetic lineages at the end of the last ice age***

**Michelle Starr**

Humans and dogs have shared a long and beautiful relationship, but the story of how we got together has been lost to the sands of time - so we don't know exactly how long we've been friends.

According to new research, though, we started dogs on the path of domestication well before 11,000 years ago. By carefully sequencing the DNA of ancient dogs, researchers found that there were already at least five distinct genetic lineages at the end of the last ice age. They also sequenced contemporaneous human DNA to trace the relationship between our two species over the millennia.

It was these early lineages, the researchers say, that were the basis for the many different dogs we know and love today.

"If we look back more than four or five thousand years ago, we can see that Europe was a very diverse place when it came to dogs," said geneticist Anders Bergström of the Francis Crick Institute in the UK.

"Although the European dogs we see today come in such an extraordinary array of shapes and forms, genetically they derive from only a very narrow subset of the diversity that used to exist."

We know that all domestic dogs (*Canis familiaris*) are descended from a wolf ancestor shared with today's grey wolf (*Canis lupus*). But precisely when that divergence occurred has been a matter of some debate. Some claim domestication - the process of slowly

breeding wolves to select for more friendly traits - began over 100,000 years ago, although that interpretation is controversial.

It's generally accepted that dog domestication began sometime between 40,000 and 20,000 years ago. And it's possible that the process began with the wolves themselves self-domesticating as they grew attached to human settlements.

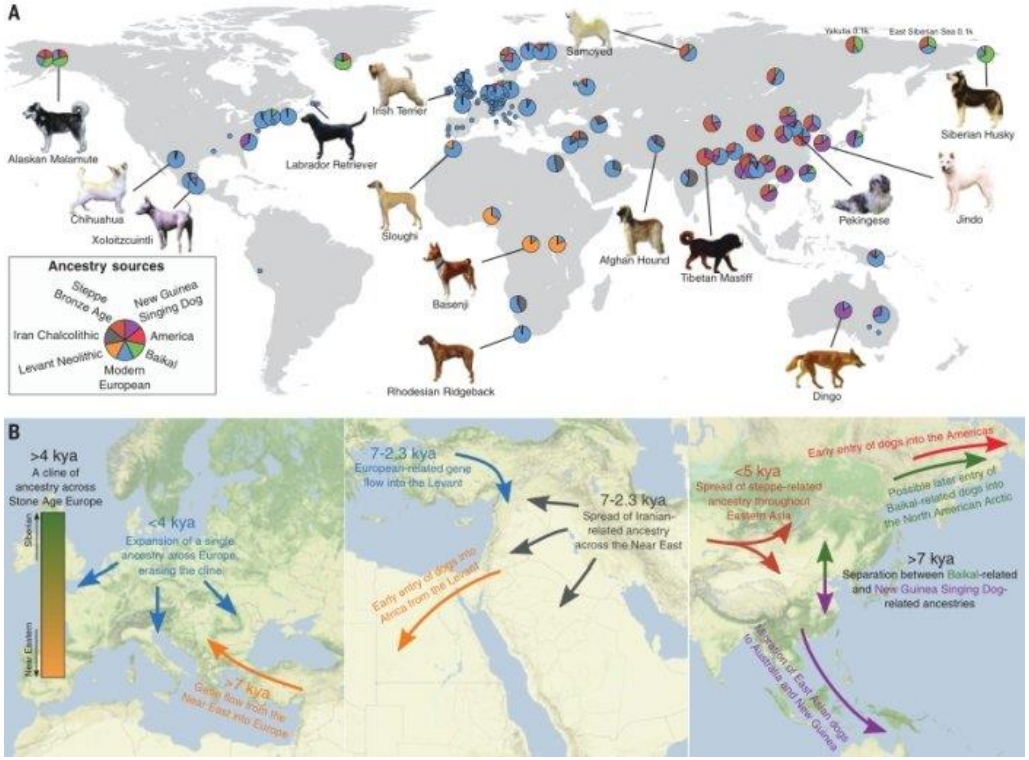
It's difficult to tell early dog fossils apart from ancient wolf fossils, and this new work makes no claims as to when or how canine domestication began - so it's not going to resolve any whats or wherefores about how it all kicked off. But it does reveal fascinating new information about the shared history of humans and dogs.

The ancient dog DNA was sourced from 32 different animals, from 100 to 10,900 years old, from Siberia, Europe and the Near East. Five of those dog genomes had been previously sequenced; the team sequenced 27 new genomes for the most complete ancient dog DNA study yet. These were compared to a selection of modern dog genomes from around the world.

This is how the team found there were at least five distinct dog lineages as early as 11,000 years ago - they describe these as Neolithic Levant, Mesolithic Karelia, Mesolithic Baikal, ancient America, and New Guinea singing dog. So the domestication process had to have started long before that point. And traces of those lineages can be found in today's dogs.

Tibetan mastiffs, for example, have a strong mix of Bronze Age steppe and New Guinea singing dog lineages. Chihuahuas and Xoloitzcuintli have traces of the ancient America lineage. Basenjis have a strong contribution from the Neolithic Levant lineage. And New Guinea singing dogs can still be found in the wild today.

Interestingly, there didn't seem to be a back-and-forth gene flow between dogs and wolves. Previous research suggested that, as the two species were diverging, they continued to interbreed, contributing to early dog diversity. They did, in fact, continue to interbreed, but the gene flow seemed to go predominantly in one direction - from dogs to wolves.




***Ancestry of global dogs today.*** ***(A) For each present-day population, the ancestry proportions estimated by the best-fitting qpAdm model, restricted to models containing up to four of seven selected sources, are displayed. Populations for which a single component accounts for ≥98% of the ancestry are collapsed to smaller circles.*** **Dog pictures were obtained from Wikimedia under the CC BY-SA 3.0 license.** (B) ***Illustrations of inferred population histories in three regions of the world.*** **(Bergström et al., Science, 2020)**

Wolf-dog hybrids do exist today, which could be a clue as to this unidirectional gene flow: These hybrids are unpredictable and often wild, poorly suited to living with humans.

To reconstruct the relationship between dogs and humans over history, the researchers also compared the ancient dog DNA to the genomes of 17 humans living in the same places at the same times as the dogs.

In many cases, similar shifts occurred in the DNA of the dogs and the humans. These, the researchers concluded, likely reflected lifestyle changes, such as moving from one place to another. This makes sense: when humans migrated, they brought along their canine BFFs. That would explain why, for example, dogs from the Middle East and humans from the Middle East ended up in Europe at the same time.

But these changes did not always align. Sometimes the human population changed, but the dogs didn't. This suggests that dogs could move between human groups, or could have been valuable trade commodities. Why these differences exist is still a mystery, and may take a lot more ancient dog DNA to figure out.

One thing is very clear, though: Dogs and humans have found each other pretty awesome for a very long time now.

"Dogs are our oldest and closest animal partner," said palaeogeneticist Greger Larson of the University of Oxford in the UK. "Using DNA from ancient dogs is showing us just how far back our shared history goes and will ultimately help us understand when and where this deep relationship began."

The research has been published in *Science*.

***https://go.nature.com/2HWhehC***

## New polio vaccine poised to get emergency WHO approval

***The vaccine, designed to prevent harmful mutations, is seen as key to eradicating polio.***

**Aisling Irwin**

A vaccine against a type of polio that is spreading in the Southern Hemisphere is expected to receive emergency approval before the end of the year. If it does, it will be the first time the World Health Organization has steered an unlicensed vaccine or drug through its emergency listing process.

Wild polio has been almost eradicated. Only two countries — Afghanistan and Pakistan — still report cases. But a version of the virus that arose naturally from the weakened polio virus used in vaccination is increasing,

What is called circulating vaccine-derived poliovirus (cVDPV) is increasing in both Afghanistan and Pakistan, as well as in the Philippines, Malaysia, Yemen and 19 African countries — with Chad, the Democratic Republic of the Congo and Côte d'Ivoire the worst affected in Africa.

So far in 2020, there have been more than 460 cases of vaccine-derived polio worldwide. This is more than 4 times the number detected by this time in 2019, which is a major problem for the 32-year, US$17-billion global campaign to wipe out the disease. Researchers who model polio infections say that for every known case, there are about 2,000 infections in the population.

"Millions of people potentially have no immunity to the vaccine-derived virus, and that's why we're very concerned," says Kathleen O'Reilly, an epidemiologist at the London School of Hygiene and Tropical Medicine who models polio infections.

Independent scientific advisers to the World Health Organization (WHO) have been assessing a vaccine that is designed specifically to protect against cVDPV. This vaccine, a decade in the making, has been tested for safety and efficacy, but is not yet licensed and still has to undergo further trials.

The WHO is in the last stages of considering whether to approve it more quickly, under what is called an emergency-use listing — a procedure that was created during the 2014–16 Ebola outbreak in West Africa, and which the agency is also preparing to use for coronavirus vaccines.

After a press conference on 9 October, Alejandro Cravioto, chair of the WHO's Strategic Advisory Group of Experts on Immunization, told *Nature* that it is the first vaccine to be considered under the emergency-use listing.

"It's going to be a very good exercise for us to look [at] how this works, because probably some of the COVID-19 vaccines will have to be authorized for use in the same way," he says.

Most cases of cVDPV are caused by mutations in a strain of poliovirus called type 2. Right now, outbreaks are being tackled using the old vaccine for type 2 polio — which risks seeding further outbreaks. If the new vaccine receives emergency-use listing, that could be a "game-changer", says Simona Zipursky, who co-chairs the working group on the vaccine at the Global Polio Eradication Initiative in Geneva, Switzerland. The initiative is a partnership between the WHO and international donors.

Results from phase I trials of the vaccine were published last year[1]. Two phase II trials have been completed, but results are as yet unpublished. However, manufacturer Bio Farma, headquartered in Bandung, Indonesia, has produced 160 million doses in anticipation that the WHO will grant an emergency-use listing while further trials are in progress.

If national medical regulators agree, the new polio vaccine could be distributed in selected pilot countries within two months of the WHO's approval, says Zipursky.

**The back story**

Medical researcher Albert Sabin developed the conventional polio vaccine in the 1950s and 1960s, by growing the virus in non-human primates and cell cultures, until it adapted to those environments and was no longer good at infecting humans.

This 'attenuated' virus is used as a vaccine — with the result that, today, just a few hundred people are infected each year, and a much smaller number paralysed, by a disease that used to infect hundreds of thousands.

The vaccine must be taken by mouth, and recipients excrete the live virus in their faeces for a period afterwards. If this virus is ingested by other people, for example in contaminated drinking water, it can infect them. This is usually harmless, because the virus is attenuated. And it could even boost immunity against polio, just as it does for those who receive the vaccine directly.

But what Sabin never knew, says Raul Andino, a virologist at the University of California, San Francisco, was that his attenuation of the virus hung by a thread. It took just one "gatekeeper mutation" in the virus's RNA to permit other changes that allowed it to regain virulence.

And this happened — possibly as early as 1988, when an outbreak of polio derived from a vaccine began in Egypt. More cases emerged in later years, even though wild polio was on its way to being eliminated in most countries.

A crucial moment came in 2015, when wild polio type 2 was declared to have been eradicated, 16 years after the last case was reported. The WHO decided to withdraw the oral type 2 vaccine around the world in one grand, coordinated act in 2016. After this, immunity to type 2 polio began to wane — leaving communities vulnerable when a few lurking type 2 viruses from vaccines became dangerous again.

**A decade of research**

Like the old polio vaccine, the new vaccine is derived from the live, infectious virus — but this time it has been 'triple-locked' using genetic engineering, to prevent it becoming harmful.

Andino started working on this redesign in 2011, with colleagues including Andrew Macadam at the UK National Institute for Biological Standards and Control and others at the US Centers for Disease Control and Prevention.

Macadam focused on parts of the RNA in Sabin's vaccine where individual bases were mutating to reinstate the virus's virulence. He swapped some of these bases for others at strategic points — chosen so it would be hard for the virus to undo the alteration[2]. "It works amazingly," says Andino. "We didn't see mutation any more in this thing, not in cell culture, not in animal models and now, not in humans".

The team made two further alterations to the virus: one to hinder it from recombining with other gut viruses; the other to slow its evolution. The result is a viral vaccine with a much-reduced chance of causing polio.

In 2015, the Bill and Melinda Gates Foundation in Seattle, Washington, agreed to fund a $150-million programme of simultaneous clinical trials and manufacturing of the new vaccine; the non-profit global health organization PATH, also based in Seattle, is coordinating the project. While the programme is under way, the WHO is sharing its trial data with the African Vaccine Regulatory Forum, a network of national regulatory authorities.

"The vaccine is never forced on a country, and it has to go through its own process to approve it," says Zipursky. But she adds that regulators are impatient to get hold of the vaccine so that they can finally rid their countries of polio and focus on other priorities. "They don't want to have to mop up other outbreaks, they don't want to have to be in this cycle," she says.

**Preparing for unexpected findings**

There's still a small risk that this vaccine, too, could revert and start causing disease, says Paul Fine, a communicable-diseases specialist at the London School of Hygiene and Tropical Medicine. "I think it's going to come down at the end of the day to: how stable is this thing," he says.

A rare adverse event would be detected only in bigger trials, says Abdhalah Ziraba, an epidemiologist at the African Population and Health Research Center in Nairobi. He has reservations about emergency roll-out; he says it "makes sense where you don't have any tool in the arsenal — such as with Ebola or with COVID. But polio and COVID are light years apart in terms of what constitutes an emergency."

Zipursky counters that the emergency-use listing requires intense monitoring in the first three months after the vaccine is deployed, so that nations can "respond to any unexpected findings". It's essential, she says, "so that we are not undermining not just the polio programme, but immunization in general".

And Nicholas Grassly, an infectious-disease epidemiologist at Imperial College London, says that the roll-out can't wait. He says the world is responding to cVDPV outbreaks using hundreds of millions of doses of the old type 2 polio vaccine, which are themselves seeding more outbreaks. The new vaccine, he adds, "is the only tool we have to stop this cycle".

He says that the absence of data from more trials is offset by historical data from the old vaccine, which is similar in many ways and shows minimal adverse effects.

Faisal Shuaib, executive director of the National Primary Health Care Development Agency in Abuja, which is responsible for eradicating polio in Nigeria, welcomes the new vaccine "provided it satisfies the safety profiles that have been set by global and national regulatory organizations".

But it is "not a silver bullet", he adds. "It is very important, but ultimately the solution is to make sure we put in all the resources that are required to improve routine immunization."

*doi: https://doi.org/10.1038/d41586-020-03045-2*

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https://bit.ly/2GgjAqU

# Brain Scans Show a Whole Spectrum of COVID-19 Abnormalities We Can't Fully Explain

***Among the many serious symptoms of COVID-19, the strange neurological effects experienced by many patients count as perhaps the most mysterious.***

**Clare Watson**

A sudden loss of smell and taste was one of the first unusual symptoms reported by COVID-19 patients, but stroke, seizures, and swelling of the brain (called encephalitis) have all been described.

Some patients diagnosed with COVID-19 also experience confusion, delirium, dizziness, and have difficulty concentrating, according to case reports and reviews.

For several months, doctors have been relentlessly trying to understand this disease, and its many manifestations that seem to affect the brain in ways we can't fully explain.

To synthesise some of the rapidly accumulating data, two neurologists have now conducted a review of research exploring how COVID-19 disturbs patterns of normal brain function, which can be measured by an EEG.

An EEG, short for electroencephalogram, records electrical activity in different parts of a person's brain, typically by using electrodes placed on their scalp.

In their review, the researchers collated data on nearly 620 COVID-positive patients from 84 studies, published in peer-reviewed journals and pre-print servers, where the EEG waveform data were available to analyse. Looking at EEG results could indicate some form of COVID-related encephalopathy in these patients – signs of impairment or disturbance to brain function.

Approximately two-thirds of the patients in the studies were male, and the median age was 61 years old. Some people also had a pre-existing condition, such as dementia, that could alter an EEG reading, which the researchers considered when evaluating their test results.

Among the 420 patients where the basis for ordering an EEG was recorded, the most common reason was an altered mental state: close to two-thirds of the patients studied had experienced some delirium, coma, or confusion.

Around 30 percent of patients had had a seizure-like event, which prompted their doctor to order an EEG, while a handful of patients had speech issues. Others experienced a sudden cardiac arrest, which could have interrupted blood flow to the brain.

The patients' EEG scans showed a whole spectrum of abnormalities in brain activity, including some rhythmic patterns and epileptic-like spikes in activity. The most common abnormality noted was diffuse slowing, which is an overall slowing of brain waves that indicates a general dysfunction in brain activity.

In the case of COVID, this impairment could be the result of widespread inflammation, as the body mounts its immune response, or possibly reduced blood flow to the brain, if the heart and lungs are weak.

As for localised effects, a third of all abnormalities detected were detected in the frontal lobe, the part of the brain which handles executive thinking tasks, such as logical reasoning and decision-making. The frontal lobe also helps us to regulate our emotions, control our behaviour, and is involved in learning and attention.

"These findings tell us that we need to try EEG on a wider range of patients, as well as other types of brain imaging, such as MRI or CT scans, that will give us a closer look at the frontal lobe," said neurologist and co-author Zulfi Haneef from Baylor College of Medicine in Houston.

In time, an EEG could help cement a COVID-19 diagnosis or hint at possible complications. Doing so might help doctors monitor the

long-term complications of COVID-19, and detect any long-lasting effects on a patient's brain function.

Unfortunately, as it stands the results don't give any indication of how rare or common these brainwave disturbances are in the broader population, since only COVID-19 patients who had an EEG test were included in the analysis.

But it does add to mounting evidence that the novel coronavirus can have a serious impact on our neurological health.

"More research is needed, but these findings show us these are areas to focus on as we move forward," Haneef said.

"EEG abnormalities affecting the frontal lobe seem to be common in COVID-19 encephalopathy, and has been proposed as a potential biomarker if recorded consistently," the authors wrote in their paper.

As the pandemic rolls on, we've come to understand just how stubborn COVID-19 can be, with patients dubbed 'long haulers' describing how they can't shake symptoms, and still feel fatigued months after they were diagnosed.

"A lot of people think they will get the illness, get well, and everything will go back to normal," Haneef said in a statement. "But these findings tell us that there might be long-term issues, which is something we have suspected and now we are finding more evidence to back that up."

The study was published in *Seizure: European Journal of Epilepsy*.

***https://wb.md/3mJIiiS***

## In Some COVID-19 Cases, Antibodies Attack Body, Not Virus

***For some people with severe COVID-19, the immune system may attack itself rather than the virus, according to a new study published on the preprint server MedRxiv.***

**Carolyn Crist**

The study has not yet been peer-reviewed. In these patients, the body creates "autoantibodies" that target human cells instead of the virus, similar to other autoimmune diseases such as lupus and rheumatoid arthritis.

If doctors can detect these autoantibodies, they may be able to treat patients with drugs that already exist for autoimmune conditions, according to *The New York Times* . The treatments aren't a "cure" but can reduce the severity of symptoms.

"It's possible that you could hit the appropriate patients harder with some of these more aggressive drugs and expect better outcomes," Matthew Woodruff, the lead author and an immunologist at Emory University in Atlanta, told the newspaper.

Woodruff and colleagues studied 52 patients in Atlanta who had severe or critical COVID-19 and no history of autoimmune disorders. They found autoantibodies in about half of the patients, and among the top 50% of the most severe cases more than 70% had autoantibodies.

Some of the autoantibodies were associated with blood clotting and blood flow problems, which could be related to the coagulation issues seen in COVID-19 patients this year. If long-lasting, the autoantibodies may create long-term issues that don't have a cure and last for life, Ann Marshak-Rothstein, an immunologist and lupus expert at the University of Massachusetts, Worcester, told the newspaper.

"You never really cure lupus — they have flares, and they get better and they have flares again," she said. "And that may have something to do with autoantibody memory."

Other viral illnesses also trigger autoantibodies, so the findings make sense, scientists who weren't involved with the study said. Certain immune cells — called B immune cells — make antibodies against virus invaders, but sometimes, the body mistakenly produces antibodies based on dead human cells killed by the virus.

"I'm not surprised, but it's interesting to see that it's really happening," Akiko Iwasaki, an immunologist at Yale University,

told the newspaper. "It's possible that even moderate to mild disease may induce this kind of antibody response."

***Source***

*MedRxiv, "Clinically identifiable autoreactivity is common in severe SARS-CoV-2 Infection."*

*New York Times, "Some Covid Survivors Have Antibodies That Attack the Body, not Virus."*

***https://bit.ly/2HZKO5S***

## A Common Type 2 Diabetes Drug Could Be Slowing The Onset of Parkinson's

***Those taking two particular types of diabetes drugs were less likely to be diagnosed with Parkinson's later in life than those on other treatments.***

**David Nield**

Medication used to treat diabetes could reduce the risk of developing Parkinson's disease, according to new research, opening up a range of potential options for treating and managing the degenerative brain disorder.

Looking at patient records for 100,288 individuals with type 2 diabetes, scientists found that while these individuals had a higher than normal risk of developing Parkinson's, commonly prescribed diabetes drugs also seemed to lower that risk.

Those who were taking two particular types of diabetes drugs – GLP-1 receptor agonists and DPP4 inhibitors – were less likely to be diagnosed with Parkinson's later in life than those on other treatments. In the case of GLP-1 receptor agonists, the likelihood dropped by 60 percent.

"Our study has strengthened evidence that there is a link between type 2 diabetes and Parkinson's disease, although it remains clear that most people with diabetes will not go on to develop Parkinson's," says neuroscientist Tom Foltynie, from University College London in the UK.

The research follows up a 2018 study that covered some 2 million individuals with type 2 diabetes, showing that while the chances of developing Parkinson's remained low, having diabetes increased that chance by around a third – though as yet it's not clear exactly why.

Scientists are particularly keen on exploring the potential of the medication exenatide, which is a GLP-1 receptor agonist: small studies have already suggested that exenatide can limit some of the degenerative effects of Parkinson's disease.

In this new study, patient records were collated for an average of just over three years, with 329 of the 100,288 individuals developing Parkinson's within that time. That's not a huge number, but it was enough to reveal a smaller fraction of people taking DPP4 inhibitors and GLP-1 receptor agonists went on to develop Parkinson's than those using a third antidiabetic drug, or those not using antidiabetic drugs at all.

"It may be helpful for doctors to consider other risk factors for Parkinson's disease when prescribing medications for type 2 diabetes, but further research will be needed to confirm clinical implications," says pharmacoepidemiologist Li Wei, from University College London.

GLP-1 receptor agonists are designed to bind onto and activate receptor proteins found on pancreas and neuron cells that stimulate insulin secretion, which lowers blood glucose levels. Animal studies have suggested this might also trigger some way of protecting neurons from harm; the new research backs that up.

This is all very promising, but there's a long way to go – the team behind the new study is about to recruit volunteers for a phase 3 clinical trial that will look more closely at the potential effects of exenatide on brain disorders.

With the number of people with Parkinson's worldwide now in the millions, and the number expected to keep on rising, new ways of at

least managing this condition and other diseases of the brain are urgently required. Exenatide could be one way forward.

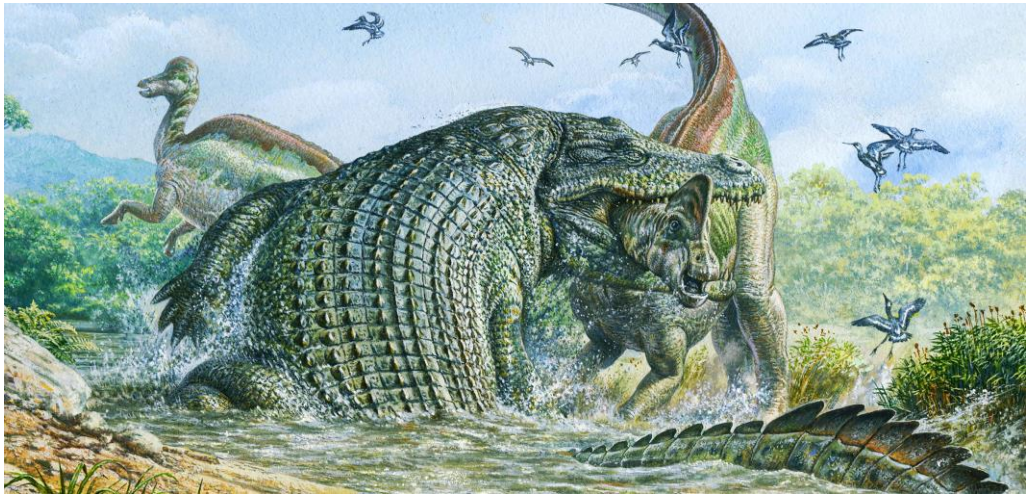
"We have added to evidence that exenatide may help to prevent or treat Parkinson's disease, hopefully by affecting the course of the disease and not merely reducing symptoms, but we need to progress with our clinical trial before making any recommendations," says Foltynie. The research has been published in *Brain*.

***https://bit.ly/2HXkpWn***

## When *Deinosuchus* Ruled the Earth

***As long as T. rex but twice as heavy, this ancient alligator makes for terrifying nightmares. Now, a new study reveals there wasn't just one Deinosuchus species, but three.***

**by Riley Black**



***Deinosuchus, a 10-meter-long alligator that ruled the Cretaceous, preyed on duckbills and other herbivorous dinosaurs.*** **Photo by John Sibbick/Science Photo Library**

More than 75 million years ago, a formidable carnivore lurked in the coastal swamps of North America. This ancient behemoth was not a dinosaur, but a 10-meter-long alligator that weighed up to seven tonnes—as much as a full-grown elephant. With its snapping jaws, *Deinosuchus* was the largest predator of its ecosystem, and it made snacks out of the duckbills and horned dinosaurs that plodded near prehistoric marshes.

Despite its menacing stature, *Deinosuchus* has largely remained an armor-encased mystery since William Jacob Holland first discovered its bones in Montana in 1909. No skull—much less a complete skeleton—had yet been found. All the same, researchers have remained fascinated with the enormous reptile. In 1954, Edwin Colbert and Roland Bird of New York's American Museum of Natural History pieced together a plaster-and-fossil model of the ancient reptile using what bones they had found, filling in missing parts with the anatomy of modern Cuban crocodiles.

Over time, paleontologists assigned various *Deinosuchus* fossil discoveries to a single species, *Deinosuchus hatcheri*, and dubbed the animal an ancient member of the croc subgroup that contains modern alligators and caimans. The sheer enormity of the alligator—and the fact that it was often presented in museums with jaws agape as if ready to snatch up a visitor—made it a fossil legend.

But according to a new study, what was once thought to be one species may have been as many as three terrifying species. That's the conclusion reached by paleontologists Adam Cossette and Christopher Brochu, from the New York Institute of Technology and the University of Iowa, respectively, after puzzling together hundreds of *Deinosuchus* fossils—including newly excavated specimens—collected from more than 10 states over the past century.

Scientists had previously identified anatomical idiosyncrasies between various *Deinosuchus* finds, but chalked those up to mere variations on a single species. Cossette and Brochu, however, found they were indicative of different animals entirely. "We used the largest number of specimens to date, and we determined that three

species of *Deinosuchus* existed in the fossil record," says Cossette. For duckbills and other herbivores, that meant contending with a whole slew of swamp-bound chompers.

The finding parallels other research on living crocodilians. "We used to think that there was only one species of Nile crocodile," says University of Tennessee, Knoxville, paleontologist Stephanie Drumheller-Horton who was not part of the new study. But genomic sequencing revealed that there are really two distinct species. Though *Deinosuchus* is too old for DNA to have been preserved, paleontologists can still pore over fine anatomical details to distinguish one species from another.

The latest research also confirms that, unlike the 1950s reproductions of Colbert and Bird, the three *Deinosuchus* species wouldn't have looked like any crocodilian swishing around in today's swamps.

"The animal's snout was both long and wide, and had an inflated end around the nose," Cossette says, making it appear as if someone had stretched out the muzzle of an American alligator. Not to mention that, in addition to its nasal passages, *Deinosuchus* had a pair of cavernous holes at the tip of its snout. What purpose they served is an enigma, but some scientists believe they could have played a role in the reptile's sinuses, or in keeping its skull lightweight.

Why these reptiles grew so stupendously—matching *Tyrannosaurus rex* by length, but outweighing it two times over—is another mystery scientists are hoping to answer.

*Deinosuchus* spent most of its time in water, which may have freed it from size restrictions imposed by gravity on land, says Cossette. Drumheller-Horton also suspects that the plethora of prey such as turtles and three-tonne hadrosaurs had something to do with their sheer enormity.

The predators' success, says Drumheller-Horton, may have hinged on the fact that they were so large that there was little they couldn't crush between their jaws. Dinosaur bones marked by *Deinosuchus* teeth are a testament to this prowess.

"*Deinosuchus* would have been an opportunistic predator," she says. "At their maximum sizes, that made almost everything else in their ecosystem a potential meal."

***https://wb.md/34MyJcU***

## Alzheimer's Blood Test Comes to the Clinic

***The first blood test to detect the presence of amyloid, a hallmark of Alzheimer's disease (AD), is now available for clinical use***

**Pauline Anderson**

The first blood test to detect the presence of amyloid, a hallmark of Alzheimer's disease (AD), is now available for clinical use, the company behind the test's development, $C_2N$ Diagnostics, has announced. The availability of the noninvasive, easily administered test is being called a milestone in the early detection and diagnosis of AD.

The blood test "introduces a new option for patients, families, and the medical community that have eagerly awaited innovative tools to address Alzheimer's troubling problems," Joel B. Braunstein, MD, CEO of $C_2N$ Diagnostics, said in a press release.

"This is really an important advance," said Howard Fillit, MD, founding executive director and chief science officer of the Alzheimer's Drug Discovery Foundation (ADDF), which partially funded the development of the test, in a separate press release.

"You can now walk into your doctor's office to get a blood test to help detect Alzheimer's disease," said Fillit. "This test answers a critical need for less costly and accessible diagnostic testing in memory and dementia care."

**A Word of Caution**

However, Maria C. Carrillo, PhD, chief science officer, Alzheimer's Association, highlighted the need for caution.

The test is "very new," experts have only "limited information" about it, and it is only available by prescription from a healthcare provider for patients with cognitive impairment, Carrillo told *Medscape Medical News*.

"The test is not FDA approved and it does not, on its own, diagnose Alzheimer's," added Carrillo. "Without FDA review, healthcare providers lack the agency's guidance for how to use it when making decisions about a person's health or treatment."

Carrillo also noted that the test has only been studied in a limited number of individuals and that few data are available regarding underrepresented populations.

"As a result, it is not clear how accurate or generalizable the results are for all individuals and populations," she noted.

Another factor to consider, said Carrillo, is that the test is not covered by insurance, including Medicare and Medicaid.

**How It Works**

The test (PrecivityAD) is for use in patients with cognitive impairment. It requires a very small blood sample — as little as a teaspoon — from the patient's forearm. The physician sends the sample to $C_2N$ Diagnostic's specialized laboratory, where it's analyzed using mass spectrometry to measure concentrations of amyloid beta 42 and 40 and to detect the presence of apolipoprotein E isoforms.

The lab report, which is sent to the patient's physician, details biomarker levels and provides an overall combined score, known as the Amyloid Probability Score, to assess the likelihood of low, intermediate, or high levels of amyloid plaque in the brain.

The company reports that, on the basis of data from 686 patients older than 60 years who had subjective cognitive impairment or dementia, the test correctly identified brain amyloid plaque status, as determined by quantitative amyloid positron-emission tomography (PET) scans, in 86% of the patients.

In the analysis, the area under the curve for the receiver operating characteristic was 0.88.

The company notes that the test, the results of which require interpretation by a healthcare provider, is an important new tool to aid physicians in the evaluation process.

The new blood test is currently available in 45 states, the District of Columbia, and Puerto Rico.

$C_2N$ Diagnostics is moving ahead with development of a brain health panel to detect multiple blood-based markers for AD to aid in disease staging, treatment monitoring, and differential diagnosis.

The ADDF believes the path to approval of treatments of AD starts with a better diagnosis, Fillit said in his organization's press release.

"Investing in biomarker research has been a core goal for the ADDF because reliable, accessible, and affordable biomarkers for Alzheimer's diagnosis are critical to our ability to find drugs to prevent, slow, and even cure the disease.

Our funding helped bring the first PET scan to market and now has helped bring the first blood test to market," he said.

*In addition to the ADDF, the National Institutes of Health, the GHR Foundation, and the BrightFocus Foundation contributed funding for the development of the amyloid blood test.*

***https://wb.md/2HZTDN2***

## About 17% of COVID-19 Survivors Retest Positive in Follow-Up Study

***For reasons unknown, about 1-in-6 people who recovered from COVID-19 subsequently retested positive at least 2 weeks later, researchers reported in a study in Italy.***

**Damian McNamara**

Sore throat and rhinitis were the only symptoms associated with a positive result. "Patients who continued to have respiratory

symptoms, especially, were more likely to have a new positive test result," lead author Francesco Landi, MD, PhD, told *Medscape Medical News.*

"This suggests the persistence of respiratory symptoms should not be underestimated and should be adequately assessed in all patients considered recovered from COVID-19," he said.

"The study results are interesting," Akiko Iwasaki, PhD, an immunobiologist at Yale University and the Howard Hughes Medical Institute, told *Medscape Medical News.*

"There are other reports of RNA detection postdischarge, but this study...found that only two symptoms out of many — sore throat and rhinitis — were higher in those with PCR-positive status." The study was published online September 18 in the *American Journal of Preventive Medicine.*

The findings could carry important implications for people who continue to be symptomatic.

"It is reasonable to be cautious and avoid close contact with others, wear a face mask and possibly undergo an additional nasopharyngeal swab," said Landi, associate professor of internal medicine at Catholic University of the Sacred Heart in Rome, Italy.

"One of most interesting findings is that persistent symptoms do not correlate with PCR positivity, suggesting that symptoms are in many cases not due to ongoing viral replication," Jonathan Karn, PhD, professor and chair of the Department of Molecular Biology and Microbiology at Case Western Reserve University School of Medicine in Cleveland, Ohio, told *Medscape Medical News* when asked to comment.

"The key technical problem, which they have discussed, is that a viral RNA signal in the PCR assay does not necessarily mean that infectious virus is present," Karn said.

He added that new comprehensive viral RNA analyses would be needed to answer this question.

**Official COVID-19 Recovery**

To identify risk factors and COVID-19 survivors more likely to retest positive, Landi and members of the Gemelli Against COVID-19 Post-Acute Care Study Group evaluated 131 people after hospital discharge.

All participants met World Health Organization criteria for release from isolation, including two negative test results at least 24 hours apart, and were studied between April 21 and May 21. Mean age was 56 and 39% were women. Only a slightly higher mean BMI of 27.6 kg/m2 in the positive group, vs 25.9 kg/m2 in the negative group, was significant.

Although 51% of survivors reported fatigue, 44% had dyspnea, and 17% were coughing, the rates did not differ significantly between groups. In contrast, 18% of positive survivors and 4% of negative survivors had a sore throat ($P$ = .04), and 27% vs 12%, respectively, reported rhinitis ($P$ = .05). People returned for follow-up visits a mean 17 days after the second negative swab test.

**Asymptomatic COVID-19 Carriers?**

"These findings indicate that a noteworthy rate of recovered patients with COVID-19 could still be asymptomatic carriers of the virus," the researchers note in the paper. "Even in the absence of specific guidelines, the 22 patients who tested positive for COVID-19 again were suggested to quarantine for a second time."

No family member or close contact of the positive survivors reported SARS-CoV-2 infection. All patients continued to wear masks and observe social distancing recommendations, which makes it "very difficult to affirm whether these patients were really contagious," the researchers note.

**Next Steps**

Evaluating all COVID-19 survivors to identify any who retest positive "will be a crucial contribution to a better understanding of

both the natural history of COVID-19 as well as the public health implications of viral shedding," the authors write.

One study limitation is that the RT-PCR test reveals genetic sequences specific to COVID-19. "It is important to underline that this is not a viral culture and cannot determine whether the virus is viable and transmissible," the researchers note.

"In this respect, we are trying to better understand if the persistence of long-time positive RT-PCR test for COVID-19 is really correlated to a potential contagiousness," they add. Landi and colleagues said their findings should be considered preliminary, and larger data samples are warranted to validate the results.

*Landi and Karn disclosed no relevant financial relationships. Iwasaki disclosed a research grant from Condair, a 5% or greater equity interest in RIGImmune, and income of $250 or more from PureTec.*

*Am J Prevent Med*. Published online September 18, 2020. Full text

***https://bit.ly/3kToxVU***

## Scientists in Japan Just Found a Detailed Record of Earth's Last Magnetic Switcharoo

***Every 200,000 to 300,000 years, Earth's magnetic poles reverse. What was once the north pole becomes the south, and vice versa. It's a time of invisible upheaval.***

**Evan Gough**

The last reversal was unusual because it was so long ago. For some reason, the poles have remained oriented the way they are now for about three-quarters of a million years. A new study has revealed some of the detail of that reversal.

The study of the Earth's magnetic field is called paleomagnetism. It involves the study of rocks and sediments and sometimes archaeological materials. Rocks that were once molten retain a record of the Earth's magnetic field as they solidified.

The related field of magnetostratigraphy studies the record of geomagnetic reversals that are contained in those rocks. By dating the rocks, researchers can construct a timeline of the Earth's reversals.

The last reversal is named the Matuyama-Brunhes geomagnetic reversal after the co-discoverers: Bernard Brunhes, a French geophysicist, and Motonori Matuyama, a Japanese geophysicist. Over the years since its discovery, researchers have tried to understand exactly when it happened, and also how long it took.

This new study is titled "A full sequence of the Matuyama–Brunhes geomagnetic reversal in the Chiba composite section, Central Japan." The lead author is Yuki Haneda, a project researcher at the National Institute of Polar Research and a postdoctoral research fellow at the National Institute of Advanced Industrial Science and Technology in Japan. The paper is published in the journal *Progress in Earth and Planetary Science*.

Lava flows are a reliable indicator of the orientation of Earth's magnetic poles at the time the lava solidified. But what they can't provide is a timeline. They're more like snapshots that freeze a moment in time.

Lava flows are very helpful when it comes to understanding the Earth's magnetic field at the time of solidification. "However, lava sequences cannot provide continuous paleomagnetic records due to the nature of sporadic eruptions," lead author Haneda said in a press release.

A better record can be found in some sediment deposits, which can form over a long period of time. One of these deposits is called the Chiba composite section. It's in Japan, and geophysicists consider it to be a very detailed record of the Matuyama-Brunhes reversal.

"In this study, we collected new samples and conducted paleo- and rock-magnetic analyses of samples from the Chiba composite section, a continuous and expanded marine succession in Central Japan, to reconstruct the full sequence of the Matuyama-Brunhes geomagnetic reversal," Haneda said.

The Chiba composite section is widely considered to contain the most detailed marine sedimentary record of the Matuyama-Brunhes geomagnetic reversal, according to Haneda.

It serves as the international standard for the lower boundary of the Middle Pleistocene Subseries and Chibanian Stage — when *Homo sapiens* emerged as a species.

The Chiba composite section is notable for its well-preserved pollen and marine micro- and macrofossils. It also contains tephra beds. Tephra is a fragmentary material produced by volcanic eruptions, normally referred to as volcanic ash.

All in all, Chiba provides the most reliable chronostratigraphic framework of the time period around the Brunhes-Matuyama reversal.

What they found goes against what some other studies have uncovered, especially when it comes to how long the reversal took to occur. Some studies suggest it took several thousand years, while another suggested that the reversal was completed in one human lifetime.

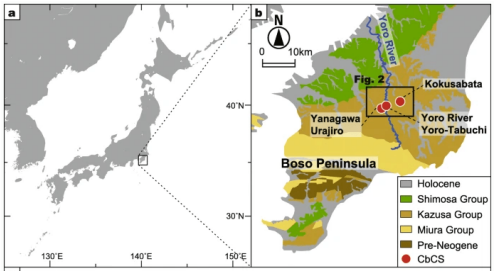
The different time estimates depend largely on where on Earth researchers gather their evidence. This study based on the Chiba composite section says it took about 20,000 years, including a 10,000 year period of instability leading up to the reversal.

"Our data is one of the most detailed paleomagnetic record during the Matuyama-Brunhes geomagnetic reversal, offering deep insight into the mechanism of the geomagnetic reversal," Haneda said.

The marine micro-fossils and pollen found in the Chiba composite section also hold clues to the magnetic reversal. The team of researchers is going to investigate fossils and pollen next to try to learn more.

The question that looms over Earth's geomagnetic reversals is 'What effect do they have?' That's outside the scope of this study, but it's the focus of other research.

Some researchers have wondered if magnetic reversals have contributed to climate change. While the evidence is nowhere near complete, some scientists have outlined how reversals might play a role.




***This figure from the study shows the location of the study area on Japan's Boso Peninsula.*** **(Haneda et al., 2020)**

In 2006 a team of researchers made a presentation to the American Geophysical Union's Fall Meeting titled "Does the Earth's Magnetic Field Influence Climate?"

When mentioning the accepted causes of climate change on Earth, the team said, "Magnetism has seldom been invoked, and evidence for connections between climate and magnetic field variations have received little attention."

"The most intriguing feature may be recently proposed archaeomagnetic jerks. These seem to correlate with significant climatic events."

Archaeomagnetic jerks are quick changes in the Earth's geomagnetic field that are localized rather than global. While there's only a correlation between them and climate, a causal link might one day be established. Could there also be a causal link between magnetic reversals and climate?

The effect that magnetic reversals have on animals is likewise a fascinating and open question. Many animals undertake long, migratory voyages. Whales, birds, and sea turtles, for example.

And there's evidence that some migratory species rely on Earth's magnetic field to navigate. The phenomenon is called magnetoreception.

How are creatures that rely on magnetoreception affected by geomagnetic reversals?

During a reversal, the magnetic poles not only switch places but the field strength drops. There may also be temporary poles at the equator or even multiple temporary poles. The poles can also wander around, leaving their original position and returning before eventually switching completely.

It's not clear what effect a reversal has on animals. But there's some evidence that solar storms, with all their magnetic activity, can create confusion for migrating whales and may even drive them to beach themselves.

During a reversal, the protective effect of the Earth's magnetic field is reduced. More solar radiation may reach the surface of Earth during a reversal, which could put animals like whales in peril the same way a solar storm might. However, the evidence for this is not clear.

In any case, life on Earth has survived many geomagnetic reversals, and still, life thrives. Modern humans haven't faced one yet, so observing the next one will be very instructive.

The most likely effect will be on our power and communications systems, including satellites. As the global magnetic field weakens, more of the Sun's radiation can get through. We know from things like the Carrington Event that that scenario can be very damaging.

While this study can't address all these questions, it does advance our understanding of the previous reversal.

"Our results provide a detailed and expanded sedimentary record of the M–B geomagnetic reversal and offer valuable new information to further understand the mechanisms and dynamics of geomagnetic reversals," the authors conclude.

***https://bit.ly/3jQcGGP***

# If You Have COVID-19, US Study Shows 50% of Your Household Will Get Sick Within Days

***People who develop COVID-19 infect around half of their household members, with adults only slightly more likely than children to spread the virus, a US government study said Friday.***

**Signe Dean**

The paper by the Centers of Disease Control and Prevention (CDC) is the latest to attempt to quantify the household transmission rate of the disease, with previous research varying widely but generally suggesting that adults are bigger drivers than children.

The new research by the CDC involved finding cases of "index" or initial patients with lab-confirmed coronavirus infection in Nashville, Tennessee, and Marshfield, Wisconsin, starting in April 2020.

Both the index patients and their household members were trained remotely to complete symptom diaries and obtain self-collected specimens, which were either nasal swabs only or nasal swabs and saliva samples, for 14 days.

A total of 191 enrolled household contacts of 101 index patients reported having no symptoms on the day of their index patient's illness onset.

In the follow-up period, 102 of the 191 contacts had SARS-CoV-2 positive tests, for a "secondary infection rate" of 53 percent.

The secondary infection rate when index patients were over 18 was 57 percent, which fell to 43 percent when the index patient was under 18.

Overall there were far fewer children index patients than there were adults: 20 compared to 82, which makes it harder to generalize the results for under-18s.

In terms of household characteristics, the median number of members per bedroom was one, 69 percent of index patients

reported spending four or more hours in the same room with one or more household member the day before, and 40 percent the day after illness onset.

Forty percent of index patients reported sleeping in the same room with one or more household members before illness onset and 30 percent after illness onset.

**Higher than reported**

Interpreting the findings, the authors of the paper wrote: "In this ongoing prospective study that includes systematic and daily follow-up, transmission of SARS-CoV-2 among household members was common, and secondary infection rates were higher than have been previously reported."

"Substantial transmission occurred whether the index patient was an adult or a child," they added.

Another important finding of the study was that fewer than half of household members with confirmed infections reported symptoms at the time infection was first detected, and many reported no symptoms throughout seven days of follow-up.

This underscores the potential for transmission for asymptomatic secondary contacts.

Other studies carried out abroad have at times found lower household infection rates.

The CDC said this might be because those studies didn't have enough follow-up, or because those patients isolated in facilities outside their houses or applied more stringent mask use.

It recommended that people who think they might have COVID-19 should isolate themselves from others in their household, including sleeping separately and using a separate bathroom if possible, and wear a mask.

People exposed should not delay isolating until their infection is confirmed by a test.

An important limitation of the study was that determining who the index patient was can be challenging.

When the calculations were changed to exclude 54 household members who had positive tests in specimens taken at enrolment, but whose results took some time to be confirmed, the overall secondary infection rate fell to 35 percent.

However, it's still thought more likely that the person who first developed symptoms is the index patient.

***https://bit.ly/322zcGo***

## Abnormal blood pressure levels while sleeping increase risk of heart disease, stroke

***Even when their daytime blood pressure is within normal ranges***

Dallas - People who experience high blood pressure while sleeping are more likely to experience future cardiovascular disease especially heart failure, even when their daytime blood pressure is within normal ranges, according to new research published today in the American Heart Association's flagship journal *Circulation*.

Health care professionals typically use in-office and daytime blood pressure measurements to determine a patient's hypertension medication needs and dosages. However, many patients may have undetected nocturnal hypertension -- high blood pressure while sleeping.

"Nighttime blood pressure is increasingly being recognized as a predictor of cardiovascular risk," said Kazuomi Kario, M.D., Ph.D., lead author of the study and a professor of cardiovascular medicine at Jichi Medical University in Tochigi, Japan. "This study provides much more in-depth information about the cardiovascular risk associated with high nighttime blood pressure and different nighttime blood pressure phenotypes than have been reported previously."

The Japan Ambulatory Blood Pressure Monitoring Prospective (JAMP) study enrolled 6,359 patients from across Japan between

2009 and 2017 and measured daytime and nighttime levels using an at-home, wearable, ambulatory monitor. Blood pressure was measured during daily activities and sleep for at least 24-hours at a time, and device data were periodically downloaded at a health care clinic. Almost half of the study participants were male, and more than half were over the age of 65 years. The patients all had at least one cardiovascular risk factor, and three-quarters of them were taking blood pressure medications, and none had symptomatic cardiovascular disease when the study began.

The study participants were instructed to rest or sleep during nighttime hours and maintain their usual daytime activities. Their daily activities and sleep and wake times were self-reported in a diary. Almost every participant recorded 20 daytime and seven nighttime automated blood pressure measurements. To determine nighttime measurements, patients self-reported the time they fell asleep and woke up. All other readings were defined as daytime.

Follow-up occurred annually via phone or clinic visit, with total follow up ranging from two to seven years. Researchers analyzed the rates of cardiovascular disease events, including heart attacks, strokes, heart failure and death, among the participants. The occurrence and timing of heart events in relation to blood pressure variations was analyzed to determine whether there were any associations. Study participants experienced a total of 306 cardiovascular events, including 119 strokes, 99 diagnoses of coronary artery disease and 88 diagnoses of heart failure.

**The analysis indicates:**

Increased levels during sleep--a systolic blood pressure measuring 20 mm Hg above a person's daytime systolic reading--was significantly associated with the risk of atherosclerotic cardiovascular disease and heart failure.

The participants who had an abnormal circadian pattern, which is when sleep blood pressure exceeds daytime readings, were at particular risk of developing heart failure and had a greater risk of experiencing any cardiovascular disease events.

Excessive reduction of blood pressure during sleep may also be detrimental. Patients with well-controlled hypertension showed a significantly increased risk of stroke when nighttime systolic pressure took extreme dips.

"Results indicate that nighttime systolic blood pressure was a significant, independent risk factor for cardiovascular events," said Kario. "The study highlights the importance of including nighttime blood pressure monitoring in patient management strategies and will hopefully encourage physicians to ensure that antihypertensive therapy is effectively lowering blood pressure throughout the 24-hour dosing period."

The authors noted that the study was not without limitations. Ambulatory data were obtained once at the start of the study, however, no information was available regarding the contributions of subsequent changes in ambulatory blood pressure levels up until the time of diagnosis of a cardiac event. The study focused on systolic, rather than diastolic, measurements due to the older age of the participants. Additionally, study evaluations did not include echocardiograms, thus preventing some degree of differentiation for types of heart failure.

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*This study was financially supported in part by a grant from the Foundation for the Development of the Community (Tochigi).*

***Additional Resources:***

*Available multimedia is on right column of release link -*
*https://newsroom.heart.org/news/abnormal-blood-pressure-levels-while-sleeping-increase-risk-of-heart-disease-stroke?preview=76b0bccb52dd04fc6faec99b26e338c9*