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# Pain Experiment Shows There Really Is Something Soothing About Saying The 'f' Word

***Saying taboo words out loud seems to make people feel less pain***

**PETER DOCKRILL**

Swearing is good for you. Well, kind of. A growing body of research suggests that, under the right circumstances, simply saying taboo words out loud seems to make people feel less pain – but not just any swear words will suffice, new findings reveal.

Exactly how and why the act of swearing manages to make things seem less painful remains largely hypothetical, and it's worth noting that much of the hypothesising to date in this area has been led by a single researcher, British psychologist Richard Stephens from Keele University.

Nonetheless, what Stephens has uncovered is certainly very interesting. A little over a decade ago, he and his team found that if people immersed their hand in ice water, the simple act of swearing during the experiment enabled participants to perceive decreased pain and tolerate increased pain.

Related follow-ups found that the benefits of this pain-lessening (hypoalgesic) effect brought about by swearing are constrained by how often you swear ordinarily, with frequent swearers receiving a lesser increase in pain tolerance than those who don't tend to swear as much.

The hypoalgesic phenomenon seems to transcend language barriers, and appears to be related to other oddities that alter people's perception and abilities; swearing seems to make people stronger too, and taboo gestures, in place of verbal swearing, can also have a positive effect when people are in pain.

Now, in his latest expert contribution to this weird tangent of psychological research, Stephens and his colleague Olly Robertson have explored what happens if we swap around the designated swear words during the ice water experiment.

Specifically, what happens if we use made-up swear words in a test like this: can a word be plucked out of thin air to represent a taboo or humorous idea, and still have a measurable effect on pain reduction in people's minds?

In the new experiment, 92 participants immersed their hand in a frigid tub of water kept at an icy constant of 3–5°C until it was no longer bearable. During this uncomfortable ordeal, participants had their heart rate monitored, and would randomly repeat one of four words every three seconds, to see what effect that might have, both on their pain perception and how long they could ultimately endure keeping their hand immersed in the water.

The four words to be spoken included a conventional swear word ('f*ck'), a neutral word (a term the participants themselves nominated to describe a table, eg. 'solid'), and two made-up swear words designed specifically for the experiment.

One of these made-up terms was 'fouch' (intended to invoke an emotional response from the participant), and the other was 'twizpipe' (intended to invoke a humorous response from the participant).

While the new swear words may have been designed to partially resemble the attention-modulating impacts of actual swear words, they didn't seem to have much effect in the experiment, at least in terms of influencing pain perception.

The results backed up Stephens' previous research, showing that conventional swearing appears to reduce the perception of pain. In this case, saying 'f*ck' was linked with a 32 percent increase in pain threshold and a 33 percent increase in pain tolerance.

In contrast, the made-up swear words had no beneficial effects for pain threshold and tolerance, which the researchers say is not altogether unsurprising. "While it is not properly understood how

swear words gain their power, it has been suggested that swearing is learned during childhood and that aversive classical conditioning contributes to the emotionally arousing aspects of swear word use," the researchers write in their paper.

"This suggests that how and when we learn conventional swear words is an important aspect of how they function."

This could mean that the made-up swear words, while designed to superficially resemble swear words in either emotional or humorous ways, cannot reduce the perception of pain, because the "surface properties of swear words (such as how they sound) do not explain the hypoalgesic effects of swearing".

Future studies might help us understand what's going on more. Until such time, the results serve as a timely reminder of the best thing to say when something really, really hurts.

The findings are reported in *Frontiers in Psychology*.

***https://bit.ly/36HtACz***

## A fidget spinner to detect urinary tract infections

***Faster, easier diagnosis means less misuse of antibiotics.***

**Cathleen O'Grady**

Urinary tract infections have been called the "canary in the coal mine" of global antibiotic resistance. With more than half of all women having a UTI in their lifetime and men increasing in susceptibility as they age, UTIs are one of the most common bacterial infections in the world.

Because it's not always possible to check for a bacterial infection in a urine sample, patients are often given antibiotics on the basis of symptoms alone—a practice that contributes to the growing resistance of many UTIs to the most common treatments.

We may be rescued by an unexpected hero: the fidget spinner. In a paper in Nature Biomedical Engineering this week, researchers in South Korea and India describe a new test for UTIs that needs nothing more than a couple of spins, by hand, of a spinner-like device. Its results—which can be read by anyone—are ready in around an hour.

**Lab on a disc**

Currently, UTIs are best diagnosed by urine culture tests, which are slow and resource-intensive. Dipstick tests—which just requires a treated paper strip to be dipped into a urine sample—are cheaper and available immediately, but they aren't as reliable.

The ideal test would not only be fast and accurate but also as resource-light as a dipstick—useable in settings with no electricity, limited cash, and few trained professionals. That's where the fidget spinner comes in.

A team of researchers led by Yoon-Kyoung Cho built a device that works on the same principles as a fidget spinner. Like the toy, it has small "wings" that spin around a central point; and like the toy, it can spin on its own for ages after just one or two nudges by hand. Unlike the three lobes of the common fidget spinner toy, this "lab on a disc" is rectangular. It makes up for that with much more interesting contents.

The testing device takes just 1ml of urine in a central chamber. When the device is spun, the centrifugal force pushes the sample through a membrane that catches any bacteria from the sample while the liquid filters through to a reservoir. When a dye is added, it filters through this sample of bacteria, changing color to indicate how high the bacterial load is. It takes less than an hour to get results visible to the naked eye.

**Field testing**

To road-test the device, the researchers took it to a clinic in Tiruchirappalli, India, where patients are usually given antibiotics based just on their symptoms. They collected samples from 39 UTI patients, and then tested them using conventional urine culture tests as well as the new device. The two methods had comparable results,

although the spinner found a few extra patients who tested negative using conventional methods.

The team also used the device to test for antimicrobial resistance. They exposed bacterial samples in the test to different drugs and then compared them to samples that hadn't been treated. The samples that stayed strongly colored by the dye were considered resistant. Although this wouldn't rival gold-standard tests for microbial resistance, it could help doctors to make a quick decision about which antibiotic to prescribe.

One more test confirmed that the spinner could be used by anyone, regardless of hand size. The researchers checked spin speed differences between ten different test spinners, five men and five women. All of them could get the device to spin all of the urine sample through the filter, although some of them needed to give it more than one spin to do so.

Of those 39 patients in Tiruchirappalli, all would normally have been prescribed antibiotics based on their symptoms. Using the spinner, that number dropped to 18, which would save 21 people from getting an unnecessary prescription—and the risks, both personal and global, that come with it.

*Nature Biomedical Engineering*, 2020. DOI: 10.1038/s41551-020-0557-2 (About DOIs).

***https://go.nature.com/36DIqT8***

## Learn from Rwanda's success in tackling COVID-19

***Country has recorded zero deaths from the disease so far***

Rwanda's strong health-care system and strictly coordinated prevention measures against COVID-19 have helped the country to record zero deaths from the disease so far. As the pandemic threatens to gather momentum in Africa, other governments there could benefit from lessons we have learnt.

Rwanda implemented full lockdown a week after its first case was reported in mid-March. A week later, it set up a contact-tracing system and implemented testing for all staff policing borders, as well as those working in public spaces such as banks and bars. By the end of April, 29,395 citizens had been tested for COVID-19 (prevalence was 0.7%). The nation's community health network has enabled the government — with help from the private sector — to identify populations in need of extra support.

Africa has so far recorded relatively few cases and deaths compared with other continents (https://covid19.who.int). Strict prevention measures that are coordinated across countries could keep it that way. Regional bodies such as the East African Community should agree guidelines for full lockdown, backed by surveillance and a supranational testing laboratory, and follow up with population-impact surveys for mental health and COVID-19 serological status.

*Nature* ***581***, *384 (2020) doi: 10.1038/d41586-020-01563-7*

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

## Women with Neandertal gene give birth to more children

***1/3 of women in Europe inherited a gene variant associated with increased fertility from Neandertals***

One in three women in Europe inherited the receptor for progesterone from Neandertals - a gene variant associated with increased fertility, fewer bleedings during early pregnancy and fewer miscarriages. This is according to a study published in *Molecular Biology and Evolution* by researchers at the Max Planck Institute for Evolutionary Anthropology in Germany and Karolinska Institutet in Sweden.

"The progesterone receptor is an example of how favourable genetic variants that were introduced into modern humans by mixing with Neandertals can have effects in people living today," says Hugo Zeberg, researcher at the Department of Neuroscience at Karolinska Institutet and the Max Planck Institute for Evolutionary Anthropology, who performed the study with colleagues Janet Kelso and Svante Pääbo.

Progesterone is a hormone, which plays an important role in the menstrual cycle and in pregnancy. Analyses of biobank data from more than 450,000 participants - among them 244,000 women - show that almost one in three women in Europe have inherited the progesterone receptor from Neandertals. 29 percent carry one copy of the Neandertal receptor and three percent have two copies.

"The proportion of women who inherited this gene is about ten times greater than for most Neandertal gene variants," says Hugo Zeberg. "These findings suggest that the Neandertal variant of the receptor has a favourable effect on fertility."

The study shows that women who carry the Neandertal variant of the receptor tend to have fewer bleedings during early pregnancy, fewer miscarriages, and give birth to more children. Molecular analyses revealed that these women produce more progesterone receptors in their cells, which may lead to increased sensitivity to progesterone and protection against early miscarriages and bleeding.

*The research was supported by the NOMIS Foundation and the Max Planck Society.*
*Publication: "The Neandertal Progesterone Receptor". Hugo Zeberg, Janet Kelso and Svante Pääbo. Molecular Biology and Evolution, online 21 May 2020, doi: 10.1093/molbev/msaa119.*

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

## Beware of false negatives in diagnostic testing of COVID-19

***Chance of a false negative result is greater than 1 in 5 and, at times, far higher***

One of the most commonly used diagnostic tools, particularly during this pandemic, is the reverse transcriptase polymerase chain reaction test (RT-PCR), which uses a person's respiratory sample to detect viral particles and determine if the person may have been exposed to a virus. Laboratory professionals across the U.S. and the globe have used RT-PCR to find out if a person has been infected with SARS-CoV-2, the virus that causes COVID-19. These tests have played a critical role in our nation's response to the pandemic. But, while they are important, researchers at Johns Hopkins have found that the chance of a false negative result -- when a virus is not detected in a person who actually is, or recently has been, infected -- is greater than 1 in 5 and, at times, far higher. The researchers caution that the predictive value of these tests may not always yield accurate results, and timing of the test seems to matter greatly in the accuracy.

In the report on the findings published May 13 in the journal *Annals of Internal Medicine*, the researchers found that the probability of a false negative result decreases from 100% on Day 1 of being infected to 67% on Day 4. The false negative rate decreased to 20% on Day 8 (three days after a person begins experiencing symptoms). They also found that on the day a person started experiencing actual symptoms of illness, the average false negative rate was 38%. In addition, the false negative rate began to increase again from 21% on Day 9 to 66% on Day 21.

The study, which analyzed seven previously published studies on RT-PCR performance, adds to evidence that caution should be used in the interpretation of negative test results, particularly for individuals likely to have been exposed or who have symptoms consistent with COVID-19.

*Lauren Kucirka, M.D., Ph.D., gynecology and obstetrics resident physician, and Justin Lessler, Ph.D., associate professor of epidemiology at the Johns Hopkins Bloomberg School of Public Health, are available for comment on false negatives in diagnostic testing for SARS-CoV-2.*

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

## Study shows patients with hemorrhagic brain disease have disordered gut microbiomes

***Results of the study, the first of its kind in any human neurovascular disease, have implications for treating cavernous angioma***

A new study shows that people with a rare genetic disease that causes bleeding in the brain have gut microbiomes distinct from those without the disease. Moreover, it is the molecules produced by this bacterial imbalance that cause lesions to form in the brains of these patients. The results are the first in any human neurovascular disease. They have implications both for treating the disease and in examining other neurovascular diseases that could be affected by a person's gut microbiome.

The study was led by investigators at University of Chicago Medicine and published May 27 in *Nature Communications*.

It examined the gut bacteria of patients with cavernous angioma (CA), a disease where blood vessel abnormalities develop in the brain and cause strokes, seizures and serious neurologic complications. The disease is caused by a genetic mutation in the lesion --which may be inherited or occurs sporadically -- and its severity and course vary widely among patients.

UChicago is a leader in studying this disease.

It has been designated as a cavernous angioma center of excellence and treats patients with the condition from all over the world.

Investigators had hints that the disease could be affected by the gut microbiome: Senior author Issam Awad, MD, the John Harper Seeley Professor of Neurosurgery and Director of Neurovascular Surgery at UChicago Medicine, was a partner in a previous study in mice, which showed that the cells that lined the blood vessels of the brain reacted to the animals' gut bacteria.

"The implications of that were very big," he said.

"But we didn't know if this concept of a unique microbiome that favors the development of lesions would be true in human beings."

To find out, UChicago researchers -- working with investigators at the University of California San Francisco, University of New Mexico, University of Pennsylvania, and the Angioma Alliance patient support group -- collected stool samples from more than 120 CA patients. The samples were then analyzed for their bacterial content and compared with samples from the general population.

The CA samples showed significantly higher amounts of gram-negative bacteria and less gram-positive bacteria.

The researchers identified a combination of three common bacterial species, whose relative abundance can distinguish CA patients from control patients without CA lesions, with high sensitivity and specificity.

The CA samples also showed an imbalanced network of bacteria that was much more disordered than the general population's bacterial network.

"The CA patients from all the different collection sites had the same distinctive microbiome, regardless of whether they had inherited the mutation or had a sporadic lesion, and regardless of the number of lesions they had," Awad said.

The investigators further showed that the bacterial imbalance in patients with CA produces lipopolysaccharide (LPS) molecules, which travel through the bloodstream to the brain and attach to the brain's blood vessel lining, facilitating lesion development.

"All this evidence pointed to the microbiome as a cause of lesions rather than an effect," Awad said.

The investigators also collected blood from several CA patients and used advanced computational machine learning to identify the combination of molecular signals associated with the disease. Those with CA had significantly different LPS-related related blood biomarkers and inflammatory molecules. The result was essentially a smart, personalized test for each CA patient.

"By looking at both bacteria combinations and the blood biomarkers, we were able to measure just how aggressive the disease was in each patient," said Sean Polster, MD, a neurosurgery resident at UChicago Medicine and first author on the paper.

Polster spent two years of his neurosurgery residency coordinating the study among the different institutions. The researchers are beginning to think about how these results affect treatment.

Earlier studies in mice showed that those fed emulsifiers -- which are often used as preservatives in processed foods -- had more bleeding in the brain, likely due to the way they disrupted the gut's bacterial network.

The researchers now tell patients to avoid these preservatives.

Though antibiotics and probiotics might seem like natural courses of treatment, they could change the bacterial balance in ways that lead to bigger problems.

"This is more complicated than it appears," said Awad.

However, he tells CA patients who have infections caused by gram-negative bacteria (such as urinary tract infections or prostatitis) to have them treated right away to avoid more potential brain lesions.

The researchers are also looking into whether this microbiome-brain connection can be examined in other diseases.

Already, they showed that the same genes and biomarkers involved in CA are also active in the human brain as we age. "Patients have a lot of hope that we are working on this," Polster said.

*The study, "Permissive microbiome characterizes human subjects with a neurovascular disease cavernous angioma," was supported by grants from the National Institutes of Health, Department of Defense, BeBrave for Life Foundation, the University of Chicago Safadi Clinical and Translational Neuroscience Awards, the American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Cerebrovascular Section Robert J. Dempsey MD Cerebrovascular Research Grant, Sigrid Juselius Foundation, and the William and Judith Davis Fund in Neurovascular Surgery Research. Additional authors include Le Shen, Jack Gilbert, Anukriti Sharma, Ying Cao, Julia?n Carrio?n-Penagos, Romauld Girard, Janne Koskima?ki, Dongdong Zhang, Agnieszka Stadnik, Sharbel G. Romanos, Sea?n B. Lyne, Robert Shenkar from the University of Chicago; Mark Kahn from the University of Pennsylvania; Kimberly Yan and Helen Kim from the University of California San Francisco; Cornelia Lee and Amy Akers from the Angioma Alliance; Leslie Morrison, Myranda Robinson, Atif Zafar from the University of New Mexico; and Kyle Bittinger from the Children's Hospital of Philadelphia.*

***https://bbc.in/36IX8zK***

# Dinosaur asteroid's trajectory was 'perfect storm'

***A clear picture is emerging of why the asteroid that struck Earth 66 million years ago was so catastrophic.***

**By Jonathan Amos BBC Science Correspondent**

The space object, which wiped out 75% of all species including the dinosaurs, hit the worst possible place on the planet and - according to new research - at the most lethal angle.

Investigations at the crater site, together with computer simulations, suggest the impactor dug into the crust at an inclination of up to 60 degrees. This exacerbated the climatic fallout.

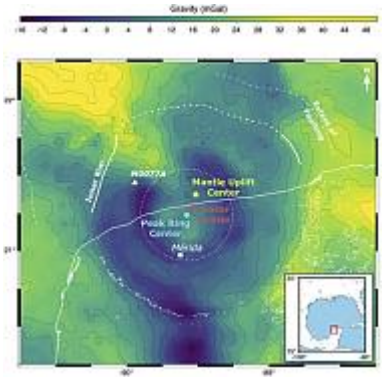
We know that the target rocks, in what is now the Gulf of Mexico, contained huge volumes of sulphur from the mineral gypsum. When this material was thrown high into the atmosphere and mixed with water vapour, it produced a "global winter". And the angle of attack ensured this environmental crisis was intense and prolonged.

"At 45 to 60 degrees, the impact is very efficient at vaporising and ejecting debris to high altitude. If the impact happens at shallower or much steeper angles, the amount of material that's put into the atmosphere that can then have climate-changing effects is significantly less," explained Prof Gareth Collins from Imperial College London. "It's evident that the nature of the location where this event happened, together with the impact angle, made for a perfect storm," he told BBC News.

The majority of plant and animal life on Earth succumbed to the the challenging conditions. Prof Collins' and colleagues' work is published in the journal Nature Communications.

Prof Collins is part of an international team that's been studying the anatomy of the crater associated with the calamitous asteroid strike. Today, this 200km-wide structure is positioned under Mexico's Yucatan Peninsula, with its best preserved central portions sitting just offshore of the port of Chicxulub.

It's hard to grasp the scale of the forces that produced it. The impactor, thought to be about 12km in diameter, punched an instantaneous hole in the crust that was probably some 30km deep. As fluidised rocks at the base of this bowl rebounded, they created in just a few minutes a mountain that was higher than Everest. This didn't last, however, and it fell back, to leave a prominent inner ring of hills, or peaks.




***Gravity measurements trace the central features of the Chicxulub Crater***
**G.Collins**

What's interesting from Prof Collins' perspective is the asymmetry that was frozen into the Chicxulub structure. For example, if you look at the centres of the crater, of its peak ring and of the uplifted rock that underlies the crust in Earth's mantle - these points do not map directly on top of each other. They're actually aligned in a northeast-southwest direction, with the crater centre in between the centres of mantle uplift and peak-ring formation.

This is a vital clue in determining not only the direction from which the asteroid arrived but the angle at which it hit the planet.

The Imperial researcher ran a number of simulations on the UK Science and Technology Facilities Council (STFC) DiRAC High Performance Computing Facility. The only way he can reproduce the geometry is by having the asteroid come in from the northeast and strike the Earth at an angle of roughly 60 degrees.

Prof Collins said: "If you run the model at different impact angles, at 30 degrees and at 45 degrees, say, you can't match the observations - you get centres of mantle uplift and of the peak ring on the downrange side of the crater centre. And for a straight overhead impact, at 90 degrees, the centres are all on top of each other. So, that's doesn't match the observations, either."

Imperial colleague and co-author Prof Joanna Morgan added: "Knowing the direction of impact means we now know which part of the target site was subjected to the greatest shock pressures.

"The sulphur-bearing and carbon-bearing sedimentary rocks actually thicken as you go from east to west, and to the south. So this result means we're degassing more of those sediments than we would if you just took an average value for their thickness."

And Prof Sean Gulick from the University of Texas at Austin, US, told BBC News: "This new modelling provides a clear answer to the angle of the impact and the direction of the impact that largely settles a long-standing debate on what was downrange of the impact.

"Also critical is that a 60-degree angle is in the range of the worst options for injecting large volumes of vaporised and ejected sulphur-rich rocks into the atmosphere.

"Thus these results are critical for understanding potential 'kill mechanisms'," the co-author explained.

Gulick and Morgan led the expedition that drilled into the Chicxulub Crater in 2016 to recover some of its rocks for an analysis. A follow-up, high-resolution seismic survey is due to take place late this summer that will provide an enhanced 3D view of the structure.

## The impact that changed life on Earth

***Scientists now think a 12km-wide object struck Earth 66 million years ago***

***The crater it produced is about 200km wide and is buried mostly offshore***

***On land, it is covered by limestone, but its rim is traced by an arc of sinkholes***

***Experts drilled into the crater to study its rocks and reconstruct the event***

***They say the impact was more than capable of driving a mass extinction***

https://bit.ly/2yH4C9A

# A special elemental magic

## *Kyoto scientists announce a 'nuclear' periodic table*

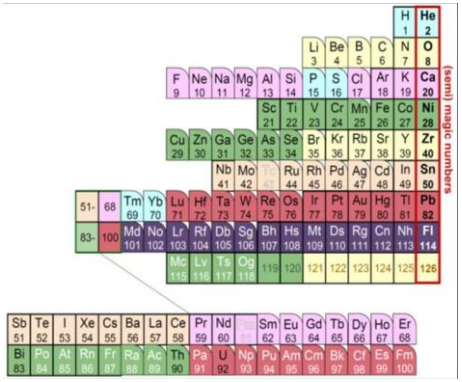
Kyoto, Japan -- A staple in every science classroom is the periodic table of elements, and for many it is their first introduction to the vast mysteries of the natural world.

Now physicists from Kyoto University have unveiled a new table that provides a different perspective on the building blocks of the universe. While the traditional table is based on the behavior of *electrons* in an atom, this new table is based on the *protons* in the nucleus.

"The periodic table of the elements is one of the most significant achievements in science, and in its familiar form it is based on the shell structure of electron orbitals in atoms," explains Yoshiteru Maeno, one of the co-developers of the new table.

"But atoms are comprised of two types of charged particles that designate each element: electrons orbiting the core and protons in the core itself."

The team's new 'Nucletouch' table -- also available as a 3D model -- was announced recently in the journal *Foundations of Chemistry*.




***The fundamental elements organized by their proton 'magic number'*** **Credit: Kyoto University/Yoshiteru Maeno/Kouichi Hagino**

Over 150 years have passed since Dmitri Mendeleev discovered the periodic law that lead him to propose the classic periodic table. He even had the foresight to add space for elements that were still unknown in his time. "Fundamentally, it comes down to the electrons in each atom. Atoms are considered to be stable when electrons completely fill their 'shell' of orbits around the nucleus," continues Maeno.

"So-called 'noble gases', inert elements such as helium, neon, and argon, rarely react with other elements. Their most stable electron numbers are 2, 10, 18, 36, and so on."

Maeno describes these as atomic 'magic numbers', and importantly the same principle can also be applied to protons. Imagining that protons in a nucleus exist in 'orbits' may seem like a stretch, but the discovery of the concept was awarded the 1963 Nobel prize in physics.

Protons have different stable magic numbers: 2, 8, 20, 28, and so on. Among these are familiar elements such at helium, oxygen, and calcium. The Nucletouch table places these 'magic nuclei' at its center, providing a new perspective on the elements.

"Similar to electrons, when nuclear orbits are filled with protons, they form stable nuclei, analogous to the noble-gas elements," says collaborator Kouichi Hagino. "In our nuclear periodic table, we also see that nuclei tend to be spherically-shaped near the magic numbers, but deformed as you move away from them."

The team made the table to highlight alternative ways to illustrate the laws of nature, and hopes that enthusiasts and academics alike will find something to enjoy and learn from this fresh new look at an old friend.

*The paper "A nuclear periodic table" appeared on 21 April 2020 in Foundations of Chemistry, with doi: 10.1007/s10698-020-09365-5*

https://bit.ly/2B6UMi6

# Collision between Milky Way and Its Satellite May Have Triggered Formation of Our Solar System

## *Collisions with the Sagittarius dwarf galaxy may have triggered major star formation episodes in our Milky Way Galaxy*

Repeated collisions with the Sagittarius dwarf galaxy may have triggered major star formation episodes in our Milky Way Galaxy,

one of which roughly coincided with the time of the formation of the Solar System some 4.7 billion years ago, according to an analysis of data from ESA's star-mapping Gaia satellite.

The Sagittarius dwarf galaxy is an elliptical loop-shaped galaxy that is currently located 78,300 light-years away.

"It is known from existing models that Sagittarius fell into the Milky Way three times — first about 5 or 6 billion years ago, then about 2 billion years ago, and finally one billion years ago," said Dr. Tomás Ruiz-Lara, an astronomer in the Instituto de Astrofísica de Canarias.

"When we looked into the Gaia data about the Milky Way, we found three periods of increased star formation that peaked 5.7 billion years ago, 1.9 billion years ago and 1 billion years ago, corresponding with the time when Sagittarius is believed to have passed through the disc of the Milky Way."

Dr. Ruiz-Lara and colleagues looked at luminosities, distances and colors of stars within a sphere of about 6,500 light-years around the Sun and compared the data with existing stellar evolution models.

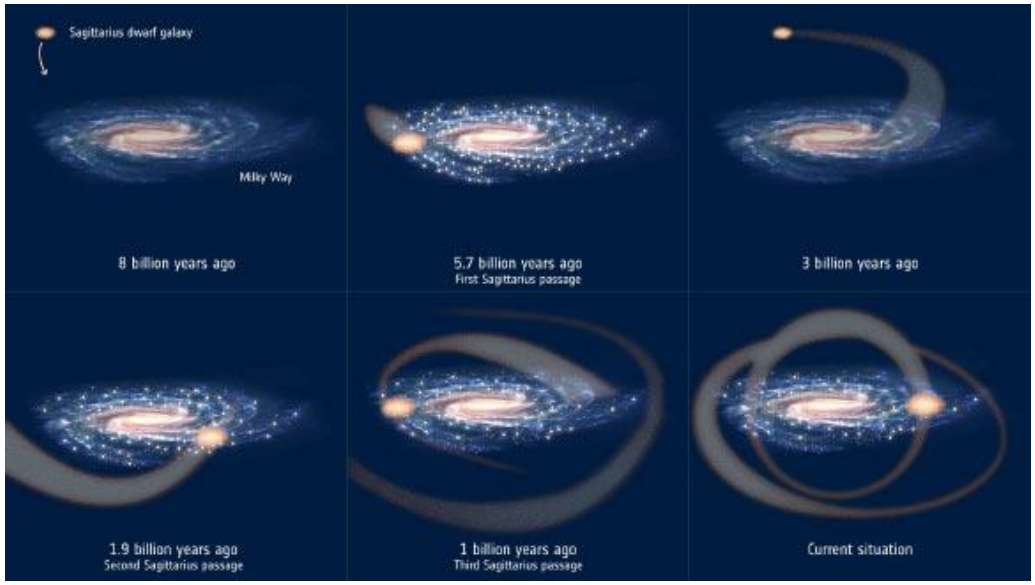
"At the beginning you have a galaxy, the Milky Way, which is relatively quiet," Dr. Ruiz-Lara explained.

"After an initial violent epoch of star formation, partly triggered by an earlier merger as we described in a previous study, the Milky Way had reached a balanced state in which stars were forming steadily."

"Suddenly, you have Sagittarius fall in and disrupt the equilibrium, causing all the previously still gas and dust inside the larger galaxy to slosh around like ripples on the water."

In some areas of the Milky Way, these ripples would lead to higher concentrations of dust and gas, while emptying others. The high density of material in those areas would then trigger the formation of new stars.

"It seems that not only did Sagittarius shape the structure and influenced the dynamics of how stars are moving in the Milky Way, it has also led to a build-up of the Milky Way," said co-author Dr. Carme Gallart, also from the Instituto de Astrofísica de Canarias.




***The Sagittarius dwarf galaxy has been orbiting the Milky Way for billions for years. As its orbit around the 10,000 more massive Milky Way gradually tightened, it started colliding with our Galaxy's disk. The three known collisions between Sagittarius and the Milky Way have triggered major star formation episodes, one of which may have given rise to the Solar System.***
**Image credit: ESA.**

"It seems that an important part of the Milky Way's stellar mass was formed due to the interactions with Sagittarius and wouldn't exist otherwise."

In fact, it seems possible that even the Sun and its planets would not have existed if the Sagittarius dwarf had not gotten trapped by the gravitational pull of the Milky Way and eventually smashed through its disc.

"The Sun formed at the time when stars were forming in the Milky Way because of the first passage of Sagittarius," Dr. Carme said.

"We don't know if the particular cloud of gas and dust that turned into the Sun collapsed because of the effects of Sagittarius or not. But it is a possible scenario because the age of the Sun is consistent with a star formed as a result of the Sagittarius effect."

The team's paper was published in the journal *Nature Astronomy*.

*T. Ruiz-Lara et al. The recurrent impact of the Sagittarius dwarf on the star formation history of the Milky Way. Nat Astron, published online May 25, 2020; doi: 10.1038/s41550-020-1097-0*

***https://bit.ly/36IbMXZ***

## Dairy consumption ineffective in preventing age-related bone loss or fractures

***New study based on SWAN data shows that despite containing essential nutrients, dairy products do not benefit lumbar spine or femoral neck bone density, nor do they protect against fracture risk***

Cleveland, Ohio -Dairy products provide more bone-beneficial nutrients than any other food group. Yet a new study based on data from the Study of Women's Health Across the Nation (SWAN) shows that during the menopause transition, when bone loss is accelerated, they offer little benefit in preventing bone mineral density loss or fractures.Study results are published online in *Menopause*, the journal of The North American Menopause Society (NAMS).

Growing up, children are often encouraged to drink milk. That's because dairy products contain more than 12 essential nutrients that promote bone mineralization, including calcium, phosphorus, vitamin D, and high-quality protein. Unfortunately, as women enter the menopause transition, bone loss accelerates and may lead to osteoporosis. According to SWAN data, this bone loss is not slowed down by the consumption of dairy products nor is fracture risk mitigated.

The new study specifically looked at the effect of dairy intake on femoral and spine bone mineral density. It is one of the few studies dedicated to examining how dairy consumption affects a woman's risk of bone loss and fractures across the menopause transition. Because two of the greatest risk factors for osteoporosis--age and sex--are beyond a woman's control, there is an increased focus on possible modifiable risk factors to slow this irreversible, age-related, progressive, degenerative skeletal disease that makes a woman more susceptible to bone fractures. Women are at greater risk for osteoporosis than men, and the risk increases significantly as women age.

Study results appear in the article "Dairy intake is not associated with improvements in bone mineral density or risk of fractures across the menopause transition: data from the Study of Women's Health Across the Nation."

"This study adds to the existing, albeit inconsistent, data suggesting a lack of benefit from dairy intake on bone mineral density and fracture risk. However, there are many other health benefits of a Mediterranean-type diet rich in fruits, vegetables, and whole grains, as well as lean protein such as fish and low-fat dairy. In addition, regular weight-bearing exercise, such as walking or jogging, can help maintain bone strength, and activities that improve strength and balance, such as yoga and tai chi, may help prevent falls," says Dr. Stephanie Faubion, NAMS medical director.

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

## No asteroids needed: ancient mass extinction tied to ozone loss, warming climate

***Earth's ozone layer was stripped away, exposing surface life to a blast of mutation-causing UV***

**By Paul Voosen**

The end of the Devonian period, 359 million years ago, was an eventful time: Fish were inching out of the ocean, and fernlike forests were advancing on land. The world was recovering from a

mass extinction 12 million years earlier, but the climate was still chaotic, swinging between hothouse conditions and freezes so deep that glaciers formed in the tropics. And then, just as the planet was warming from one of these ice ages, another extinction struck, seemingly without reason. Now, spores from fernlike plants, preserved in ancient lake sediments from eastern Greenland, suggest a culprit: The planet's protective ozone layer was suddenly stripped away, exposing surface life to a blast of mutation-causing ultraviolet (UV) radiation.

Just as the extinction set in, the spores became misshapen and dark, indicating DNA damage, John Marshall, a palynologist at the University of Southampton, and his co-authors say in a paper published today in *Science Advances*. It's evidence, he says, that "all of the ozone protection is gone."

Scientists have long believed—at least before humanity became a force for extinction—that there were just two ways to wipe out life on Earth: an asteroid strike or massive volcanic eruptions. But 2 years ago, researchers found evidence that in Earth's worst extinction—the end-Permian, 252 million years ago—volcanoes lofted Siberian salt deposits into the stratosphere, where they might have fed chemical reactions that obliterated the ozone layer and sterilized whole forests.

Now, spores from the end-Devonian make a compelling case that, even without eruptions, a warming climate can deplete the ozone layer, says Lauren Sallan, a paleobiologist at the University of Pennsylvania. "Because the evidence is so strong, it will make people rethink other mass extinction events."

The end-Devonian die-off has long sat in the shadow of the Late Devonian extinction 12 million years earlier, one of the planet's largest. Likely driven by volcanoes that emitted gases that drastically cooled and warmed the planet, it killed most corals and many shelled sea creatures. But 10 years ago, work by Sallan and others revealed the end-Devonian was mighty in its own right, wiping out many plants and vertebrates, including most tetrapods, the four-limbed fish that had begun to evolve fingers and toes. Only the five-toed tetrapods survived.

"It resets our own evolution," Marshall says. "All these archaic lineages, it kicked them out of the frame."

What the end-Devonian lacked was a cause. There was no evidence for volcanism or a giant impact, but one alluring clue was seen in the rapid formation and disappearance of rock deposits associated with glaciers, Sallan says. "Something was really screwed up with climate at that time."

Over the past 3 decades, Marshall has explored rocks surviving from this time in eastern Greenland. At the time, this terrain lay far from the arctic, at lower latitudes, locked in the arid interior of a landmass called the Old Red Sandstone Continent. As the climate warmed after the Devonian's last ice age, lakes formed and filled with sediment that slowly turned to mudstone, recording conditions before and during the extinction. In 2017, Marshall exhumed the perfect mudstone in a 6-meter-long drilled core.

It captures a startling transformation: Healthy fossilized spores, coated in distinctive symmetrical spikes, suddenly grow misshapen, their spikes dilapidated and uneven. Spores are a common fossil because of their armored coat, but they are vulnerable to UV radiation, much like humans; spores can even develop a "tan" in response to UV. The damage Marshall saw is consistent with such exposure, says Jeffrey Benca, an experimental paleobotanist who has linked such damage to the end-Permian extinction. "What they propose seems quite plausible," he says.

Marshall argues that the warming climate drove more powerful summer thunderstorms, which could have injected an ozone-depleting mix of water and salts into the stratosphere. As UV rays killed off forests, nutrient runoff into the sea could have caused

blooms of plankton and algae, which would have produced more ozone-destroying salts in a runaway feedback. “It looks like it might be a perfect storm,” he says.

Marshall’s scenario could explain not just the extinction, but also the many natural gas deposits dating from the period, says Sarah Carmichael, a geochemist at Appalachian State University. They formed from decaying organic matter, but no one has explained the needed surge in plankton growth. Nutrient runoff from dead forests could have fertilized the marine life.

It’s also a portent of what could happen in today’s warming world, where more powerful thunderstorms sometimes “overshoot” the troposphere and inject moisture into the dry, cold stratosphere. When combined with aerosol particles and chlorine molecules, the moisture may eat away ozone.

But atmospheric scientists can barely agree on whether these ozone depletions are happening now, let alone hundreds of millions of years ago. More overshoots occur now than expected, but whether they are spurring damaging reactions is not yet clear. Elliot Atlas, an atmospheric chemist at the University of Miami who studies this dynamic, is skeptical of Marshall’s theory. It needs much more rigorous testing in models, he says. “Is it impossible? I can’t say that.”

Carmichael, for her part, would like to see evidence beyond the pollen grains that UV drove the extinction. “I’m wary of saying UV radiation is the reason,” she says. “But I think it’s a reason.”

*Posted in: Climate doi:10.1126/science.abd0309*

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

## Giant eruptions belched toxic metal during the ‘Great Dying’

***Volcanoes in Siberia poisoned the planet with mercury, contributing to a global mass extinction.***

Mercury from volcanic eruptions poisoned the planet 252 million years ago during the Great Dying, the greatest extinction in Earth’s history.

Rocks worldwide that formed at the time of this event have high mercury levels. This mercury has been attributed to Siberian volcanoes that poured forth massive amounts of lava during the extinction.

Stephen Grasby at the Geological Survey of Canada in Calgary and his colleagues sought to understand how these mercury emissions affected ancient Earth. The researchers modelled how much mercury the volcanoes emitted during the peak of their activity — a period that lasted 300,000 years — and the fate of the erupted element.

According to the team’s models, mercury drifted through the air and dropped into the ocean, or settled onto the land and eventually washed into the sea. Levels of one form of mercury might have reached more than 450 times the norm on the land and at sea. Animals throughout Earth’s environments would have been exposed to the toxic element.

These spikes of mercury could help to explain the worldwide nature of the extinction, in which more than 90% of marine species and 70% of land species were wiped out.

*Geology* (2020)

***https://bit.ly/3ezU4Zm***

## New report discusses coffee's effect on digestion and digestive disorders

***Research suggests that drinking coffee may help to reduce the risk of certain digestive disorders, including gallstone disease and pancreatitis, and benefit some elements of the digestive process, such as gut motility.***

A new report from the Institute for Scientific Information on Coffee (ISIC), entitled 'Coffee and its effect on digestion' reviews the latest

research into coffee's effect on digestion, and indicates a potential protective effect against gallstones and gallstone disease,[1,2,3] and pancreatitis[4,5]. The report also highlights other beneficial effects that coffee consumption may have on the process of digestion[6-11], including supporting gut microflora[17-19] and promoting gut motility[12,13-16].

The report was authored by Professor Carlo La Vecchia, at the Department of Clinical Sciences and Community Health, University of Milan, Italy, who commented: "*The effect of coffee on digestion is an evolving area of research. Data indicates benefits against common digestive complaints such as constipation, as well as a potential reduction in the risk of more serious conditions like chronic liver diseases, from non alcoholic fatty liver disease (NAFLD), gallstones and related pancreatitis*".

Gallstone disease is a common digestive disorder, caused by the accumulation of gallstones in the gallbladder or bile duct, which affects approximately 10-15% of the adult population[20]. While the mechanism by which coffee may protect against gallstone disease is not yet known[1-3], it has been observed that the risk for the condition declines with increasing daily consumption of coffee[1,2]. Caffeine is thought to play a role in these associations, as the same effect is not observed with decaffeinated coffee[3].

A common question among consumers and focus area for research is whether coffee is associated with heartburn or gastro-oesophageal reflux disease (GORD). Heartburn is a mild form of acid reflux that can affect most people on occasion, while GORD is a chronic and severe acid reflux condition that affects up to one in five adults[21], and is characterised by frequent heartburn, regurgitation of food or liquid, and difficulty swallowing. While a small number of studies have suggested an association between coffee drinking and GORD[22-24], the majority of studies reviewed suggest that coffee is not a major trigger of these conditions[12,25-31].

The report also reviewed a growing area of health and nutrition research, namely: the effect of coffee on the gut microflora (microorganism populations)[17-19]. Recent studies suggest that populations of the beneficial gut bacteria Bifidobacterium spp., increase after drinking coffee[19,32]. It is thought that the dietary fibre and polyphenols found in coffee, support the healthy growth of microflora populations[18,19].

Additional research findings highlighted in the report include:

***Coffee can stimulate gut motility[12,13-16].***

***Coffee consumption is thought to stimulate digestion by encouraging the release of gastric acid, bile and pancreatic secretions[6-11].***

Coffee is already one of the most widely researched components of the diet, and its effect on digestion remains a growing area of research. While this report highlights a number of the more interesting findings that have emerged in recent years, it also provides insight into areas where further research would be beneficial, to better understand the mechanisms behind some of the beneficial effects observed.

*Readers interested in finding out more about coffee & health can visit: http://www.coffeeandhealth.org*

***Notes to editors***

- *Moderate coffee consumption can be defined as 3-5 cups per day, based on the European Food Safety Authority's review of caffeine safety[33].*
- *To read a full overview of coffee and digestion, please click here.*

***Author of the report***

*Professor Carlo La Vecchia, Department of Clinical Sciences and Community Health, University of Milan, Italy.*

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***https://bit.ly/2B8tVSP***

# Cincinnati children's HLH research points to treatment for COVID-19 cytokine storms

## *How mice that model immune disease's cytokine storms may point to solution for global pandemic*

Cincinnati - A transgenic mouse developed at Cincinnati Children's to model the deadly childhood immune disease HLH (hemophagocytic lymphohistiocytosis) may play a key role in saving lives during the COVID-19 virus pandemic.

One of the genetically engineered mouse strain's inventors--Cincinnati Children's cancer pathologist Gang Huang, PhD-- is co-investigator on a small clinical trial that successfully tested a drug used to treat to HLH (ruxolitinib) to dramatically reverse respiratory and multi-system inflammation in severely ill COVID-19 patients. Data from the Phase II clinical study is published in the *Journal of Allergy and Clinical Immunology*.

The study involved 43 hospitalized patients diagnosed with severe COVID-19 between February 9 and February 28 in Wuhan, China, believed to be ground zero for the pandemic. The multi-center study was led by Jianfeng Zhou, MD, PhD, Department of Hematology at Tongji Hospital, Tongji Medical College and Huazhong University of Science in Wuhan.

Zhou is a longtime collaborator of Huang and colleagues at the Cincinnati Children's HLH Center of Excellence, part of the Cancer and Blood Diseases Institute.

**Ruxolitinib Shows Signs of Benefit**

Patients taking ruxolitinib were randomly selected to receive two daily 5mg oral doses of the anti-inflammatory drug, plus the standard of care treatment for COVID-19. A randomly selected control group of 21 patients received a placebo along with the standard of care treatment.

"Ruxolitinib recipients had a numerically faster clinical improvement," study authors write in their report. "Significant chest CT improvement, a faster recovery from lymphopenia and favorable side-effect profile in ruxolitinib group were encouraging and informative to future trials to test efficacy of ruxolitinib in a larger population."

Patients treated with ruxolitinib saw a shorter median time to clinical improvement compared to the control group. Patients treated with ruxolitinib saw a shorter median time to clinical improvement compared to the control group. Researchers reported that 90 percent of ruxolitinib patients showed CT scan improvement within 14 days, compared with 61. 9 percent of patients from the control group. Three patients in the control group eventually died of respiratory failure. All the severely ill patients who received ruxolitinib survived.

More clinical testing of the drug is needed. A larger Phase III clinical trial RUXCOVID by Incyte and Novartis is now testing up to 400 severely ill COVID-19 patients with the drug, according to Huang. Preliminary clinical data from the study is expected during the summer, he added.

"This is the first therapy we know of that appears to work effectively to quiet the cytokine storm and inflammation in severe COVID-19 disease, and there are no significant toxicities to patients who take the drug by two pills a day," Huang said. "This is critical until we can develop and distribute enough effective vaccine to help prevent people from becoming infected."

**Calming the 'Cytokine Storm'**

The so-called cytokine storm that inundates the bodies of severely ill COVID-19 patients with inflammatory cells produced by the immune system is a common feature of children battling secondary HLH, which happens in patients where initial HLH treatment has not worked. Huang, who along with a large portion of the world's scientific community was busy trying to study and find solutions to COVID-19, noticed this common clinical feature of both illnesses.

He also noticed that severe COVID-19 disease clinical manifestations are very similar to those seen in transgenic laboratory mice created to faithfully mimic human secondary HLH in the lab. That preclinical laboratory research, some of it in collaboration with the researchers in Wuhan, China, helped identify the drug ruxolitinib for treating secondary HLH. The anti-inflammatory drug is also used to treat other blood diseases including leukemia.

"I approached our research colleagues in Wuhan and explained our observations and recommended this drug be tested to quiet the cytokine storm in the multi-system inflammation in patients with severe COVID-19 disease," Huang said. "The disease was spreading very rapidly and many people were dying. We believed the existing clinical drug would help save lives. So, we worked to push it forward before there is an effective vaccine for everyone."

Huang said the work with colleagues in China was completed on a compressed timeframe as scientists around the world went on high alert to battle the pandemic in January. During their work, Huang and researchers in China found other clinical studies involving other diseases where ruxolitinib also had worked well at quieting inflammation, and testing on COVID-19 patients proceeded.

*Funding support for the JACI study came as part of an Emergency Research Project of Tongji Hospital, Huazhong University of Science and Technology (2020kfyXGYJ045), an Emergency Research Project of Hubei province (2020FCA006).*

***https://bit.ly/2McX6qf***

## ESPRESSO confirms the presence of an Earth around the nearest star

***Existence of a planet the size of Earth around the closest star in the solar system, Proxima Centauri, has been confirmed***

The existence of a planet the size of Earth around the closest star in the solar system, Proxima Centauri, has been confirmed by an international team of scientists including researchers from the University of Geneva (UNIGE).

The results, which you can read all about in the journal *Astronomy & Astrophysics*, reveal that the planet in question, Proxima b, has a mass of 1.17 earth masses and is located in the habitable zone of its star, which it orbits in 11.2 days.

This breakthrough has been possible thanks to radial velocity measurements of unprecedented precision using ESPRESSO, the Swiss-manufactured spectrograph - the most accurate currently in operation - which is installed on the Very Large Telescope in Chile. Proxima b was first detected four years ago by means of an older spectrograph, HARPS - also developed by the Geneva-based team - which measured a low disturbance in the star's speed, suggesting the presence of a companion.

The ESPRESSO spectrograph has performed radial velocity measurements on the star Proxima Centauri, which is only 4.2 light-years from the Sun, with an accuracy of 30 centimetres a second (cm/s) or about three times more precise than that obtained with

HARPS, the same type of instrument but from the previous generation.

"We were already very happy with the performance of HARPS, which has been responsible for discovering hundreds of exoplanets over the last 17 years", begins Francesco Pepe, a professor in the Astronomy Department in UNIGE's Faculty of Science and the man in charge of ESPRESSO. "We're really pleased that ESPRESSO can produce even better measurements, and it's gratifying and just reward for the teamwork lasting nearly 10 years."

Alejandro Suarez Mascareño, the article's main author, adds: "Confirming the existence of Proxima b was an important task, and it's one of the most interesting planets known in the solar neighbourhood."

The measurements performed by ESPRESSO have clarified that the minimum mass of Proxima b is 1.17 earth masses (the previous estimate was 1.3) and that it orbits around its star in only 11.2 days.

"ESPRESSO has made it possible to measure the mass of the planet with a precision of over one-tenth of the mass of Earth", says Michel Mayor, winner of the Nobel Prize for Physics in 2019, honorary professor in the Faculty of Science and the 'architect' of all ESPRESSO-type instruments. "It's completely unheard of."

**And what about life in all this?**

Although Proxima b is about 20 times closer to its star than the Earth is to the Sun, it receives comparable energy, so that its surface temperature could mean that water (if there is any) is in liquid form in places and might, therefore, harbour life.

Having said that, although Proxima b is an ideal candidate for biomarker research, there is still a long way to go before we can suggest that life has been able to develop on its surface. In fact, the Proxima star is an active red dwarf that bombards its planet with X rays, receiving about 400 times more than the Earth.

"Is there an atmosphere that protects the planet from these deadly rays?" asks Christophe Lovis, a researcher in UNIGE's Astronomy Department and responsible for ESPRESSO's scientific performance and data processing. "And if this atmosphere exists, does it contain the chemical elements that promote the development of life (oxygen, for example)? How long have these favourable conditions existed? We're going to tackle all these questions, especially with the help of future instruments like the RISTRETTO spectrometer, which we're going to build specially to detect the light emitted by Proxima b, and HIRES, which will be installed on the future ELT 39 m giant telescope that the European Southern Observatory (ESO) is building in Chile."

**Surprise: is there a second planet?**

In the meantime, the precision of the measurements made by ESPRESSO could result in another surprise. The team has found evidence of a second signal in the data, without being able to establish the definitive cause behind it. "If the signal was planetary in origin, this potential other planet accompanying Proxima b would have a mass less than one third of the mass of the Earth. It would then be the smallest planet ever measured using the radial velocity method", adds Professor Pepe.

It should be noted that ESPRESSO, which became operational in 2017, is in its infancy and these initial results are already opening up undreamt of opportunities.

The road has been travelled at breakneck pace since the first extrasolar planet was discovered by Michel Mayor and Didier Queloz, both from UNIGE's Astronomy Department. In 1995, the 51Peg b gas giant planet was detected using the ELODIE spectrograph with an accuracy of 10 meters per second (m/s). Today ESPRESSO, with its 30 cm/s (and soon 10 after the latest adjustments) will perhaps make it possible to explore worlds that remind us of the Earth.

https://wb.md/3qAQNe7

# Let's Stop the Draconian Visiting Restrictions

***Patients with COVID-19 isolated and treated as social pariahs, and families are helpless in their efforts to touch and comfort a loved***

**Tom Alsaigh, MD**

As society grapples with the multifaceted devastation caused by the COVID-19 pandemic, patients and families worldwide are left to wonder what the path forward will be to mitigate the profound psychological fallout from visitor restrictions imposed by hospitals, nursing homes, and care facilities. As F. Scott Fitzgerald wrote, "The loneliest moment in someone's life is when they are watching their whole world fall apart, and all they can do is stare blankly."

His words capture the feeling around the deeply disturbing visitation policies in place from both the patient and the family perspective. Not only are patients with COVID-19 isolated and treated as social pariahs, but families are helpless in their efforts to touch and comfort a loved one in a time of exquisite need.

Consider non-COVID-19 hospitalized patients as well; their trauma is just as distressing as they live a digital nightmare with their families via blurry videochatting about risky surgeries and end-of-life care. The despair felt by forced separation of patients and families during this time is overwhelming. A meta-analysis showing loneliness as a key driver for all-cause mortality underscores the critical need for in-person social support for patients. Anecdotal sentiment from patients and family members suggests that while videochatting services help somewhat, they are inadequate at alleviating the consequences of physical isolation.

Families' descriptions of the intense trauma they experience because of these restrictions should also worry society about the unintended consequences of such draconian policies, including a widespread increase in post-traumatic stress disorder (PTSD) in both patients and families.

One particularly poignant moment shared by a colleague involves the desperation of a dying father—with a non-COVID-19–related illness—to see his son with autism one last time before passing away. Despite multiple attempts by staff to grant this dying wish, the request was ultimately denied due to a nebulous on-the-spot policy decision that a child with autism may not be able to appropriately wear a mask while in the hospital. The father died shortly afterwards without seeing his son. That same day, a hospital staff member whose father was intubated due to COVID-19 was agonized by the difficulty in obtaining updates about her loved one's medical status. It was gut-wrenching to watch.

***[I]t is not impossible to imagine a scenario where the benefits outweigh the risks of reuniting family members, if done carefully and methodically.***

The consequences of this are real and tangible. For example, in women, PTSD is associated with significantly higher total healthcare costs, even after controlling for depression, chronic medical illness, and demographic differences. Failure to address this visitation quandary will almost certainly mean a significant increase in PTSD and other psychological sequelae, the impact of which will last years if not decades.

Is society willing to accept this as the status quo until the crisis resolves?

Surely reconsideration of this policy requires a thoughtful approach in light of the dire consequences of continued societal spread of the virus. So, what is the solution? A measured policy based on compassion and scientific merit should be foundational and guide decision-making on visitation privileges. The devastating lack of personal protective equipment has made this prospect more difficult. Understandably, hospital systems cannot afford to distribute this

equipment liberally to family members, as it is essential to protect the health of frontline workers. Because of this, any policy that eases visitor restrictions will undoubtedly invite risk to patients and family members, but it is not impossible to imagine a scenario where the benefits outweigh the risks of reuniting family members, if done carefully and methodically.

First, limiting the number of visitors is necessary. A one-visitor-per-patient rule will help minimize overall exposure. The visitor is screened at the entrance for fever and, if afebrile, is escorted directly to the patient's room by a dedicated staff member. The visitor may not leave the room for other purposes until ready to leave the hospital. Once ready, the visitor is given instructions to minimize contact outside the home environment and is escorted out of the hospital.

Next, face masks have garnered significant attention lately as a way to mitigate viral spread. Culturally driven opinion about face masks aside, the efficacy of these masks in reducing the emission of coronavirus in large droplets and aerosols is generally accepted. This has led to systemic societal change, with the CDC now recommending the use of cloth face coverings in addition to social distancing while out in public. This policy would accompany any visitor to a hospital or other healthcare center. Face masks must be worn at all times, without exception. Instructions on proper face mask hygiene, including not touching the front of the face mask directly, should be provided to both patients and family members.

Finally, appropriate social distancing, both in patient rooms and outside of the hospital, should be stressed to every visitor. Reminders of the importance of this in reducing viral spread should be reiterated at every opportunity.

I argue that this is a worthwhile risk which may significantly alter the trajectory of the unimaginable despair felt by family members affected by this crisis. We must care about this. We must address this issue and challenge the current dogma, if for no other reason than to prevent a significant portion of humanity from staring blankly as their whole world falls apart.

***https://nyti.ms/2XgbRPs***

## Coronavirus Epidemics Began Later Than Believed, Study Concludes

***In Washington State and Italy, the first confirmed cases were not linked to the outbreaks that followed, the analysis found. The epidemics were seeded later.***

**By Carl Zimmer Published May 27, 2020 Updated May 29, 2020**

The first confirmed coronavirus infections in Europe and the United States, discovered in January, did not ignite the epidemics that followed, according to a close analysis of hundreds of viral genomes. Instead, the outbreaks plaguing much of the West began weeks later, the study concluded. The revised timeline may clarify nagging ambiguities about the arrival of the pandemic.

For example, while President Trump has frequently claimed that a ban on travelers from China prevented the epidemic from becoming much worse, the new data suggest that the virus that started Washington State's epidemic arrived roughly two weeks after the ban was imposed on Feb. 2.

And the authors argue that the relatively late emergence of the outbreak means that more lives could have been saved by early action, such as testing and contact tracing.

The new analysis is not the last word. Scientific understanding of the coronavirus is evolving almost daily, and this type of research yields a range of possible results, not complete certainty.

Many infections in Washington State seem to have occurred in early February, and other models suggested that the epidemic there began closer to the beginning of the month. But a number of virus

experts said that the new report convincingly rules out a connection between the first confirmed cases and the later outbreaks.

“This paper clearly shows this didn’t happen,” said Kristian Andersen, a computational biologist at the Scripps Research Institute in San Diego, who was not involved in the research.

Michael Worobey, an evolutionary biologist at the University of Arizona, and his colleagues posted a preliminary version of their study online on Saturday. It has not yet been published in a scientific journal.

Viruses develop genetic mutations at a roughly regular rate as they multiply. Scientists can use these mutations to reconstruct a virus’s movement through a population and to estimate when an outbreak began in a region.

The first confirmed coronavirus case in the United States was a man who flew from China to the Seattle-Tacoma International Airport on Jan. 15. Researchers sequenced the genome of his virus, which came to be known as WA1.

The man, who lived in Snohomish County, was hospitalized in isolation and recovered. On Feb. 24, a Snohomish teenager with flulike symptoms also tested positive for the coronavirus.

Trevor Bedford, a geneticist at the University of Washington and the Fred Hutchinson Cancer Research Center, and his colleagues discovered that this viral genome was nearly identical to WA1, except for two new mutations. They called the second virus WA2.

Alarmed, he and his colleagues concluded that the most likely explanation for the slight difference was that WA1 had circulated in Washington State for six weeks, gaining the mutations along the way.

The implication was that there might be hundreds of people already infected in the state, setting the stage for an explosion of cases. Officials reacted to the news with aggressive measures that public health experts credit with reining in the outbreak.

Initially, Dr. Worobey found the work by Dr. Bedford and his colleagues “pretty darn convincing.” But as time passed, he said in an interview, “something at the back of my mind started niggling away.”

Viruses are far more prone to genetic mutations than other living things. But as viruses go, the new coronavirus is a slowpoke — much more stable than influenza viruses, for example.

It seemed unlikely to Dr. Worobey for the coronavirus to have gained two mutations in just weeks.

As the epidemic spread, Dr. Bedford and his colleagues examined hundreds of coronavirus genomes from Washington State. None of the genomes matched WA1. They all shared the two mutations found in WA2.

Dr. Worobey and his colleagues decided to take a further look. They replayed the outbreak thousands of times on a computer running a program that simulates what we know so far about how the new coronavirus spreads and mutates.

When the researchers modeled WA1 as the source of the Washington State outbreak, the computer could not reproduce the viral mutations found there in later weeks. It was close to impossible for WA1 to have seeded the outbreak, the scientists decided.

It was far more likely that the WA2 group of viruses was introduced to Washington from China sometime around Feb. 13th and set off the epidemic.

That was about two weeks after Mr. Trump banned most travelers from China. According to an analysis by The New York Times, however, about 40,000 people made the journey to the United States in the two months after those restrictions were imposed.

Many were admitted under rules that exempted American citizens and others. They were funneled to a few international hubs, including Seattle-Tacoma International Airport.

Dr. Worobey speculated that the virus that started the state's epidemic arrived by that route, or perhaps to the Seattle area via Vancouver. There was no stealthy community spread of the coronavirus in January in the state, the analysis concluded; the epidemic began soon after the virus that started it arrived.

In an interview, Dr. Bedford said of the new research, "I think it's a very clever way to do things." On Twitter, he accepted many of the conclusions: "I believe I was wrong in the original assessment of a WA1 introduction," he wrote. Still, Dr. Bedford and his colleagues have continued their own study of the Washington State outbreak, and they now estimate it began around Feb. 1 - about two weeks earlier than Dr. Worobey's estimate.

Dr. Bedford found it unlikely that a virus that appeared around Feb. 13 could produce a large outbreak by the end of the month. But Dr. Worobey's team found a similar pattern in the arrival of the new coronavirus in Europe.

On Jan. 20, a woman who had traveled from China to Germany met with her colleagues at an auto supply company. She didn't realize she was sick, and infected a man at the meeting. Scientists gathered that virus's genetic signature and called it BavPat1. That virus spread to 16 people in the company — but then disappeared.

At the end of February, Italy saw Europe's first outbreak. The coronaviruses there were genetically very close to BavPat1, scientists found, leading to suspicions that a German traveler had brought the virus to Italy.

That's not the case, according to Dr. Worobey's analysis. According to the computer simulations, another introduction of the coronavirus from China probably was responsible, and it may have arrived in early or mid-February. "The lineage just happened to get into Europe and run wild," Dr. Worobey said.

This viral line then hopped from Europe to New York several times, Dr. Worobey and his colleagues found, confirming previous studies. They estimated that the coronaviruses circulating in the city by March were introduced into the city around Feb. 20.

Around the world, the new study suggests, the coronavirus arrived more than once without starting runaway outbreaks. In these cases, there was little or no transmission, and the virus simply died out.

To Dr. Worobey, the time before the pandemic took off in the United States was a lost opportunity, when testing and contact tracing could have made a big difference.

"There were weeks before the virus really got a foothold," he said. "It does start to make those missteps seem much more consequential."

The study is "a very careful and rigorous analysis of what we can and can't say about the U.S. and European outbreaks from genomic data," said Edward Holmes, a virologist at the University of Sydney who was not involved in the study.

"To me, what this all highlights are the challenges about drawing strong conclusions on virus introductions and spread based on limited data."

This updated view of the history of the pandemic is exactly how science is supposed to work, said Dr. Andersen of Scripps Research. Scientists look for the best interpretation of data — and then keep looking. But it can be unsettling for the public to watch scientific consensus shift in real time. "We have to live with that uncertainty," Dr. Andersen said.

***https://bit.ly/36LZDB6***

## Ancient antidotes

***Favourites of emperors and royalty, theriacs were the universal cures of their day***

**By Raychelle Burks**

His fears were not irrational. His father was poisoned by his enemies and it has been said he had good reason to fear his mother would dispatch him in the same fashion. His name was Mithridates

VI (c.132–63 BCE) and, like his father before him, he became King of Pontus, a state along the Black Sea. Mithridates' fears spurred him to action – both as poisoner and poison scholar.

Mithridates has been called the first experimental toxicologist, with his primary goal being the creation of 'a "universal antidote" to make himself and his friends immune to all poisons and toxins'.[1] His experimental methods would now be considered dubious at best, including self-dosing with poisons and their supposed antidotes. His practice of taking a bit of poison regularly toward acquiring a tolerance bears his name – mithridatism.

Mithridates' personal physician Crateuas, perhaps collaborating with his ruler, formulated a much sought-after universal antidote and dubbed it 'Mithridatum'.[2] With approximately 40 ingredients, it certainly aimed to protect Mithridates and his friends from 'all poisons and toxins'. Like Mithridates' practice of self-dosing with poisons and protectors, Mithridatum contained both toxins and their counterparts. It's likely that the toxins present – probably insect and reptile venoms, arsenic, mercury and others – were in tiny, non-lethal amounts. Mithridatum's ingredient list is thought to have included cinnamon, cassia, frankincense, myrrh, honey, garlic, musk, rue, tannin, Lemnian earth, wine, charcoal, ginger, rhubarb, St. John's wort, saffron, walnuts, carrot, cardamom, anise, opium and more.

As discussed in the fascinating book *Toxicology in Antiquity*, chemicals in these ingredients have since been found to provide medicinal benefit or have a link to modern medicines. For instance, both cinnamon and cassia contain coumarin, a chemical compound found in a variety of plants that proved pivotal in the development of the anticoagulation medicine warfarin. Cinnamon also contains eugenol, an antibacterial agent and local anaesthetic long used in dentistry. The boswellic acids in frankincense resin have anti-inflammatory and anti-arthritic effects. Opium poppy sap contains morphine, an important compound in pain management – but one that requires great care-in-use given that it is addictive.

Theriac formulations span cultures and centuries because poisonings occurred fairly often in the ancient world

Mithridatum falls into a long line of universal antidotes known as theriacs. As its name suggests, coming from the Greek word *theia* (wild beasts), theriacs were thought to protect from toxins of certain animals. Later formulations expanded to (hopefully) guard against all manner of poison. We might be tempted to look back to ancient times with rose coloured glasses and see only delights, when the truer picture includes significant dangers. Theriac formulations span cultures and centuries because poisonings occurred fairly often in the ancient world. Poisonings in antiquity were not only murders, executions, assassinations and suicides – though there were plenty of those.[3] Then, like now, there were a plethora of accidental poisonings. Having a theriac, which was ingested or used topically, can be thought of as having a well-stocked medicine cabinet in a single jar. And those jars could be quite pricey. A theraic's container could be expensive and ornate – like the fabulously intricate gilded jar shown above. Then, like now, branding mattered and everyone seemed to have their favourite theriac.

The most celebrated theriac was one prepared for Roman Emperor Nero (37–68 CE) by imperial physician and botanist Andromachus. This theriac boasted 64 ingredients and Andromachus claimed it could treat all manner of ills – including plague. Nero probably did not have Mithridates' toxicological knowledge, but Nero certainly used poisons – or ordered their use – to rid of himself of foes and family.[4] Nero is implicated in the death of his stepbrother Britannicus, his rich aunt Domita, Burrus, the Prefect of the Praetorian Guard and others. Nero's mother Agrippina the Younger is said to have survived her son's attempts to poison her as she

practised mithridatism. She did not, however, survive his other weapons of choice.

Cleopatra VII (69–30 BCE), embattled ruler of the Egyptian empire, 'had a deep understanding of poisons' and might have used a theriac.[5] But if she did, it did not protect her. Cleopatra was lethally poisoned – and it might not have been the self-envenomation with an asp that we grew up reading about and seeing on screen. Some scholars have argued that the details of Cleopatra's demise are more aligned with an assassination-by-poisoning on the orders of Octavian, Julius Caesar's adopted son and future emperor of the Roman Empire.

Whether suicide or murder, the possible failure of Cleopatra's theriac highlights what has been known of these medicinal concoctions since their inception. Each theriac has its limits. Each theriac hoped to improve on the last. While it is now known no true medicinal panacea exists, history is replete with humankind's attempts to find one. From the rulers of societies to society's most vulnerable, people craved safety and wellness. We still do.

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

## Modified Parkinson's drug shows potential in treating nonalcoholic fatty liver disease

***Scientists spur advances in fatty liver disease therapy by modifying an existing neurological drug***

Nonalcoholic fatty liver disease (NAFLD) is a condition characterized by excessive fat accumulation in the liver. It can cause serious complications, including nonalcoholic steatohepatitis, cirrhosis, and cancer.

Although prevalent, there is a dearth of drugs to treat NAFLD, with current therapies revolving around lifestyle interventions.

In a recent study published in *Journal of Medicinal Chemistry*, scientists from Gwangju Institute of Science and Technology, Korea, led by Prof Jin Hee Ahn, aimed to find new therapeutic options for NAFLD.

Prof Ahn says, "*NAFLD is a serious public health problem worldwide. However, no pharmacological agents have been specifically approved for its treatment yet*."

For their study, the scientists focused on a well-known neurotransmitter called serotonin. Serotonin is widely known as the "happy" neurotransmitter, and its deficiency in the central nervous system (CNS) can cause various brain disorders. But, not many know that it is also found in the gastrointestinal tract; here, it is called "peripheral" serotonin, which has different functions altogether, such as regulating lipid metabolism in the liver.

In a previous study published in *Nature Communications*, Prof Hail Kim, the co-corresponding author of this study, had investigated peripheral serotonin as a drug target with knockout mice models (mice lacking functional peripheral serotonin). This study reported that these mice showed reduction in liver weight, hepatic lipid accumulation, and hepatic triglyceride content and improved NAFLD activity.

These findings formed the basis of Prof Ahn's study and prompted the research group to identify new peripheral serotonin antagonists. The scientists selected a CNS drug approved for the treatment of Parkinson's, called pimavanserin.

Pimavanserin acts as an "antagonist" to serotonin, mimicking its effect in the CNS. The scientists then structurally modified this drug such that it cannot permeate the blood-brain barrier, by adding different types of molecules to it.

In this way, they generated an array of novel compounds. On testing these, the scientists found one compound in particular to show promising results: it showed very low blood-brain barrier permeation and thus had the potential to target peripheral serotonin systems.

The scientists tested this compound in obese mice with impaired liver function. Interestingly, the mice showed improvement in symptoms of fatty liver disease, such as improved glucose tolerance. Additionally, their body fat decreased while lean body mass increased. Prof Ahn says, "*Through the chemical optimization of an existing drug, pimavanserin, we identified a new peripheral agent for the possible treatment of NAFLD*."

Although this novel compound is yet to be tested in humans, these findings show that it has remarkable potential in treating fatty liver disease.

Optimistic about these findings, Prof Ahn concludes, "*We hope that our novel drug candidate will offer relief to patients bearing the brunt of NAFLD*."

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

## The coronavirus didn't really start at that Wuhan 'wet market'

***Early reports blamed a market where live animals were sold, but evidence now shows they were wrong.***

**By Rafi Letzter - Staff Writer 3 days ago**

The first case of SARS-CoV-2 didn't emerge from a Wuhan wet market, according to experts at the Wuhan Institute of Virology (WIV).

Instead, the live animal market may have been the site of a superspreader event, where one person spread the virus to many other people, one US-based expert told Live Science.

Since the early days of the coronavirus pandemic, reports have suggested that SARS-CoV-2 (the virus that causes COVID-19) jumped from animals to humans in Wuhan's Huanan Seafood Wholesale Market.

Now, experts at the WIV have said publicly that the theory was wrong, and that the virus must have originated elsewhere, according to a Wall Street Journal report.

"I haven't seen anything that makes me feel, as a researcher who studies zoonotic disease, that this market is a likely option," said Colin Carlson, a professor at Georgetown University who studies the spread of such zoonotic viruses, which transmit between animals and humans. Carlson does not work for the WIV.

The theory was plausible, he said. For a virus to jump from animals to humans, the animal host needs to come into contact with humans somewhere.

And viruses often jump from one animal to another before breaking into the human population. In fact, the genome of SARS-CoV-2 is most closely related to coronaviruses isolated from horseshoe bats in China.

From there, scientists suspect the virus may have jumped to another animal and then hopped to humans.

Wet markets, where lots of different species of live animals are clustered, and lots of humans come into contact with them, offer opportunities for that sort of transmission.

And the outbreak of another coronavirus, dubbed SARS, began at a similar market in 2002, after that virus spread from bats to civets.

A number of early cases of the outbreak in Wuhan were tied to the Huanan Seafood Wholesale Market. Later, researchers took

environmental samples that suggested the virus had landed on surfaces in the market.

But in the period since, tissue samples from the market's animals have revealed no trace of the virus. For the virus to jump from animals to humans, the animals have to actually be carrying it.

"None of the animals tested positive. So since January, this has not actually been particularly conclusive. But this has developed into a narrative," he said.

Carlson said his colleagues in China have been careful and precise in their work, publishing data according to international regulations that any scientist anywhere in the world can examine, and that strongly supports the conclusion that the Huanan Seafood Wholesale Market wasn't the source of the virus.

One reason this idea has gained such traction is that it dovetails with conservation efforts.

Many wet markets sell exotic, endangered and highly trafficked animals such as pangolins. And it would be a victory for animal conservation, he said, if markets like this one were shut down after being blamed for the disease. But that doesn't mean that the evidence is there.

"This is an animal-origin virus that made the leap, maybe from bats to humans, maybe through… another animal, maybe through livestock. And we don't have the data yet to know where or how," he said. "That takes time. The study that really definitively showed the bats that SARS came from was published in 2017," roughly 15 years after the outbreak first occurred.

"It took that long to go through caves, to go through samples, and build an evidence base where we could confidently say: 'This was the sort of bat, in this cave, at this time," Carlson said.

So when will we know for sure where SARS-CoV-2 came from? Ruling out one site took a few months. Finding the definitive origin site will likely take much longer, he said.

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

# How the U.S. Fought the 1957 Flu Pandemic

***The story of the medical researcher whose quick action protected millions of Americans from a new contagion***

**By Emily Moon**

In April 1957, a new strain of a lethal respiratory virus emerged in East Asia, caught local health authorities by surprise and eventually killed masses of people worldwide.

Today, in the age of Covid-19, that scenario sounds frighteningly familiar—with one key difference.

Maurice Hilleman, an American microbiologist then running influenza monitoring efforts at the Walter Reed Army Institute of Research, saw the problem coming and prepared the United States ahead of time. “This is the pandemic,” he recalled saying. “It’s here.”

Hilleman arranged for the U.S. military to ship samples of the pathogen, believed to be a novel influenza virus, from Hong Kong to his lab in Washington, D.C.

For five days and nights, his team tested it against blood from thousands of Americans. They found that this strain, H2N2, was unlike any flu that humans were known to have encountered. When it reached the United States, no one would be immune.

Hilleman moved quickly to alert the government, even predicting when the virus would hit U.S. shores: the first week of September, right when schools would reopen.

In the years since the 1918 pandemic, health officials had lost sight of the deadly power of aggressive strains of influenza viruses, and the U.S. Public Health Service ignored Hilleman’s warnings. “I was declared crazy,” Hilleman told the pediatrician Paul Offit, who reports the conversation in his book *Vaccinated*.

Still, having identified the new strain, Hilleman sent samples of the virus to the six biggest pharmaceutical companies, directing them to

produce a vaccine for this new flu—and they did, partly out of respect for Hilleman himself. “He had that sort of clout” within the industry, says George Dehner, a historian.

The pandemic of 1957-58 ultimately caused 1.1 million deaths worldwide, and it follows the 1918 crisis as the second-most severe influenza outbreak in U.S. history. Some 20 million Americans were infected, and 116,000 died.

Yet researchers estimate that a million more Americans would have died if not for the pharmaceutical companies that distributed 40 million doses of Hilleman’s vaccine that fall, inoculating about 30 million people.

His swift and perceptive response to the virus led one expert to predict, according to the *New York Times*, that Americans could look forward “to the time when common virus diseases will be preventable and treatable and even curable.”

Hilleman went on to join Merck & Co., where he developed vaccines for more than 40 diseases, including measles, mumps and meningitis. But as these illnesses faded from public memory, so did Hilleman, who died in 2005 at age 85.

Alexandra Lord, chair and curator of medicine and science at the National Museum of American History, says one irony of public health is that “the more successful experts are, the more people forget about the dangers.”

***https://wb.md/2yRMf1W***

## COVID-19 Data Dives: Why Don't We Have a Vaccine for SARS or MERS?

***These diseases have been around longer than COVID-19. Is there reason to be worried?***

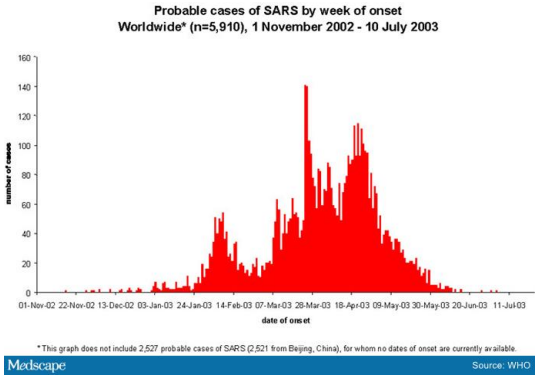
**Natalie E. Dean, PhD**

It is easy to point to the fact that we don't have licensed vaccines for severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), or HIV/AIDS as reasons to be discouraged about COVID-19. These diseases have been around longer than COVID-19. In the case of HIV/AIDS, much longer. Is there reason to be worried?

Let me attempt to provide some perspective and even a small dose of optimism. We are not in the same situation here.

First, HIV is a uniquely challenging virus, and it is possible that we may never have an HIV vaccine. HIV attacks the host immune system, making it difficult to design an effective vaccine. It also mutates rapidly, diversifying within a person over the course of their infection. Viral diversity within a single person has been shown to be comparable to viral diversity of influenza across the globe. In comparison, SARS-CoV-2 mutates even more slowly than seasonal influenza, making it a more stable target for vaccines.

Next, SARS caused an explosive outbreak in 2003 (Figure 1). Fortunately, that outbreak was contained, in part because SARS-CoV caused severe illness that was less likely to be missed during tracing, and there was no presymptomatic or asymptomatic transmission.

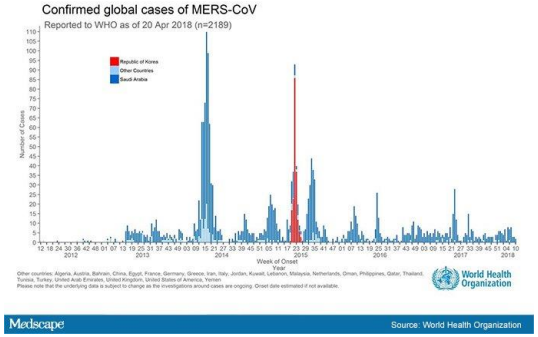



After being contained in 2003, there have been no SARS outbreaks since.

While several SARS vaccine candidates were developed, funding dried up to test them further. In addition, there has been no clear pathway for testing the efficacy of SARS vaccine and getting it approved for use. How can we determine whether a vaccine prevents SARS if there is no SARS to prevent? Thus, these candidates have been stalled at earlier stages of development.

Finally, MERS was first reported in 2012. Since then, there have been regular "spillover" events whereby the virus jumps from the camel reservoir into humans and may transmit directly between humans.

Some early MERS outbreaks were explosive, including an exported outbreak in South Korea in 2015. But Saudi Arabia, where the majority of transmission occurs, has made great improvements to its infection control procedures to prevent hospital spread. As a result, recent outbreaks have been much smaller (Figure 2).




Organizations like the Coalition for Epidemic Preparedness Innovations (CEPI) have been funding research for MERS vaccine candidates, but one persistent challenge is identifying strategies to evaluate the efficacy of these vaccines. Along with other researchers involved in the WHO R&D Blueprint, we have discussed potential strategies for a MERS vaccine efficacy trial. But given the relatively low incidence even in high-risk groups (camel workers, their families, healthcare workers), trials could need 100,000-plus participants, which isn't feasible. As a result, there still isn't a clear path forward for testing a vaccine and getting it approved by regulators.

Of course we all would be better off with effective SARS, MERS, and HIV/AIDS vaccines. In particular, if we had licensed SARS and MERS vaccines, they could be modified for COVID-19. Indeed, many of these candidates were brought back off the shelf for exactly this purpose. But the fact that approved vaccines for these diseases do not exist reflects other challenges in their development as much as anything else. For COVID-19, with widespread transmission and active funding, we should expect large trials to soon begin testing the many vaccine candidates being pursued in parallel. So if one or more of them works, we should be able to figure this out quickly.

***https://bit.ly/3qFH8TC***

## Earliest 'Chickens' Were Actually Pheasants

***A new analysis ruffles the story of poultry domestication***

**By Rachel Nuwer**

Chickens are by far the most numerous birds on the planet, with a population of around 23 billion. But new research suggests that another species was once a strong contender to become the world's favorite poultry: ancient bird remains in China have turned out to be not from the first domesticated chickens, as researchers long assumed, but from pheasants. The study further indicates that wild pheasants lived side by side with people, shedding light on the early domestication process.

***Modern pheasant.*** **Credit: J. Mrocek Getty Images**

"It's uncommon for us to have evidence of deer, for example, living with hunter-gatherers," says Loukas Barton, an archaeologist at California-based environmental consulting firm Dudek. "But in this case, we see what otherwise is considered a wild animal living in the human biome." Barton is lead author on the study, published in February in *Scientific Reports*.

Most archaeologists had assumed that bird bones found with those of pigs and dogs, along with agricultural tools, at 8,000-year-old sites in northern China were the earliest evidence of chicken domestication. But many wondered how red jungle fowl—known to be chickens' wild ancestors—could suddenly appear more than 1,000 miles from their native range in Southeast Asia. In 2015

researchers raised the possibility that the bones belonged to pheasants, which are native to northern China.

For a definitive answer, Barton and his colleagues analyzed the bones of eight birds found at Gansu Province's 7,500-year-old Neolithic Dadiwan site that were previously identified as chickens. Researchers at the University of Oklahoma used two different methods, including sequencing the full mitochondrial genome, to genetically confirm that the bones belonged to pheasants.

Biochemistry tests revealed that these pheasants subsisted on a diet heavy in millet, a human-grown crop, suggesting that the birds lived alongside people year-round—a first step toward domestication. Barton says the process likely paralleled early chicken domestication: wild birds started interacting closely with humans and eventually formed lasting, interdependent relationships with them. True domestication, however, entails physical or genetic change brought about by artificial human selection; the ancient pheasant genomes match modern ones, so these birds were still technically “wild.”

Yu Dong, a geneticist at Shandong University in China, who was not involved in the research, says these “very important” findings provide significant insight into the history of domestication. She wonders, though, whether Neolithic people would have been likely to welcome pheasants. “In many places nowadays,” Dong notes, “a net is put up in fields to prevent birds from eating up crops.”

Barton says humans probably considered pheasants a good meat source. But he suspects that pheasants' intermittent egg laying may be why the more consistent chicken was ultimately domesticated instead—perhaps explaining, he says, “why today we don't eat Kentucky Fried Pheasant.”

*This article was originally published with the title "Tastes Like Pheasant" in Scientific American 322, 6, 16 (June 2020)*
*doi:10.1038/scientificamerican0620-16a*

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

## Anesthesia's effect on consciousness solved, settling century-old scientific debate

### *Billiard-like break shot to cell-membrane structures triggers brain's loss of consciousness from anesthesia, scientists find*

La Jolla, Calif. And Jupiter, Fla.- Surgery would be inconceivable without general anesthesia, so it may come as a surprise that despite its 175-year history of medical use, doctors and scientists have been unable to explain how anesthetics temporarily render patients unconscious.

A new study from Scripps Research published Thursday evening in the *Proceedings of the National Academies of Sciences* (*PNAS*) solves this longstanding medical mystery. Using modern nanoscale microscopic techniques, plus clever experiments in living cells and fruit flies, the scientists show how clusters of lipids in the cell membrane serve as a missing go-between in a two-part mechanism. Temporary exposure to anesthesia causes the lipid clusters to move from an ordered state, to a disordered one, and then back again, leading to a multitude of subsequent effects that ultimately cause changes in consciousness.

The discovery by chemist Richard Lerner, MD, and molecular biologist Scott Hansen, PhD, settles a century-old scientific debate, one that still simmers today: Do anesthetics act directly on cell-membrane gates called ion channels, or do they somehow act on the membrane to signal cell changes in a new and unexpected way? It has taken nearly five years of experiments, calls, debates and challenges to arrive at the conclusion that it's a two-step process that begins in the membrane, the duo say. The anesthetics perturb ordered lipid clusters within the cell membrane known as "lipid rafts" to initiate the signal.

"We think there is little doubt that this novel pathway is being used for other brain functions beyond consciousness, enabling us to now chip away at additional mysteries of the brain," Lerner says.

Lerner, a member of the National Academy of Sciences, is a former president of Scripps Research, and the founder of Scripps Research's Jupiter, Florida campus. Hansen is an associate professor, in his first posting, at that same campus.

**The Ether Dome**

Ether's ability to induce loss of consciousness was first demonstrated on a tumor patient at Massachusetts General Hospital in Boston in 1846, within a surgical theater that later became known as "the Ether Dome." So consequential was the procedure that it was captured in a famous painting, "First Operation Under Ether," by Robert C. Hinckley. By 1899, German pharmacologist Hans Horst Meyer, and then in 1901 British biologist Charles Ernest Overton, sagely concluded that lipid solubility dictated the potency of such anesthetics.

Hansen recalls turning to a Google search while drafting a grant submission to investigate further that historic question, thinking he couldn't be the only one convinced of membrane lipid rafts' role. To Hansen's delight, he found a figure from Lerner's 1997 *PNAS* paper, "A hypothesis about the endogenous analogue of general anesthesia," that proposed just such a mechanism. Hansen had long looked up to Lerner--literally. As a predoctoral student in San Diego, Hansen says he worked in a basement lab with a window that looked directly out at Lerner's parking space at Scripps Research.

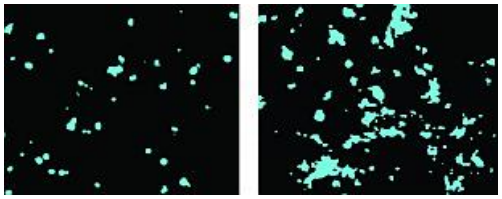
"I contacted him, and I said, 'You are never going to believe this. Your 1997 figure was intuitively describing what I am seeing in our data right now,'" Hansen recalls. "It was brilliant."

For Lerner, it was an exciting moment as well.

"This is the granddaddy of medical mysteries," Lerner says. "When I was in medical school at Stanford, this was the one problem I wanted to solve. Anesthesia was of such practical importance I couldn't believe we didn't know how all of these anesthetics could cause people to lose consciousness."

Many other scientists, through a century of experimentation, had sought the same answers, but they lacked several key elements, Hansen says: First, microscopes able to visualize biological complexes smaller than the diffraction limits of light, and second, recent insights about the nature of cell membranes, and the complex organization and function of the rich variety of lipid complexes that comprise them.

"They had been looking in a whole sea of lipids, and the signal got washed out, they just didn't see it, in large part for a lack of technology," Hansen says.



***An ordered cholesterol cluster in a cell membrane briefly becomes disordered on exposure to chloroform.*** **Hansen lab, Scripps Research**

**From order to disorder**

Using Nobel Prize-winning microscopic technology, specifically a microscope called dSTORM, short for "direct stochastical optical reconstruction microscopy," a post-doctoral researcher in the Hansen lab bathed cells in chloroform and watched something like the opening break shot of a game of billiards. Exposing the cells to chloroform strongly increased the diameter and area of cell membrane lipid clusters called GM1, Hansen explains.

What he was looking at was a shift in the GM1 cluster's organization, a shift from a tightly packed ball to a disrupted mess, Hansen says. As it grew disordered, GM1 spilled its contents, among them, an enzyme called phospholipase D2 (PLD2).

Tagging PLD2 with a fluorescent chemical, Hansen was able to watch via the dSTORM microscope as PLD2 moved like a billiard ball away from its GM1 home and over to a different, less-preferred lipid cluster called PIP2. This activated key molecules within PIP2 clusters, among them, TREK1 potassium ion channels and their lipid activator, phosphatidic acid (PA). The activation of TREK1 basically freezes neurons' ability to fire, and thus leads to loss of consciousness, Hansen says.

"The TREK1 potassium channels release potassium, and that hyper-polarizes the nerve--it makes it more difficult to fire--and just shuts it down," Hansen says.

Lerner insisted they validate the findings in a living animal model. The common fruit fly, drosophila melanogaster, provided that data. Deleting PLD expression in the flies rendered them resistant to the effects of sedation. In fact, they required double the exposure to the anesthetic to demonstrate the same response.

"All flies eventually lost consciousness, suggesting PLD helps set a threshold, but is not the only pathway controlling anesthetic sensitivity," they write.

Hansen and Lerner say the discoveries raise a host of tantalizing new possibilities that may explain other mysteries of the brain, including the molecular events that lead us to fall asleep.

Lerner's original 1997 hypothesis of the role of "lipid matrices" in signaling arose from his inquiries into the biochemistry of sleep, and his discovery of a soporific lipid he called oleamide. Hansen and Lerner's collaboration in this arena continues.

"We think this is fundamental and foundational, but there is a lot more work that needs to be done, and it needs to be done by a lot of people," Hansen says. Lerner agrees.

"People will begin to study this for everything you can imagine: Sleep, consciousness, all those related disorders," he says. "Ether was a gift that helps us understand the problem of consciousness. It has shined a light on a heretofore unrecognized pathway that the brain has clearly evolved to control higher-order functions."

*The paper, "Studies on the mechanism of general anesthesia," appears May 29, 2020, in PNAS. In addition to Lerner and Hansen, the authors are Mahmud Arif Pavel, E. Nicholas Petersen and Hao Wang, all of Scripps Research.*

***https://bit.ly/2ZUZ72v***

## New model predicts the peaks of the COVID-19 pandemic

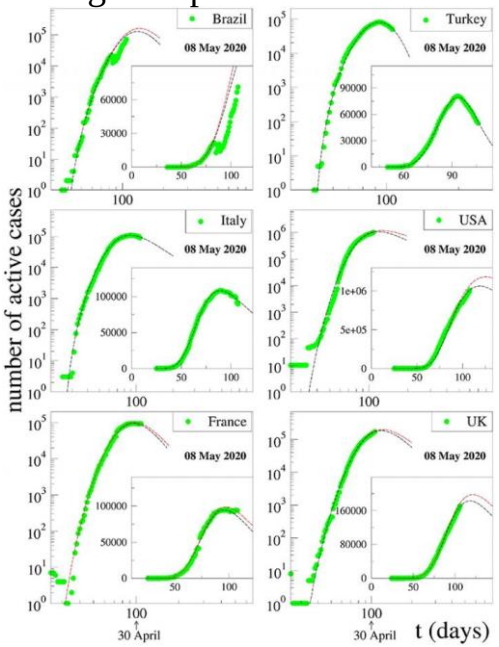
### *Function accurately describes all existing available data on active cases and deaths--and predicts forthcoming peaks*

As of late May, COVID-19 has killed more than 325,000 people around the world. Even though the worst seems to be over for countries like China and South Korea, public health experts warn that cases and fatalities will continue to surge in many parts of the world. Understanding how the disease evolves can help these countries prepare for an expected uptick in cases.

This week in the journal *Frontiers*, researchers describe a single function that accurately describes all existing available data on active cases and deaths--and predicts forthcoming peaks. The tool uses q-statistics, a set of functions and probability distributions developed by Constantino Tsallis, a physicist and member of the Santa Fe Institute's external faculty. Tsallis worked on the new model together with Ugur Tirnakli, a physicist at Ege University, in Turkey.

"The formula works in all the countries in which we have tested," says Tsallis.

Neither physicist ever set out to model a global pandemic. But Tsallis says that when he saw the shape of published graphs representing China's daily active cases, he recognized shapes he'd seen before--namely, in graphs he'd helped produce almost two decades ago to describe the behavior of the stock market. "The shape was exactly the same," he says. For the financial data, the function described probabilities of stock exchanges; for COVID-19, it described daily the number of active cases--and fatalities--as a function of time.




***Fits of the data for active cases available on 08 May 2020 for various severely affected countries around the world.*** **Constantino Tsallis and Ugur Tirnakli, Frontiers**

Modeling financial data and tracking a global pandemic may seem unrelated, but Tsallis says they have one important thing in common. "They're both complex systems," he says, "and in complex systems, this happens all the time." Disparate systems from a variety of fields--biology, network theory, computer science, mathematics--often reveal patterns that follow the same basic shapes and evolution.

The financial graph appeared in a 2004 volume co-edited by Tsallis and the late Nobelist Murray Gell-Mann. Tsallis developed q-statitics, also known as "Tsallis statistics," in the late 1980s as a generalization of Boltzmann-Gibbs statistics to complex systems.

In the new paper, Tsallis and Tirnakli used data from China, where the active case rate is thought to have peaked, to set the main parameters for the formula. Then, they applied it to other countries including France, Brazil, and the United Kingdom, and found that it matched the evolution of the active cases and fatality rates over time.

The model, says Tsallis, could be used to create useful tools like an app that updates in real-time with new available data, and can adjust its predictions accordingly. In addition, he thinks that it could be fine-tuned to fit future outbreaks as well.

"The functional form seems to be universal," he says, "Not just for this virus, but for the next one that might appear as well."

***https://bit.ly/2XjL3xv***

## Ancient people in the Kingdom of Judah may have gotten high off weed

***First known evidence of hallucinogenic substance found in the Kingdom of Judah***

**By Laura Geggel - Associate Editor**

More than 2,700 years ago, worshipers at a "holy of holies" shrine in Israel may have gotten high on weed. Researchers discovered burnt cannabis and frankincense at the site, which was located in the Kingdom of Judah.

***An aerial view of the Tel Arad fortress that stands in what was once the Kingdom of Judah.*** **© Asaf. Z; Public Domain**

Researchers made the discovery after analyzing ancient residues left on two altars at the shrine. The burnt cannabis is "the first known evidence of [a] hallucinogenic substance found in the Kingdom of Judah," a region that now includes parts of the West Bank and central Israel, the researchers wrote in the study.

Once the cannabis was burned at the Iron Age site, "we can assume that the religious altered state of consciousness in this shrine was an

important part of the ceremonies that took place here," study lead researcher Eran Arie, the curator of Iron Age and Persian period archaeology at the Israel Museum in Jerusalem, told Live Science in an email.

Archaeologists first excavated the site in the 1960s; they unearthed two fortresses, dating to from the ninth to the early sixth centuries B.C., that flanked the southern border of the Kingdom of Judah. During these excavations, archaeologists found a well-preserved shrine dating to about 750 B.C. to 715 B.C.

At the shrine's entrance were two limestone altars, one standing 18 inches (40 centimeters) high and the other 20 inches (50 cm) tall. Each altar had a shallow depression on top containing "round heaps of black solidified organic material," the researchers wrote in the study. Based on the altars' characteristics, researchers concluded this was a "holy of holies" shrine, meant to evoke the inner sanctum of the Tabernacle of the Israelites, where God was thought to appear. Tests of this black gunk in the 1960s gave mostly inconclusive results, noting only that one clump contained animal fat.

The shrine was rebuilt at the Israel Museum. (Image credit: Israel Antiquities Authority Collection, Photo © The Israel Museum, Jerusalem, by Laura Lachman)

Arie decided to reanalyze this black material, especially since some residue still remained on the altars. He teamed up with study co-researcher Dvory Namdar, a senior research fellow at the Institute of Plant Sciences at the Volcani Center of Agricultural Research in Israel. Namdar has expertise in analyzing residue from ancient burned incense, but "we never thought we [would] reveal such an amazing find" as the cannabis, Arie said.

However, Namdar was worried that the sample could have been contaminated; at the time, she worked in a lab that conducted cannabinoid research. So, the researchers "re-sampled the altars and verified the results in another laboratory at the Hebrew University of Jerusalem," Arie said. "The results were the same."

**Ceremonial burning**

The new tests revealed that the smaller altar contained burned cannabis and animal droppings. It appears that "animal dung was used as the fuel [to burn] the cannabis," Arie said. Dung burns more slowly than herbs, so it would have slowed down the burning process, he said.

The taller altar contained the remnants of frankincense and animal fat, which would have promoted evaporation of the aromatic tree resin. It's the earliest evidence that frankincense was used in a cultic practice in the Kingdom of Judah, Arie said.

Both of these findings provide clues about cultic practices in the Kingdom of Judah. In particular, the cannabis finding indicates that people may have purposefully used the plant for its "hallucinogenic ingredients," to stimulate ecstasy during cultic ceremonies, at least during the eighth century B.C., Arie said.

Practices at this shrine may also shed light on the First Temple, also known as Solomon's Temple, which was also in the Kingdom of Judah and in use at the same time. The shrine at Arad "was an official shrine of the Kingdom of Judah," Arie said, so it's possible that these findings can be "extra-biblical evidence" that similar practices were used in the First Temple, Arie said.

In other words, the bible mentions that frankincense was burned in the First Temple, but because this shrine used both cannabis and frankincense, these substances "were probably also (at least) part of the components of the incense that was burnt in the Temple in Jerusalem," Arie said.

Where did these burned ingredients originate? Frankincense comes from Arabia, so it's likely that the Kingdom of Judah took part in the south Arabian trade, even before the Assyrian empire encouraged such practices starting in 701 B.C., the researchers said.

Moreover, it probably wasn't cheap. "The high value of frankincense is further reflected in the Bible, where its price is compared several times with that of gold and precious stones, and it is often described as a royal treasure," the researchers wrote in the study.

Cannabis, in contrast, isn't local to the Middle East. Rather, cannabis originated high on the Tibetan Plateau, according to a study of fossil pollen. What's more, there aren't any cannabis seeds or pollen remains known in the ancient Near East's archaeological record. So, it's possible that cannabis plants "may have been imported from distant origins and were transported as dried resin (commonly known as hashish)," the researchers wrote in the study.

The new finding "is revolutionary in making a case for the use of specialized psychoactive plants in early Israelite religion," said Patrick McGovern, the scientific director of the Biomolecular Archaeology Project at the Penn Museum in Philadelphia, who was not involved in the study.

However, McGovern said the study could have delved deeper into the cannabis findings. "The proposal that the cannabis was heated to release psychoactive compounds, rather than for its aroma as an incense (provided by the frankincense, in any case), is an intriguing proposition," he said.

It's interesting that the Hebrew Bible doesn't appear to mention cannabis use, and that there isn't any known archaeobotanical evidence for the plant at the shrine, he noted. That said, it may not be far-fetched, given that people in the Kingdom of Judah did use another mind-altering substance in rituals, namely alcohol, McGovern said. The study doesn't mention "the psychoactive properties of grape wine, which we know to have played a central role in early Israelite religion," McGovern said.

The study was published online yesterday (May 28) in the journal Tel Aviv.

***https://bit.ly/36PmWKr***

## Boys End Up in Hospital After Trying to Gain Superpowers From a Black Widow Bite

***Brothers believed the bite would give them superpowers***

**Jacob Sarkisian, Business Insider**

Three boys from Bolivia let a black widow spider bite them in the hopes of gaining Spider-Man's powers, but they ended up in hospital instead.

**Mark Kostich/iStock/Getty Images Plus**

The brothers, aged 12, 10, and 8, were herding goats in Chayanta when they found a spider, Telemundo first reported after a Ministry of Health official revealed the details at a coronavirus briefing.

The official, Virgilio Pietro, said that the three boys repeatedly poked the deadly spider with a stick until it bit each one of the brothers in turn. They believed the bite would give them superpowers.

Their mother found them crying, and they were soon transferred to a hospital after visiting a nearby health centre. They began to suffer fevers, tremors, and muscle pains and were therefore transferred a third time to the Children's Hospital in La Paz. They were treated there and, a week after they were bitten, were finally discharged.

Telemundo reported that Pietro detailed the story during his briefing as a warning to parents: "For children, everything is real, movies are real."

According to *National Geographic*, black widow spiders, one of the most feared breeds in the world and the most venomous in North America, have venom 15 times more powerful than a rattlesnake's.

*National Geographic* also says that black widows only bite in self-defence, and that while their bites are not usually fatal, children are most at risk along with the elderly and infirm.

***This article was originally published by Business Insider.***

https://nyti.ms/3qIFctq

# How Line-Dried Laundry Gets That Fresh Smell

***This is what happens when atmospheric chemists hang towels on drying racks around their chemistry building.***

**By Cara Giaimo**

People have written poems about it. It has been imitated by candles and air fresheners. At least one person has even fought in court for the right to produce it naturally.

It's the smell of line-dried laundry.

Some atmospheric chemists like that scent, too. In a paper published this year in Environmental Chemistry, researchers examined line-dried towels at the molecular level, to try to pinpoint the source of their specific fragrance.

Silvia Pugliese led the research while she was a master's student at the University of Copenhagen. When Ms. Pugliese was a child, her mother line-dried laundry, and she still does it whenever she can.

"The fresh smell reminds me of home," she said. So she was excited to rigorously pursue such an everyday research subject.

In between their more official thesis work, Ms. Pugliese and two labmates, with their adviser Matthew Stanley Johnson, commandeered two little-used areas of the university's chemistry building — a dark, empty office and a small, fifth-floor balcony — and obtained materials, including ultrapurified water and a set of cotton towels from Ikea.

Each towel got washed three times in the water, and then hung out: inside the office, on the balcony under a plastic shade or on the balcony in the sun.

When they came across the drying racks, "a lot of colleagues laughed," Ms. Pugliese said. "But we had a lot of support."

When a towel finished drying, the researchers sealed it in a bag for 15 hours. As the towel sat in the bag, they sampled the chemical compounds it released into the air around it. The researchers performed similar sampling on an empty bag, an unwashed towel and the air around the drying sites.

By comparing the experimental towels' chemical profiles to those controls and to each other, the researchers were able to tease out which compounds popped up only when they hung wet towels in

Line-drying uniquely produced a number of aldehydes and ketones: organic molecules our noses might recognize from plants and perfumes. For example, after sunbathing, the towels emitted pentanal, found in cardamom, octanal, which produces citrusy aromas, and nonanal, which smells roselike.

Why is that? It may have to do with exposure to ozone, an atmospheric chemical that can transform some common chemicals into those aldehydes and ketones.

A more fundamental contribution, she thinks, may come from the sun itself. When exposed to ultraviolet light, certain molecules "get excited" and form highly reactive compounds called radicals, Ms. Pugliese said. Those radicals then recombine with other nearby molecules, processes that often lead to the creation of aldehydes as well as ketones.

It's possible that the water on a wet towel gathers a lot of these excitable molecules together, and then works "like a magnifying glass," concentrating the sunlight and speeding up these reactions, Ms. Pugliese said.

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Similar processes are likely occurring on any number of natural outdoor surfaces, including bare soil and individual blades of grass — perhaps part of the reason that sun after a rainstorm makes the world smell fresh. (Although the scent seems to last longer on clothes, potentially because aldehydes bond with cotton, said Ms. Pugliese.)

Ricardo López, a chemist at the Lab for Flavor Analysis and Enology at the University of Zaragoza in Spain who was not

involved in the research, thinks the aldehydes and ketones may not tell the whole story. “When testing for key flavor compounds, sometimes compounds in low concentrations are as important as those in high concentrations,” he said. Additional forms of testing might be helpful to get the full bouquet.

Ms. Pugliese has, for now, moved onto headier things — her doctoral research involves artificial photosynthesis — but she hopes to dig into similar topics in the future.

“I thought it was a really nice way to do science,” she said.

***https://nyti.ms/2zP8nKD***

## It’s Not Whether You Were Exposed to the Virus. It’s How Much.

***The pathogen is proving a familiar adage: The dose makes the poison.***

**By Apoorva Mandavilli**

When experts recommend wearing masks, staying at least six feet away from others, washing your hands frequently and avoiding crowded spaces, what they’re really saying is: Try to minimize the amount of virus you encounter.

A few viral particles cannot make you sick — the immune system would vanquish the intruders before they could. But how much virus is needed for an infection to take root? What is the minimum effective dose?

A precise answer is impossible, because it’s difficult to capture the moment of infection. Scientists are studying ferrets, hamsters and mice for clues but, of course, it wouldn’t be ethical for scientists to expose people to different doses of the coronavirus, as they do with milder cold viruses.

“The truth is, we really just don’t know,” said Angela Rasmussen, a virologist at Columbia University in New York. “I don’t think we can make anything better than an educated guess.”

Common respiratory viruses, like influenza and other coronaviruses, should offer some insight. But researchers have found little consistency.

For SARS, also a coronavirus, the estimated infective dose is just a few hundred particles. For MERS, the infective dose is much higher, on the order of thousands of particles.

The new coronavirus, SARS-CoV-2, is more similar to the SARS virus and, therefore, the infectious dose may be hundreds of particles, Dr. Rasmussen said.

But the virus has a habit of defying predictions.

Generally, people who harbor high levels of pathogens — whether from influenza, H.I.V. or SARS — tend to have more severe symptoms and are more likely to pass on the pathogens to others.

But in the case of the new coronavirus, people who have no symptoms seem to have viral loads — that is, the amount of virus in their bodies — just as high as those who are seriously ill, according to some studies.

And coronavirus patients are most infectious two to three days before symptoms begin, less so after the illness really hits.

Some people are generous transmitters of the coronavirus; others are stingy. So-called super-spreaders seem to be particularly gifted in transmitting it, although it’s unclear whether that’s because of their biology or their behavior.

On the receiving end, the shape of a person’s nostrils and the amount of nose hair and mucus present — as well as the distribution of certain cellular receptors in the airway that the virus needs to latch on to — can all influence how much virus it takes to become infected.

A higher dose is clearly worse, though, and that may explain why some young health care workers have fallen victim even though the virus usually targets older people.

The crucial dose may also vary depending on whether it's ingested or inhaled.

People may take in virus by touching a contaminated surface and then putting their hands on their nose or mouth. But "this isn't thought to be the main way the virus spreads," according to the Centers for Disease Control and Prevention.

That form of transmission may require millions more copies of the virus to cause an infection, compared to inhalation.

Coughing, sneezing, singing, talking and even heavy breathing can result in the expulsion of thousands of large and small respiratory droplets carrying the virus.

"It's clear that one doesn't have to be sick and coughing and sneezing for transmission to occur," said Dr. Dan Barouch, a viral immunologist at Beth Israel Deaconess Medical Center in Boston.

Larger droplets are heavy and float down quickly — unless there's a breeze or an air-conditioning blast — and can't penetrate surgical masks. But droplets less than 5 microns in diameter, called aerosols, can linger in the air for hours.

"They travel further, last longer and have the potential of more spread than the large droplets," Dr. Barouch said.

Three factors seem to be particularly important for aerosol transmission: proximity to the infected person, air flow and timing.

A windowless public bathroom with high foot traffic is riskier than a bathroom with a window, or a bathroom that's rarely used. A short outdoor conversation with a masked neighbor is much safer than either of those scenarios.

Recently, Dutch researchers used a special spray nozzle to simulate the expulsion of saliva droplets and then tracked their movement. The scientists found that just cracking open a door or a window can banish aerosols.

"Even the smallest breeze will do something," said Daniel Bonn, a physicist at the University of Amsterdam who led the study.

Observations from two hospitals in Wuhan, China, published in April in the journal Nature, determined much the same thing: more aerosolized particles were found in unventilated toilet areas than in airier patient rooms or crowded public areas.

This makes intuitive sense, experts said. But they noted that aerosols, because they are smaller than 5 microns, would also contain much less, perhaps millions-fold less, virus than droplets of 500 microns.

"It really takes a lot of these single-digit size droplets to change the risk for you," said Dr. Joshua Rabinowitz, a quantitative biologist at Princeton University.

Apart from avoiding crowded indoor spaces, the most effective thing people can do is wear masks, all of the experts said. Even if masks don't fully shield you from droplets loaded with virus, they can cut down the amount you receive, and perhaps bring it below the infectious dose.

"This is not a virus for which hand washing seems like it will be enough," Dr. Rabinowitz said. "We have to limit crowds, we have to wear masks."

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

## New study shows how ketamine combats depression

***Researchers have identified a key target for the drug: specific serotonin receptors in the brain.***

The anaesthetic drug ketamine has been shown, in low doses, to have a rapid effect on difficult-to-treat depression. Researchers at Karolinska Institutet now report that they have identified a key target for the drug: specific serotonin receptors in the brain. Their findings, which are published in *Translational Psychiatry*, give hope of new, effective antidepressants.

Depression is the most common psychiatric diagnosis in Sweden, affecting one in ten men and one in five women at some point

during their lives. Between 15 and 30 per cent of patients are not helped by the first two attempts at therapy, in which case the depression is designated difficult to treat. Studies have shown that low doses of the anaesthetic drug ketamine are rapid acting on certain sufferers, but exactly how it works is unknown. A nasal spray containing ketamine has recently been approved in the USA and EU for patients with treatment-resistant depression.

Researchers at Karolinska Institutet in Sweden have now imaged the brains of study participants using a PET (positron emission tomography) camera in connection with ketamine treatment.

"In this, the largest PET study of its kind in the world, we wanted to look at not only the magnitude of the effect but also if ketamine acts via serotonin 1B receptors," says the study's first author Mikael Tiger, researcher at the Department of Clinical Neuroscience, Karolinska Institutet. "We and another research team were previously able to show a low density of serotonin 1B receptors in the brains of people with depression."

In the first phase of the study, 30 people with difficult-to-treat depression were randomly assigned to either a ketamine-infusion group (20 individuals) or a placebo (saline) group. It was a randomised double-blind study, so neither patient nor doctor initially knew who received the active substance. The participants' brains were imaged with a PET camera before the infusion and 24-72 hours afterwards.

In the next phase, those who so wished (29 individuals) received ketamine twice a week for two weeks. The result was that over 70 per cent of those treated with ketamine responded to the drug according to a rating scale for depression.

Serotonin plays a key role in depression and low levels are thought to be linked to more serious disease. There are 14 different kinds of receptor for this neurotransmitter on the surface of neurons. For their PET imaging, the researchers used a radioactive marker that binds specifically to serotonin 1B receptors. They found that the ketamine operated via these receptors in a formerly unknown mechanism of action. Binding to this receptor reduces the release of serotonin but increases that of another neurotransmitter called dopamine. Dopamine is part of the brain's reward system and helps people to experience positive feelings about life, something that is often lacking in depression.

"We show for the first time that ketamine treatment increases the number of serotonin 1B receptors," says the study's last author Johan Lundberg, research group leader at the Department of Clinical Neuroscience, Karolinska Institutet. "Ketamine has the advantage of being very rapid-acting, but at the same time it is a narcotic-classed drug that can lead to addiction. So it'll be interesting to examine in future studies if this receptor can be a target for new, effective drugs that don't have the adverse effects of ketamine."

*The study was conducted in association with North Stockholm Psychiatry and was financed by the Swedish Research Council, the Söderström König Foundation, the Centre for Psychiatry Research, Region Stockholm, the Swedish Psychiatric Foundation and Karolinska Institutet.*

*Publication: "A randomized placebo controlled PET study of ketamine's effect on serotonin 1B receptor binding in patients with SSRI resistant depression." Mikael Tiger, Emma R. Veldman, Carl-Johan Ekman, Christer Halldin, Per Svenningsson and Johan Lundberg. Translational Psychiatry, online 1 June 2020, doi: 10.1038/s41398-020-0844-4.*