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Can a century-old TB vaccine steel the immune system against the new coronavirus?

Researchers will test whether bacillus Calmette-Guérin can rev up the human immune system in a broad way

By Jop de Vrieze

Researchers in four countries will soon start a clinical trial of an unorthodox approach to the new coronavirus. They will test whether a century-old vaccine against tuberculosis (TB), a bacterial disease, can rev up the human immune system in a broad way, allowing it to better fight the virus that causes coronavirus disease 2019 and, perhaps, prevent infection with it altogether. The studies will be done in physicians and nurses, who are at higher risk of becoming infected with the respiratory disease than the general population, and in the elderly, who are at higher risk of serious illness if they become infected.

A team in the Netherlands will kick off the first of the trials this week. They will recruit 1000 health care workers in eight Dutch hospitals who will either receive the vaccine, called bacillus Calmette-Guérin (BCG), or a placebo.

BCG contains a live, weakened strain of *Mycobacterium bovis*, a cousin of *M. tuberculosis*, the microbe that causes TB. (The vaccine is named after French microbiologists Albert Calmette and Camille Guérin, who developed it in the early 20th century.) The vaccine is given to children in their first year of life in most countries of the world, and is safe and cheap—but far from perfect: It prevents about 60% of TB cases in children on average, with large differences between countries.

Vaccines generally raise immune responses specific to a targeted pathogen, such as antibodies that bind and neutralize one type of virus but not others. But BCG may also increase the ability of the immune system to fight off pathogens other than the TB bacterium, according to clinical and observational studies published over several decades by Danish researchers Peter Aaby and Christine Stabell Benn, who live and work in Guinea-Bissau. They concluded the vaccine prevents about 30% of infections with any known pathogen, including viruses, in the first year after it's given. The studies published in this field have been criticized for their methodology, however; a 2014 review ordered by the World Health Organization concluded that BCG appeared to lower overall mortality in children, but rated confidence in the findings as "very low." A 2016 review was a bit more positive about BCG's potential benefits but said randomized trials were needed.

Since then, the clinical evidence has strengthened and several groups have made important steps investigating how BCG may generally boost the immune system. Mihai Netea, an infectious disease specialist at Radboud University Medical Center, discovered that the vaccine may defy textbook knowledge of how immunity works.

When a pathogen enters the body, white blood cells of the "innate" arm of the immune system attack it first; they may handle up to 99% of infections. If these cells fail, they call in the "adaptive" immune system, and T cells and antibody-producing B cells start to divide to join the fight. Key to this is that certain T cells or antibodies are specific to the pathogen; their presence is amplified the most. Once the pathogen is eliminated, a small portion of these pathogen-specific cells transform into memory cells that speed up T cell and B cell production the next time the same pathogen attacks. Vaccines are based on this mechanism of immunity.

The innate immune system, composed of white blood cells such as macrophages, natural killer cells, and neutrophils, was supposed to have no such memory. But Netea's team discovered that BCG, which can remain alive in the human skin for up to several months,

triggers not only *Mycobacterium*-specific memory B and T cells, but also stimulates the innate blood cells for a prolonged period. "Trained immunity," Netea and colleagues call it. In a randomized placebo-controlled study published in 2018, the team showed that BCG vaccination protects against experimental infection with a weakened form of the yellow fever virus, which is used as a vaccine. Together with Evangelos Giamarellos from the University of Athens, Netea has set up a study in Greece to see whether BCG can increase resistance to infections overall in elderly people. He is planning to start a similar study in the Netherlands soon. The trial was designed before the new coronavirus emerged, but the pandemic may reveal BCG's broad effects more clearly, Netea says.

For the health care worker study, Neeta teamed up with epidemiologist and microbiologist Marc Bonten of UMC Utrecht. "There is a lot of enthusiasm to participate," among the workers, Bonten says. The team decided not to use actual infection with coronavirus as the study outcome, but "unplanned absenteeism." "We don't have a large budget and it won't be feasible to visit the sick professionals at home," Bonten says. Looking at absenteeism has the advantage that any beneficial effects of the BCG vaccine on influenza and other infections may be captured as well, he says.

Although the study is randomized, participants will likely know if they got the vaccine instead of a placebo. BCG often causes a pustule at the injection site that may persist for months, usually resulting in a scar. But the researchers will be blinded to which arm of the study—vaccine or placebo—a person is in.

A research group at the University of Melbourne is setting up a BCG study among health care workers using the exact same protocol. Another research group at the University of Exeter will do a similar study in the elderly. And a team at the Max Planck Institute for Infection Biology last week announced that—inspired by Netea's work—it will embark on a similar trial in elderly people and health workers with VPM1002, a genetically modified version of BCG that has not yet been approved for use against TB.

Eleanor Fish, an immunologist at the of the University of Toronto, says the vaccine probably won't eliminate infections with the new coronavirus completely, but is likely to dampen its impact on individuals. Fish says she'd take the vaccine herself if she could get a hold of it, and even wonders whether it's ethical to withhold its potential benefits from trial subjects in the placebo arm.

But Netea says the randomized design is critical: "Otherwise we would never know if this is good for people." The team may have answers within a few months.

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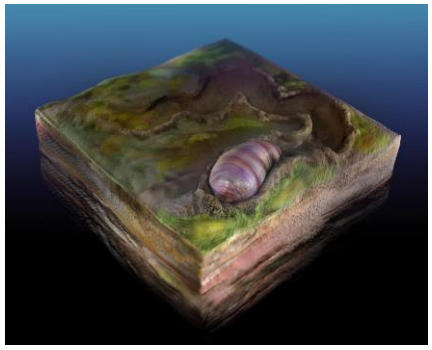
Ancestor of all animals identified in Australian fossils

A wormlike creature that lived more than 555 million years ago is the earliest bilaterian

A team led by UC Riverside geologists has discovered the first ancestor on the family tree that contains most familiar animals today, including humans.



Artist's rendering of Ikaria wariootia. **Sohail Wasif/UCR**

The tiny, wormlike creature, named *Ikaria wariootia*, is the earliest bilaterian, or organism with a front and back, two symmetrical sides, and openings at either end connected by a gut. The paper is published today in *Proceedings of the National Academy of Sciences*.

The earliest multicellular organisms, such as sponges and algal mats, had variable shapes. Collectively known as the Ediacaran Biota, this group contains the oldest fossils of complex, multicellular organisms.

However, most of these are not directly related to animals around today, including lily pad-shaped creatures known as *Dickinsonia* that lack basic features of most animals, such as a mouth or gut.

The development of bilateral symmetry was a critical step in the evolution of animal life, giving organisms the ability to move purposefully and a common, yet successful way to organize their bodies. A multitude of animals, from worms to insects to dinosaurs to humans, are organized around this same basic bilaterian body plan.

Evolutionary biologists studying the genetics of modern animals predicted the oldest ancestor of all bilaterians would have been simple and small, with rudimentary sensory organs. Preserving and identifying the fossilized remains of such an animal was thought to be difficult, if not impossible.

For 15 years, scientists agreed that fossilized burrows found in 555 million-year-old Ediacaran Period deposits in Nilpena, South Australia, were made by bilaterians. But there was no sign of the creature that made the burrows, leaving scientists with nothing but speculation.

Scott Evans, a recent doctoral graduate from UC Riverside; and Mary Droser, a professor of geology, noticed miniscule, oval impressions near some of these burrows.

With funding from a NASA exobiology grant, they used a three-dimensional laser scanner that revealed the regular, consistent shape of a cylindrical body with a distinct head and tail and faintly grooved musculature. The animal ranged between 2-7 millimeters long and about 1-2.5 millimeters wide, with the largest the size and shape of a grain of rice -- just the right size to have made the burrows.

"We thought these animals should have existed during this interval, but always understood they would be difficult to recognize," Evans said. "Once we had the 3D scans, we knew that we had made an important discovery."

The researchers, who include Ian Hughes of UC San Diego and James Gehling of the South Australia Museum, describe *Ikaria wariootia*, named to acknowledge the original custodians of the land.

The genus name comes from Ikara, which means "meeting place" in the Adnyamathanha language. It's the Adnyamathanha name for a grouping of mountains known in English as Wilpena Pound. The species name comes from Warioota Creek, which runs from the Flinders Ranges to Nilpena Station.

"Burrows of *Ikaria* occur lower than anything else. It's the oldest fossil we get with this type of complexity," Droser said. "*Dickinsonia* and other big things were probably evolutionary dead ends. We knew that we also had lots of little things and thought these might have been the early bilaterians that we were looking for."

In spite of its relatively simple shape, *Ikaria* was complex compared to other fossils from this period. It burrowed in thin layers of well-oxygenated sand on the ocean floor in search of organic matter, indicating rudimentary sensory abilities. The depth and curvature of *Ikaria* represent clearly distinct front and rear ends, supporting the directed movement found in the burrows.

The burrows also preserve crosswise, "V"-shaped ridges, suggesting *Ikaria* moved by contracting muscles across its body like a worm, known as peristaltic locomotion. Evidence of sediment displacement in the burrows and signs the organism fed on buried organic matter reveal *Ikaria* probably had a mouth, anus, and gut.

"This is what evolutionary biologists predicted," Droser said. "It's really exciting that what we have found lines up so neatly with their prediction."

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Extract from seeds of the Melinjo tree may improve obesity and diabetes

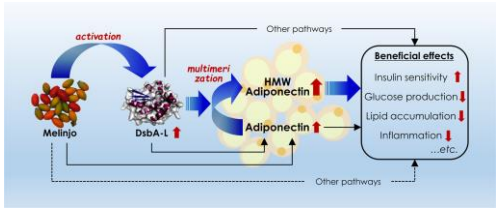
Melinjo seed extract activates the physiologically beneficial substance adiponectin which improves obesity and diabetes

日本のニュース

In Southeast Asia, the fruit, flowers, and leaves of Indonesia's "Melinjo" tree are traditional foods. Researchers from Kumamoto University, Japan who study plants from around the world for useful medicinal properties have found that Melinjo seed extract (MSE) stimulates the production of adiponectin, a beneficial hormone that improves obesity and diabetes. They also discovered that individual genotype differences were responsible for variations in its efficacy.

Melinjo fruit have high antioxidant and antibacterial qualities and are known to contain large amounts of polyphenols. One such compound, resveratrol, has been shown to induce adiponectin and may improve lifestyle-related diseases like metabolic syndrome.

Gnetin C, a type of resveratrol abundant in MSE, is known to have higher antioxidant activity and stays in the body longer than resveratrol. However, the detailed mechanism by which these compounds exert their biological activity is still unknown.



Proposed mechanism by which MSE promotes the expression of DsbA-L in the living body, increases the amount of activated adiponectin, and improves obesity and diabetes symptoms. DsbA-L, disulfide-bond A oxidoreductase-like protein; HMW, high-molecular-weight. **Credit: Associate Professor Tsuyoshi Shuto**

Kumamoto University's Global Center for Natural Resources Sciences conducts component isolation and identification of useful plants and natural products from around the world and evaluates their pharmacological activities. Within the center, Dr. Kentaro Oniki's research team used genetic analysis to find that differences in the type of DsbA-L (Disulfide-bond-A oxidoreductase-like protein) gene affects adiponectin activation. In other words, DsbA-L induction may promote adiponectin activation and improve lifestyle-related diseases. In their recent work, they attempted to determine 1) whether MSE enhances the function of DsbA-L, 2) whether MSE promotes adiponectin activation, and 3) whether MSE has a therapeutic effect on obesity and diabetes.

In their first study (double-blind, placebo-controlled, randomized controlled), 42 healthy adult men took MSE supplements orally for 14 days. They found that taking 300 mg of MSE per day activated adiponectin in human males. They also found that effects varied depending on the differences in the type of DsbA-L gene (G/G, G/T, T/T) possessed by the individual. MSE effects were large in G/T or T/T genotype carriers whose gene expression level was presumed to be low.

Following the results of the clinical trials, another of the center's researchers, Dr. Tsuyoshi Shuto, and his research team tested the compound in a high fat diet mouse model with obesity-induced diabetes. By measuring the effects of MSE on DsbA-L expression and blood adiponectin concentration in various tissues, they found that daily oral administration of MSE over a period of four weeks increased the expression of DsbA-L and the amount of activated adiponectin in the body. Diabetic pathologies, in muscle tissue also improved. Symptoms such as increased fat accumulation and fasting blood sugar levels significantly improved.

These research results show that MSE promotes DsbA-L expression, increases the amount of activated adiponectin, and may improve obesity and diabetic symptoms in living organisms, especially in mice.

"We believe that our findings can benefit human health through the treatment of obesity and diabetes by focusing on the induction of the DsbA-L gene using MSE," said Associate Professor Shuto. "We hope that this work contributes to a healthier society through the creation of innovative medicines and products from plants and other natural resources. It is important to provide solid scientific evidence that supports the use of natural resources in emerging countries and using them for beneficial drug discovery and health."

*This research was posted online in "*Scientific Reports*" on 9 March 2020.*

[Source]

Oniki, K., Kawakami, T., Nakashima, A., Miyata, K., Watanabe, T., Fujikawa, H., ... Shuto, T. (2020). Melinjo seed extract increases adiponectin multimerization in physiological and pathological conditions. Scientific Reports, *10(1). doi:10.1038/s41598-020-61148-2*

https://wb.md/2WJOwpp

Coming Out of Retirement During a Pandemic -- Is It Possible?

Retired nurses and advanced practice providers may want to help their former colleagues cope with the waves of sick patients

Carolyn Buppert, MSN, JD

With the COVID-19 pandemic, we are hearing about healthcare provider shortages on a daily basis, and these staffing crunches could get much worse. Retired nurses and advanced practice providers may want to help their former colleagues cope with the waves of sick patients pouring into the healthcare system.

The questions most often asked are whether lapsed licenses can be reinstated, and do any national emergency declaration provisions allow nurses in one state to cross state lines and work in another state?

To answer either of these questions, the nurse should check the state board of nursing, and check back daily, because the rules are changing day by day. Governors of some states are authorizing boards of nursing, pharmacy, and medicine to cut through red tape to allow nurses, as well as pharmacists and physicians, who are retired or are licensed in other states to be licensed as quickly as possible.

For example, Gov Jared Polis of Colorado has authorized emergency provisions for nurses licensed in other states but living in Colorado and for retired Colorado nurses. In a guidance document issued March 13, 2020, existing licensing exemptions allow for individuals in the healthcare field who either hold licenses in other states or who have allowed their license to expire in Colorado to immediately resume work within their scope of practice, provided their out-of-state or expired license is/was in good standing.

The National Council of State Boards of Nursing has compiled a State COVID-19 Response Document with information about emergency action by states.

The retired nurse's inactive license usually can be reactivated by filing forms with the board of nursing. It is likely to be more complicated if the nurse has been retired for more than 5 years. For example, in Maryland, nurses who have practiced 1000 hours in the past 5 years do not need to complete a refresher course and may reactivate their license by filing the application and paying a modest fee.

Those who have been retired for more than 5 years usually will need to undergo a refresher course. Again, check with your Board of Nursing, and check frequently.

Note that some Board of Nursing staff may not be in the office during this time of social distancing. Some staff may be able to conduct business from their homes.

In regard to working across state lines, nurses registered in states that are part of the Enhanced Nurse Licensure Compact (eNLC) may work in a compact state without obtaining another license. Check the website of the Board of Nursing in the state where you want to work to verify that state's policy on eNLC.

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Coronavirus Could Be a 'Chimera' of Two Different Viruses, Genome Analysis Suggests

In the space of a few weeks, we have all learned a lot about COVID-19 and the virus that causes it: SARS-CoV-2. But there have also been a lot of rumours.

Alexandre Hassanin, The Conversation

And while the number of scientific articles on this virus is increasing, there are still many grey areas as to its origins.

In which animal species did it occur? A bat, a pangolin or another wild species? Where does it come from? From a cave or a forest in the Chinese province of Hubei, or elsewhere?

In December 2019, 27 of the first 41 people hospitalised (66 percent) passed through a market located in the heart of Wuhan city in Hubei province. But, according to a study conducted at Wuhan Hospital, the very first human case identified did not frequent this market. Instead, a molecular dating estimate based on the SARS-CoV-2 genomic sequences indicates an origin in November. This raises questions about the link between this COVID-19 epidemic and wildlife.

Genomic data

The SARS-CoV-2 genome was rapidly sequenced by Chinese researchers. It is an RNA molecule of about 30,000 bases containing 15 genes, including the S gene which codes for a protein located on the surface of the viral envelope (for comparison, our genome is in the form of a double helix of DNA about 3 billion bases in size and contains about 30,000 genes).

Comparative genomic analyses have shown that SARS-CoV-2 belongs to the group of *Betacoronaviruses* and that it is very close to SARS-CoV, responsible for an epidemic of acute pneumonia which appeared in November 2002 in the Chinese province of Guangdong and then spread to 29 countries in 2003.

A total of 8,098 cases were recorded, including 774 deaths. It is known that bats of the genus *Rhinolophus* (potentially several cave species) were the reservoir of this virus and that a small carnivore, the palm civet (*Paguma larvata*), may have served as an intermediate host between bats and the first human cases.

Since then, many *Betacoronaviruses* have been discovered, mainly in bats, but also in humans. For example, RaTG13, isolated from a bat of the species *Rhinolophus affinis* collected in China's Yunan Province, has recently been described as very similar to SARS-CoV-2, with genome sequences identical to 96 percent.

These results indicate that bats, and in particular species of the genus *Rhinolophus*, constitute the reservoir of the SARS-CoV and SARS-CoV-2 viruses.

But how do you define a reservoir? A reservoir is one or several animal species that are not or not very sensitive to the virus, which will naturally host one or several viruses.

The absence of symptoms of the disease is explained by the effectiveness of their immune system, which allows them to fight against too much viral proliferation.

Recombination mechanism

On 7 February, 2020, we learned that a virus even closer to SARS-CoV-2 had been discovered in pangolin. With 99 percent of genomic concordance reported, this suggested a more likely reservoir than bats.

However, a recent study under review shows that the genome of the coronavirus isolated from the Malaysian pangolin (*Manis javanica*) is less similar to SARS-Cov-2, with only 90 percent of genomic concordance. This would indicate that the virus isolated in the pangolin is not responsible for the COVID-19 epidemic currently raging.

However, the coronavirus isolated from pangolin is similar at 99 percent in a specific region of the S protein, which corresponds to

the 74 amino acids involved in the ACE (Angiotensin Converting Enzyme 2) receptor binding domain, the one that allows the virus to enter human cells to infect them.

By contrast, the virus RaTG13 isolated from bat *R. affinis* is highly divergent in this specific region (only 77 percent of similarity). This means that the coronavirus isolated from pangolin is capable of entering human cells whereas the one isolated from bat *R. affinis* is not.

In addition, these genomic comparisons suggest that the SARS-Cov-2 virus is the result of a recombination between two different viruses, one close to RaTG13 and the other closer to the pangolin virus. In other words, it is a chimera between two pre-existing viruses. This recombination mechanism had already been described in coronaviruses, in particular to explain the origin of SARS-CoV. It is important to know that recombination results in a new virus potentially capable of infecting a new host species.

For recombination to occur, the two divergent viruses must have infected the same organism simultaneously.

Two questions remain unanswered: in which organism did this recombination occur? (a bat, a pangolin or another species?) And above all, under what conditions did this recombination take place?

Alexandre Hassanin, Maître de Conférences (HDR) à Sorbonne Université, ISYEB - Institut de Systématique, Evolution, Biodiversité (CNRS, MNHN, SU, EPHE, UA), Muséum national d'histoire naturelle (MNHN).

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Superconductivity Has Been Discovered in Meteorites For The First Time

Scientists have found naturally occurring superconductive grains embedded inside two distinct meteorites

Peter Dockrill

Scientists have found naturally occurring superconducting materials in extraterrestrial objects for the first time, discovering superconductive grains embedded inside two distinct meteorites that crash-landed on Earth.

The discovery is just the latest to show that meteorites are much more than space debris that falls out of the sky. Recent investigations have turned up meteorite-borne deliveries of possible extraterrestrial proteins, minerals we've never encountered, and materials older than the Solar System itself. But we've never seen something quite like this before.

Superconductivity is a set of physical properties that ensures 'perfect' electrical conductivity in a material, meaning all electrical resistance inside the material vanishes, among other effects. This prized phenomenon is incredibly rare in natural materials that haven't been specially treated – or, at least, it's rare on Earth.

In the distant sky above, things could be very, very different, researchers say, with extreme environments in space creating exotic material phases not seen on Earth, via astronomical events that can unleash incredibly high temperatures and extremely high amounts of pressure.

Because of this, the thinking goes, meteorites could be good candidates for finding naturally formed superconducting materials forged in the strangeness of space. The only problem is, previous searches have never identified any such superconducting compounds. At least, not until now.

In a new study led by researchers from UC San Diego, scientists investigated fragments from 15 different meteorites, using a technique called magnetic field modulated microwave spectroscopy to detect traces of superconductivity inside the samples.

A fragment of the Mundrabilla meteorite. **(James Wampler)**

They got two hits: one, in an iron meteorite called Mundrabilla, one of the largest meteorites ever found, which was discovered in

Australia in 1911; the other, a rare ureilite meteorite called GRA 95205, located in Antarctica a quarter-century ago.

According to the team's measurements, which also drew upon vibrating sample magnetometry (VSM) and energy dispersive X-ray spectroscopy (EDX) methods, both of these space rocks contain minute amounts of extraterrestrial superconductive grains.

"Naturally occurring superconductive materials are unusual, but they are particularly significant because these materials could be superconducting in extraterrestrial environments," says physicist and nanoscientist James Wampler. "These measurements and analysis identified the likely phases as alloys of lead, indium, and tin." It's a major find – and not only because it's a first in meteorites. "Even the simplest superconducting mineral, lead, is only rarely found naturally in its native form, and, to our knowledge, there are no previous reports of natural lead samples superconducting," the authors explain in their paper.

"In fact, we are only aware of one previous report of superconductivity in natural materials, in the mineral covellite."

That said, the fact that these superconducting grains were discovered in two separate meteorites – and from such a small sampler overall of space rocks – means more of these superconducting phase materials are likely to exist in astronomical environments, and their superconducting properties could in turn have all manner of effects on their extraterrestrial surroundings.

"Superconducting particles within cold regions of space could have implications on the structure of stellar objects," the team writes.

"Specifically, superconducting particles could sustain microscopic current loops generated by transient fields and contribute to nearby magnetic fields."

Just how substantial these phenomena would end up being is anybody's guess, but there are lots of new questions to ask, and now's the time to get wondering. The findings are reported in *PNAS*.

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Turning Back the Clock on Aging Cells

Researchers report that they can rejuvenate human cells by reprogramming them to a youthful state.

By Nicholas Wade

Researchers at Stanford University report that they can rejuvenate human cells by reprogramming them back to a youthful state. They hope that the technique will help in the treatment of diseases, such as osteoarthritis and muscle wasting, that are caused by the aging of tissue cells.

A major cause of aging is thought to be the errors that accumulate in the epigenome, the system of proteins that packages the DNA and controls access to its genes. The Stanford team, led by Tapash Jay Sarkar, Dr. Thomas A. Rando and Vittorio Sebastiano, say their method, designed to reverse these errors and walk back the cells to their youthful state, does indeed restore the cells' vigor and eliminate signs of aging.

In their report, published on Tuesday in Nature Communications, they described their technique as "a significant step toward the goal of reversing cellular aging" and could produce therapies "for aging and aging-related diseases."

Leonard P. Guarente, an expert on aging at M.I.T., said the method was "one of the most promising areas of aging research" but that it would take a long time to develop drugs based on RNA, the required chemical.

The Stanford approach utilizes powerful agents known as Yamanaka factors, which reprogram a cell's epigenome to its time zero, or embryonic state.

Embryonic cells, derived from the fertilized egg, can develop into any of the specialized cell types of the body. Their fate, whether to become a skin or eye or liver cell, is determined by chemical groups, or marks, that are tagged on to their epigenome.

In each type of cell, these marks make accessible only the genes that the cell type needs, while locking down all other genes in the DNAs. The pattern of marks thus establishes each cell's identity.

As the cell ages, it accumulates errors in the marking system, which degrade the cell's efficiency at switching on and off the genes needed for its operations.

In 2006 Dr. Shinya Yamanaka, a stem-cell researcher at Kyoto University, amazed biologists by showing that a cell's fate could be reversed with a set of four transcription factors — agents that activate genes — that he had identified. A cell dosed with the Yamanaka factors erases the marks on the epigenome, so the cell loses its identity and reverts to the embryonic state. Erroneous marks gathered during aging are also lost in the process, restoring the cell to its state of youth. Dr. Yamanaka shared the 2012 Nobel Prize in medicine for the work.

But the Yamanaka factors are no simple panacea. Applied to whole mice, the factors made cells lose their functions and primed them for rapid growth, usually cancerous; the mice all died.

In 2016, Juan Carlos Izpisua Belmonte, of the Salk Institute for Biological Studies in San Diego, found that the two effects of the Yamanaka factors — erasing cell identity and reversing aging — could be separated, with a lower dose securing just age reversal. But he achieved this by genetically engineering mice, a technique not usable in people.

In their paper on Tuesday, the Stanford team described a feasible way to deliver Yamanaka factors to cells taken from patients, by dosing cells kept in cultures with small amounts of the factors.

If dosed for a short enough time, the team reported, the cells retained their identity but returned to a youthful state, as judged by several measures of cell vigor.

Dr. Sebastiano said the Yamanaka factors appeared to operate in two stages, as if they were raising the epigenome's energy to one level, at which the marks of aging were lost, and then to a higher level at which cell identity was erased.

The Stanford team extracted aged cartilage cells from patients with osteoarthritis and found that after a low dosage of Yamanaka factors the cells no longer secreted the inflammatory factors that provoke the disease. The team also found that human muscle stem cells, which are impaired in a muscle-wasting disease, could be restored to youth. Members of the Stanford team have formed a company, Turn Biotechnologies, to develop therapies for osteoarthritis and other diseases.

The study is "definitively a step forward in the goal of reversing cellular aging," Dr. Izpisua Belmonte said.

https://bit.ly/2UAYuXC

Crumpled graphene makes ultra-sensitive cancer DNA detector

Crumpling graphene in DNA sensors made it tens of thousands of times more sensitive, making it a feasible platform for liquid biopsy.

Graphene-based biosensors could usher in an era of liquid biopsy, detecting DNA cancer markers circulating in a patient's blood or serum. But current designs need a lot of DNA. In a new study, crumpling graphene makes it more than ten thousand times more sensitive to DNA by creating electrical "hot spots," researchers at the University of Illinois at Urbana-Champaign found.

Crumpled graphene could be used in a wide array of biosensing applications for rapid diagnosis, the researchers said. They published their results in the journal *Nature Communications*.

"This sensor can detect ultra-low concentrations of molecules that are markers of disease, which is important for early diagnosis," said study leader Rashid Bashir, a professor of bioengineering and the dean of the Grainger College of Engineering at Illinois. "It's very

sensitive, it's low-cost, it's easy to use, and it's using graphene in a new way."

While the idea of looking for telltale cancer sequences in nucleic acids, such as DNA or its cousin RNA, isn't new, this is the first electronic sensor to detect very small amounts, such as might be found in a patient's serum, without additional processing.

"When you have cancer, certain sequences are overexpressed. But rather than sequencing someone's DNA, which takes a lot of time and money, we can detect those specific segments that are cancer biomarkers in DNA and RNA that are secreted from the tumors into the blood," said Michael Hwang, the first author of the study and a postdoctoral researcher in the Holonyak Micro and Nanotechnology Lab at Illinois.

Graphene—a flat sheet of carbon one atom thick—is a popular, low-cost material for electronic sensors. However, nucleic-acid sensors developed so far require a process called amplification—isolating a DNA or RNA fragment and copying it many times in a test tube. This process is lengthy and can introduce errors. So Bashir's group set out to increase graphene's sensing power to the point of being able to test a sample without first amplifying the DNA.

Many other approaches to boosting graphene's electronic properties have involved carefully crafted nanoscale structures. Rather than fabricate special structures, the Illinois group simply stretched out a thin sheet of plastic, laid the graphene on top of it, then released the tension in the plastic, causing the graphene to scrunch up and form a crumpled surface.

They tested the crumpled graphene's ability to sense DNA and a cancer-related microRNA in both a buffer solution and in undiluted human serum, and saw the performance improve tens of thousands of times over flat graphene.

"This is the highest sensitivity ever reported for electrical detection of a biomolecule. Before, we would need tens of thousands of molecules in a sample to detect it. With this device, we could detect a signal with only a few molecules," Hwang said. "I expected to see some improvement in sensitivity, but not like this."

To determine the reason for this boost in sensing power, mechanical science and engineering professor Narayana Aluru and his research group used detailed computer simulations to study the crumpled graphene's electrical properties and how DNA physically interacted with the sensor's surface.

They found that the cavities served as electrical hotspots, acting as a trap to attract and hold the DNA and RNA molecules.

"When you crumple graphene and create these concave regions, the DNA molecule fits into the curves and cavities on the surface, so more of the molecule interacts with the graphene and we can detect it," said graduate student Mohammad Heiranian, a co-first author of the study. "But when you have a flat surface, other ions in the solution like the surface more than the DNA, so the DNA does not interact much with the graphene and we cannot detect it."

In addition, crumpling the graphene created a strain in the material that changed its electrical properties, inducing a bandgap—an energy barrier that electrons must overcome to flow through the material—that made it more sensitive to the electrical charges on the DNA and RNA molecules.

"This bandgap potential shows that crumpled graphene could be used for other applications as well, such as nano circuits, diodes or flexible electronics," said Amir Taqieddin, a graduate student and coauthor of the paper.

Even though DNA was used in the first demonstration of crumpled graphene's sensitivity for biological molecules, the new sensor could be tuned to detect a wide variety of target biomarkers.

Bashir's group is testing crumpled graphene in sensors for proteins and small molecules as well.

"Eventually the goal would be to build cartridges for a handheld device that would detect target molecules in a few drops of blood, for example, in the way that blood sugar is monitored," Bashir said. "The vision is to have measurements quickly and in a portable format."

More information: *"Ultrasensitive detection of nucleic acids using deformed graphene channel field effect biosensors" Nature Communications (2020).* DOI: 10.1038/s41467-020-15330-9

https://bit.ly/2xsz71Y

Solar system acquired current configuration not long after its formation

Model developed by Brazilian researchers shows chaotic phase that placed objects in current orbits beginning within first 100 million years after formation of giant planets.

by José Tadeu Arantes, FAPESP

The hypothesis that the solar system originated from a gigantic cloud of gas and dust was first floated in the second half of the 18th century by German philosopher Immanuel Kant and further developed by French mathematician Pierre-Simon de Laplace. It is now a consensus among astronomers. Thanks to the enormous amount of observational data, theoretical input and computational resources now available, it has been continually refined, but this is not a linear process.

Nor is it without controversies. Until recently, the solar system was thought to have acquired its present features as a result of a period of turbulence that occurred some 700 million years after its formation. However, some of the latest research suggests it took shape in the more remote past, at some stage during the first 100 million years.

A study conducted by three Brazilian researchers offers robust evidence of this earlier structuring. Reported in an article published in the journal *Icarus*, the study was supported by São Paulo Research Foundation—FAPESP. The authors are all affiliated with São Paulo State University's Engineering School (FEG-UNESP) in Guaratinguetá (Brazil).

The lead author is Rafael Ribeiro de Sousa. The other two authors are André Izidoro Ferreira da Costa and Ernesto Vieira Neto, principal investigator for the study.

"The large amount of data acquired from detailed observation of the solar system enables us to define with precision the trajectories of the many bodies that orbit the sun," Ribeiro said. "This orbital structure enables us to write the history of the formation of the solar system. Emerging from the gas and dust cloud that surrounded the sun some 4.6 billion years ago, the giant planets formed in orbits closer to each other and also closer to the sun. The orbits were also more co-planar and more circular than they are now, and more interconnected in resonant dynamic systems. These stable systems are the most likely outcome of the gravitational dynamics of planet formation from gaseous protoplanetary disks."

Izidoro offered more details: "The four giant planets—Jupiter, Saturn, Uranus and Neptune—emerged from the gas and dust cloud in more compact orbits," he said. "Their motions were strongly synchronous owing to resonant chains, with Jupiter completing three revolutions around the sun while Saturn completed two. All the planets were involved in this synchronicity produced by the dynamics of the primordial gas disk and the gravitational dynamics of the planets."

However, throughout the formation region of the outer solar system, which includes the zone located beyond the current orbits of Uranus and Neptune, the solar system had a large population of

planetesimals, small bodies of rock and ice considered the building blocks of planets and forerunners of asteroids, comets and satellites. The outer planetesimal disk began disturbing the system's gravitational balance. The resonances were disrupted after the gas phase, and the system entered a period of chaos in which the giant planets interacted violently and ejected matter into space.

"Pluto and its icy neighbors were pushed into the Kuiper Belt, where they're located now, and the entire group of planets migrated to orbits more distant from the sun," Ribeiro said.

The Kuiper Belt, whose existence was proposed in 1951 by Dutch astronomer Gerard Kuiper and later confirmed by astronomical observations, is a toroidal (doughnut-shaped) structure made up of thousands of small bodies orbiting the sun.

The diversity of their orbits is not seen in any other part of the solar system. The Kuiper Belt's inner edge begins at the orbit of Neptune about 30 astronomical units (AUs) from the sun. The outer edge is about 50 AUs from the sun. One AU is approximately equal to the average distance from Earth to the sun.

Returning to the disruption of synchronicity and the onset of the chaotic stage, the question is when this happened—very early in the life of the solar system, when it was 100 million years old or less, or much later, probably about 700 million years after the planets formed?

"Until recently, the late instability hypothesis predominated," Ribeiro said. "Dating of the moon rocks brought back by the Apollo astronauts suggested they were created by asteroids and comets crashing into the lunar surface at the same time. This cataclysm is known as the "Late Heavy Bombardment' of the moon. If it happened on the moon, it presumably also happened on Earth and the solar system's other terrestrial planets. Because a great deal of matter in the form of asteroids and comets was projected in all directions in the solar system during the period of planetary instability, it was deduced from the moon rocks that this chaotic period occurred late, but in recent years, the idea of a "Late Bombardment' of the moon has fallen out of favor."

According to Ribeiro, if the late chaotic catastrophe had occurred, it would have destroyed Earth and the other terrestrial planets, or at least caused disturbances that would have placed them in totally different orbits from those we observe now.

Furthermore, the moon rocks brought back by the Apollo astronauts were found to have been produced by a single impact. If they had originated in late giant planet instability, there would be evidence of several impacts, given the scattering of the planetesimals by the giant planets.

"The starting point for our study was the idea that the instability should be dated dynamically. The instability can only have happened later if there was a relatively large distance between the inner edge of the disk of planetesimals and Neptune's orbit when the gas was exhausted. This relatively large distance proved unsustainable in our simulation," Ribeiro said.

The argument is based on a simple premise: The shorter the distance between Neptune and the planetesimal disk, the greater the gravitational influence, and hence the earlier the period of instability. Conversely, later instability requires a larger distance.

"What we did was sculpt the primordial planetesimal disk for the first time. To do so, we had to go back to the formation of the ice giants Uranus and Neptune. Computer simulations based on a model constructed by Professor Izidoro [Ferreira da Costa] in 2015 showed that the formation of Uranus and Neptune may have originated in planetary embryos with several Earth masses. Massive collisions of these super-Earths would explain, for example, why Uranus spins on its side," Ribeiro said, referring to Uranus's "tilt," with north and south poles located on its sides rather than top and bottom.

Previous studies had pointed to the importance of the distance between Neptune's orbit and the inner boundary of the planetesimal disk, but they used a model in which the four giant planets were already formed.

"The novelty of this latest study is that the model doesn't begin with completely formed planets. Instead, Uranus and Neptune are still in the growth stage, and the growth driver is two or three collisions involving objects with up to five Earth masses," Izidoro said.

"Imagine a situation in which Jupiter and Saturn are formed, but we have five to 10 super-Earths instead of Uranus and Neptune. The super-Earths are forced by the gas to synchronize with Jupiter and Saturn, but being numerous, their synchronicity fluctuates, and they end up colliding. The collisions reduce their number, making synchronicity possible. Eventually, Uranus and Neptune are left. While the two ice giants were forming in the gas, the planetesimal disk was being consumed. Part of the matter was accreted to Uranus and Neptune, and part was propelled to the outskirts of the solar system. The growth of Uranus and Neptune therefore defined the position of the inner boundary of the planetesimal disk. What was left of the disk is now the Kuiper Belt. The Kuiper Belt is basically a relic of the primordial planetesimal disk, which was once far more massive."

The proposed model is consistent with the giant planets' current orbits and with the structure observed in the Kuiper Belt. It is also consistent with the motion of the Trojans, a large group of asteroids that share Jupiter's orbit and were presumably captured during the disruption of synchronicity.

According to a paper published by Izidoro in 2017, Jupiter and Saturn were still in formation, with their growth contributing to displacement of the asteroid belt. The latest paper is a kind of continuation, starting from a stage in which Jupiter and Saturn were fully formed but still synchronized, and describing the evolution of the solar system from there on.

"Gravitational interaction between the giant planets and the planetesimal disk produced disturbances in the gas disk that spread in the form of waves. The waves produced compact and synchronous planetary systems. When the gas ran out, interaction between the planets and planetesimal disk disrupted the synchronicity and gave rise to the chaotic phase. Taking all this into account, we discovered that the conditions simply didn't exist for the distance between Neptune's orbit and the inner boundary of the planetesimal disk to become large enough to sustain the late instability hypothesis. This is the main contribution of our study, which shows that the instability occurred in the first 100 million years, and may have occurred, for example, before the formation of Earth and the moon," Ribeiro said.

More information: *Rafael de Sousa Ribeiro et al, Dynamical evidence for an early giant planet instability, Icarus (2019).* *DOI: 10.1016/j.icarus.2019.113605*

https://bit.ly/2UFTGzV

Regular tub bathing linked to lower risk of death from cardiovascular disease

Daily hot bath seems to be more effective than once to twice weekly one or none at all

Regular tub bathing is linked to a lower risk of death from heart disease and stroke, indicates a long term study, published online in the journal *Heart*. And the higher the 'dose,' the better it seems to be for cardiovascular health, with a daily hot bath seemingly more protective than a once or twice weekly one, the findings indicate.

A linked editorial sounds a note of caution, however, because sudden death associated with hot baths is relatively common in Japan, where the study was conducted.

Having a bath is associated with good sleep quality and better self-rated health, but it's not clear what its long term impact might be on

cardiovascular disease risk, including heart attack, sudden cardiac death, and stroke.

To explore this further, the researchers drew on participants in The Japan Public Health Center based Study Cohort 1, a population based tracking study of more than 61,000 middle aged adults (45 to 59 years).

At the start of the study in 1990, some 43,000 participants completed a detailed questionnaire on their bathing habits and potentially influential factors: lifestyle, to include exercise, diet, alcohol intake, weight (BMI); average sleep duration; and medical history and current medicines use.

Each participant was monitored until death or completion of the study at the end of December 2009, whichever came first, with the final analysis based on 30,076 people.

During the monitoring period, 2097 cases of cardiovascular disease occurred: 275 heart attacks; 53 sudden cardiac deaths; and 1769 strokes.

After taking account of potentially influential factors, analysis of the data showed that compared with a once or twice weekly bath or no bath at all, a daily hot bath was associated with a 28% lower overall risk of cardiovascular disease, and a 26% lower overall risk of stroke.

The frequency of tub bathing wasn't associated with a heightened risk of sudden cardiac death, or with a particular type of stroke, called subarachnoid haemorrhage (bleed into the space surrounding the brain).

Further analysis of preferred water temperature indicated 26% lower and 35% lower risks of overall cardiovascular disease for warm and hot water, respectively.

But no significant associations emerged for overall stroke risk and water temperature.

After excluding those participants who developed cardiovascular disease within 5 or 10 years of the start of the study, the associations found weren't quite as strong, but nevertheless still remained statistically significant.

This is an observational study, and as such, can't establish cause, added to which changes in bathing frequency weren't tracked during the monitoring period.

The typical style of Japanese bathing also includes immersion to shoulder height, and this may be a critical factor.

But, say the researchers, previously published research has pointed to a link between heat exposure and cardiovascular disease prevention: this is because the effects of heat on the body are not dissimilar to those of exercise.

"We found that frequent tub bathing was significantly associated with a lower risk of hypertension, suggesting that a beneficial effect of tub bathing on risk of [cardiovascular disease] may in part be due to a reduced risk of developing hypertension," write the researchers.

They acknowledge that taking a hot bath is not without its risk, particularly if the temperature is too high, a point that is taken up by Dr Andrew Felix Burden in a linked editorial.

"There can be no doubt about the potential dangers of bathing in hot water, and the occurrence of death from this increases with age, as well as with the temperature of the water," he writes.

Although cardiovascular disease itself is unlikely to be the cause of these deaths, overheating, leading to confusion and drowning, most likely is, he suggests.

"Investigations into the potential cardiovascular benefit of heat-free immersion in warm to hot water are needed," he says. "In the meanwhile, caution is needed because of the higher mortality associated with such bathing in an unselected population."

Ukai T, Iso H, Yamagishi K, et al. Habitual tub bathing and risks of incident coronary heart disease and stroke. Heart2020:[e pub ahead of print: heartjnl-2019-315752].

https://bit.ly/2y3tWG6

Wuhan study shows lying face down improves breathing in severe COVID-19

Prone ventilation shown to improve breathing in severe COVID-19 patients.

In a new study of patients with severe COVID-19 (SARS-CoV-2) hospitalized on ventilators, researchers found that lying face down was better for the lungs. The research letter was published online in the American Thoracic Society's *American Journal of Respiratory and Critical Care Medicine*.

In "Lung Recruitability in SARS--CoV-2 Associated Acute Respiratory Distress Syndrome: A Single-Center, Observational Study," Haibo Qiu, MD, Chun Pan, MD, and co-authors report on a retrospective study of the treatment of 12 patients in Wuhan Jinyintan Hospital, China, with severe COVID-19 infection-related acute respiratory distress syndrome (ARDS) who were assisted by mechanical ventilation.

Drs. Qiu and Pan were in charge of the treatment of these patients, who were transferred from other treatment centers to Jinyintan Hospital.

A majority of patients admitted to the ICU with confirmed COVID-19 developed ARDS. The observational study took place during a six-day period the week of Feb. 18, 2020.

"This study is the first description of the behavior of the lungs in patients with severe COVID-19 requiring mechanical ventilation and receiving positive pressure," said Dr. Qiu, professor, Department of Critical Care Medicine, Zhangda Hospital, School of Medicine, Southeast University, Nanjing, China.

"It indicates that some patients do not respond well to high positive pressure and respond better to prone positioning in bed (facing downward)."

The clinicians in Wuhan used an index, the Recruitment-to-Inflation ratio, that measures the response of lungs to pressure (lung recruitability). Members of the research team, Lu Chen, PhD, and Laurent Brochard, PhD, HDR, from the University of Toronto, developed this index prior to this study.

The researchers assessed the effect of body positioning. Prone positioning was performed for 24-hour periods in which patients had persistently low levels of blood oxygenation.

Oxygen flow, lung volume and airway pressure were measured by devices on patients' ventilators. Other measurements were taken, including the aeration of their airway passages and calculations were done to measure recruitability.

Seven patients received at least one session of prone positioning. Three patients received both prone positioning and ECMO (life support, replacing the function of heart and lungs). Three patients died.

Patients who did not receive prone positioning had poor lung recruitability, while alternating supine (face upward) and prone positioning was associated with increased lung recruitability.

"It is only a small number of patients, but our study shows that many patients did not re-open their lungs under high positive pressure and may be exposed to more harm than benefit in trying to increase the pressure," said Chun Pan, MD, also a professor with Zhongda Hospital, School of Medicine, Southeast University.

"By contrast, the lung improves when the patient is in the prone position.

Considering this can be done, it is important for the management of patients with severe COVID-19 requiring mechanical ventilation."

The team consisted of scientists and clinicians affiliated with four Chinese and two Canadian hospitals, medical schools and universities.

https://nyti.ms/33OXEdO

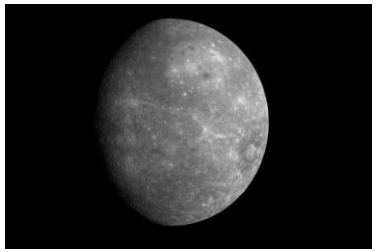
Life on the Planet Mercury? 'It's Not Completely Nuts'

A new explanation for the rocky world's jumbled landscape opens a possibility that it could have had ingredients for habitability.

By Shannon Hall

Mercury — a planet with a surface hot enough to melt lead — might once have contained ingredients needed for life. Though that's a pretty big might.

The new theory, published last week in the journal Scientific Reports, is based on a particularly muddled feature on the planet orbiting closest to the sun, known as "chaotic terrain." Here, the cracked, uneven and jumbled landscape consists of fractured rock, mismatched peaks and collapsed craters.



The study theorizes that the "chaotic terrain" on Mercury's surface was formed by activity underneath the planet's barren, scorched exterior, and not a collision. **NASA/Johns Hopkins University Applied Physics Laboratory/Carnegie Institution of Washington**

"Think of a kid throwing up a bunch of building blocks and how they land," said Deborah Domingue, a co-author of the study from the Planetary Science Institute, headquartered in Tucson, Ariz. "Some are up, some are down, some are tilted — that's chaotic terrain."

For nearly 50 years, scientists have thought the chaos on Mercury was caused by earthquakes that raced throughout the planet when a massive asteroid struck the planet's far side.

But the new study, led by Dr. Domingue's colleague Alexis Rodriguez, upends that notion. It suggests the terrain could not possibly have formed in response to the collision because it occurred 2 billion years after the impact crater formed.

In addition, Dr. Rodriguez and his colleagues discovered that areas within the chaotic terrain appear to have dropped. It's as though the layer of crust just below the surface had simply disappeared.

The easiest explanation is that subsurface volatiles — elements that can easily switch from a solid to a liquid or a gas — heated up as a result of the intrusion of magma below. That caused those elements to transform into a gas, forcing the terrain above them to collapse into a jumbled mess.

"Let's say I have a house on stilts, and I kick one out," Dr. Domingue said. "My house is going to tilt right? That's what's going on here."

Paul Hayne, a planetary scientist at the University of Colorado Boulder who was not involved in the study, agrees that the prevailing explanation for Mercury's mishmash — which has long been unchallenged — is likely wrong. He also notes that the new story is consistent with what scientists have observed on Mars, where similar terrain was likely caused by the release of volatiles.

It's a thrilling prospect given that volatiles — particularly water — are needed to kick-start life. Though the team cannot say which volatiles were present, there is reason to hope that water might be one of them, Dr. Domingue said.

The finding runs against the notion that Mercury is inhospitable. At such a close distance to the sun, its surface reaches a scorching 800 degrees Fahrenheit during its day. Then, because the planet has no atmosphere to retain the heat, its surface plummets to minus 290 degrees Fahrenheit during its night.

But a short distance below the surface, the temperatures are much cooler, even pleasant — at least for some life-forms, said Jeffrey Kargel, a co-author of the study who is also from the Planetary Science Institute.

"It is possible that as long as there was water, the temperatures would be appropriate for the survival and possibly the origin of life," Dr. Kargel said. But at first, even he was not convinced.

"I thought Alexis had lost it at some point," he said, referring to Dr. Rodriguez. "But the more I dug into the geologic evidence and the more I thought about the chemistry and physical conditions there, the more I realized that this idea — well it might be nuts, but it's not completely nuts."

Dr. Hayne, however, thinks that water is an unlikely culprit. The only scenario in which it might be possible is one where water is bound to the rocks.

"So you could have transient pockets of high water activity, but I don't think this is a case where we'd see massive pools of water and subsurface lakes and that sort of thing," Dr. Hayne said.

Nonetheless, the suggestion that water could exist at all on a planet like Mercury provides a compelling clue toward the search for life across the galaxy. Astronomers have discovered thousands of planets orbiting other stars — some of which look similar to Mercury. "If it's happening here, it's happening somewhere else," Dr. Rodriguez said.

https://bit.ly/2vOEWq6

Doctors hoard unproven COVID-19 meds by writing prescriptions for selves, families

Pharmacists seeing fraudulent activity with unproven drugs endorsed by President Trump.

Topher Sanders, David Armstrong, and Ava Kofman, ProPublica

A nationwide shortage of two drugs touted as possible treatments for the coronavirus is being driven in part by doctors inappropriately prescribing the medicines for family, friends, and themselves, according to pharmacists and state regulators.

"It's disgraceful, is what it is," said Garth Reynolds, executive director of the Illinois Pharmacists Association, which started getting calls and emails Saturday from members saying they were receiving questionable prescriptions. "And completely selfish."

Demand for chloroquine and hydroxychloroquine surged over the past several days as President Donald Trump promoted them as possible treatments for the coronavirus and online forums buzzed with excitement over a small study suggesting the combination of hydroxychloroquine and a commonly used antibiotic could be effective in treating COVID-19.

Reynolds said the Illinois Pharmacists Association has started reaching out to pharmacists and medical groups throughout the state to urge doctors, nurses, and physician assistants not to write prescriptions for themselves and those close to them.

"We even had a couple of examples of prescribers trying to say that the individual they were calling in for had rheumatoid arthritis," he said, explaining that pharmacists suspected that wasn't true. "I mean, that's fraud."

In one case, Reynolds said, the prescriber initially tried to get the pills without an explanation and only offered up that the individual had rheumatoid arthritis after the pharmacist questioned the prescription.

In a bulletin to pharmacists on Sunday, the state association wrote that it was "disturbed by the current actions of prescribers" and instructed members on how to file a complaint against physicians and nurses who were doing it.

"People are losing their minds about this product," said Brian Brito, president of SMP Pharmacy Solutions in Miami. "We're selling so much of this stuff and people are just stockpiling it prophylactically if anybody in their family gets sick—they're just holding on to it."

The two drugs are only available through a prescription and cannot be purchased over the counter. Hydroxychloroquine, sold under the brand name Plaquenil, is approved to treat lupus and rheumatoid arthritis while chloroquine is an anti-malarial treatment.

There is little evidence that the drugs work to treat coronavirus, although clinical trials are underway to find out. But as coronavirus cases multiply and protective gear for medical workers vanishes from emergency rooms, many patients and physicians see the drugs as the only hope to reverse the course of serious disease.

Brito said his pharmacy had about 800 tablets on Monday and were nearly sold out in about an hour.

One doctor called and asked for 200 tablets, but the company refused. “He was a little upset about it but he understood and he went quickly from 200 to 42 tablets, which is essentially treating two people,” Brito said. “So yeah, they’re stockpiling it.”

A pharmacist in Houston, who asked to remain anonymous for fear of retaliation and violating patient privacy, said he was recently asked by a surgeon for an unusually large quantity with unlimited refills. “He said it was because his wife had lupus,” the pharmacist said, “but when I asked him for her name and diagnosis, he told me just to put it in his.”

Lupus patients are reporting difficulty in refilling their prescriptions for the drug. On Monday, the Lupus Foundation of America issued a joint statement asking the White House Coronavirus Task Force to “take action to ensure current supplies are allocated for patients taking them for indicated uses.”

Several states in the past few days have already moved to limit prescriptions of the drugs, neither of which is approved to treat the coronavirus. Trump, in press conferences and tweets over the past week, has promoted the use of the drugs as potentially blunting the impact of the COVID-19 outbreak.

“It’s unfortunate that a news conference, I think prematurely, made it sound like this was the answer, and that’s led to this panic,” Michelle Petri, director of Johns Hopkins University School of Medicine’s Lupus Center, said Friday. “I have spent the last two days trying to help lupus patients who actually need their refills.” She said some patients have refills on back order while others are being provided smaller amounts than usual.

The West Virginia Board of Pharmacy, in an alert Saturday, ordered pharmacists to limit new prescriptions to no more than 30 tablets and only to cases where the drugs were being used for approved indications.

“Currently, both nationally and in West Virginia, some prescribers have begun writing prescriptions for these drugs for family, friends, and coworkers in anticipation of COVID-19 related illness,” the board wrote.

Texas and Ohio have also restricted prescribing of the drugs. Louisiana on Sunday also issued an emergency rule limiting when the drugs can be prescribed, citing “inappropriate use” and “hoarding.” On Monday, the Louisiana Board of Pharmacy said it was rescinding that order because manufacturers had boosted distribution of the drugs.

Experts are warning that any use of the drugs outside of a hospital setting can be dangerous, and admonished doctors to stop prescribing the medicines inappropriately.

Daniel Brooks, the medical director of the Banner Poison and Drug Information Center in Phoenix, said it was “immoral” for physicians to hoard the medications. “One should not be selfish and scared, especially medical providers,” he said. “I find it incredibly embarrassing and unfortunate that physicians appear to be prescribing these medications inappropriately.”

This weekend Brooks cared for a man in his 60s who died after ingesting a version of chloroquine commonly used to clean fish tanks. The man, who thought he might have COVID-19, took a small amount of the substance in a misguided effort to treat his symptoms. His wife was also hospitalized after taking the substance but survived.

Brooks said the amount the couple ingested was equivalent to a couple days' worth of prescription chloroquine.

Ken Thai, the owner of a chain of Los Angeles-area pharmacies, said his stores are witnessing a rash of inappropriate prescribing.

"A lot of physicians, unfortunately, are writing high amounts for more than the required number of tablets and calling in five, six, seven and eight prescriptions at a time," he said. "I don't want to insinuate what is going on, but it is very unusual."

He said his pharmacists are declining to fill suspicious orders and telling prescribers they don't have enough of the medication on hand to complete those requests. Among the prescriptions flagged are those for people who have not previously taken the drug as well as orders from doctors who do not typically treat lupus and rheumatoid arthritis patients.

"If a doctor is writing a prescription for himself or aunts and uncles, that is usually a red flag for us," he said. "Whatever we have in stock, we have to preserve for the patients we currently service."

On Twitter, pharmacy workers traded stories about dentists and opthamologists requesting hydroxychloroquine under dubious pretenses. "A dentist just tried to call in scripts for hydroxychloroquine + azithromycin for himself, his wife, & another couple (friends)," tweeted a pharmacist in Eugene, Oregon. "I have patients with lupus that have been on HCQ [Hydroxychloroquine] for YEARS and now can't get it because it's on backorder."

Steve Moore, president of the Pharmacists Society of the State of New York, said medical providers hoarding the drugs is occurring in the state, which has the highest number of coronavirus cases in the country.

"That's a double whammy," he said. "We're potentially taking that medication away from patients with autoimmune conditions and patients with the actual virus that may need treatment."

https://bit.ly/2xwo9Zi

Rare disease designation for coronavirus drug is just a tax break [Updated]

As a patent holder, it can jack up the prices regardless of orphan drug status.

Jonathan M. Gitlin - 3/25/2020, 4:07 AM

Update: On March 25, Gilead announced that it had asked the Food and Drug Administration to rescind the orphan drug designation:

Gilead has submitted a request to the U.S. Food and Drug Administration to rescind the orphan drug designation it was granted for the investigational antiviral remdesivir for the treatment of COVID-19 and is waiving all benefits that accompany the designation. Gilead is confident that it can maintain an expedited timeline in seeking regulatory review of remdesivir, without the orphan drug designation. Recent engagement with regulatory agencies has demonstrated that submissions and review relating to remdesivir for the treatment of COVID-19 are being expedited.

Original story:

On Monday night, a panicked headline at The Intercept proclaimed that a potential treatment for COVID-19 had been classified as what's known as an "orphan drug," which is a class given to treatments for rare diseases, and that such a classification runs the danger of "potentially limiting [the drug's] affordability." At first glance, describing a COVID-19 treatment like this sounds absurd, given that a pandemic is the exact opposite of a rare disease. So what exactly is going on, and does it mean that Gilead Sciences, the biotechnology company that makes the drug (called remdesivir) is going to jack up its prices so that only the rich survive?

It all goes back to 1983

By the late 1970s, it was clear that the incentives for profit-making drug companies did not align with the needs of people with rare diseases. Developing a new drug was extremely expensive even 40

years ago, and so if a drug company wanted to make its money back, it would focus on conditions where it could expect plenty of sales rather than those with just a handful of patients. The rare-disease advocacy community was understandably outraged by this cold-hearted economic analysis, and by 1983 it had successfully cajoled Congress into passing the Orphan Drug Act.

Once the law passed, the FDA was given the power to grant a drug "orphan" status, even to compounds without patent protection. If a company got its product approved as an orphan drug, it gained a period of market exclusivity, meaning that for seven years no one else would be allowed to sell that same product to treat that specific disease. What's more, all the costs associated with developing that orphan drug—including payroll for scientists and so on—was subject to a handy tax credit. Since the passage of the Orphan Drug Act, more than 800 orphan drugs and biologics have been approved by the FDA out of more than 5,300 applications.

How is a pandemic "rare"?!

When we say "rare disease," it's generally accepted that this means a condition that affects fewer than 200,000 individuals in the United States. Obviously the predictions for COVID-19 are for many times that number—it's a pandemic, after all. However, the Orphan Drug Act does have an exception for more common diseases with unmet needs. So the FDA is allowed to consider granting orphan drug status to a treatment for "[a] disease affecting over 200,000 persons in the US, but for which there is no reasonable expectation that the cost of developing and making available a drug for such disease will be recovered from sales in the US." It's this provision that Gilead used with its remdesivir orphan drug application.

The FDA has *not* approved remdesivir as an orphan drug

At this point, it's important to make something clear: the FDA has not *approved* remdesivir as an orphan drug. It has *designated* it as an orphan drug (as of yesterday), which means that Gilead can start tracking all of its expenses for studying remdesivir as a treatment for COVID-19 to satisfy the IRS. But getting something designated as an orphan drug by the FDA is pretty easy—the agency tries to respond to applications within 90 days and doesn't even charge user fees.

Getting FDA approval as an orphan drug is another matter—that requires actual clinical data, and approval typically happens four or five years after designation. (In remdesivir's case, I could see approval happening much quicker given the public health emergency, but again it would still require clinical trial data to be collected, analyzed, and then reviewed.) This approval is by no means guaranteed; Gilead applied for orphan drug status for remdesivir in September 2014 as a treatment for Ebola. But as of March 2020, that approval has not been granted.

Is it time to grab my torch and pitchfork?

In its article, The Intercept notes that Gilead is no longer allowing new patients access to remdesivir through a "compassionate use" exemption that allows a drug to be given to a patient for a disease for which that drug was not FDA approved. But we should also note that, until the clinical trials are complete, it's yet to be proven that remdesivir will actually be effective with SARS-CoV-2 infections. A Phase 3 clinical trial is underway in the US, but it only began in February. (Another trial is also underway in China.) And the seven years of orphan drug exclusivity—and those potentially outrageous prices—can only happen after any FDA approval.

In fact, there's another complicating factor in all of this. While the FDA is empowered to grant seven years of market exclusivity, that's a separate power to the one given to the US Patent and Trademark Office. A patent awarded by USPTO is an intellectual property right, which can be much broader than the narrow

definition of an orphan drug for a particular condition, and patents last for 20 years. And Gilead already has a patent for remdesivir in the US, so it will probably be in a position to charge what it wants for the drug whether or not it also gets approved as an orphan drug. In fact, any patent protection would likely extend to 2037, long past any orphan drug market exclusivity, as the two can and do run at the same time.

Finally, there is a provision in the law that would allow the FDA to give permission to other companies to sell remdesivir if the secretary of Health and Human Services found that Gilead could not "assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated." (Whether or not an HHS secretary of this particularly business-friendly regime would ever do such a thing is a different question.)

That's not to say that criticisms of the Orphan Drug Act are completely off-base. Orphan drugs often come with high prices, and 95 percent of the 7,000-or-so identified rare diseases lack any effective treatment. While the market exclusivity granted under the act is beneficial for about a third of orphan drugs, more often it's the sweet corporate-tax advantages that are driving that calculation.

https://bit.ly/2WLlDJr

Fleeing Nazis shaped Austrian politics for generations after World War II: study

Migrating extremists can shape political developments in their destination regions for generations.

A new study in *The Economic Journal*, published by Oxford University Press, suggests that migrating extremists can shape political developments in their destination regions for generations. Regions in Austria that witnessed an influx of Nazis fleeing the Soviets after WWII are significantly more right-leaning than other parts of the country. There were no such regional differences in far-right values before World War Two.

There is a long history of ideological radicals who have moved abroad to spread their political views: From the anarchist Mikhail Bakunin over the revolutionary Che Guevara to Jihadist fighters returning to their home countries from the Islamic State. Governments fear that these immigrants bring political turmoil and often react with travel bans or harsh surveillance. Beyond anecdotal evidence, however, researchers have not yet identified effects of migrating extremists on the spread of actual political beliefs.

The researchers use the Allied occupation of Austria after World War Two as a natural experiment. In the summer of 1945, occupation zones in the Austrian federal state of Upper Austria were unexpectedly reallocated between the United States and the Soviets. US-liberated regions north of the Danube River were reassigned to the Soviets, while the southern bank remained under US control. People started to flee to the US zone in large numbers immediately. Primarily Nazi elites fearing Soviet punishment migrated to the south bank of the Danube River. The zoning along the Danube River divided an otherwise historically, economically and culturally homogeneous region into two areas—one with a high density and another one with comparably low density of Nazi elite members.

Austria's long tradition of far-right populism allows the authors to trace the effects of migrated Nazi elites since the late 1940s until today. The results indicate a substantial and persistent increase in extreme right-wing attitudes in the destinations of migrating extremists. Even seventy years after the Nazi influx, vote shares for far-right parties are still much higher in places where Nazi elites settled.

The authors provide two main explanations for the long-term persistence of far-right values: local institutions and family ties.

Migrated Nazis founded and penetrated local party branches at their destination. Those institutions multiplied their impact. The researchers found that migrating Nazis leverage far-right votes by at least a factor of 1.3 up to a factor of 2.5. Another explanation for persistence is intergenerational transmission. The authors collected pre-war phone book entries and show that names of far-right politicians today still reflect long-gone migration of Nazi elites after the war. All results hold when including controls for socio-economic and time invariant geographic characteristics.

It appears that political preferences are transmitted from generation to generation. Even after three or four generations, attitudes and beliefs of Nazi migrant families and communities continue to differ. Descendants of migrating extremists together with local party institutions are continuously spreading their beliefs to residents through active engagement in local politics.

"We were surprised to learn that imported extremism can survive for generations and does not fade away," said the paper's lead author Felix Roesel. "The good news is that liberal and democratic values spread in a very similar manner. This is what new research has shown. Populism is not more contagious than other political ideas."

More information: *Christian Ochsner et al, Migrating Extremists, The Economic Journal (2020).* *DOI: 10.1093/ej/ueaa017*

https://bit.ly/2QTqJ2J

Bricks can act as 'cameras' for characterizing past presence of radioactive materials

Technique for determining the historical location and distribution of radioactive materials

Researchers from North Carolina State University have developed a new technique for determining the historical location and distribution of radioactive materials, such as weapons grade plutonium. The technique may allow them to use common building materials, such as bricks, as a three-dimensional "camera," relying on residual gamma radiation signatures to take a snapshot of radioactive materials even after they've been removed from a location.

"This research builds on our previous work, which was an empirical demonstration that we could turn a brick into a gamma ray spectrometer - characterizing the energy distribution of a radiation source," says Robert Hayes, an associate professor of nuclear engineering at NC State and first author of a paper on the work.

"Our new work effectively shows that we could take an array of bricks and turn them into a gamma ray camera, characterizing the location and distribution of a radiation source," Hayes says. "Although this time we did not use bricks, instead relying on commercial dosimeters, since it's a proof of concept study. Also, the radiation source we imaged this time was 4.5 kilograms of weapons grade plutonium, whereas we previously used a commercial americium source for the spectrometry demonstration. In this most recent study, we were able to rather accurately predict not only the location of the weapons grade plutonium, but even the radius of the source, just with passive dosimeters.

"Even though we used commercial dosimeters here, our findings strongly suggest that we could do the same using building materials, such as brick," Hayes says. "That's because the silicates in brick - such as quartz, feldspars, zircons, and so on - are all individual dosimeters. It is a tedious process to remove those grains from the brick for measurements, but we have done it multiple times. For the goals of this new research, it wasn't necessary to use brick - we've already shown we can do that. This was simply a question of determining how much information we could glean from this approach. And the answer is that we could learn a lot - about the size and shape of the radiation source, as well as the nature of the radioactive material itself."

"This ability for three-dimensional imaging is a novel capability, meaning we can basically see into history in terms of what nuclear material was where or when," says Ryan O'Mara, a Ph.D. student at NC State and coauthor of the work.

The paper, "Retrospective characterization of special nuclear material in time and space," is published in the journal Radiation Measurements.

This work was funded in part by federal grant NRC-HQ-84-14-G-0059 from the Nuclear Regulatory Commission; and through a joint faculty appointment between North Carolina State University and Oak Ridge National Laboratory in coordination with the Office of Defense Nuclear Nonproliferation of the National Nuclear Security Administration sponsored Consortium for Nonproliferation Enabling Capabilities under Award Number DE-NA0002576.

https://bit.ly/2UGV85n

New feathered dinosaur was one of the last surviving raptors

Feathered dinosaur that lived in New Mexico 67 million years ago is one of the last known surviving raptor species

A new feathered dinosaur that lived in New Mexico 67 million years ago is one of the last known surviving raptor species, according to a new publication in the journal *Scientific Reports*.

Dineobellator notohesperus adds to scientists' understanding of the paleo-biodiversity of the American Southwest, offering a clearer picture of what life was like in this region near the end of the reign of the dinosaurs. **Sergey Krasovskiy**

Dineobellator notohesperus adds to scientists' understanding of the paleo-biodiversity of the American Southwest, offering a clearer picture of what life was like in this region near the end of the reign of the dinosaurs.

Steven Jasinski, who recently completed his Ph.D. in Penn's Department of Earth and Environmental Sciences in the School of Arts and Sciences, led the work to describe the new species, collaborating with doctoral advisor Peter Dodson of the School of Veterinary Medicine and Penn Arts and Sciences and as well as Robert Sullivan of the New Mexico Museum of Natural History and Science in Albuquerque.

In 2008, Sullivan found fossils of the new species in Cretaceous rocks of the San Juan Basin, New Mexico. He, along with his field team of Jasinski and James Nikas, collected the specimen on U.S. federal land under a permit issued by the Bureau of Land Management. The entire specimen was recovered over four field seasons. Jasinski and his coauthors gave the species its official name, Dineobellator notohesperus, which means "Navajo warrior from the Southwest," in honor of the people who today live in the same region where this dinosaur once dwelled.

Dineobellator, as well as its Asian cousin Velociraptor, belong to a group of dinosaurs known as the dromaeosaurids. Members of this group are commonly referred to as "raptor" dinosaurs, thanks to movies such as "Jurassic Park" and "Jurassic World." But unlike the terrifying beasts depicted in film, Dineobellator stood only about 3.5 feet (about 1 meter) at the hip and was 6 to 7 feet (about 2 meters) long--much smaller than its Hollywood counterparts.

Raptor dinosaurs are generally small, lightly built predators. Consequently, their remains are rare, particularly from the southwestern United States and Mexico. "While dromaeosaurids are better known from places like the northern United States, Canada, and Asia, little is known of the group farther south in North America," says Jasinski.

While not all of the bones of this dinosaur were recovered, bones from the forearm have quill nobs--small bumps on the surface where feathers would be anchored by ligaments--an indication that Dineobellator bore feathers in life, similar to those inferred for Velociraptor.

Features of the animal's forelimbs, including enlarged areas of the claws, suggest this dinosaur could strongly flex its arms and hands. This ability may have been useful for holding on to prey--using its hands for smaller animals such as birds and lizards, or perhaps its arms and feet for larger species such as other dinosaurs.

Its tail also possessed unique characteristics. While most raptors' tails were straight and stiffened with rod-like structures, Dineobellator's tail was rather flexible at its base, allowing the rest of the tail to remain stiff and act like a rudder.

"Think of what happens with a cat's tail as it is running," says Jasinski. "While the tail itself remains straight, it is also whipping around constantly as the animal is changing direction. A stiff tail that is highly mobile at its base allows for increased agility and changes in direction, and potentially aided Dineobellator in pursuing prey, especially in more open habitats."

This new dinosaur provides a clearer picture of the biology of North American dromaeosaurid dinosaurs, especially concerning the distribution of feathers among its members.

"As we find evidence of more members possessing feathers, we believe it is likely that all the dromaeosaurids had feathers," says Jasinski. The discovery also hints at some of the predatory habits of a group of iconic meat-eating dinosaurs that lived just before the extinction event that killed off all the dinosaurs that weren't birds.

Jasinski plans to continue his field research in New Mexico with the hope of finding more fossils.

"It was with a lot of searching and a bit of luck that this dinosaur was found weathering out of a small hillside," he says. "We do so much hiking and it is easy to overlook something or simply walk on the wrong side of a hill and miss something. We hope that the more we search, the better chance we have of finding more of Dineobellator or the other dinosaurs it lived alongside."

Steven E. Jasinski is a curator of paleontology and geology at the State Museum of Pennsylvania and earned his doctoral degree in the Department of Earth and Environmental Science in the University of Pennsylvania's School of Arts and Sciences. Peter Dodson is a professor of veterinary gross anatomy in the School of Veterinary Medicine and a professor of earth and environmental science in the School of Arts and Sciences at the University of Pennsylvania.

Robert Sullivan is a research associate at the New Mexico Museum of Natural History and Science in Albuquerque.

Jasinski was supported by Geo. L. Harrison and Benjamin Franklin fellowships. The research was also partially funded by a Walker Endowment Research Grant and a University of Pennsylvania Paleontology Research Grant.

https://bit.ly/3axyO4Y

Brain mapping study suggests motor regions for the hand also connect to the entire body

An area believed to control only one body part actually operates across a wide range of motor functions

Mapping different parts of the brain and determining how they correspond to thoughts, actions, and other neural functions is a central area of inquiry in neuroscience, but while previous studies using fMRI scans and EEG have allowed researchers to rough out brain areas connected with different types of neural activities, they have not allowed for mapping the activity of individual neurons.

Now in a paper publishing March 26 in the journal *Cell*, investigators report that they have used microelectrode arrays implanted in the brains of two people to map out motor functions down to the level of the single nerve cell. The study revealed that an area believed to control only one body part actually operates across a wide range of motor functions. It also demonstrated how different neurons coordinate with each other.

"This research shows for the first time that an area of the brain previously thought to be connected only to the arm and hand has information about the entire body," says first author Frank Willett, a postdoctoral fellow in the Neural Prosthetics Translational Laboratory at Stanford University and the Howard Hughes Medical

Institute. "We also found that this area has a shared neural code that links all the body parts together."

The study, a collaboration between neuroscientists at Stanford and Brown University, is part of BrainGate2, a multisite pilot clinical trial focused on developing and testing medical devices to restore communication and independence in people affected by neurological conditions like paralysis and locked-in syndrome. A major focus of the Stanford team has been developing ways to restore the ability of these people to communicate through brain-computer interfaces (BCIs).

The new study involved two participants who have chronic tetraplegia--partial or total loss of function in all four limbs. One of them has a high-level spinal cord injury and the other has amyotrophic lateral sclerosis. Both have electrodes implanted in the so-called hand knob area of the motor cortex of their brains. This area--named in part for its knoblike shape--was previously thought to control movement in the hands and arms only.

The investigators used the electrodes to measure the action potentials in single neurons when the participants were asked to attempt to do certain tasks--for example, lifting a finger or turning an ankle. The researchers looked at how the microarrays in the brain were activated. They were surprised to find that the hand knob area was activated not only by movements in the hand and arm, but also in the leg, face, and other parts of the body.

"Another thing we looked at in this study was matching movements of the arms and legs," Willett says, "for example, moving your wrist up or moving your ankle up. We would have expected the resulting patterns of neural activity in motor cortex to be different, because they are a completely different set of muscles. We actually found that they were much more similar than we would have expected." These findings reveal an unexpected link between all four limbs in motor cortex that might help the brain to transfer skills learned with one limb to another one.

Willett says that the new findings have important implications for the development of BCIs to help people who are paralyzed to move again. "We used to think that to control different parts of the body, we would need to put implants in many areas spread out across the brain," he notes. "It's exciting, because now we can explore controlling movements throughout the whole body with an implant in only one area."

One important potential application for BCIs is allowing people who are paralyzed or have locked-in syndrome to communicate by controlling a computer mouse or other device. "It may be that we can connect different body movements to different types of computer clicks," Willett says. "We hope we can leverage these different signals more accurately to enable someone who can't talk to use a computer, since neural signals from different body parts are easier for a BCI to tease apart than those from the arm or hand alone."

This work was supported by the Office of Research and Development, Rehabilitation R and D Service, Department of Veterans Affairs, the Executive Committee on Research of Massachusetts General Hospital, NIDCD, NINDS, Larry and Pamela Garlick, Samuel and Betsy Reeves, the Wu Tsai Neuroscience Institute at Stanford, the Simons Foundation Collaboration on the Global Brain, the Office of Naval Research, and the Howard Hughes Medical Institute.

Cell, Willett et al. "Hand Knob Area of Premotor Cortex Represents the Whole Body in a Compositional Way" https://www.cell.com/cell/fulltext/S0092-8674(20)30220-8

https://bit.ly/2Jo9Ys4

The Atmosphere of Uranus Is Literally Leaking Gas Into Space

Poor old Uranus just can't seem to catch a break.

Michelle Starr

Something already tipped the planet on its side, so its orbit is perpendicular to those of the other Solar System planets. It

probably smells terrible. And now scientists have discovered that the atmosphere of Uranus is leaking out into space.

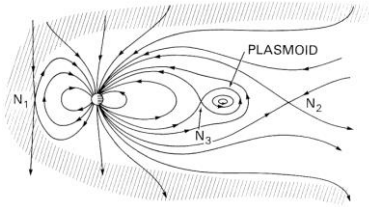
Hidden in the data from Voyager 2's historic 1986 encounter with the icy planet, and undiscovered until now, was the presence of a plasmoid - a pocket of atmospheric material being funnelled away from Uranus by the planet's magnetic field.

(Voyager 2/NASA/Erich Karkoschka)

It's the first time a plasmoid has been spotted in connection with an ice giant, and it doesn't just show us that Uranus' atmosphere is leaking. It's also revealing some of the dynamics of this planet's peculiar, twisted magnetic field.

Actually, leaky atmospheres aren't that uncommon. It's called atmospheric escape, and it's how Mars, for example, turned from what we think was quite a damp planet into a dusty barren wasteland. Venus is leaking hydrogen.

Jupiter's moon Io and Saturn's moon Titan are leaking. Even Earth is losing about 90 tonnes of atmospheric material a day (don't worry, we have around 5,140 trillion tonnes, it will take a long time to completely disappear).



(David Stern, Reviews of Geophysics, 1996)

There are several mechanisms whereby this can occur, and one of those is through plasmoids. These are large, cylindrical bubbles of plasma - ionised gas - bound by magnetic field lines streaming away from the Sun, the region known as the magnetotail. The image above shows what that looks like for Earth.

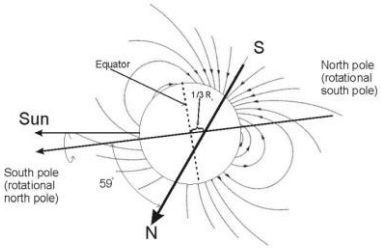
Ions from the atmosphere are channelled along the magnetic field into this region. When the solar wind causes the magnetic field to break at the side facing the Sun - the bow shock - they whip around and reconnect in the tail, pinching off spinning plasmoids. Some of the ions bounce back towards the planet (producing, on Earth, auroras), and the plasmoid hurtles off in the opposite direction, taking the atmospheric ions with it.

For Earth, that's pretty straightforward and well understood. And there's evidence solar wind tears plasmoids off Mars on a daily basis in a slightly different fashion, since Mars doesn't have a global magnetic field.

But Uranus is a tricky beast of a planet, and let's be honest, its magnetic field is a straight-up mess.

Where Earth's magnetic field is more or less consistent with the planet's orientation, Uranus' is all twisted sideways, with the magnetic poles angled 59 degrees away from the geographic poles.

And it's not even centred. If you were to draw a line between those two poles, it would miss the centre of Uranus by quite a large distance. There's even evidence to suggest that the magnetic field opens at night and closes during the day. Seriously, look at this. Who came up with this.



(Wikimedia Commons/Public Domain)

It was this mess of a magnetic field that drew the attention of astronomers Gina DiBraccio and Dan Gershman of NASA Goddard Space Flight Center, who were planning potential planetary missions and thought this particular oddity would be a good starting point.

They were studying the data collected by Voyager 2's magnetometer in January 1986 in higher resolution than any previous research when they noticed a wiggle in the data, a blip in the magnetic field.

They processed the data and came to the conclusion that, yep. Even though Uranus has a weirdly skewed, wobbly magnetic field, that

blip did indeed represent a plasmoid, roughly 204,000 kilometres in length and 400,000 kilometres across (127,000 by 250,000 miles), likely full of ionised hydrogen, moving away from the planet.

And this reveals some new information about that magnetic field. According to the researchers' analysis, it shows that Uranus' magnetic field reconnects at the tail, like Earth's. It also suggests that internal forces play a role in the planet's magnetic dynamics.

And, of course, it reveals a mechanism whereby Uranus could be losing a substantial amount of mass, transported away by plasmoids.

The Voyager data used for this analysis is over two decades old, so the researchers suggest the best way to find out more is to send another probe to check it all out.

"The nature of magnetospheric circulation and mass-loss processes remain outstanding and essential topics at both Uranus and Neptune," they wrote in their paper.

"In order to definitively determine the relative contributions of planetary rotation and solar wind forcing in driving global plasma dynamics, new in situ measurements will be necessary. Until then, the enigmatic ice giant magnetospheres await further exploration."

The research has been published in *Geophysical Research Letters*.

https://bit.ly/3avV13a

How can I treat myself if I've got – or think I've got – coronavirus?

New cases of the coronavirus are reported every day, and as yet there's no vaccine. So what treatments are available if you're one of the unlucky ones who gets infected?

David King *

If your symptoms are mild, you should treat them the same way you would a cold or flu.

A spectrum of severity

SARS-CoV-2, the virus that causes COVID-19, is one of hundreds of viruses that cause colds and flu symptoms in humans.

The infection ranges in severity from almost silent (asymptomatic), to a mild cold, all the way to lung and organ failure. The symptoms may be worse than a normal cold or flu because this coronavirus is new (or "novel") to our species and we haven't built up herd immunity to it yet. But current estimates suggest about 80% of cases will have relatively mild to moderate illness.

If you're one of these, you might not know for sure whether you have COVID-19, as you may not be eligible for testing. It's important you self-isolate if you're unwell regardless.

But from the perspective of treatment, if your illness is reasonably mild, it doesn't really matter whether you have a confirmed COVID-19 diagnosis or not.

So how do I treat the symptoms?

The World Health Organisation (WHO) says the most common symptoms of COVID-19 are fever, tiredness, and dry cough. Some patients may have aches and pains, nasal congestion, runny nose, a sore throat or diarrhoea. The most bothersome symptoms tend to be fever and muscle pains. You can safely treat these with paracetamol.

The WHO initially recommended people with COVID-19 avoid taking ibuprofen to relieve symptoms. But it retracted that advice days later, so it seems reasonable to also consider using anti-inflammatory drugs.

You can treat nasal congestion with decongestants and nasal saline. Effective treatments for a sore throat include honey, salt water gargles, and sore throat sprays or gargles. Cough is a more difficult symptom to control, but you may be able to improve it with honey, steam inhalations and saline nose sprays. Cough suppressants have only minimal benefit in reducing a dry cough.

It's also important to support your immune system, particularly with rest and a healthy diet. There's some evidence zinc lozenges may shorten the duration of some colds and flus, including COVID-19. But this evidence is conflicting and not of high quality.

Meanwhile, there's no convincing evidence beyond the placebo effect for a range of other common treatments, such a vitamin C and echinacea. But these are unlikely to cause harm.

Don't try this at home

It's important not to take medicines that haven't been approved for the treatment of colds and flus. Anecdotal reports and a small case series of patients in China have suggested a role for the antimalarial drug chloroquine in treating COVID-19.

Further clinical trials of this drug are currently underway, but at this stage it's recommended as treatment only in COVID-19 cases complicated by viral or bacterial pneumonia, and under the guidance of medical professionals. One HIV antiviral combination drug, lopinavir-ritonavir, seemed promising. But it failed to make a significant difference in 199 patients with COVID-19 in China.

So there are no effective curative treatments as yet, but clinical trials of different antiviral agents are continuing.

While lots of information about prevention and treatments for coronavirus is circulating online, a good rule of thumb is if it sounds too good to be true, it probably is.

If you're unsure about anything, look to reliable sources like the Australian government or the WHO, or consult a doctor.

What about people with more serious illness?

About five to seven days after the onset of symptoms, some patients develop shortness of breath and trouble breathing, which will require medical attention. Shortness of breath occurs when pneumonia develops, causing a buildup of thick mucus in the lungs that blocks the transfer of oxygen into the blood vessels.

If your condition deteriorates, call ahead to a doctor or hospital and inform them of your COVID-19 status. If you're experiencing severe symptoms, such as shortness of breath, call an ambulance.

How long before I'm not infectious anymore?

If you're hospitalised with COVID-19, you will remain in isolation until you're no longer experiencing symptoms and a test confirms you're no longer infectious.

In a group of hospitalised patients in China, the average duration of virus still detected in the respiratory tract was 20 days.

Mild cases, however, have a shorter duration of illness, and the virus clears more quickly from their bodies.

Australian guidelines state that cases with a mild illness not requiring hospitalisation can end their self-isolation if they meet these two criteria:

**** at least ten days have passed since the onset of symptoms***

**** all symptoms of acute illness have been resolved for the previous 72 hours.***

[*]Senior Lecturer, The University of Queensland

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https://bit.ly/2UHvIEM

COVID-19 linked to cardiac injury, worse outcomes for patients with heart conditions

It is likely that even in the absence of previous heart disease, the heart muscle can be affected by coronavirus disease

COVID-19 can have fatal consequences for people with underlying cardiovascular disease and cause cardiac injury even in patients without underlying heart conditions, according to a review published today in *JAMA Cardiology* by experts at The University of Texas Health Science Center at Houston (UTHealth).

Experts have known that viral illnesses such as COVID-19 can cause respiratory infections that may lead to lung damage and even death in severe cases. Less is known about the effects on the cardiovascular system.

"It is likely that even in the absence of previous heart disease, the heart muscle can be affected by coronavirus disease," said Mohammad Madjid, MD, MS, the study's lead author and an assistant professor of cardiology at McGovern Medical School at UTHealth. "Overall, injury to heart muscle can happen in any patient with or without heart disease, but the risk is higher in those who already have heart disease."

The study authors explained that research from previous coronavirus and influenza epidemics suggest that viral infections can cause acute coronary syndromes, arrhythmias, and the development of, or exacerbation of, heart failure.

In a clinical bulletin issued by the American College of Cardiology, it was revealed that the case fatality rate of COVID-19 for patients with cardiovascular disease was 10.5%. Data also points to a greater likelihood that individuals over the age of 65 with coronary heart disease or hypertension can contract the illness, as well experience more severe symptoms that will require critical care.

According to the study authors, critical cases are those that reported respiratory failure, septic shock, and/or multiple organ dysfunction or failure that resulted in death. "It is reasonable to expect that significant cardiovascular complications linked to COVID-19 will occur in severe symptomatic patients because of the high inflammatory response associated with this illness," said Madjid, who also sees patients at the UT Physicians Multispecialty - Bayshore clinic.

The novel virus that causes COVID-19 was first identified in January 2020. This novel virus originated in Wuhan, China, and by March 11, 2020, the World Health Organization had declared it a global pandemic. The three most common symptoms of COVID-19 include fever, cough, and shortness of breath. Other less common symptoms are muscle pain, sore throat, nasal congestion, and headache. Symptoms can appear as soon as two days after exposure to the virus to up to14 days after. There is a high viral load in both symptomatic and asymptomatic patients, meaning asymptomatic spread between person to person is likely.

Previously identified coronaviruses known to cause severe illness in humans include Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome (MERS-CoV). SARS-CoV was first identified in southern China in 2002, and by 2003 it had killed over 8,000 individuals in 29 countries. Data suggests that SARS-CoV may have resulted in cardiovascular complications, such as acute coronary syndrome and myocardial infarction. MERS-CoV was first discovered in 2012 in Saudi Arabia. As of 2019, 2,494 cases have been confirmed along with 858 deaths in 26 countries.

Current COVID-19 treatment options are being researched, and there is a large effort to develop vaccines for prevention and to test antivirals for the treatment of the disease. In the meantime, the study authors encourage all individuals to consult with their health care providers about being vaccinated against influenza and that at-risk patients seek advice on receiving a pneumonia vaccine from their primary care physician. While these vaccines will not provide specific protection against COVID-19, they can help prevent superimposed infections alongside COVID-19.

Study co-authors include Payam Safavi-Naeini, MD, of the Texas Heart Institute; Scott Solomon, MD, of Harvard Medical School; and Orly Vardeny, PharmD, of the University of Minnesota.

https://bit.ly/2WT2DZA

Some COVID-19 patients still have coronavirus after symptoms disappear

Half of patients treated for mild COVID-19 infection still had coronavirus for up to eight days after symptoms clear

In a new study, researchers found that half of the patients they treated for mild COVID-19 infection still had coronavirus for up to

eight days after symptoms disappeared. The research letter was published online in the American Thoracic Society's *American Journal of Respiratory and Critical Care Medicine*.

In "Time Kinetics of Viral Clearance and Resolution of Symptoms in Novel Coronavirus Infection," Lixin Xie, MD, Lokesh Sharma, PhD, and co-authors report on a study of 16 patients with COVID-19, who were treated and released from the Treatment Center of PLA General Hospital in Beijing between January 28 and Feb. 9, 2020. Patients studied had a median age of 35.5 years.

Researchers collected samples from throat swabs taken from all patients on alternate days and analyzed. Patients were discharged after their recovery and confirmation of negative viral status by at least two consecutive polymerase chain reaction (PCR) tests.

"The most significant finding from our study is that half of the patients kept shedding the virus even after resolution of their symptoms," said co-lead author Dr. Sharma, instructor of medicine, Section of Pulmonary, Critical Care & Sleep Medicine, Department of Medicine, Yale School of Medicine. "More severe infections may have even longer shedding times."

The primary symptoms in these patients included fever, cough, pain in the pharynx (pharyngalgia) and difficult or labored breathing (dyspnea). Patients were treated with a range of medications.

The time from infection to onset of symptoms (incubation period) was five days among all but one patient. The average duration of symptoms was eight days, while the length of time patients remained contagious after the end of their symptoms ranged from one to eight days. Two patients had diabetes and one had tuberculosis, neither of which affected the timing of the course of COVID-19 infection.

"If you had mild respiratory symptoms from COVID-19 and were staying at home so as not to infect people, extend your quarantine for another two weeks after recovery to ensure that you don't infect other people," recommended corresponding author Lixin Xie, MD, professor, College of Pulmonary and Critical Care Medicine, Chinese PLA General Hospital, Beijing.

The authors had a special message for the medical community: "COVID-19 patients can be infectious even after their symptomatic recovery, so treat the asymptomatic/recently recovered patients as carefully as symptomatic patients."

The researchers emphasized that all of these patients had milder infections and recovered from the disease, and that the study looked at a small number of patients. They noted that it is unclear whether similar results would hold true for more vulnerable patients such as the elderly, those with suppressed immune systems and patients on immunosuppressive therapies.

"Further studies are needed to investigate if the real-time PCR-detected virus is capable of transmission in the later stages of COVID-19 infection," Dr. Xie added.

https://bit.ly/3an1L3j

Astronaut urine to build moon bases

European researchers have found that urea could be used as a plasticizer in the concrete

The modules that the major space agencies plan to erect on the Moon could incorporate an element contributed by the human colonizers themselves: the urea in their pee. European researchers have found that it could be used as a plasticizer in the concrete of the structures.

Future moon bases could be built with 3D printers that mix materials such as moon regolith, water and astronauts' urine **Credit: ESA, Foster and Partners**

NASA, the European Space Agency (ESA) and its Chinese counterpart plan to build moon bases in the coming decades, as part

of a broader space exploration plan that will take humans to more distant destinations, such as Mars.

However, the colonization of the Moon poses problems such as high levels of radiation, extreme temperatures, meteorite bombardment and a logistical issue: how to get construction materials there, although it may not be necessary.

Transporting about 0.45 kg from the Earth to space costs about $10,000, which means that building a complete module on our satellite in this way would be very expensive. This is the reason why space agencies are thinking of using raw materials from the moon's surface, or even those that astronauts themselves can provide, such as their urine.

Scientists from Norway, Spain, the Netherlands and Italy, in cooperation with ESA, have conducted several experiments to verify the potential of urine urea as a plasticizer, an additive that can be incorporated into concrete to soften the initial mixture and make it more pliable before it hardens. Details are published in the *Journal of Cleaner Production*.

"To make the geopolymer concrete that will be used on the moon, the idea is to use what is there: regolith (loose material from the moon's surface) and the water from the ice present in some areas," explains one of the authors, Ramón Pamies, a professor at the Polytechnic University of Cartagena (Murcia), where various analyses of the samples have been carried out using X-ray diffraction.

"But moreover," he adds, "with this study we have seen that a waste product, such as the urine of the personnel who occupy the moon bases, could also be used. The two main components of this body fluid are water and urea, a molecule that allows the hydrogen bonds to be broken and, therefore, reduces the viscosities of many aqueous mixtures."

Using a material developed by ESA, which is similar to moon regolith, together with urea and various plasticizers, the researchers, using a 3D printer, have manufactured various 'mud' cylinders and compared the results.

The experiments, carried out at Østfold University College (Norway), revealed that the samples carrying urea supported heavy weights and remained almost stable in shape. Once heated to 80°C, their resistance was also tested and even increased after eight freeze-thaw cycles like those on the Moon.

"We have not yet investigated how the urea would be extracted from the urine, as we are assessing whether this would really be necessary, because perhaps its other components could also be used to form the geopolymer concrete," says one of the researchers from the Norwegian university, Anna-Lena Kjøniksen, who adds: "The actual water in the urine could be used for the mixture, together with that which can be obtained on the Moon, or a combination of both."

The scientists stress the need for further testing to find the best building material for the moon bases, where it can be mass-produced using 3D printers.

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https://bit.ly/2QVovj4

Experts Increasingly Question Advice Against Widespread Use of Face Masks

Health authorities in some Asian countries have been calling on everyone to wear face masks to prevent the virus from spreading

By Daniel Politi

Since the beginning of the coronavirus crisis, the message from Western public health authorities has been pretty uniform in stating that the public at large shouldn’t be wearing face masks to protect

against COVID-19. Surgeon General Jerome Adams even sent an all-caps message to all Americans in late February imploring them to "STOP BUYING MASKS!" because they are "NOT effective" for the general public. Experts, however, aren't so sure that's the case, particularly considering that health authorities in some Asian countries have been calling on everyone to wear face masks to prevent the virus from spreading.

These experts insist that while it's true that face masks are hardly a cure-all and don't replace more important measures such as social distancing, they could still help. That's particularly the case for essential workers who can't avoid crowded areas like public transportation. Although regular surgical masks are hardly ideal for protection they do seem to be better than nothing. The New York Times cites a study of strategies used during the 2003 SARS outbreak that found washing hands 10 times a day was 55 percent effective in stopping transmission. But wearing a mask was more effective at around 68 percent.

One key point is that health authorities have long recommended masks for those who are sick in order to prevent them from infecting others. And considering COVID-19 has a lot of asymptomatic cases, widespread use of masks could help prevent those who do not know they are carrying the virus from spreading it to others. "It's really a perfectly good public health intervention that's not used," KK Cheng, a public health expert at the University of Birmingham, tells Science. "It's not to protect yourself. It's to protect people against the droplets coming out of your respiratory tract." Plus if everyone is wearing them it reduces any stigma attached to the face masks themselves.

Another side benefit of wearing masks, some experts say, is that it can help people avoid touching their face (although to be fair, some have said the exact opposite, that wearing a face mask actually encourages people to touch their face). But in order to be most effective, the general public needs to receive some training on how to properly wear protective equipment. "I think the average person, if they were taught how to wear a mask properly … would have some protection against infection in the community," Benjamin Cowling, an epidemiologist at the University of Hong Kong, said.

The key problem though is supply. As surely everyone knows by now, masks are really difficult to obtain and calling on the general public to wear them would decrease those available for health care workers and other emergency workers. After all, it's difficult to call for a widespread use of masks when hospital workers are being told to reuse their protective gear because there is a shortage. Still, Dan McCarthy, an assistant professor of medicine at Weill Cornell, tweeted that the Centers for Disease Control would be changing its guidelines on masks over the next 10 days to advise Americans to wear them. The CDC replied to the tweet saying there is no schedule to update its guidance on the issue.

https://nyti.ms/2WRevuZ

Early Graduation Could Send Medical Students to Virus Front Lines

Hundreds of fourth-year students at universities in Boston and New York could start caring for patients months ahead of schedule.

By Emma Goldberg

The battle to treat an ever-growing number of patients infected with the new coronavirus just gained its newest recruits: soon-to-be medical graduates. Several medical schools in Massachusetts and New York announced this week that they intended to offer early graduation to their fourth-year students, fast-tracking them into front-line hospital care as the need for medical workers surges.

On Tuesday, the Grossman School of Medicine at New York University became the first in the United States to announce an offer of early graduation, in an email to students. That followed

similar moves earlier this year in Italy and Britain, which advanced many final-year medical students into intermediate clinical service.

On Thursday, the medical schools at Tufts University, Boston University and the University of Massachusetts announced that they planned to move up their graduation dates to April from May, after a request from the state of Massachusetts to help expand the medical work force. Harvard Medical School said it was "actively considering" the same step.

In Massachusetts, the state would provide 90-day provisional licenses for early graduates, allowing almost automatic entry into clinical work. The move would make some 700 medical students in Massachusetts eligible to offer patient care at least eight weeks earlier than expected.

On Friday, Columbia's Vagelos College of Physicians and Surgeons became the latest to announce that final year students would graduate early, on April 15, rather than May 20. Graduates would have the option to temporarily join the staff at NewYork-Presbyterian Hospital.

Dr. Steven Abramson, vice dean for education, faculty and academic affairs at N.Y.U. Grossman, said the school's decision came as its hospitals were overwhelmed with an increasing number of Covid-19 patient cases, including in critical care. He said several fourth-year students had approached school administrators to volunteer their service.

"We're running into issues of manpower," Dr. Abramson said. "That led us to conclude: Why not graduate students who are interested in serving in hospitals now? They've completed their requirements and they're prepared."

Most American medical schools last four years, at which point the medical degree is granted, followed by residencies and internships to develop the specialties of new doctors.

At N.Y.U., Dr. Abramson said, fourth-year students would be able to graduate in early April and begin patient care at N.Y.U.'s hospitals, on medicine floors and in the emergency room. They would then depart in late June or July for the start of their scheduled residency programs, with a two-week quarantine in between. Of 120 fourth-year students surveyed this week, he said 69 responded that they would be interested in early clinical service.

While the Liaison Committee on Medical Education, which accredits medical degree programs in the United States, has offered guidelines for early graduation, N.Y.U.'s decision awaits final approval from the New York State Department of Education.

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A number of New York medical schools are still developing proposals for early graduations. Dr. David Muller, dean for medical education at the Icahn School of Medicine at Mount Sinai, said the school hoped to have a proposal ready to share with students by early next week. The early graduation would most likely occur in mid-April, he added, and would be voluntary, although details need to be worked out. The Albert Einstein College of Medicine also is working toward early graduation.

Medical students around the country have spent recent weeks mobilizing to support local physicians. They have staffed coronavirus hotlines, coordinated meal deliveries and even offered their time as babysitters to other medical workers. Many said they were excited to contribute their medical training.

"We see everything the physicians around us are going through and we're excited we can bring some relief to the physicians who trained and mentored us," said Greg Peters, a fourth-year student at Harvard who plans to start a residency in emergency care in Boston. He added, though, that the prospect of early graduation and fast-tracked service came as a surprise. "My classmates and I are Type

A people who plan everything out, and our plans are out the window," he said. "We're confident in our training, but we're a little worried about getting thrown in there."

The Association of American Medical Colleges, a research and advocacy group for medical schools and major teaching hospitals, said it supported the early graduations following L.C.M.E. guidelines, but emphasized the importance of supervision for new graduates.

"As we think about what the role of these new graduates would be, it would need to be under supervision," said Dr. Alison Whelan, the association's chief medical education officer.

Dr. Abramson said he expected more medical schools around the country to move toward early graduations.

"We aren't the only school that has needs for taking care of patients in this Covid environment," he said. "I fully anticipate other schools will look at this and do it as well."

https://bit.ly/33VFZ45

Scientists Trace Neutron Star Crash That Helped Form Our Solar System

The collision helped seed Earth with its precious metals

By Nola Taylor Redd, SPACE.com

Astronomers are on the hunt for the remnants of the neutron-star collision that gave Earth its precious metals.

When neutron stars merge, they spew a wealth of short-lived elements into their surroundings, and these materials become part of later-forming solar systems. Now scientists are trying to close in on the merger that seeded our solar system by tracing the elements produced by the original decaying material. From that work, they believe the responsible merger occurred 100 million years before and 1,000 light-years away from the birth of our solar system.

"It was close," the project's lead scientist, Szabolcs Marka, who is a physicist at Columbia University, told Space.com. "If you look up at the sky and you see a neutron-star merger 1,000 light-years away, it would outshine the entire night sky."

Marka and his colleague Imre Bartos, an astrophysicist at the University of Florida, used meteorites from the dawn of the solar system to track down the collision. They analyzed the isotopes—flavors of elements with different numbers of neutrons in their atoms—in these rocks.

First, they calculated the quantity of radioactive isotopes in the early solar system; then the researchers compared their measurements with the amount of isotopes produced by neutron-star mergers. Marka presented the results of their research in January at the winter meeting of the American Astronomical Society in Honolulu.

"Our" neutron-star merger

The universe's heavy elements, such as gold, platinum and plutonium, form when neutrons bombard existing atoms. During such collisions, a neutral neutron can emit a negatively charged electron, becoming a positively charged proton and changing the atom's identity.

This process, known as rapid neutron capture, occurs only during the most powerful explosions, such as supernovas and neutron-star mergers. But scientists continue to debate which of these extreme events is responsible for the bulk of heavy elements in the universe.

So Marka and Bartos turned to ancient meteorites in an effort to understand which type of event may have seeded the early solar system. Locked inside of those rocks from the young solar system is material that spewed from an explosion, and although those initial elements were radioactive and rapidly decayed, they left behind signatures of their past presence.

And as the Laser Interferometer Gravitational-Wave Observatory (LIGO) begins to identify potential neutron-star mergers, scientists are applying its observations to help identify the

most likely contributors of material formed in a nearby merger, what Marka called “the witch’s brew of the galaxy,” the slowly decaying material that made its way to the solar system.

Previous studies estimated that a supernova occurs in the Milky Way once every 50 years or so. LIGO’s new observations suggest that neutron-star mergers occur much less frequently, approximately once every 100,000 years. The amount of heavy elements in the solar system suggested that they came from a nearby neutron-star merger, as supernova origins would have yielded more material.

From there, the pair relied on the individual isotopes to determine where and when the solar system’s local neutron-star merger had occurred.

“Each isotope is a stopwatch starting at the explosion,” Marka said. By studying how much of each isotope was left when the material was captured, he was able to pin down the age of the collision that showered the solar system. “There is only one point in time when they all agree," he said. That point occurred roughly 100 million years before the solar system formed, an eye blink in astronomical time scales. The team also calculated how far away the stars collided, a distance of 1,000 light-years, based on how much material ended up in the solar system.

What the team could not figure out was the direction at which these heavy elements entered the neighborhood that would become our solar system, a discovery that could theoretically allow scientists to pinpoint the remnants of the collision. The problem is that the sun hasn’t been sitting still for the 4.5 billion years since it formed; instead, it’s been traveling around the galaxy.

Along the way, it has left behind the stars that formed near it in the same cluster, stars that astronomers have long hunted in vain. Marka hopes that one day, astronomers will find those sister stars and the remnants of the neutron-star merger that formed the solar system.

According to Marka, the new discovery hit close to home. “People were actually crying," he said, referring to members of his team.

He said he thinks that strong emotional reaction arose because this neutron-star merger wasn’t just an event that happened out in space. It was one that contributed to each of us, personally.

“This is not esoteric, it’s ours,” Marka said. “Not ours in the galaxy but ours in the solar system.”

https://bit.ly/2WO8ijD

America Needs Plasma From COVID-19 Survivors Now

People who have recovered from the disease have antibodies that might help those still suffering from it.

Sarah Zhang

Tatiana Prowell knew it was a long shot, but she didn’t know what else to do. Her brother-in-law’s father, the man she knew affectionately as “Papa Doc,” was in the ICU with COVID-19, and things were not looking good. “HELP!,” she tweeted late on Wednesday night: She needed to find someone who had recovered from COVID-19, and then ask for their blood.

The day before Prowell tweeted her plea, the Food and Drug Administration began allowing doctors to use plasma, the yellow fluid in which blood cells are suspended, as a Hail Mary to treat very ill COVID-19 patients. The idea of using plasma from survivors, also known as convalescent-plasma therapy, dates back to the late 19th century. Doctors have transfused the blood of recovered patients into those still sick with the 1918 flu, measles, polio, chickenpox, SARS, and Ebola—to varying degrees of success. Given the dearth of treatments for COVID-19, convalescent plasma has gained new prominence. The blood of survivors, the thinking goes, contains proteins called antibodies that

can neutralize the coronavirus. Early data from very small numbers of COVID-19 patients in China show some promise. But the first hurdle is finding the recovered patients who can give plasma.

"We can't go to that warehouse and get the 100 bottles on the shelf," says Liise-anne Pirofski, the chief of the infectious-disease department at the Montefiore Medical Center, in New York. So doctors, scientists, blood banks, and government agencies have begun mobilizing to collect, distribute, and study plasma from COVID-19 survivors. The advantage of plasma is that you don't need to develop a vaccine or treatment from scratch. But in these early days of the pandemic, when the number of recovered and confirmed patients is still relatively small, finding them will take time. The irony is that the bigger the pandemic gets, the easier finding donors will be.

Prowell, who had been following the prospects of convalescent plasma closely because she is also a doctor at Johns Hopkins University, was overwhelmed—in a good way—by the response to her tweet. She got hundreds of replies from people who offered to donate or knew someone who might. "That's very powerful, but it's obviously not the right way to do this at scale," she told me. "We're going to have millions of cases." The family is still looking for a donor who fits all the criteria.

The way to do this at scale is a national network that connects donors, patients, and their doctors. Such an effort began in late February, when Arturo Casadevall, an immunologist at Johns Hopkins, published an op-ed in *The Wall Street Journal* suggesting the use of convalescent plasma for COVID-19. He started connecting interested doctors, virologists, immunologists, and blood-banking experts, who all came together to launch the National COVID-19 Convalescent Plasma Project.

The movement has gained traction. This week, New York announced that it would be the first state to try convalescent-plasma therapy, and the New York Blood Center, a major blood bank, began collecting plasma from people who have recovered from COVID-19.

For now, this plasma is going to hospitals in New York, which are using it on a case-by-case basis. A spokesperson at Mount Sinai told me that the hospital expects to transfuse its first patient this weekend. Mount Sinai's call for donors got thousands of responses, which an army of medical students is now sifting through.

A single plasma donation from a COVID-19 survivor could go to multiple patients. Donating plasma is similar to donating whole blood, except the red blood cells are separated out by a machine and returned to the donor. "We can do two to three people from one donor," says Bruce Sachais, the chief medical officer at the New York Blood Center. But the majority of these interested donors will not be suitable for one reason or another: The criteria, set by the FDA, suggest that donors should have had no symptoms for at least 14 days. They should have had a lab test confirming COVID-19, which is hard to get now and was even harder to get when the donors would have first gotten sick, several weeks ago. And, as with normal blood donation, patients and donors have to be matched by blood type. Prowell, for example, is looking for someone who is A-positive or AB-positive for Papa Doc.

In addition to using plasma on a case-by-case basis for very ill patients, doctors are also planning to study convalescent-plasma therapy for COVID-19 more systematically. Soon, the New York Blood Center plans to send out plasma for clinical trials at several hospitals, such as Johns Hopkins, the Mayo Clinic, and Montefiore Medical Center. To help find the right donors for the trials, Shmuel Shoham, an infectious-disease doctor who is involved in the Johns Hopkins trial, told me he leaned on a friend who is an organizer in the Orthodox Jewish community. Orthodox Jews in New York were

at the center of an early coronavirus outbreak, which means those who have recovered could become donors right now.

Michael J. Joyner, a doctor at the Mayo Clinic, likened this phase to the "craft brewing" of convalescent-plasma therapy. It's available at only a few academic centers, and doctors are reliant on personal connections to recruit donors. Getting to the "national-brewery model," he says, requires involving bigger players. The FDA could help identify donors, and a network of national blood banks could send COVID-19 plasma to hospitals in small cities and towns. Eventually, pharmaceutical companies might be interested in pooling and purifying plasma down to a concentrated dose of antibodies—at which point convalescent plasma truly would be a standardized product you pull off the shelf.

All of this, of course, is contingent on plasma actually working against COVID-19. The clinical trials that are planned in the U.S. will focus on patients who are less ill—ideally those not in the ICU. Some evidence suggests that the antibodies in plasma are useful early on in the immune response, but less so once a patient has reached the stage of organ failure that requires hospitalization. No one knows why, Pirofski told me, but one reason could be that antibodies help prevent the virus from spreading from the nose and throat into the lungs.

At Mayo and Montefiore, the trials will be focused on people early into their infections. The Johns Hopkins trial will enroll people who have been exposed to COVID-19—maybe because a family member tested positive—but who do not yet have symptoms. If plasma can lessen the severity of COVID-19, it could be key to alleviating the strain on hospitals. "The idea is if we give this to people who have respiratory symptoms like cough and chest pain, maybe they won't require supplemental oxygen, won't require intubation," Pirofski said.

Papa Doc has gotten slightly better in the days since Prowell tweeted for help. But he's still sedated and on a ventilator; no visitors are allowed, due to the risk of infection. "That is so emotionally excruciating," says Jason Constantine, Prowell's brother-in-law. His father doesn't know that they are trying to find him a plasma donor or that hundreds of strangers have taken an interest in him. But they are still looking for the right stranger who might be able to help.

https://wb.md/2QWbaHs

Steps to Boost Your Facility's Capacity Before COVID-19 Surge Hits

Reporting from an alliance for health policy webinar

Kari Oakes

Ramping up health system capacity for the coming surge of U.S. COVID-19 cases requires a commitment to boosting safety, capacity, and communication, according to a physician leader and a health workforce expert.

Polly Pittman, PhD, is hearing a lot of concern among health care workers that it's difficult to find definitive and accurate information about how best to protect themselves and their families, she said during a webinar by the Alliance for Health Policy titled Health System Capacity: Protecting Frontline Health Workers. "The knowledge base is evolving very quickly," said Dr. Pittman, Fitzhugh Mullan Professor of Health Workforce Equity at the Milken Institute School of Public Health, George Washington University, Washington.

Stephen Parodi, MD, agreed that effective communication is job one in the health care workplace during the crisis. "I can't stress enough ... that communications are paramount and you can't overcommunicate," said Dr. Parodi, executive vice president of external affairs, communications, and brand at the Permanente

Federation and associate executive director of the Permanente Medical Group, Vallejo, Calif.

"We're in a situation of confusion and improvisation right now," regarding protection of health care workers, said Dr. Pittman. The potential exists for "a downward spiral where you have the lack of training, the shortages in terms of protective gear, weakening of guidelines, and confusion regarding guidelines at federal level, creating a potential cascade" that may result in "moral distress and fatigue. ... That's not occurring now, but that's the danger" unless the personal protective equipment (PPE) situation is adequately addressed very soon, she said.

Dr. Pittman also pointed out the concerns that many of the 18 million U.S. health care workers have for their families should they themselves fall ill or transmit coronavirus to family members. "The danger exists of a mass exodus. People don't have to show up at work, and they won't show up at work if they don't feel supported and safe."

Dr. Parodi said that the Permanente organization is on a better footing than many workplaces. "We actually had an early experience because of the work that we did to support the Diamond Princess cruise ship evacuees from Yokohama in February." That ship was quarantined upon arrival in Yokohama on Feb. 3 because a passenger had a confirmed test for SARS-CoV-2 infection, and a quarter of the 428 Americans on board subsequently tested positive. Most of them were evacuated to California or Texas. "That actually gave us the experience for providing care within the hospital setting — and also for containment strategies," he said.

"We quickly understood that we needed to move to a mitigation strategy," said Dr. Parodi. Use of PPE has been "tailored for how the virus is spread." In the absence of the risk of aerosol transmission from certain procedures, health care workers use gowns, gloves, surgical masks, and goggles.

Because of anticipated "supply chain shortfalls," Dr. Parodi said that his organization implemented Centers for Disease Control and Prevention guidelines for reuse and extended use of N95 respirators early on. "Even if you're not in a locale that's been hit, you need to be on wartime footing for preserving PPE."

Telehealth, said Dr. Parodi, has been implemented "in a huge way" throughout the Permanente system. "We have reduced primary care visits by 90% in the past week, and also subspecialty visits by 50%. … A large amount of the workforce can work from home. We turned off elective surgeries more than a week ago to reduce the number of patients who are requiring intensive care." Making these changes means the organization is more prepared now for a surge they expect in the coming weeks.

Dr. Pittman voiced an opinion widely shared by those who are implementing large-scale telehealth efforts "We're going to learn a lot. Many of the traditional doctor-patient visits can be done by telemedicine in the future."

Knowledge about local trends in infection rates is key to preparedness. "We've ramped up testing, to understand what's happening in the community," said Dr. Parodi, noting that test turnaround time is currently running 8-24 hours. Tightening up this window can free up resources when an admitted patient's test is negative.

Still, some national projections forecast a need for hospital beds at two to three times current capacity — or even more, said Dr. Parodi. He noted that Permanente is "working hand in glove with state authorities throughout the country." Efforts include establishing alternative sites for assessment and testing, as well as opening up closed hospitals and working with the National Guard and the Department of Defense to prepare mobile hospital units that can be deployed in areas with peak infection rates. "Having all of those options available to us is critically important," he said.

To mitigate potential provider shortages, Dr. Pittman said, "All members of the care team could potentially do more" than their current licenses allow. Expanding the scope of practice for pharmacists, clinical laboratory staff, licensed practical nurses, and medical assistants can help with efficient care delivery.

Other measures include expedited licensing for near-graduates and nonpracticing foreign medical graduates, as well as relicensing for retired health care personnel and those who are not currently working directly with patients, she said.

Getting these things done "requires leadership on behalf of the licensing bodies," as well as coordination with state regulatory authorities, Dr. Pittman pointed out.

Dr. Parodi called for state and federal governments to implement emergency declarations that suspend some existing health codes to achieve repurposing of staff. Getting these measures in place now will allow facilities "to be able to provide that in-time training now before the surge occurs. ... We are actively developing plans knowing that there's going to be a need for more critical care."

The game plan at Permanente, he said, is to repurpose critical care physicians to provide consultations to multiple hospitalists who are providing the bulk of frontline care. At the same time, they plan to repurpose other specialists to backfill the hospitalists, and to repurpose family medicine physicians to supplement staff in emergency departments and other frontline intake areas.

All the organizational measures being taken won't be in vain if they increase preparedness for the long battle ahead, he said. "We need to double down on the work. ... We need to continue social distancing, and we've got to ramp up testing. Until we do that we have to hold the line on basic public health measures."

Dr. Parodi is employed by Permanente. The panelists reported no disclosures relevant to the presentation, which was sponsored by the Alliance for Health Policy, the Commonwealth Fund, and the National Institute for Health Care Management Foundation. This article originally appeared on MDedge.com.

https://bit.ly/2QPA3ob

How to make a coronavirus vaccine

Dr. William Haseltine, a biologist, explains how one goes about the task of vaccinating for the coronavirus

Matthew Rozsa

The coronavirus pandemic may seem like something out of a horror movie — an invisible enemy that kills millions of people and shuts down society, reducing vibrant communities to ghost towns — but it is important to remember that the virus itself is not some supernatural monster. It is a thing that lives by and through infecting other cells,it has tangible physical characteristics — meaning it can be captured and therefore killed.

The question nowis how? Fortunately, the COVID-19 virus isn't entirely new. It is closely related to the SARS-1 virus, which like COVID-19 originated from China. That disease infected roughly 8,000 people from 2002 to 2003, a mild outbreak compared to the global pandemic caused by COVID-2, also known as SARS-CoV-2. Yet despite President Donald Trump suggesting a vaccine would be ready in November, it is quite possible that there will be a long road ahead of us before this thing is licked.

To learn more about the fight against COVID-19 and the possibility of a vaccine, Salon spoke with Dr. William Haseltine, a biologist renowned for his work in confronting the HIV/AIDS epidemic, for fighting anthrax, and for advancing our knowledge of the human genome. He is also the founder and former CEO of Human Genome Sciences, and is currently the chair and president of the global health think tank Access Health International. As usual, this interview had been edited for clarity and context.

Why is it so difficult to develop a vaccine?

It may be simple and it may be difficult. We still don't know… With SARS 1, people tried to make vaccines in animals, including monkeys, but it didn't work very well. So they tried what they

thought would work, which was using a surface protein of the virus. And they didn't work very well to stop the virus and they didn't last for very long. So there hasn't been a successful virus vaccine developed for any of the coronaviruses. That suggests it might be difficult but we don't know yet. I'm hoping it's going to be easy, but nobody knows.

It is an unresolved question at this point. If you want to know why, I can give you some information about why.

Indeed I would, yes.

Many natural infections, and most of the work I'm going to refer to, refers to HIV, but many natural infections present themselves to the body in a way that the body reacts to, but is harmless to the virus. So essentially they throw up a lot of decoys and they protect the most sensitive part, which is that part which has to attach to the receptor of the surface. Think of it like a fuzzy basketball with a big dent in it, or maybe a Pac-Man. The Pac-Man is what holds that dent and it is what's going to grab a hold of the receptor. The outsides of the virus can be all fuzzy and that's what it presents to the immune system and it's hard for the immune system to see into the mouth of the Pac-Man. And so many viruses use that kind of trick. So you make a lot of antibodies but they don't stop the virus from working, from getting into your body.

Does that effect our ability to develop a vaccine?

It does, because then if you take the same protein and you use that outside protein to raise antibodies like you do in a vaccine, it means you're going to raise the wrong kind of antibodies. And then the antibodies you raised, you'll get a good immune response but it won't stop the virus. And so that's the fear. It's not certain yet whether that happens, but there are early experiments that were done many years ago with the SARS-1 virus which showed that it was not as simple as people were hoping for. So it may not be simple for this, but we might be lucky.

For people who are not familiar with epidemiology, explain how you develop vaccines and whether it is easier to defeat a disease like COVID-19 than it is to defeat a retrovirus [RNA viruses which inject a DNA copy of their genome into a host cell] like AIDS.

The prospects of a vaccine for coronavirus are not straightforward. It may be possible to make one using traditional methods, but they've so far not been proven effective for any animal against the coronavirus.

There are several ways to make a vaccine. One way is to grow up the virus and kill it. That's what polio virus is. That's a polio vaccine, and that's relatively simple because the polio virus doesn't have the kind of envelope around it. There is a membrane around the coronavirus. So when you grow a polio and you kill it, that makes a good vaccine, and that's the way to make vaccines. And you could try that with this virus. It's unlikely to work, but you can try it.

A second way is to actually produce a purified protein from the virus and you mix that with an adjuvant and that becomes the vaccine.

A third way is to take the genes that specify the virus proteins you want to make and you put those into a different viral vector that is itself harmless. When you use that as a vaccine it produces the protein that raises the immune responses that are protective.

To date though, no one has been successful in creating a vaccine that protects any animal from a coronavirus. Vaccine trials have not been attempted in humans for any members of the coronavirus family.

Why aren't coronaviruses a more common type of virus in terms of pandemics from an evolutionary perspective, given that they seem to be so effective?

They are quite common! About one third of all your colds are coronaviruses. They're very effective. It's just they're usually not lethal, mostly they give mild symptoms. By the way, the same thing is true about the polio virus. The polio virus is a cold virus. It causes paralysis in about one out of a hundred people. But there are many similar viruses, polio-like viruses, and all they do is cause colds. And so the coronavirus is a virus like that. Most of the time it just causes mild infections. And in the '50s, they were discovered and people were surprised to find about one-third of all colds are caused by coronaviruses. So they are successful.

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https://bit.ly/3byclVl

The COVID-19 Virus May Have Been in Humans For Years, Study Suggests

Virus may have been circulating harmlessly in human populations for quite a while

Jacinta Bowler

As COVID-19 has hitchhiked around the globe, causing lockdowns, pneumonia and fear, scientists have been racing to determine where the SARS-CoV-2 coronavirus has come from.

While we don't have all the answers yet - including whether it came from an animal reservoir - a new analysis has definitively put to rest the conspiracies that claim it's a lab-made disease.

The study raises some interesting possibilities regarding the origin of the new coronavirus. One of the scenarios suggests the virus may have been circulating harmlessly in human populations for quite a while before it became the pandemic that's now stopped the world in its tracks.

"It is possible that a progenitor of SARS-CoV-2 jumped into humans, acquiring [new genomic features] through adaptation during undetected human-to-human transmission," the team from the US, UK and Australia writes in the study.

"Once acquired, these adaptations would enable the pandemic to take off and produce a sufficiently large cluster of cases."

The researchers analysed genomic data available from SARS-CoV-2 and other similar coronaviruses, showing that the receptor-binding domain (RBD) sections of SARS-CoV-2 spike proteins were so effective at binding to human cells, they had to be caused by natural selection.

"By comparing the available genome sequence data for known coronavirus strains, we can firmly determine that SARS-CoV-2 originated through natural processes," said one of the researchers, immunologist Kristian Andersen at Scripps Research.

"Two features of the virus, the mutations in the RBD portion of the spike protein and its distinct backbone, rules out laboratory manipulation as a potential origin for SARS-CoV-2."

With 'laboratory experiment gone wrong' out of the way, the team explored two viable hypotheses. First, that the natural selection occurred in an animal host *before* the virus was transmitted to humans. The team explains that although samples of coronaviruses in bats and pangolins have shown similar genomes, none of them fit perfectly just yet.

"Although no animal coronavirus has been identified that is sufficiently similar to have served as the direct progenitor of SARS-CoV-2, the diversity of coronaviruses in bats and other species is massively undersampled," the researchers write.

The second hypothesis is that the natural selection happened in humans - *after* the virus was transmitted from an animal host.

"The second scenario is that the new coronavirus crossed from animals into humans before it became capable of causing human disease," director of the National Institute of Health, Francis Collins explains on the NIH blog.

"Then, as a result of gradual evolutionary changes over years or perhaps decades, the virus eventually gained the ability to spread from human-to-human and cause serious, often life-threatening disease."

Although we don't yet know which of the two hypotheses is correct, the researchers think that more evidence might tip the scales in favour of one or the other - but we'll have to wait for that research to be done.

In the meantime, wash your hands, stay home, and help with the effort if you can.

The correspondence has been published in Nature Medicine.

https://nyti.ms/2Jr6hCa

What Social Distancing Looked Like in 1666

Humanity has been surviving plagues for thousands of years, and we have managed to learn a lot along the way.

By Annalee Newitz

A lot of English people believed 1666 would be the year of the apocalypse. You can't really blame them. In late spring 1665, bubonic plague began to eat away at London's population. By fall, roughly 7,000 people were dying every week in the city.

Credit...Sophy Hollington

The plague lasted through most of 1666, ultimately killing about 100,000 people in London alone — and possibly as many as three-quarters of a million in England as a whole.

Perhaps the greatest chronicler of the Great Plague was Samuel Pepys, a well-connected English administrator and politician who kept a detailed personal diary during London's darkest years. He reported stumbling across corpses in the street, and anxiously reading the weekly death tolls posted in public squares.

In August of 1665, Pepys described walking to Greenwich, "in my way seeing a coffin with a dead body therein, dead of the plague, lying in [a field] belonging to Coome farme, which was carried out last night, and the parish have not appointed any body to bury it, but only set a watch there day and night, that nobody should go thither or come thence, which is a most cruel thing." To ensure that no one — not even the family of the dead person — would go near the corpse or bury it, the parish had stationed a guard. "This disease making us more cruel to one another than if we are doggs."

It felt like Armageddon. And yet it was also the beginning of a scientific renaissance in England, when doctors experimented with quarantines, sterilization and social distancing. For those of us living through these stay-at-home days of Covid-19, it's useful to look back and see how much has changed — and how much hasn't. Humanity has been guarding against plagues and surviving them for thousands of years, and we have managed to learn a lot along the way.

When a plague hit England during the summer of 1665, it was a time of tremendous political turmoil. The nation was deep into the Second Anglo-Dutch War, a nasty naval conflict that had torpedoed the British economy. But there were deeper sources of internal political conflict. Just five years earlier in 1660, King Charles II had wrested back control of the government from the Puritan members of Parliament led by Oliver Cromwell.

Though Cromwell had died in 1658, the king had him exhumed, his corpse put in chains and tried for treason. After the inevitable guilty verdict, the King's henchmen mounted Cromwell's severed head on a 20-foot spike over Westminster Hall, along with the heads of two co-conspirators. Cromwell's rotting head stayed there, gazing at London, throughout the plague and for many years after.

War and social upheaval hastened the spread of the plague, which had broken out several years earlier in Holland. But when he wasn't

displaying the severed heads of his enemies, the king was invested in scientific progress. He sanctioned the founding of the Royal Society of London for Improving Natural Knowledge, a venerable scientific institution known today as The Royal Society.

It was most likely thanks to his interest in science that government representatives and doctors quickly used social distancing methods for containing the spread of bubonic plague. Charles II issued a formal order in 1666 that ordered a halt to all public gatherings, including funerals. Already, theaters had been shut down in London, and licensing curtailed for new pubs. Oxford and Cambridge closed. Isaac Newton was one of the students sent home, and his family was among the wealthy who fled the cities so they could shelter in place at their country homes. He spent the plague year at his family estate, teasing out the foundational ideas for calculus.

Things were less cozy in London. Quarantining was invented during the first wave of bubonic plague in the 14th century, but it was deployed more systematically during the Great Plague. Public servants called searchers ferreted out new cases of plague, and quarantined sick people along with everyone who shared their homes. People called warders painted a red cross on the doors of quarantined homes, alongside a paper notice that read "LORD HAVE MERCY UPON US." (Yes, the all-caps was mandatory).

The government supplied food to the housebound. After 40 days, warders painted over the red crosses with white crosses, ordering residents to sterilize their homes with lime. Doctors believed that the bubonic plague was caused by "smells" in the air, so cleaning was always recommended. They had no idea that it was also a good way to get rid of the ticks and fleas that actually spread the contagion.

Of course, not everyone was compliant. Legal documents at the U.K. National Archives show that in April 1665, Charles II ordered severe punishment for a group of people who took the cross and paper off their door "in a riotious manner," so they could "goe abroad into the street promiscuously, with others." It's reminiscent of all those modern Americans who went to the beaches in Florida over spring break, despite what public health experts told them.

Pepys was a believer in science, and he tried to follow the most cutting-edge advice from his doctor friends. This included smoking tobacco as a precautionary measure, because smoke and fire would purify the "bad air." In June of 1665, as the plague began, Pepys described seeing red crosses on doors for the first time. "It put me into an ill conception of myself and my smell," he writes, "so that I was forced to buy some roll-tobacco to smell and chaw, which took away the apprehension."

Quack medicine will always be with us. But there was some good advice, too. During the Great Plague, shopkeepers asked customers to drop their coins in dishes of vinegar to sterilize them, using the 1600s version of hand sanitizer.

Just as some American politicians blame the Chinese for the coronavirus, there were 17th century Brits who blamed the Dutch for spreading the plague. Others blamed Londoners. Mr. Pepys had relocated his family to a country home in Woolwich, and writes in his diary that the locals "are afeard of London, being doubtfull of anything that comes from thence, or that hath lately been there … I was forced to say that I lived wholly at Woolwich."

By late 1666, the plague had begun its retreat from England, but one disaster led to another. In autumn, the Great Fire of London destroyed the city's downtown in a weeklong conflagration. The damage was so extensive in part because city officials were slow to respond, having already spent over a year dealing with plague. The fire left 70,000 Londoners homeless and angry, threatening to riot.

While the mayor of London issued orders to evacuate the city, Pepys had more pedestrian concerns: He wrote about helping a friend dig a pit in his garden, where the two men buried "my

Parmazan cheese, as well as my wine and some other things." Even in the middle of a civilization-shaking event, people will still hoard odd things, like toilet paper — or cheese.

Despite the war, the plague and the fire, London survived. Urbanites rebuilt relatively quickly, using the same basic street layout. In 1667, Pepys was bustling around the healing city, putting his rooms back in order and turning his thoughts to new developments in politics.

Pepys survived. Scholars are still not sure whether he ever retrieved his cheese.

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