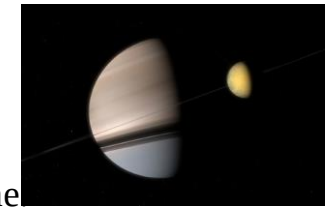
https://go.nature.com/2M8JVua

The moon that made Saturn a pushover

Scientists have a new theory for how the ringed planet got its tilt. Titan, Saturn's biggest moon, probably helped to cause the ringed planet to start tipping off-kilter long ago.



Saturn is tilted with respect to its orbit around the Sun, by a little bit more than Earth is. Planetary scientists had thought that Saturn acquired its tilt more than 4 billion years ago, thanks to the gravitational influence of Neptune

Saturn (left) might have the migration of its moon Titan (right) to thank for its conspicuous tilt. **Credit: Mark Garlick/Science Photo Library**

But recent measurements made with NASA's Cassini spacecraft show that Titan is moving relatively rapidly away from Saturn. Melaine Saillenfest at the Paris Observatory and his colleagues capitalized on that finding to suggest that Titan is to blame for Saturn's tilt.

Their calculations suggest that, around one billion years ago, Titan was migrating away from Saturn and led the planet into a gravitational interaction with Neptune — which steadily tilted Saturn over. Big migrating moons could similarly cause giant planets in other solar systems to keel over.

Correction 27 January 2021: An earlier version of this article incorrectly used the gender pronoun 'her' for Melaine Saillenfest. It also misstated the journal that published the paper.

Correction 28 January 2021: This article has been changed to correctly describe how Titan influenced Saturn and how Saturn's motion responded to that influence.

Nature Astron. (2021)

http://bit.ly/2YnbwKq

Scientists use a novel ink to 3D print 'bone' with living cells

May allow surgeons in the future to 3D-print bone parts complete with living cells

Scientists from UNSW Sydney have developed a ceramic-based ink that may allow surgeons in the future to 3D-print bone parts complete with living cells that could be used to repair damaged bone tissue.

Using a 3D-printer that deploys a special ink made up of calcium phosphate, the scientists developed a new technique, known as ceramic omnidirectional bioprinting in cell-suspensions (COBICS), enabling them to print bone-like structures that harden in a matter of minutes when placed in water.

While the idea of 3D-printing bone-mimicking structures is not new, this is the first time such material can be created at room temperature - complete with living cells - and without harsh chemicals or radiation, says Dr Iman Roohani from UNSW's School of Chemistry. "This is a unique technology that can produce structures that closely mimic bone tissue," he says.

"It could be used in clinical applications where there is a large demand for in situ repair of bone defects such as those caused by trauma, cancer, or where a big chunk of tissue is resected."

Associate Professor Kristopher Kilian who co-developed the breakthrough technology with Dr Roohani says the fact that living cells can be part of the 3D-printed structure, together with its portability, make it a big advance on current state-of-the-art technology.

Up until now, he says, making a piece of bone-like material to repair bone tissue of a patient involves first going into a laboratory to fabricate the structures using high-temperature furnaces and toxic chemicals. "This produces a dry material that is then brought into a clinical setting or in a laboratory, where they wash it profusely and then add living cells to it," Professor Kilian says.

"The cool thing about our technique is you can just extrude it directly into a place where there are cells, like a cavity in a patient's bone. We can go directly into the bone where there are cells, blood

vessels and fat, and print a bone-like structure that already contains living cells, right in that area."

"There are currently no technologies that can do that directly."

In a research paper published recently in *Advanced Functional Materials*, the authors describe how they developed the special ink in a microgel matrix with living cells.

"The ink takes advantage of a setting mechanism through the local nanocrystallisation of its components in aqueous environments, converting the inorganic ink to mechanically interlocked bone apatite nanocrystals," Dr Roohani says.

"In other words, it forms a structure that is chemically similar to bone-building blocks. The ink is formulated in such a way that the conversion is quick, non-toxic in a biological environment and it only initiates when ink is exposed to the body fluids, providing an ample working time for the end-user, for example, surgeons."

He says when the ink is combined with a collagenous substance containing living cells, it enables in-situ fabrication of bone-like tissues which may be suitable for bone tissue engineering applications, disease modelling, drug screening, and in-situ reconstruction of bone and osteochondral defects.

Already there has been keen interest from surgeons and medical technology manufacturers. A/Prof. Kilian thinks while it's early days, this new bone-printing process could open up a whole new way of treating and repairing bone tissue.

"This advance really paves the way for numerous opportunities that we believe could prove transformational - from using the ink to create bone in the lab for disease modelling, as a bioactive material for dental restoration, to direct bone reconstruction in a patient," says A/Prof. Kilian.

"I imagine a day where a patient needing a bone graft can walk into a clinic where the anatomical structure of their bone is imaged, translated to a 3D printer, and directly printed into the cavity with their own cells. "This has the potential to radically change current practice, reducing patient suffering and ultimately saving lives."

Next up the duo will be performing in vivo tests in animal models to see if the living cells in the bone-like constructs continue to grow after being implanted in existing bone tissue.

http://nyti.ms/2MFA9j6

In Ice Age Siberia, a Meeting of Carnivores May Have Given Us Dogs

Researchers propose that some remote ancestors of Native Americans may have been the first humans to forge the bond with wolves that led to domestication.

By James Gorman

Climate data and archaeological and DNA evidence show that 23,000 years ago, horses, mammoths and other prey animals were abundant in Siberia, attracting humans and other carnivores. **Credit...Ettore Mazza**

Twenty-three thousand years ago, in the cold of the last ice age, some humans found a place where the climate was marginally better: Siberia.

While many people associate the region that is now in Russia with forbidding cold today, climate data as well as archaeological and DNA evidence show that this was where horses, mammoths and other prey animals found enough to eat, which attracted humans and other carnivores. Hemmed in by worse conditions, the humans, some of them the ancestors of Native Americans, were isolated for thousands of years. So were wolves.

It is there and then that dogs were first domesticated, according to a new hypothesis from a group of archaeologists and ancient DNA experts who specialize in the deep history of humans and canines. They published their analysis on Monday in Proceedings of the National Academy of Sciences.

Angela R. Perri, an archaeologist at Durham University who studies the domestication of dogs, said the new hypothesis emerged in informal discussions among the authors. As they assembled archaeological and DNA data on the peopling of the Americas and the origins of dogs, they came up with an idea that was lurking in the data all along, one that she said, "I'm frankly embarrassed I didn't have earlier."

David Meltzer, another author who is an archaeologist at Southern Methodist University in Dallas specializing in the peopling of the Americas, recalled one whiteboard session at Oxford in which he and other authors, including Dr. Perri, brainstormed the complicated chain of reasoning based on DNA evidence that has allowed the tracing of population movement of ancient humans and more recently dogs.

He said to Greger Larson, an Oxford scientist who has orchestrated a number of dog domestication studies, including this one: "I've seen your dog dates. And my people dates, they kind of look the same." By the time the whiteboard was filled, he said, they had the bones of the new paper.

Ancient canine history is murky and in the past decade alone, researchers have suggested Europe, Eurasia, East Asia and Africa as the first home of dogs, starting at least 15,000 years ago. Some researchers push the origin back much further, but whether some of the earliest fossils are dogs or wolves is debated.

A starting point for the new proposal is the date when humans first came to the Americas, probably around 15,000 years ago. Another is that ancient DNA shows that dog and human populations have similar histories of migration and divergence.

Dr. Perri said that among ancient American dogs, which disappeared, leaving only traces of their genetics in a few modern breeds, "there are two main groups which share a common ancestor about 23,000 years ago."

On the human side there is a similar split.

The names get a bit hard to keep track of, but one group called the Ancient North Siberians mixed with another group from which Ancestral Native Americans split about 21,000 years ago. The hypothesis suggests that in addition to providing some genes, the ancient North Siberians also gave dogs to people, some of whom eventually migrated to North America, taking the dogs with them. As Dr. Meltzer said, "Dogs are not going to go to the new world without people."

But the several different groups in Siberia appear to have been isolated from outside contact from about 30,000 years ago to 15,000 years ago. So, Dr. Perri said, if there is "this isolated population who had no interaction with anyone outside of Siberia after 30,000 years ago, who gave the dogs to the ancestors of Native Americans?"

The data suggest that it was the ancient North Siberians, who, having been isolated for thousands of years, must have been the people who first domesticated wolves, or with whom wolves domesticated themselves, feeding on leftovers or discards from the hunt.

Dr. Meltzer said these Siberians lived in small groups of 25 or so in a vast, open landscape. Ancient DNA evidence shows that they married outside of their small groups, and so had to seek one another out. "People are exchanging information, they're exchanging mates, they're maybe exchanging their wolf pups," he said.

Pontus Skoglund, an ancient DNA expert who studies the origin of dogs at the Crick Institute in London and was not involved in the research, said, "Siberia could very well be the origin of dogs. Absolutely." But, he said this was one possibility only. He said the analysis in the paper depended largely on mitochondrial DNA, which traces only the maternal line and is therefore incomplete.

"It's still an open question for me," he said. "It could be many other corners of Eurasia as well."

New information on ancient DNA recovered from Siberian dog fossils that are 18,000 or more years old could help prove or disprove the hypothesis, Dr. Perri said, and she and her colleagues are working on those studies now.

http://bit.ly/2Md8xSq

COVID-19 warnings were on Twitter well before the outbreak of the pandemic

New study shows that posts revealing concern for 'pneumonia' circulated very early, suggesting social media can be an effective tool for epidemiological surveillance.

Even before public announcements of the first cases of COVID-19 in Europe were made, at the end of January 2020, signals that something strange was happening were already circulating on social media. A new study of researchers at **IMT School for Advanced Studies Lucca**, published in *Scientific Reports*, has identified tracks of increasing concern about pneumonia cases on posts published on Twitter in seven countries, between the end of 2019 and the beginning of 2020. The analysis of the posts shows that the "whistleblowing" came precisely from the geographical regions where the primary outbreaks later developed.

To conduct the research, the authors first created a unique database with all the messages posted on Twitter containing the keyword "pneumonia" in the seven most spoken languages of the European Union - English, German, French, Italian, Spanish, Polish, and Dutch - from December 2014 until 1 March 2020. The word "pneumonia" was chosen because the disease is the most severe condition induced by the SARS-CoV-2, and also because the 2020 flu season was milder than the previous ones, so there was no reason to think it to be responsible for all the mentions and worries. The researchers then made a number of adjustments and corrections to the posts in the database to avoid overestimating the number of tweets mentioning pneumonia between December 2019 and January 2020, that is to say in the weeks between the World Health Organization (WHO) announcement that the first "cases of pneumonia of unknown etiology" had been identified - on 31 December 2019 - and the official recognition of COVID19 as a serious transmissible disease, on 21 January 2020. In particular, all the tweets and retweets containing links to news about the emerging virus were eliminated from the database to exclude from the count the mass media coverage of the emerging pandemic.

The analysis of the authors shows an increase in tweets mentioning the keyword "pneumonia" in most of the European countries included in the study as early as January 2020, such as to indicate an ongoing concern and public interest in pneumonia cases. In Italy, for example, where the first lock-down measures to contain COVID-19 infections were introduced on 22 February 2020, the increase rate in mentions of pneumonia during the first few weeks of 2020 differs substantially from the rate observed in the same weeks in 2019. That is to say that potentially hidden infection hotspots were identified several weeks before the announcement of the first local source of a COVID-19 infection (20 February, Codogno, Italy). France exhibited a similar pattern, whereas Spain, Poland, and the UK witnessed a delay of 2 weeks.

The authors also geo-localized over 13,000 pneumonia-related tweets in this same period, and discovered that they came exactly from the regions where the first cases of infections were later reported, such as the Lombardia region in Italy, Madrid, Spain, and Île de France.

Following the same procedure used for the keyword "pneumonia", the researchers also produced a new dataset containing the keyword "dry cough", one of the other symptoms later associated with the COVID-19 syndrome. Even then, they observed the same pattern,

namely an abnormal and statistically significant increase in the number of mentions of the word during the weeks leading up to the surge of infections in February 2020.

"Our study adds on to the existing evidence that social media can be a useful tool of epidemiological surveillance. They can help intercept the first signs of a new disease, before it proliferates undetected, and also track its spread" says Massimo Riccaboni, full professor of Economics at the IMT School, who coordinated the research.

This is especially true in a situation like the current pandemic, when lapses in identifying early-warning signals left many national governments blind to the unprecedented scale of the looming public health emergency. In a successive phase of the pandemic, monitoring social media could help public health authorities mitigate the risks of contagion resurgence, for example by adopting stricter measures of social distancing where the infections appear to be increasing, or vice versa relaxing them in other regions. These tools could also pave the way to an integrated epidemiological surveillance system globally managed by international health organizations.

The paper "Early warnings of COVID-19 outbreaks across Europe from social media" is available after publication at: http://www.nature.com/articles/s41598-021-81333-1

http://bit.ly/39vnCaN

Competition among human females likely contributed to concealed ovulation

Might have actually evolved to allow females to hide their fertility status from other females

Human females rely on aids like charting, test strips or wearable tech to identify periods of fertility. Some animals, like baboons, undergo obvious physical changes during ovulation. How did fertility become so hard to detect in humans?

For nearly half a century, the evolution of concealed ovulation in human females has been explained as useful for securing male partners to help raise and support children. A study published on January 25 in *Nature Human Behaviour* casts doubt on this long-standing idea. Using agent-based computational models, a team of evolutionary scientists has shown that concealed ovulation might have actually evolved to allow females to hide their fertility status from other females.

"The study of human evolution has tended to look at things from a male perspective, and even adaptations specific to females—like their social behavior and concealed ovulation—are have been viewed in terms of how males shape them. This study challenges the idea that the role of female sociality is to better secure male partners and their resources; our computational model shows female sociality is about much more than securing male investment," said Athena Aktipis, associate professor of psychology at Arizona State University and senior author on the paper.

Out with the old, in with the new

The idea that females evolved to conceal ovulation from males to encourage them to help with children, called the male investment hypothesis, was proposed as a way of understanding why human females do not advertise ovulation. This hypothesis has been the predominant explanation for female sociality and concealed ovulation for decades, though it has undergone few empirical tests and has not been formally modeled until now.

But females do not just interact with males. They interact with each other, sometimes cooperating and other times engaging in conflict.

"I have been puzzling over the male investment hypothesis for years, and because you cannot argue with a verbal hypothesis, I started work on how to test it," Aktipis said. "At the same time, I was working on female sociality and it struck me that females could have been aggressing against other females showing ovulatory cues, which then would create a benefit to concealing ovulation."

The team of evolutionary scientists tested the idea that female conflict might have driven the evolution of concealed ovulation, which they call the female rivalry hypothesis, using an agent-based computational model. Evolutionary adaptations in humans happen on the timescale of many generations, which makes it hard to test whether or how traits might evolve. Computational modeling allows researchers to test ideas that would be hard to test in the real world.

In agent-based computational models, an agent represents an individual whose behavior can be programmed and analyzed. Each agent follows a specific set of rules and can interact with other agents and with the environment. In the model developed to test the female rivalry hypothesis, male and female agents followed rules governing their movement, reproductive behavior and attractiveness. The male agents varied in terms of their promiscuity. Promiscuous males did not partner with females to help raise subsequent children, while male agents that were not promiscuous stuck around to share resources and support future children.

Female agents either had physical cues indicating when they were ovulating or ovulation was concealed. The female agents could also aggress against each other.

The female and male agents interacted with each other and had opportunities to procreate and form parenting partnerships. The model supported the female rivalry hypothesis by showing that females who concealed ovulation fared better. They had more children, avoided female-female aggression and succeeded in forming parenting relationships with males.

"Work in social science has tended to assume that male cognition and behavior is the default. But females recurrently face some unique challenges—particularly in their interactions with other females. This work is the result, in part, of taking that idea seriously. When we do that, I think we'll learn more, not just about the female mind, but about the human mind," said Jaimie Arona Krems, assistant professor of psychology at Oklahoma State University and first author on the paper.

The research team also used the model to test the male investment hypothesis, by running scenarios that did not allow females to aggress against each other. But there was no clear benefit from concealing ovulation in this scenario, suggesting that concealed ovulation in females might not have evolved because of interactions with males, but rather because of interactions with other females.

"This work represents a necessary shift in thinking about how human females have evolved. Female sociality and other adaptations are not just about securing male investment, even though that has long been the underlying assumption about the purpose of female social behavior," Aktipis said.

More information: *An agent-based model of the female rivalry hypothesis for concealed ovulation in humans, Nature Human Behaviour (2021). DOI: 10.1038/s41562-020-01038-9, www.nature.com/articles/s41562-020-01038-9*

http://bit.ly/2Yrs1W4

Change of course on the journey to the island of stability

Center of the island of stability is not located at element 114 -- Heavier elements will move into the spotlight

An international research team succeeded in gaining new insights into the artificially produced superheavy element flerovium, element 114, at the accelerator facilities of the GSI Helmholtzzentrum für Schwerionenforschung in Darmstadt, Germany. Under the leadership of Lund University in Sweden and with significant participation of Johannes Gutenberg University Mainz (JGU) as well as the Helmholtz Institute Mainz (HIM) in Germany and other partners, flerovium was produced and investigated to determine whether it has a closed proton shell. The results suggest that, contrary to expectations, flerovium is not a so-

called "magic nucleus". The results were published in the journal *Physical Review Letters*.

In the late 1960s, Sven-Gösta Nilsson, then a physics professor at Lund University, and others formulated a theory about the possible existence of still unknown superheavy elements. In the meantime, such elements have been created and many predictions have been confirmed. The discovery of the six new elements 107 to 112 was achieved at GSI in Darmstadt, and further ones up to element 118 are now known as well. Strongly increased half-lives for the superheavy elements due to a "magic" combination of protons and neutrons were also predicted. This occurs when the shells in the nucleus, each holding a certain number of protons and neutrons, are completely filled. "Flerovium, element 114, was also predicted to have such a completed, 'magic' proton shell structure. If this were true, flerovium would lie at the center of the so-called 'island of stability', an area of the chart of nuclides where the superheavy elements should have particularly long lifetimes due to the shell closures," explains Professor Dirk Rudolph of Lund University, who is the spokesperson of the international experiment.

Nilsson's theories inspired the international collaboration led by the Lund group to investigate whether flerovium nuclei indeed exhibit the predicted magical properties. Their experiments, performed at the UNILAC accelerator at GSI in Darmstadt in the framework of the FAIR Phase 0 experimental program, lasted 18 days. Every second, four trillion calcium-48 nuclei with 20 protons were accelerated to ten percent of the speed of light. They irradiated a thin foil containing rare plutonium-244 with 94 protons to produce atomic nuclei of flerovium, which has 114 protons, by nuclear fusion. This so-called target was produced at the Department of Chemistry at JGU, using, plutonium provided, among others, by the Lawrence Livermore National Laboratory, USA. Strong magnets of the GSI recoil separator TASCA separated the flerovium nuclei from the intense calcium ion beam; subsequently they were registered in a detector setup specifically developed in Lund for this experiment.

The detector measured the radioactive decay of 30 flerovium nuclei -- i.e., the emission of nuclear fragments of flerovium -- with high efficiency and accuracy. By precisely analyzing these fragments and their emission times, the team was able to determine unusual decay channels of flerovium nuclei that could not be reconciled with its originally predicted "magical" properties. "Our study shows that element 114 is no more stable than others in its vicinity. This is a very important piece of the puzzle in the continued search for the center of the coveted island of stability," said Professor Christoph Düllmann, professor of nuclear chemistry at JGU and head of the research groups at GSI and HIM.

The new results will be of great benefit to science. Instead of continuing to search for the center of the island of stability in the region of element 114, even heavier ones like the as yet undiscovered element 120, will now move into the spotlight.

http://bit.ly/3aa1z8w

International team of scientists identifies new treatment for COVID-19 that appears to be far more effective than drugs in use now

Proven 27.5 times more effective than the well-known remdesivir in human cells

Mark Johnson

From a rare marine sea squirt found only in the waters around the Spanish island of Ibiza comes a potential COVID-19 treatment called Aplidin that researchers say has proven 27.5 times more effective than the well-known remdesivir in human cells in the lab.

The finding, reported Monday by an international team in the journal Science, comes at a time when potential treatments have

been overshadowed by the U.S. vaccination campaign, now trying to recover from a slower-than-expected start.

A related preprint that has yet to be peer-reviewed says that tests have shown the drug is equally effective against the highly infectious new variant of the virus discovered recently in the United Kingdom.

Aplidin, already approved in Australia for treating multiple myeloma, has been developed as a potential COVID-19 treatment by the Spanish drug company PharmaMar.

So far, Aplidin, also known as Plitidepsin, has gone through a Phase II clinical trial against COVID-19 and is now awaiting the start of Phase III testing. It comes from sea squirts, marine creatures that look like plants and have tubular openings allowing them to draw in and expel water.

The drug was identified as a potential coronavirus treatment back in March after scientists at the University of California, San Francisco and elsewhere tried an unconventional approach.

Instead of randomly testing vast libraries of existing drugs or targeting key proteins in the virus, as other research groups were doing, the San Francisco team focused on the human proteins needed by the virus. The scientists then looked for existing drugs that would prevent the coronavirus from hijacking those human proteins.

"This was data driven instead of just randomly screening drugs," stressed Nevan Krogan, one of three co-leaders of the new study in Science and director of the Quantitative Biosciences Institute at the University of California, San Francisco.

Krogan said focusing on human, rather the viral, proteins, offered a powerful advantage in the fight against the new coronavirus.

"If you target a human protein that the virus needs," he said, "the virus will never mutate away from being reliant on that human protein."

Fear that the virus could thwart vaccines and treatments by mutating has taken on greater urgency since the discovery of a new, significantly more infectious variant of SARS-CoV-2 identified in the United Kingdom.

However, work finalized this weekend by Greg Towers and colleagues at University College London show that Aplidin was effective when used against two different human lung and epithelial cells infected with the newly discovered variant.

'Easy to hit the ground running'

Krogan's co-leaders in the study published in Science were Kris M. White and Adolfo García-Sastre, both of whom work at the Icahn School of Medicine at Mount Sinai.

Researchers who did not participate in the Science study, or in the unpublished preprint, said the results are encouraging. They added that Aplidin will require further testing in people to better pin down its effectiveness and possible side effects.

"The drug performs quite well in mice and the authors hint at it having potential against other viruses too," said David H. O'Connor, a professor of pathology and laboratory medicine at the University of Wisconsin-Madison. "It is premature to say if it will have clinical benefit, but it definitely merits clinical trials."

At the University of Minnesota Medical School, Susan Kline said, "It's not typical that we think of drugs that treat cancer being used also to treat viruses." She said that even though "a drug is effective in cells in the laboratory, we don't know what effect it will have on cells in the human body."

Kline, who serves as interim director of infectious disease in the university's Department of Medicine, also expressed concern that a drug used to kill cancer cells might harm human cells.

Krogan, however, said the dose of Aplidin used against the new coronavirus was far smaller than the dose used to treat multiple myeloma. Also, the drug would only be used for a matter of days

against COVID-19; it is used for weeks or months against multiple myeloma.

The Science study found that the drug was effective treating infected human kidney cells and primary lung cells in the lab. In another experiment described in the paper, the drug was used to treat mice infected with a version of the new coronavirus, and reduced the infection 100-fold.

Early in the institute's work on COVID-19, it formed an international team with scientists from the Icahn School of Medicine at Mount Sinai in New York, the Institut Pasteur in Paris, and the J. David Gladstone Institutes in San Francisco, among others.

Known as the QBI Coronavirus Research Group, the team now includes scientists from the European Bioinformatics Institute in Cambridge, England, and University of Freiburg in Germany.

"The institute's mission are these collaborations," said Jacqueline M. Fabius, one of the paper's authors and the institute's chief operating officer. "That's why it was so easy to hit the ground running (when the new coronavirus was discovered)."

In previous papers published in Cell, Science and Nature, the QBI Coronavirus Research Group mapped out the molecular interactions shared by coronaviruses that cause COVID-19, Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome.

Early on, the group homed in on 332 proteins found in human lung cells and also in blood vessel cells that help the virus when it invades the body. Using cutting edge technology, they investigated how the virus was affected when they eliminated each protein one by one, and then when they lowered the levels of each protein.

Krogan has said that he hopes knowledge of these interactions will help researchers find treatments that address the new coronavirus but also the next one that appears.

Research on potential COVID-19 treatments is important, not only because it will take months to vaccinate the majority of Americans, but also because it's unclear whether the vaccines in use can prevent transmission of the virus.

"Work on treatments has been ongoing since the outbreak began and we have seen the benefits," said Chris Beyrer, professor of public health and human rights at Johns Hopkins Bloomberg School of Public Health. "Survival is actually better than it was in March, April, May."

http://bit.ly/3t40SGy

A CubeSat will test out water as a propulsion system

Water has plenty of advantages going for it as a propellant

by Andy Tomaswick, Universe Today

Novel propulsion systems for CubeSats have been on an innovative tear of late. UT has reported on propulsion systems that use everything from solid iodine to the Earth's own magnetic field as a way of moving a small spacecraft. Now, there is a potential solution using a much more mundane material for a propellant—water.

Water has plenty of advantages going for it as a propellant. Most obviously, it is not volatile or toxic, making it much easier to handle than conventional rocket fuel. One design flaw holding back the adoption of regular rocket fuel into widespread use in CubeSats is their explosive potential. CubeSats are usually housed next to larger, more expensive satellites in the payloads of rockets. If the rocket fuel loaded into a small CubeSat were to ignite unintentionally, it could completely destroy the much larger, more expensive telescope. So CubeSat designers rightfully shy away from including such a dangerous propellant in their small satellites.

Without access to regular rocket fuel, designers are left with much less desirable choices for propellant, such as ion thrusters. Some do not even select a propellant system at all. This lack of ability to controllable navigate space results in defunct CubeSat cluttering up orbital trajectories as well as unintentionally deorbiting in an

uncontrolled, and potentially dangerous, descent.

What makes water such a special propellant is that it is completely stable under normal conditions, but it can also be split to create hydrogen and oxygen, two of the main components of normal rocket fuel. This split is accomplished by a process known as electrolysis, which separates that oxygen and hydrogen molecules from the water from one another. Then each individual element can be funneled into a rocket nozzle and exploded to push the craft in a given direction.

Electrolysis will actually take place inside the CubeSat in a special miniaturized chamber, which is the true heart of this propulsion innovation, and was developed by Tethers Unlimited, a start-up based in Washington. Its system, Hydros, could add its name to the growing list of CubeSat propulsion technologies, if it is successfully tested later this year as part of NASA's Pathfinder Technology Demonstration-1 mission. Given the advantages of its propellant, it has a lot of potential to become a standard propulsion platform for CubeSats for years to come.

http://wb.md/2YuhWYs

Drug-Impaired Doctor Sentenced to 20 Years in Prison

Misdiagnosed and/or made medical errors in more than 3000 cases while intoxicated

Deborah Brauser

An Arkansas pathologist who misdiagnosed and/or made medical errors in more than 3000 cases while intoxicated has been sentenced to 20 years in federal prison for manslaughter and mail fraud, the US Department of Justice (DOJ) has announced.

Robert Morris Levy of Fayetteville was chief of pathology and laboratory medical services at the Veterans Health Care System of the Ozarks until he was fired in 2018. Two years earlier, Levy had his clinical privileges suspended when testing revealed a blood alcohol level of .396 mg/dL. He then attended an inpatient alcohol treatment program for 3 months. After treatment completion, he returned to medical practice on condition that he maintain his sobriety and submit to random urine or blood drug screens.

Federal charges were filed after it was discovered that during this time Levy purchased and used 2-methyl-2-butanol (2M-2B), a substance that induces intoxication but is not detectable on drug testing. The colorless, liquid substance has been used as an anesthetic but is also used recreationally.

Levy was accused of entering "inaccurate and misleading" diagnoses while intoxicated that led to at least one patient's death, as well as adding false information to medical files.

In addition, Levy had the substance mailed across state lines to his home in Fayetteville, which led to mail fraud charges.

After his sentencing trial last week, Levy received 8 years for involuntary manslaughter and 20 years for mail fraud. Because the sentences are concurrent, the maximum time he will serve is 20 years. He was also ordered by the court to pay almost $500,000 in restitution.

"This sentence should send a strong message that those who abuse their positions of trust in caring for veterans will be held accountable," Michael J. Missal, Inspector General of the Department of Veterans Affairs, said in a press release from the DOJ.

These patients "deserve to have doctors in charge of their treatment who are dedicated and vigilant, just as these victims were in their service to our country. Instead, this defendant's criminal conduct in this case caused irreparable harm to the victims and their families," added David Clay Fowlkes, acting US Attorney for the Western District of Arkansas.

Troubling Timeline

Levy first appeared before an "administrative fact-finding panel" in 2015. Although there were reports that he showed signs of alcohol

intoxication while on the job, he denied the allegations. A year later, he was again accused of being intoxicated on the job and he acknowledged test results showing a high blood alcohol content.

The Veterans Health Care System of the Ozarks (Fayetteville VA) "summarily suspended Levy's privileges to practice medicine and issued Levy a written notice of removal and revocation of clinical privileges," the DOJ reported.

It was during this time that he entered the 3-month, in-patient treatment program that started in July and ended in October 2016. Upon completion, Levy signed a strict new contract undertaking to "abstain completely" from alcohol or any other mood-altering substance. In addition, he agreed to submit to random drug testing and returned to medical practice. Any breach of these conditions would result in the loss of his medical license and employment.

All blood and urine tests collected from November 2016 through June 2018 were negative for drugs or alcohol. However, authorities subsequently discovered that Levy had purchased 2M-2B during this period.

When the charges were filed in 2019, Duane "Dak" Kees, US Attorney for the Western District of Arkansas, said in an interview with *40/29 News* that Levy was "skilled in toxicology and had the medical expertise…and the equipment to know exactly how much of this substance to take. He had the ability to do the proper calculus to know how much to use, in order for it not to be fatal."

In July 2017, a package with 2M-2B was shipped to Levy's home from a chemical supply company by United Parcel Service, a commercial interstate carrier.

"Wanton, Reckless Disregard"

It also became known that over the course of his career Levy misdiagnosed many patients while he was intoxicated. In February 2014, he diagnosed a VA patient with diffuse large B-cell lymphoma after a "cursory and rudimentary" workup.

He ignored a note from another pathologist asking Levy to perform more tests — and went back and falsely entered into the medical record that a different pathologist had agreed with his diagnosis. After receiving no life-prolonging treatment, the patient, who was a military veteran, died in July 2014 of small cell carcinoma.

"The veteran was not treated for small cell carcinoma due to Levy's grossly and criminally negligent conduct that demonstrated a wanton and reckless disregard for the veteran's life," the DOJ stated. In total, a review showed that 3007 cases of Levy's had a patient error or misdiagnosis.

As reported by *Medscape Medical News* at the time, Levy was indicted by a federal grand jury in August 2019 on twelve counts of both wire fraud and mail fraud, four counts of making false statements, and three counts of involuntary manslaughter. He entered a guilty plea for one count of involuntary manslaughter and one count of mail fraud last June.

During the sentencing trial, *40/29 News* noted, "sentencing guidelines recommend 9 to 11 years behind bars, but the judge went above and beyond that." In addition to receiving a sentence of 240 months to be served in federal prison and then 3 years of supervised release, Levy must pay $497,745.70 in restitution.

http://bit.ly/3tbdyvy

Melatonin produced in the lungs prevents infection by novel coronavirus

The hormone acts as a barrier against SARS-CoV-2, blocking the expression of genes that encode proteins in cells serving as viral entry points

By Elton Alisson | Agência FAPESP

Melatonin synthesized in the lungs acts as a barrier against SARS-CoV-2, preventing expression of genes that encode proteins in cells such as resident macrophages in the nose and pulmonary alveoli, and epithelial cells lining the alveoli, all of which are entry points

for the virus. The hormone, therefore, prevents infection of these cells by the virus and inhibits the immune response so that the virus remains in the respiratory tract for a few days, eventually leaving to find another host.

The discovery by researchers at the University of São Paulo (USP), in Brazil, helps understand why some people are not infected or do not manifest symptoms of COVID-19 even when reliably diagnosed as carriers of the virus by RT-PCR. In addition, it offers the prospect of nasal administration of melatonin, in drops or as a spray, to prevent disease from developing in pre-symptomatic patients.

Pre-clinical and clinical trials will be needed to prove the therapeutic efficacy of melatonin against the virus, the researchers stress in an **article** on the study published in the journal *Melatonin Research*. The study was **supported by FAPESP**.

"We showed that melatonin produced in the lung acts as a barrier against SARS-CoV-2, preventing the virus from entering the epithelium, activating the immune system and triggering the production of antibodies," **Regina Pekelmann Markus**, a professor at USP's Institute of Biosciences (IB) and principal investigator for the project, told **Agência FAPESP**.

"This action mechanism by pulmonary melatonin must also involve other respiratory viruses such as influenza," she added.

Markus began researching melatonin in the 1990s. In a study involving rodents, she showed that the hormone, produced at night by the pineal gland in the brain to tell the organism daylight has gone and it should prepare for sleep, can be produced in other organs, such as the lungs.

In a **study** also involving rodents, published in early 2020 in the *Journal of Pineal Research*, Markus and collaborators showed that resident macrophages in the pulmonary airspace absorb (phagocytize) particles of pollution. This aggressive stimulus induced the production of melatonin and other molecules by the macrophages, engulfing the particulate matter in the air breathed in by the animals and stimulating mucous formation, coughing, and expectoration to expel the particles from the respiratory tract.

When they blocked melatonin synthesis by resident macrophages, the researchers observed that the particles entered the bloodstream and spread throughout the organism, even invading the brain.

Based on the finding that melatonin produced in the lungs altered the entry points for particulate matter from air pollution, Markus and collaborators decided to investigate whether the hormone performed the same function with regard to SARS-CoV-2. "If so, the virus wouldn't be able to bind to the ACE-2 receptor on cells, enter the epithelium and infect the organism," Markus said.

Analysis of gene expression

To test this hypothesis, the researchers analyzed 455 genes associated in the literature with COVID-19 comorbidities, interaction between SARS-CoV-2 and human proteins, and viral entry points. The genes had been identified in studies conducted, among others, by **Helder Nakaya**, a professor at USP's School of Pharmaceutical Sciences (FCF) and a co-author of the study on lung melatonin.

From this group of genes, they selected 212 genes involved in viral cell entry, intracellular traffic, mitochondrial activity, and transcription and post-translation processes, to create a physiological signature of COVID-19.

Using RNA sequencing data downloaded from a public database, they quantified the level of expression of the 212 COVID-19 signature genes in 288 samples from healthy human lungs.

They then correlated these gene expression levels with a gene index that estimated the capacity of the lungs to synthesize melatonin (MEL-Index), based on their analysis of the lungs in healthy rodents. They found that the lower the index the higher the level of

expression of genes that encode proteins for resident macrophages and epithelial cells.

The index also correlated negatively with genes that modify proteins in cell receptor CD147, a viral entry point in macrophages and other immune cells, indicating that normal lung melatonin production may be a natural protector against the virus.

The results were corroborated by three statistical techniques: the Pearson test, which measures the degree of linear correlation between two variables; a gene set enrichment analysis; and a network analysis tool that maps the connections among the most expressed genes so as to compare the same set of genes in different states. The latter was developed by **Marcos Buckeridge**, a professor at IB-USP and also a co-author of the study.

"We found that when MEL-Index was high the entry points for the virus in the lungs were closed, and when it was low these 'doors' were open. When the doors are shut, the virus wanders around for a time in the pulmonary airspace and then tries to escape in search of another host," Markus said.

Because lung melatonin inhibits transcription of these genes that encode proteins for viral entry point cells, application of melatonin directly into the lungs in the form of drops or spray could block the virus. More research is required to prove that this is indeed the case, however, the researchers note. Another idea could be to use MEL-Index, the pulmonary melatonin metric, as a prognostic biomarker to detect asymptomatic carriers of SARS-CoV-2.

http://bit.ly/3qXDmcy

Scientists jump-start two people's brains after coma

'Stunning to see with your own eyes,' says UCLA neuroscientist

In 2016, a team led by UCLA's Martin Monti reported that a 25-year-old man recovering from a coma had made remarkable progress following a treatment to jump-start his brain using ultrasound.

Wired U.K. called the news one of the best things that happened in 2016. At the time, Monti acknowledged that although he was encouraged by the outcome, it was possible the scientists had gotten a little lucky.

Now, Monti and colleagues report that two more patients with severe brain injuries -- both had been in what scientists call a long-term "minimally conscious state" -- have made impressive progress thanks to the same technique. The results are published online in the journal *Brain Stimulation*.

"I consider this new result much more significant because these chronic patients were much less likely to recover spontaneously than the acute patient we treated in 2016 -- and any recovery typically occurs slowly over several months and more typically years, not over days and weeks, as we show," said Monti, a UCLA professor of professor of psychology and neurosurgery and co-senior author of the new paper. "It's very unlikely that our findings are simply due to spontaneous recovery."

The paper notes that, of three people who received the treatment, one -- a 58-year-old man who had been in a car accident five-and-a-half years prior to treatment and was minimally conscious -- did not benefit. However, the other two did.

One is a 56-year-old man who had suffered a stroke and had been in a minimally conscious state, unable to communicate, for more than 14 months. After the first of two treatments, he demonstrated, for the first time, the ability to consistently respond to two distinct commands -- the ability to drop or grasp a ball, and the ability to look toward separate photographs of two of his relatives when their names were mentioned. He also could nod or shake his head to indicate "yes" or "no" when asked questions such as "Is X your name?" and "Is Y your wife's name?"

Small but significant improvement

In the days following the second treatment, he also demonstrated,

for the first time since the stroke, the ability to use a pen on paper and to raise a bottle to his mouth, as well as to communicate and answer questions.

"Importantly," Monti said, "these behaviors are diagnostic markers of emergence from a disorder of consciousness."

The other patient who improved is a 50-year-old woman who had been in even less of a conscious state for more than two-and-a-half years following cardiac arrest. In the days after the first treatment, she was able, for the first time in years, according to her family, to recognize a pencil, a comb and other objects.

Both patients showed the ability to understand speech.

"What is remarkable is that both exhibited meaningful responses within just a few days of the intervention," Monti said. "This is what we hoped for, but it is stunning to see it with your own eyes. Seeing two of our three patients who had been in a chronic condition improve very significantly within days of the treatment is an extremely promising result."

The changes the researchers saw are small, but Monti said even the smallest form of communication means a way to reconnect. One powerful moment during the study was when the wife of the 56-year-old man showed him photos and asked whether he recognized who he saw.

"She said to us, 'This is the first conversation I had with him since the accident,'" Monti said. "For these patients, the smallest step can be very meaningful -- for them and their families. To them it means the world."

Using acoustic energy

The scientists used a technique called low-intensity focused ultrasound, which uses sonic stimulation to excite the neurons in the thalamus, an egg-shaped structure that serves as the brain's central hub for processing. After a coma, thalamus function is typically weakened, Monti said.

Doctors use a device about the size of a saucer creates a small sphere of acoustic energy they can aim at different brain regions to excite brain tissue. The researchers placed the device by the side of each patient's head and activated it 10 times for 30 seconds each in a 10-minute period. Each patient underwent two sessions, one week apart.

Monti hopes to eventually translate the technology into an inexpensive, portable device so the treatment could be delivered not only at state-of-the-art medical centers, but also at patients' homes, to help "wake up" patients from a minimally conscious or vegetative state.

The treatment appears to be well tolerated; the researchers saw no changes to the patients' blood pressure, heart rate or blood oxygen levels, and no other adverse events. Monti said the device is safe because it emits only a small amount of energy, less than a conventional Doppler ultrasound.

While the scientists are excited by the results, they emphasize that the technique is still experimental and likely will not be available to the public for at least a few years. For now, there is little that can be done to help patients recover from a severe brain injury that results in either a chronic vegetative state or a minimally conscious state, Monti said.

Monti said his team is planning additional studies to learn exactly how thalamic ultrasound modifies brain function; he hopes to start those clinical trials once the researchers and patients are assured of being safe from COVID-19.

The study's lead author is Josh Cain, a UCLA graduate student in psychology, and a co-senior author is Caroline Schnakers, a former UCLA researcher who is now assistant director of research at Casa Colina Hospital and Centers for Healthcare in Pomona, California. The work was funded by the Tiny Blue Dot Foundation and the Dana Foundation.

Understanding the terminology

People in a coma appear as if they are under general anesthesia; their eyes are closed, and they do not wake up even if someone tries to rouse them. Some people do eventually recover from a coma and regain significant cognitive function. Others move into a puzzling condition called a vegetative state in which they are awake -- that is, their eyes open and close as if they are waking up and falling asleep -- but they show no signs of consciousness.

A minimally conscious state is a condition in which people are awake (they wake up and fall asleep periodically) but show subtle signs that they are conscious -- for example, the ability to blink their eyes in response to a command.

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

Fossilised glider takes the origin of mammals back to the Triassic

New fossil suggests mammals evolved earlier than previously thought

Dan Fox

A new fossil specimen of *Vilevolodon diplomylos*, an ancient herbivore similar to a flying squirrel, may push the origin of mammals back millions of years earlier than previously thought.

*Vilevolodo*n is a haramiyid, an ancient group of animals that lived during the mesozoic era. Until recently they were only known through a few fossilised teeth, but new finds are shedding more light on these enigmatic creatures.

This new specimen features a well preserved middle ear, revealing more advanced structures than had previously been seen. These ear bones could place haramiyids within mammals as a group – settling an argument between palaeontologists and pushing back the origin of mammals to the late Triassic.

doi: https://doi.org/10.1038/d41586-021-00247-0

http://bit.ly/3tbhOv2

Findings may help close door on COVID-19

Finding may help close the door on COVID-19 and possibly head off future pandemics

Researchers at Vanderbilt University Medical Center (VUMC) and the University of Texas Medical Branch (UTMB) at Galveston have discovered what may be the Achilles' heel of the coronavirus, a finding that may help close the door on COVID-19 and possibly head off future pandemics.

The coronavirus is an RNA virus that has, in its enzymatic toolkit, a "proofreading" exoribonuclease, called nsp14-ExoN, which can correct errors in the RNA sequence that occur during replication, when copies of the virus are generated.

Using cutting-edge technologies and novel bioinformatics approaches, the researchers discovered that this ExoN also regulates the rate of recombination, the ability of the coronavirus to shuffle parts of its genome and even pull in genetic material from other viral strains while it replicates in order to gain evolutionary advantage.

These patterns of recombination, the researchers reported last week in the journal *PLOS Pathogens*, are conserved across multiple coronaviruses, including SARS-CoV-2, which causes COVID-19, and MERS-CoV, which causes a similar illness, Middle Eastern respiratory syndrome.

"The coronavirus exoribonuclease is therefore a conserved, important target for inhibition and attenuation in the ongoing pandemic of SARS-CoV-2, and in preventing future outbreaks of novel coronaviruses," concluded the paper's first author, Jennifer Gribble, a VUMC graduate student in the laboratory of Mark Denison, MD.

"If you can find a drug that prevents RNA recombination, you

really shut down the virus," added Andrew Routh, PhD, assistant professor of Biochemistry and Molecular Biology at UTMB and, with Denison, the paper's co-corresponding author. "It's really intriguing in terms of what we understand about virus adaptation and evolution."

Previous studies have shown that coronaviruses are resistant to many nucleoside antiviral drugs, which work by introducing errors in the viral genetic code to block replication. The coronavirus proofreader corrects the errors so replication can proceed.

Only a few drugs are capable of circumventing the proofreader. They include an approved drug, remdesivir, and EIDD-2801 (molnupiravir), an investigational drug now in clinical trials. Both were developed with the help of VUMC scientists.

"Finding that the viral ExoN plays a key role in recombination is exciting," said Denison, director of the Division of Pediatric Infectious Diseases at VUMC who has studied coronaviruses for more than 30 years.

"Knocking out this function (in laboratory studies) leads to decreased recombination and a weaker virus," Denison said. "So we think it may be possible to block this process with drugs as well (and) that it may make other drugs like remdesivir and molnupiravir work even better and last longer."

In 2007 Denison and his colleagues discovered the coronaviruses proofreader. They also found that blocking the enzyme accelerated the rate of uncorrected errors -- mutations--and crippled its ability to cause disease in animals.

Several years later they discovered that remdesivir, an investigational antiviral drug, had highly potent activity against a wide range of coronaviruses, both in laboratory and animal tests. In October 2020 remdesivir was approved for emergency use in patients hospitalized with COVID-19.

For the past two years, Gribble and Routh have collaborated in an effort to understand the role of recombination in the replication of RNA viruses, which include influenza, polio, measles, hepatitis C, HIV and Ebola, as well as the coronaviruses.

Using computational software Routh had developed, which can scour virus-sequencing datasets for evidence of "recombination events," Gribble was studying recombination in model experimental viruses, such as coronaviruses that infect mice.

Once the pandemic hit, Routh, Gribble and their colleagues were quickly able to apply this approach to SARS-CoV-2 and other coronaviruses that cause disease in humans. Other VUMC co-authors were Laura Stevens, MS, Maria Agostini, PhD, Jordan Anderson-Daniels, PhD, James Chappell, MD, PhD, Xiaotao Lu, MS, and Andrea Pruijssers, PhD.

Recombination does not always result in a "fitter," potentially more virulent virus, Routh noted. If during recombination, for example, some of the genome is deleted, the result is a "defective" viral genome that can mix with, and disable, the more virulent strain.

Coronaviruses frequently produce defective genomes, the researchers found. "That could be useful," Routh said. "You might be able to exploit defective genomes as a way of making new vaccines ... or to perturb replication (of a more virulent strain) ... in the patient."

Much remains to be learned about recombination and the role that plays in the continued spread of evolving variants of SARS-CoV-2 around the world and the ability of anti-viral drugs and vaccines to stop it.

That's why basic science is so important, said Denison, who holds the Edward Claiborne Stahlman Chair in Pediatric Physiology and Cell Metabolism in the Vanderbilt University School of Medicine.

"We need to understand the capacity of all kinds of viruses to move between species and the mechanisms by which they cause disease," he said. "We need to make sure that there are fundamental things

that we know about all identified viruses -- their genomic sequences, for example, and some basics about their biology."

That takes a lot of creativity, determination -- and money. *Funding for this study was provided by National Institutes of Health grants AI108197, GM065086 and AI133952, the Dolly Parton COVID-19 Research Fund and the Elizabeth B. Lamb Center for Pediatric Research at Vanderbilt.*

http://bit.ly/36qPZFj

Cell death shines a light on the origins of complex life

Organelles continue to thrive after the cells within which they exist die, a team of University of Bristol scientists have found, overturning previous assumptions that organelles decay too quickly to be fossilized.

As described in the journal *Sciences Advances* today, researchers from Bristol's School of Earth Sciences were able to document the decay process of eukaryotic algal cells, showing that nuclei, chloroplasts and pyrenoids (organelles found within chloroplasts) can persist for weeks and months after cell death in eukaryote cells, long enough to be preserved as fossils.

Emily Carlisle, a Ph.D. student from Bristol's School of Earth Sciences and co-author, was able to characterize the transformation of the organelles into something resembling snot. She said: "I spent several weeks photographing algal cells as they decayed, checking the condition of the nuclei, chloroplasts and pyrenoids. From this, we could tell that these organelles don't decay immediately after cell death, but actually take many weeks to dissolve."

When life first appeared on Earth it was limited to simple bacteria. Two billion years later, complex life emerged in the form of large eukaryote cells with membrane-bound organelles, such as a nucleus and chloroplasts. The evolution of fungi, plants and animals followed.

However, precisely when complex life emerged has proved difficult to say. Previous genomic studies suggested that eukaryote cells could have evolved anywhere from 800 million to 1,800 million years ago, an imprecise range that needs fossils to narrow it down.

"The evolution of eukaryotes was a hugely important event in the history of life on Earth, but fossils of these cells are difficult to interpret," said Professor Phil Donoghue, expert in molecular palaeobiology and one of the co-authors of the study. "Some of them have structures that could be organelles, but there's long been this assumption that organelles cannot be preserved because they would decay too quickly."

Although living eukaryotes include large forms that are easily spotted, early eukaryotes were predominantly single cells, difficult to distinguish from bacterial cells.

Historically, large size and intricate cell walls have been used to identify early eukaryotes, but some bacteria can attain large size, and cell wall decorations might be lost to the ravages of time and erosion. Organelles such as nuclei and chloroplasts are not found in bacteria, and would therefore be a definitive indicator of complex life, but they have been assumed to decay too quickly to be fossilized.

The results of these experiments shed light on the controversial fossils of early complex life that include structures within the cells. Dr. John Cunningham, a Bristol co-author, said: "The structures in *Shuiyousphaeridium*, a fossil from 1,700 million years ago, closely resemble nuclei. This interpretation has previously been dismissed because of the assumed rapid decay of nuclei. Our decay experiments have shown that nuclei can persist for several weeks, meaning the structures in *Shuiyousphaeridium* are likely to be nuclei."

By revealing the decay patterns of organelles, the study's authors say they can demonstrate the presence of complex life to 1,700 million years ago, helping to elucidate their evolutionary history with greater precision and clarity.

More: *"Experimental taphonomy of organelles and the fossil record of early eukaryote evolution" Sciences Advances, advances.sciencemag.org/lookup ... .1126/sciadv.abe9487*

http://bit.ly/2L5cqs5

How coronavirus damages lung cells within mere hours

Multipronged BU research team finds 18 FDA-approved drugs that could halt coronavirus infection earlier

What if scientists knew exactly what impact the SARS-CoV-2 virus had inside our lung cells, within the first few hours of being infected? Could they use that information to find drugs that would disrupt the virus' replication process before it ever gets fully underway? The discovery that several existing FDA-approved drugs--including some originally designed to fight cancer--can stop coronavirus in its tracks indicates the answer is a resounding yes.

A team of Boston University researchers--hailing from BU's National Emerging Infectious Diseases Laboratories (NEIDL), the Center for Regenerative Medicine (CReM) at BU's Medical Campus, and BU's Center for Network Systems Biology (CNSB)--embarked on a months-long, collaborative and interdisciplinary quest, combining multiple areas of expertise in virology, stem cell-derived lung tissue engineering, and deep molecular sequencing to begin answering those questions. They simultaneously infected tens of thousands of human lung cells with the SARS-CoV-2 virus, and then tracked precisely what happens in all of those cells during the first few moments after infection. As if that was not complicated enough, the team had to cool their entire high-containment research facility inside the NEIDL to a brisk 61 degrees Fahrenheit.

The result of that challenging and massive undertaking? The BU team has revealed the most comprehensive map to date of all the molecular activities that are triggered inside lung cells at the onset of coronavirus infection. They also discovered there are at least 18 existing, FDA-approved drugs that could potentially be repurposed to combat COVID-19 infections shortly after a person becomes infected. Experimentally, five of those drugs reduced coronavirus spread in human lung cells by more than 90 percent. Their findings were recently published in *Molecular Cell*.

Now, academic and industry collaborators from around the world are in contact with the team about next steps to move their findings from bench to bedside, the researchers say. (Although COVID-19 vaccines are starting to be rolled out, it's expected to take the better part of a year for enough people to be vaccinated to create herd immunity. And there are no guarantees that the current vaccine formulations will be as effective against future SARS-CoV-2 strains that could emerge over time.) More effective and well-timed therapeutic interventions could help reduce the overall number of deaths related to COVID-19 infections.

"What makes this research unusual is that we looked at very early time points [of infection], at just one hour after the virus infects lung cells. It was scary to see that the virus already starts to damage the cells so early during infection," says Elke Mühlberger, one of the study's senior investigators and a virologist at BU's NEIDL. She typically works with some of the world's most lethal viruses like Ebola and Marburg.

"The most striking aspect is how many molecular pathways are impacted by the virus," says Andrew Emili, another of the study's senior investigators, and the director of BU's CNSB, which specializes in proteomics and deep sequencing of molecular interactions. "The virus does wholesale remodeling of the lung cells--it's amazing the degree to which the virus commandeers the cells it infects."

Viruses can't replicate themselves because they lack the molecular machinery for manufacturing proteins--that's why they rely on infecting cells to hijack the cells' internal machinery and use it to spread their own genetic material. When SARS-CoV-2 takes over, it completely changes the cells' metabolic processes, Emili says,

and even damages the cells' nuclear membranes within three to six hours after infection, which the team found surprising. In contrast, "cells infected with the deadly Ebola virus don't show any obvious structural changes at these early time points of infection, and even at late stages of infection, the nuclear membrane is still intact," Mühlberger says.

The nuclear membrane surrounds the nucleus, which holds the majority of a cell's genetic information and controls and regulates normal cellular functions. With the cell nucleus compromised by SARS-CoV-2, things rapidly take a bad turn for the entire cell. Under siege, the cells--which normally play a role in maintaining the essential gas exchange of oxygen and carbon dioxide that occurs when we breathe--die. As the cells die, they also emit distress signals that boost inflammation, triggering a cascade of biological activity that speeds up cell death and can eventually lead to pneumonia, acute respiratory distress, and lung failure.

"I couldn't have predicted a lot of these pathways, most of them were news to me," says Andrew Wilson, one of the study's senior authors, a CReM scientist, and a pulmonologist at Boston Medical Center (BMC), BU's teaching hospital. At BMC, Boston's safety net hospital, Wilson has been on the front lines of the COVID-19 pandemic since March 2020, trying to treat and save the sickest patients in the hospital's ICU. "That's why our [experimental] model is so valuable."

The team leveraged the CReM's organoid expertise to grow human lung air sac cells, the type of cell that lines the inside of lungs. Air sac cells are usually difficult to grow and maintain in traditional culture and difficult to extract directly from patients for research purposes. That's why much coronavirus research to date by other labs has relied on the use of more readily available cell types, like kidney cells from monkeys. The problem with that is kidney cells from monkeys don't react the same way to coronavirus infection as lung cells from humans do, making them a poor model for studying the virus--whatever is learned from them doesn't easily translate into clinically relevant findings for treating human patients.

"Our organoids, developed by our CReM faculty, are engineered from stem cells--they're not identical to the living, breathing cells inside our bodies, but they are the closest thing to it," says Darrell Kotton, one of the study's senior authors. He is a director of the CReM and a pulmonologist at BMC, where he has worked alongside Wilson in the ICU treating COVID-19 patients. The two of them often collaborated with Mühlberger, Emili, and other members of their research team via Zoom calls that they managed to join during brief moments of calm in the ICU.

In another recent study using the CReM's engineered human lung cells, the research team confirmed that existing drugs remdesivir and camostat are effective in combating the virus, though neither is a perfect fix for controlling the inflammation that COVID-19 causes. Remdesivir, a broad-use antiviral, has already been used clinically in coronavirus patients. But based on the new study's findings that the virus does serious damage to cells within hours, setting off inflammation, the researchers say there's likely not much that antiviral drugs like remdesivir can do once an infection has advanced to the point where someone would need to be put on a ventilator in the ICU. "[Giving remdesivir] can't save lives if the disease has already progressed," Emili says.

Seeing how masterfully SARS-CoV-2 commandeers human cells and subverts them to do the manufacturing work of replicating the viral genome, it reminded the researchers of another deadly invader. "I was surprised that there are so many similarities between cancer cells and SARS-CoV-2-infected cells," Mühlberger says. The team screened a number of cancer drugs as part of their study and found that several of them are able to block SARS-CoV-2 from multiplying. Like viruses, cancer cells want to replicate their own

genomes, dividing over and over again. To do that, they need to produce a lot of pyrimidine, a basic building block for genetic material. Interrupting the production of pyrimidine--using a cancer drug designed for that purpose--also blocks the SARS-CoV-2 genome from being built. But Mühlberger cautions that cancer drugs typically have a lot of side effects. "Do we really want to use that heavy stuff against a virus?" she says. More studies will be needed to weigh the pros and cons of such an approach.

The findings of their latest study took the four senior investigators and scientists, postdoctoral fellows, and graduate students from their laboratories almost four months, working nearly around the clock, to complete the research. Of critical importance to the team's leaders was making sure that the experimental setup had rock-solid foundations in mimicking what's actually happening when the SARS-CoV-2 virus infects people.

"Science is the answer--if we use science to ask the lung cells what goes wrong when they are infected with coronavirus, the cells will tell us," Kotton says. "Objective scientific data gives us hints at what to do and has lessons to teach us. It can reveal a path out of this pandemic."

He's particularly excited about the outreach the team has received from collaborators around the world. "People with expertise in supercomputers and machine learning are excited about using those tools and the datasets from our publication to identify the most promising drug targets [for treating COVID-19]," he says.

Kotton says the theme that's become obvious among COVID-19 clinicians and scientists is understanding that timing is key. "Once a patient is on a ventilator in the ICU, we feel limited in what we can do for their body," he says. "Timing is everything, it's crucial to identify early windows of opportunity for intervention. You can keep guessing and hope we get lucky--or you [do the research] to actually understand the infection from its inception, and take the guesswork out of drug development."

http://bit.ly/2MaKyU3

First evidence that water can be created on the lunar surface by Earth's magnetosphere

Particles from Earth can seed the moon with water

by Emmanuel Masongsong, UCLA Earth, Planetary, and Space Sciences

Before the Apollo era, the moon was thought to be dry as a desert due to the extreme temperatures and harshness of the space environment. Many studies have since discovered lunar water: ice in shadowed polar craters, water bound in volcanic rocks, and unexpected rusty iron deposits in the lunar soil. Despite these findings, there is still no true confirmation of the extent or origin of lunar surface water.

The prevailing theory is that positively charged hydrogen ions propelled by the solar wind bombard the lunar surface and spontaneously react to make water (as hydroxyl (OH^-) and molecular (H_2O)). However, a new multinational study published in *Astrophysical Journal Letters* proposes that solar wind may not be the only source of water-forming ions. The researchers show that particles from Earth can seed the moon with water, as well, implying that other planets could also contribute water to their satellites.

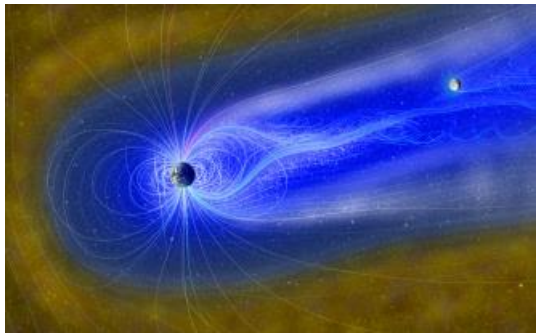
Water is far more prevalent in space than astronomers first thought, from the surface of Mars to Jupiter's moons and Saturn's rings, comets, asteroids and Pluto; it has even been detected in clouds far beyond our solar system. It was previously assumed that water was incorporated into these objects during the formation of the solar system, but there is growing evidence that water in space is far more dynamic.

Though the solar wind is a likely source for lunar surface water, computer models predict that up to half of it should evaporate and disappear at high-latitude regions during the approximately three

days of the full moon when it passes within Earth's magnetosphere. Surprisingly, the latest analysis of surface hydroxyl/water surface maps by the Chandrayaan-1 satellite's Moon Mineralogy Mapper (M^3) showed that lunar surface water does not disappear during this magnetosphere shielding period. Earth's magnetic field was thought to block the solar wind from reaching the moon so that water could not be regenerated faster than it was lost, but the researchers found this was not the case.

By comparing a time series of water surface maps before, during and after the magnetosphere transit, the researchers argue that lunar water could be replenished by flows of magnetospheric ions, also known as "Earth wind."

The presence of these Earth-derived ions near the moon was confirmed by the Kaguya satellite, while THEMIS-ARTEMIS satellite observations were used to profile the distinctive features of ions in the solar wind versus those within the magnetosphere Earth wind.



Artist's depiction of the Moon in the magnetosphere, with "Earth wind" made up of flowing oxygen ions (gray) and hydrogen ions (bright blue), which can react with the lunar surface to create water. The Moon spends >75% of its orbit in the solar wind (yellow), which is blocked by the magnetosphere the rest of the time. **Credit: E. Masongsong, UCLA EPSS, NASA GSFC SVS.**

Previous Kaguya satellite observations during the full moon detected high concentrations of oxygen isotopes that leaked out of Earth's ozone layer and embedded in lunar soil, along with an abundance of hydrogen ions in our planet's vast extended atmosphere, known as the exosphere. These combined flows of magnetosphere particles are fundamentally different from those in the solar wind. Thus, the latest detection of surface water in this study refutes the shielding hypothesis and instead suggest that the magnetosphere itself creates a "water bridge" that can replenish the moon.

The study employed a multidisciplinary team of experts from cosmochemistry, space physics and planetary geology to contextualize the data. Prior interpretations of surface water did not consider the effects of Earth ions and did not examine how surface water changed over time. The only surface maps and particle data available during a full moon in the magnetosphere were in winter and summer 2009, and it took the past several years to analyze and interpret the results. The analysis was especially difficult due to the scarce observations, which were required to compare the same lunar surface conditions over time and to control for temperature and surface composition.

In light of these findings, future studies of the solar wind and planetary winds can reveal more about the evolution of water in our solar system and the potential effects of solar and magnetosphere activity on other moons and planetary bodies. Expanding this research will require new satellites equipped with comprehensive hydroxyl/water mapping spectrometers, and particle sensors in orbit and on the lunar surface to fully confirm this mechanism.

These tools can help to predict the best regions for future exploration, mining and eventual settlement on the moon. Practically, this research can influence the design of upcoming space missions to better safeguard humans and satellites from particle radiation hazards, and also improve computer models and laboratory experiments of water formation in space.

More information: *Earth Wind as a Possible Exogenous Source of Lunar Surface Hydration, Astrophysical Journal Letters (2021).* *iopscience.iop.org/article/10. ... 847/2041-8213/abd559* *. On Arxiv:* *arxiv.org/abs/1903.04095*

http://wb.md/3ra1n0e

One in Five TIA Patients Go on to Stroke, Even in Current Era

The real incidence of transient ischemic attack (TIA) is higher than previously reported and the subsequent risk of stroke remains highly elevated for the foreseeable future, a new study shows.

Sue Hughes

"While stroke rate after TIA has come down in recent years, which is reassuring and probably due to improved secondary prevention, it is still very high — with around 20% of individuals who have had a TIA going on to have a stroke," lead author Vasileios-Arsenios Lioutas, MD, told *Medscape Medical News*.

Another finding from the study showed that the risk of stroke remained high many years after a TIA.

"It has generally been thought that stroke after a TIA is something that happens in the first few months, but our data show it is actually a significant long-term risk, with half the strokes occurring more than 1 year after the TIA, and the risk remaining elevated even after 10 years, Lioutas, who is assistant professor of neurology at Beth Israel Deaconess Medical Center, Boston, Massachusetts, noted.

"So this data is telling us we cannot relax after a TIA — action to reduce future stroke risk really is a lifelong process," he added.

The study, using data from the Framingham Heart Study, was published online in *JAMA* on January 26.

In the article, the authors conclude: "Taken together, these findings suggest that patients with TIA represent a particularly high-risk group in need of vigorous surveillance beyond the early, high-risk period and with special attention to hypertension monitoring and treatment."

The researchers believe this study is a more accurate estimate of TIA in the general population compared with other reports, as they used systematically gathered longitudinal data from Framingham Heart Study participants over almost 70 years.

"Unique features of this study include use of a population-based cohort, whereas other recent studies have been prospective registries, usually from specialized centers, so our data is a better reflection of real life in the community where it cannot be ensured that all participants have access to specialists and received optimal secondary preventive care," Lioutas commented.

Although TIA is easily missed, Lioutas believes the vast majority of cases were picked up in this study by active surveillance monitoring.

"All Framingham participants have a biannual exam and an annual update by phone, and they are asked pertinent questions including whether they have had any focal neurologic symptoms that could have been a TIA, and all their medical records are also reviewed, so our case ascertainment was truly rigorous," he explained. "We also had the unique opportunity to track TIA/stroke risk over time in a uniform way so we can see how rates have changed over time."

The study also included a cohort of matched controls, who provide a comparator group to help ascertain the increased risk of stroke after TIA, and had a longer observation period than any other TIA incidence study.

The authors analyzed prospectively collected data from 14,059 participants in the Framingham Heart Study with no history of TIA or stroke at baseline followed from 1948 to 2017.

They identified 435 individuals who experienced a TIA who were matched with 2175 controls without TIA. The estimated incidence rate of TIA was 1.19 per 1000 person-years.

Over a median of 8.9 years of follow-up after TIA, 130 participants (29.5%) had a stroke. Of these, 21.5% occurred within 7 days, 30.8% occurred within 30 days, 39.2% occurred within 90 days, and 48.5% occurred more than 1 year after the index TIA.

"Overall, we found that almost 30% of TIA patients went on to have a stroke, although this figure is a blanket estimate over the whole time period studied.

"The 30% figure is higher than reported before, but we had a much longer follow up than previous studies," Lioutas commented.

The age- and sex-adjusted cumulative 10-year hazard of incident stroke for patients with TIA was 0.46 and for matched controls without TIA was 0.09 — a fourfold increased risk of stroke in patients with TIA (adjusted hazard ratio, 4.37).

"We found individuals who had had a TIA had a risk of stroke four- or fivefold higher than controls even after adjusting for other comorbidities, and this holds through all the subsets," Lioutas said.

Compared with a 90-day stroke risk after TIA of 16.7% in 1948-1985, the risk was 11.1% in 1986-1999 and 5.9% in 2000-2017.

"The figures show a much lower stroke risk after TIA in recent years, probably because of better public awareness and improved secondary prevention. But we are still seeing long-term stroke rates of 20% in patients who have had a TIA," Lioutas noted. "For the period 2000-2017, our figures show a stroke rate of 6% at 90 days, 7.6% at 1 year, 16% at 5 years, and 20% at 10 years."

Although it is generally thought that stroke after a TIA is an early event, 49% of strokes in the study occurred more than 1 year after the TIA, Lioutas reported. He emphasized that these latest data highlight just how serious a TIA is.

"The general public also need to understand that symptoms of a TIA need to be taken extremely seriously and treated as a medical emergency," he said. "The symptoms may resolve quite quickly so people don't bother accessing medical help, and this is happening more in the current COVID crisis, but that can have devastating consequences. Our figures really drum this message home."

TIA should not be ignored because the symptoms go away, he added. "Patients should receive the same work up as if they have had a full-blown stroke, with major efforts to optimize blood pressure, diabetes, cholesterol, and these need to be continued for life. Patients should also receive antiplatelet medication and a cardiac work up to assess heart disease and look for atrial fibrillation."

Lioutas stressed that these secondary prevention measures need to be continued for life. "When we look at the cumulative risk of stroke over time, we really see how the TIA and control curves diverge more and more over time. This is very telling and highlights that we mustn't let our guard down."

Lioutas believes that awareness of TIA is improving among the medical profession, but he points out that it is not a straightforward diagnosis.

"By definition, TIA does not leave a signature on imaging," he said. "It is a clinical diagnosis and some judgment is needed. TIA is characterized by focal neurological symptoms which appear abruptly, and patients are generally of older age with cardiovascular risk factors. These are the red flags. But my message to doctors is if there is any in doubt treat like it is a TIA — refer to a neurologist or a TIA clinic for a work up. Overcalling is better than undercalling."

The study was funded by grants from the National Institutes of Health. Lioutas has reported receiving personal fees from Qmetis and serving as the continuing medical education editor for Stroke (American Heart Association).

JAMA. Published online January 26, 2021. Abstract

http://bit.ly/3r2nXre

Heparin targets coronavirus spike protein, research shows

Common anticoagulant drug could be repurposed for Covid-19 treatment

An international team of researchers led by the Universities of Liverpool and Keele, working with Public Health England, has found that the common anticoagulant drug heparin inhibits the SARS-Cov2 virus spike protein, by reducing the virus' ability to

attach to human cells and infect them.

The research, published in the journals *British Journal of Pharmacology*, and *Thrombosis and Haemostasis*, found that heparin interacts with the spike protein on the surface of coronavirus (SARS-CoV2), destabilising its structure and preventing it from docking with the ACE2 receptor on human cells.

Molecular modelling by collaborators at Queensland University in Australia showed how heparin can stick to the surface of the spike protein to achieve these effects, and studies with live SARS-CoV2 virus carried out at Public Health England's Porton Down laboratory showed that unfractionated heparin (but not low molecular weight heparins) could inhibit cell infectivity at doses similar to those currently used in clinical settings as an anticoagulant.

Crucially, the data strongly supported the clinical testing of inhaled ("nebulised") unfractionated heparin, since the doses known to be delivered to the lungs would have very strong anti-viral effects.

Professor Jeremy Turnbull from the Department of Biochemistry and Systems Biology at the University of Liverpool said: "This is exciting news since heparin could be rapidly repurposed to help alleviate Covid-19 infections, or possibly as a prophylactic treatment for high-risk groups such as medical staff or care workers. The results have also led us to investigate other novel compounds which mimic heparin that could potentially be effective against SARS-CoV2."

Dr Mark Skidmore from the School of Life Sciences at Keele University co-led the research. He said: "We also know that heparins inhibit a range of other viruses, so studying these drugs could provide new therapeutic strategies, and possibly a first-line of defence against emerging viral threats in the future, for example while vaccines are developed."

Professor Miles Carroll, of the National Infection Service, Public Health England added: "New treatments which target the SARS-CoV2 virus are urgently needed. Heparin, with its well-known clinical safety profile, is certainly an interesting candidate for repurposing against Covid-19."

"The Covid-19 pandemic has had a significant impact on the delivery of NHS services and local communities. These results strengthen the need for further investigation of heparin as a treatment in Covid-19 patients," said Dr Quentin Nunes, Consultant at the East Lancashire Hospitals NHS Trust, who is leading efforts to begin clinical trial of nebulised heparin in ITU patients in the UK.

The early release of preprint data from this study in March 2020, now published in peer-reviewed journals, has stimulated international efforts to explore the use of heparins for Covid-19 treatment. Further work is now ongoing to explore the potential of heparin and heparin-mimicking compounds as potential broad-spectrum antiviral drugs for Covid-19 and other emerging viral threats.

http://bit.ly/2NQXgaW

'COVID Tongue' Could Be One of The Signs of Infection, Doctors Warn

A swollen or patchy tongue may be a sign of coronavirus infection, according to new research.

Gabby Landsverk, Business Insider

Researchers found that one in four coronavirus patients noticed changes to their tongue, including swelling, sores, raised bumps on the surface of the tongue, indentations, and/or discolored patches. A small percentage of patients also reported a burning sensation in their mouth. These findings were based on observations from 666 patients with COVID-19 and mild or moderate pneumonia at a field hospital in Spain. The symptoms were often combined with patients losing their sense of taste, which has emerged as an increasingly common sign of the virus.

It's not yet clear whether these symptoms may be widespread. Since the patients included in the study had moderate cases of infection, researchers aren't sure whether these symptoms, dubbed "COVID tongue," might also affect people with severe coronavirus, or those with milder cases.

While viral infections are known to cause symptoms in the mouth and tongue, there hasn't been much data on this phenomenon in COVID-19 patients. That may be partly because medical experts avoid spending too much time in patients' mouth due to safety concerns about the highly infectious virus.

The new findings were presented in January 26, but first published in September in the *British Journal of Dermatology*.

Skin rashes are also linked COVID-19, but there's a lot we don't know

This study also found that about 40 percent of patients experienced skin problems on the palms of their hands or soles of their feet. These included burning sensation, redness, peeling skin, and small bumps. About one in ten patients also experienced a rash.

Previous research has also found coronavirus infection can affect the hands, feet, and skin. In May, dermatologists reported patients with red, swollen toes and rashes associated with COVID-19. And "long haulers" or people with prolonged symptoms, have also reported skin conditions, which may be a sign of inflammation caused by the virus.

The research is mixed on how common it is for the coronavirus to cause rashes and other dermatological symptoms. This most recent study found more examples of skin-related symptoms than many previous studies, so there may have been other factors involved.

Scientists also don't fully understand when these types of symptoms tend to emerge, so at this point, so it's difficult to know if they might help predict more severe cases or long-term cases of COVID-19.

http://bit.ly/2MaQpZx

Modeling study of ancient thumbs traces the history of hominin thumb dexterity

New insight into when human-like manual dexterity and efficient thumb use arose

by Cell Press

Despite long-standing ideas about the importance of thumb evolution in tool use and development, questions remain about exactly when human-like manual dexterity and efficient thumb use arose—and which hominin species was the first to have this ability. Now, researchers who've analyzed the biomechanics and efficiency of the thumb across different fossil human species using virtual muscle modeling have new insight into when these abilities first arose and what they've meant for the development of more complex human culture. The findings, appearing January 28 in the journal *Current Biology*, suggest that a fundamental aspect of human thumb opposition first appeared approximately 2 million years ago and was not found in the earliest proposed stone tool makers.

"Increased manual dexterity in the form of efficient thumb opposition was among the early defining characteristics of our lineage, providing a formidable adaptive advantage to our ancestors," said Katerina Harvati of the Eberhard Karls University of Tübingen. "It is likely a crucial element underlying the development of complex culture over the last 2 million years, shaping our biocultural evolution."

Earlier attempts to study thumb dexterity evolution had relied on comparisons between the skeletal anatomy of modern humans and earlier hominin species. The assumption was that similarities in skeletal remains to the human form could be taken as evidence of dexterity. In the new study, the team led by Harvati took a new and more comprehensive approach.

"Our methodology integrates cutting-edge virtual muscle modeling

with three-dimensional analysis of bone shape and size," first author and hand biomechanics expert Alexandros Karakostis, explains. "This process includes the precise 3-D study of the areas of the bones where muscles attach in life. Importantly, we were able to validate the predictions of our models by confirming that the differences observed between living taxa—chimpanzees and modern humans—reflect those reported from past experimental studies."

By applying this new approach to answer the question, the researchers showed that thumb efficiency and dexterity had increased to a significant extent in hominins that lived 2 million years ago in South Africa. At the same time, they found that the degree of this dexterity was consistently lower in the earliest proposed tool-making species, the Australopithecines. That includes the species Australopithecus sediba, which is also dated to approximately 2 million years ago. That's notable because researchers had previously suggested that the human-like thumb proportions of A. sediba reflected tool-making capabilities.

"One of the greatest surprises was to find that hominin hand fossils from the Swartkrans site in South Africa, which date to ca. 2 million years ago and are attributed to either early Homo or to the extinct hominin side branch Paranthropus robustus, could achieve a thumb-using dexterity similar to that of modern humans," Karakostis said.

The new findings further show that later-arising species, belonging to our own genus Homo— including Neanderthals as well as early and recent Homo sapiens—share similarly high degrees of manual dexterity. Those findings applied also to the small-brained species Homo naledi, despite the fact that this species has not yet been found in association with stone tools.

"These consistently high dexterity levels in species of Homo are indicative of the great adaptive value of thumb opposition for human biocultural evolution," Harvati says.

The researchers note that the most important implication of their new findings is that an early increase of thumb dexterity about 2 million years ago may have been a foundation for the gradual development of complex culture. They highlight that this timeframe includes important biocultural developments such as the appearance of the large-brained Homo erectus lineage and its dispersal out of Africa. Around the same time, humans gradually began to exploit animal resources and to rely more heavily on stone tool technologies.

The researchers now plan to look even more closely at specific groups, such as Neanderthals, so as to further elucidate the details of their manual dexterity and how they may have differed from that of modern humans. They'll also more closely investigate the habitual manual activities of early hominins to further shed light on the behaviors that marked the transition to systematic tool production and use among our distant ancestors.

More information: *Current Biology, Karakostis et al.: "Biomechanics of the human thumb and the evolution of dexterity" www.cell.com/current-biology/f ... 0960-9822(20)31893-5 , DOI: 10.1016/j.cub.2020.12.041*

http://bit.ly/39yXGv5

Drug prices in the U.S. are 2.56 times those in other nations

Study provides updated look at U.S. drug costs

RAND Corporation Research News

Prescription drug prices in the United States are significantly higher than in other nations, with prices in the U.S. averaging 2.56 times those seen in 32 other nations, according to a new RAND Corporation report. The gap between prices in the U.S. and other countries is even larger for brand-named drugs, with U.S. prices averaging 3.44 times those in comparison nations.

The RAND study found that prices for unbranded generic drugs --

which account for 84% of drugs sold in the U.S. by volume but only 12% of U.S. spending -- are slightly lower in the U.S. than in most other nations.

"Brand-name drugs are the primary driver of the higher prescription drug prices in the U.S.," said Andrew Mulcahy, lead author of the study and a senior health policy researcher at RAND, a nonprofit, nonpartisan research organization. "We found consistently high U.S. brand name prices regardless of our methodological decisions."

The RAND analysis is based on 2018 data and provides the most up-to-date estimates of how much higher drug prices are in the U.S. as compared to other countries in the Organisation for Economic Co-operation and Development.

Researchers calculated price indexes under a wide range of methodological decisions. While some sensitivity analyses lowered the differences between U.S. prices compared to those in other nations, under all the scenarios overall prescription drug prices remained substantially higher in the U.S.

The analysis used manufacturer prices for drugs because net prices -- that is, the prices ultimately paid for drugs after negotiated rebates and other discounts are applied -- are not systematically available. Even after adjusting U.S. prices downward based on an approximation of these discounts to account for these discounts, U.S. prices remained substantially higher than those in other countries.

The one consistent area where prices were lower in the U.S. was generic drugs, where prices were 84% of the average paid in other nations. "For the generic drugs that make up a large majority of the prescriptions written in the U.S., our costs are lower," Mulcahy said. "It's just for the brand name drugs that we pay through the nose."

The study found that among G7 nations, the United Kingdom, France and Italy generally have the lowest prescription drug prices, while Canada, Germany and Japan tend to have higher prices.

Although several prior studies compared drug prices in the United States with those in other countries, the most recent of these studies used data that are almost a decade old.

RAND researchers compiled their estimates by examining industry-standard IQVIA MIDAS data on drug sales and volume for 2018, comparing the U.S. to 32 nations that belong to the OECD. The data include most prescription drugs sold in the U.S. and comparison countries.

Researchers say that conducting such comparisons requires a variety of decisions and assumptions to calculate price indexes. The U.S. had consistently higher drug prices regardless of how the researchers calculated price indexes and treated outliers in the data.

The RAND team examined several subsets of prescription drugs, including brand-name originator drugs, unbranded generic drugs, biologics and nonbiologic drugs.

Some of the highest-priced drugs in the United States are brand-name drugs that can cost thousands of dollars per treatment and treat life-threatening illness such as hepatitis C or cancers.

"Many of the most-expensive medications are the biologic treatments that we often see advertised on television," Mulcahy said. "The hope is that competition from biosimilars will drive down prices and spending for biologics. But biosimilars are available for only a handful of biologics in the United States."

Researchers estimated that across all of the OECD nations studied, total drug spending was $795 billion. The U.S. accounted for 58% of sales, but just 24% of the volume.

Recent estimates are that prescription drug spending in the U.S. accounts for more than 10 percent of all health care spending. Drug spending in the U.S. jumped by 76% between 2000 and 2017, and the costs are expected to increase faster than other areas of health care spending over the next decade as new, expensive specialty drugs are approved.

The study was sponsored by the Office of the Assistant Secretary for Planning and Evaluation in the U.S. Department of Health and Human Services.
The report, "International Prescription Drug Price Comparisons: Current Empirical Estimates and Comparison to Previous Studies," is available on the website of the U.S. Department of Health and Human Services and on http://www.rand.org.
Other authors of the report are Christopher Whaley, Mahlet Tebeka, Daniel Schwam, Nathaniel Edenfield and Alejandro U. Becerra-Ornelas.
RAND Health Care promotes healthier societies by improving health care systems in the United States and other countries.

http://bit.ly/36sN4Ma

Hurricanes and typhoons moving 30km closer to coasts every decade

High-intensity tropical cyclones have been moving closer to coasts over the past 40 years, potentially causing more destruction than before.

The trend of tropical cyclones - commonly known as hurricanes or typhoons - increasingly moving towards coasts over the past 40 years appears to be driven by a westward shift in their tracks, say the study's authors from Imperial College London.

While the underlying mechanisms are not clear, the team say it could be connected to changes in tropical atmospheric patterns possibly caused by climate change. The research is published today in *Science*. Globally, 80 to 100 cyclones develop over tropical oceans each year, impacting regions in the Pacific, Atlantic and Indian Oceans and causing billions of dollars of damage.

Lead author Dr Shuai Wang, from the Department of Physics at Imperial, said: "Tropical cyclones are some of the most devastating natural hazards in terms of how destructive and frequent they are in coastal regions.

"Our study shows they are likely becoming more destructive as they spend more time along coastlines at their highest intensities. The risk to some coastal communities around the world may be increasing and that will have profound implications over the coming decades."

The team analysed global data from 1982-2018 on tropical cyclone formation, movement and intensity mainly gathered from satellite observations. They found that at maximum intensity, cyclones were on average getting 30km closer to coastlines per decade. There were also on average two more cyclones per decade within 200km of land.

These increases did not necessarily mean more cyclones made landfall (reached land). However, the 'near-misses' or 'indirect-hit' cyclones near coasts can still cause damage, such as Hurricane Sandy in 2012 and Hurricane Dorian in 2019, both of which skirted along the US coast for a considerable time before making landfall.

The paper's other author, Professor Ralf Toumi from the Department of Physics and Co-Director of the Grantham Institute - Climate Change and Environment at Imperial, said: "We need to understand all aspects of tropical cyclones and this new study shows how their locations are changing. This often gets less attention than changes in their intensity but is at least as important."

Previously, studies have shown that the maximum intensity of tropical cyclones is found further towards the poles. However, this does not necessarily mean these more poleward storms are more devastating. The new findings show cyclones at maximum intensity are also migrating westward, bringing them closer to coastlines and increasing their potential for damage.

The westward migration appears to be driven by anomalous 'steering' - the underlying flow in the atmosphere that carries cyclones along their tracks. The exact mechanism for this enhanced westward steering is unknown, but it may be due to the same underlying mechanism for poleward migration of cyclones as rising temperatures cause atmospheric patterns to shift.

The team will next use climate simulations to determine the underlying mechanism behind these historical shifts and project potential future shifts in tropical cyclone tracks towards global

coastal regions.

http://bit.ly/3r3QVqX

Constructing the first version of the Japanese reference genome

The Japanese now have their own reference genome thanks to researchers at Tohoku University who completed and released the first Japanese reference genome (JG1).

Their study was published in the journal *Nature Communications* on January 11, 2021. "JG1 can aid with the clinical sequence analysis of Japanese individuals with rare diseases as it eliminates the genomic differences from the international reference genome," said Jun Takayama, co-author of the study.

Back in 2003, the Human Genome Project, through a gargantuan global effort, cracked the code of life and mapped all the genes of the human genome.

Since then, more accurate versions of the human reference genome have been realized. Aiding this has been the advancement in next-generation sequencing technologies that allow for short read of approximately several hundred bases in a massively parallel way, reducing the costs and time to sequence DNA and RNA.

The international reference genome is based on an individual of African-European descent. This hampers investigating genetic variants or rare disease and cancer driving genes in Japanese owing to natural genomic difference reflective in different populations.

Associate professor Takayama and professor Gen Tamiya from Tohoku University's Tohoku Medical Megabank Organization (ToMMo) and the Advanced Research Center for Innovations in Next-Generation Medicine (INGEM) and colleagues from Tohoku University School of Medicine, School of Information Sciences, RIKEN AIP Center, and Miyagi Cancer Research Institute developed JG1 as the first part of the Japanese Reference Genome Assembly (JRGA) project.

This high-precision reference sequence is applicable to the whole human genome analysis and was constructed by analyzing the genomes of three Japanese individuals using high-coverage, long-read next-generation sequencing technologies.

Researchers can efficiently investigate the causal genetic variants of rare diseases and cancer driver genes with JG1.

"JG1 may be applicable to other populations, especially those from Asia. In addition, with the JG1, the accuracy of the Japanese allele frequency and haplotype reference panels gets improved," added Takayama.

More information: *Jun Takayama et al. Construction and integration of three de novo Japanese human genome assemblies toward a population-specific reference, Nature Communications (2021). DOI: 10.1038/s41467-020-20146-8*

http://wb.md/3r4OsfO

COVID Vaccine Anaphylaxis: Who Is at Risk?

Here are the answers to some questions you might have.

Gary J. Stadtmauer, MD

Some of the celebration and excitement over the approval of the COVID vaccines has been dampened by recent reports of allergic complications. Twenty-one cases of confirmed anaphylaxis were identified after the first 1.8 million doses of the Pfizer-BioNTech vaccine were administered (roughly 1 in 87,000 injections). Though rare, this is substantially higher than the risk associated with other vaccines (1.3 per million).

So far, the majority of episodes of anaphylaxis occurred within 30 minutes of receiving the vaccine and readily responded to treatment. Of 21 identified case reports, five patients were food allergic, of whom three also had a history of drug allergy. A total of 12 patients had had prior allergic reactions to medications or vaccines, and one patient had environmental allergies.

As for the Moderna vaccine, a couple of cases of delayed facial swelling have occurred without serious consequences. The Centers

for Disease Control and Prevention (CDC) now recommends a brief period of observation after vaccination in a facility that is capable of and prepared to treat anaphylaxis. So, what's the most likely cause of these reactions, and how can we keep our patients safe? Here are the answers to some questions you might have.

Are Vaccine Allergies Common?

Vaccine allergy is rare. The cause of these rare allergic reactions to vaccines is usually not the antigen but an excipient — additives that may include antibiotics, preservatives, or adjuvants. Meat proteins (gelatin and, rarely, alpha-gal) have also been identified as causes of IgE-mediated reactions in vaccines with higher gelatin content (MMR and VZV). Therefore, in some instances, atopy (especially food allergy) may be a risk factor for reactions to certain vaccines. On the other hand, influenza vaccine cultured in eggs contains so little egg allergen that it is no longer a concern for patients with even severe egg allergy.

What Might Be Causing COVID-19 Vaccine Anaphylaxis?

It was recently proposed that the cause of these reactions is the known allergen polyethylene glycol (PEG), which is present in both the Moderna and Pfizer vaccines to help stabilize the mRNA. PEG has been identified as the cause of reactions to colonoscopy preparations; stool softeners (such as Miralax); and medications, including topical and parenteral corticosteroids, as well as PEG-coated tablets and toothpaste. The high molecular weight of PEG may be immunogenic. Both IgE and IgG antibodies to these excipients, along with positive skin tests, support this.

Who Is At Risk for COVID-19 Vaccine Anaphylaxis?

This remains to be determined and may be different for each COVID-19 vaccine. Operating under the assumption that the causative agent *may* be PEG, then patients with a history suspicious for IgE-mediated reactions to a stool softener, colonoscopy prep, and other products containing PEGylated products may be considered at risk.

How Do You Evaluate Patients Who Could Be At Risk?

Skin prick and intradermal testing to PEG-3350 (the polyethylene glycol in Miralax stool softener) has been reported and was positive in some patients with a history of anaphylaxis to this product; the skin test resulted in a mild urticarial rash with dyspnea and diffuse pruritus. Because there is at least some experience with PEG skin testing, this could be done in patients with a questionable history of PEG allergy. But how to proceed beyond that would still be uncharted territory.

How Should We Manage Higher-Risk Patients?

The CDC recommends that patients who have an anaphylactic reaction to the first dose of the COVID-19 vaccine not receive the second dose. When the diagnosis is in doubt — for example, in the setting of a possible vasovagal reaction post-vaccination — measuring serum tryptase (or SC5b-9, the terminal complement complex) may confirm the diagnosis of anaphylaxis. I advise interpretation of the test result in consultation with an allergist-immunologist. A history of an anaphylactic reaction to any polysorbate (such as PEG) is also a contraindication to the Pfizer and Moderna vaccines.

How Should We Manage Patients With Vaccine Contraindications?

The Johnson & Johnson COVID-19 vaccine utilizes an adenovirus vector rather than mRNA. For patients who *may* have had anaphylaxis after the first dose but in whom the reaction is seriously in doubt, an allergist could consider performing a scratch test with sequential challenge. It's debatable whether that is worth the risk, because the first vaccine dose has moderate efficacy and an alternative vaccine is on the horizon.

Gary J. Stadtmauer, MD, is an allergist-immunologist in New York City. His areas of clinical interest include asthma, eczema, chronic cough, and sinusitis. He has been a Medscape contributor since 2014.

http://bit.ly/3oxCoCh

'Flatliners' still have heartbeats left. But death comes within 5 minutes.

During the death process, the heartbeat often stops and starts. Death is not a linear process.

By Stephanie Pappas - Live Science Contributor

New research finds that it's fairly common for the heart to restart — usually just for a beat or two — after a person initially flatlines. No one in the study, which took place in intensive care units (ICUs) in three countries, survived or even regained consciousness. The longest gap between someone's heart stopping and restarting again was 4 minutes and 20 seconds.

That's an important number, according to study leader Dr. Sonny Dhanani, chief of the pediatric intensive care unit at the Children's Hospital of Eastern Ontario in Canada. Most organ transplant programs require doctors to wait 5 minutes before beginning to remove organs from a deceased donor, though protocols differ from country to country, province to province and state to state. There are cases where programs wait only 2 minutes, or stretch the waiting period up to 10 minutes.

"We're very confident when we look at the findings of this study that, actually, we've got the scientific evidence to reaffirm our current standards in organ donation, to wait 5 minutes," Dhanani said during a press conference.

Defining death

Dhanani and his team focused on circulatory death, or death that occurs when the heart stops, they said in their research published Jan. 28 in The New England Journal of Medicine. The other type of death relevant to organ donation, brain death, occurs when the brain is irrevocably injured and the person has no reflexes or ability to breathe independently. In brain death, life support machines can keep the heart pumping even after a person is declared legally dead.

Declaring brain death requires its own set of criteria to test reflexes and ability of the patient to breathe. Circulatory death is simpler: It occurs once a person's heart stops. But there are occasional anecdotes of people's hearts restarting after cardiopulmonary resuscitation ends, a phenomenon known as "autoresuscitation" or "Lazarus syndrome." This sometimes leads families considering organ donation to worry whether their relative is truly beyond saving, Dhanani said.

What's more, protocols around organ donation can differ. In 2008, doctors in Colorado waited only 75 seconds after the death of a newborn to begin removing that baby's heart for donation, raising ethical questions about how soon is too soon, Reuters reported at the time. On the other end of the spectrum, waiting 10 minutes can lead to tissue damage that results in a useless organ for transplantation, Dhanani said.

Dhanani and colleagues at 20 adult ICUs in Canada, the Czech Republic and the Netherlands approached 631 families of patients who were about to have life-saving supports removed after doctors confirmed that they had no hope of survival. They asked the families if they could use monitors to track the dying patients' blood pressure, heart rhythms and oxygen saturation levels for 15 minutes prior to removing life support and 30 minutes after death.

Because of the horrors of what families were experiencing, the research team consulted with families who had been through the experience themselves when designing the study. One Ontario mother, Heather Talbot, lost her 22-year-old son to a car crash in 2008 and became involved in the research due to her subsequent advocacy around organ donation. Talbot said that monitoring in the ICU actually gave her peace of mind after her son died.

"To watch the monitors at the end, it was really relieving for me to see, 'okay, he never took another breath, it was just the machines

keeping him alive,'" she said in the press conference.

The process of death

Of 695 families approached for the study, only 48 declined participation. Another 16 were found not to meet criteria for the study, leaving 631 patients as participants.

At the bedside, clinicians reported that in seven cases, a patient's heart restarted after periods of stillness ranging from 64 seconds to 3 minutes. Dhanani and his team were able to confirm five of those reports with data from the monitors. They then did an analysis of a subset of 480 patients with complete monitoring records and found that, in fact, 67 patients had experienced at least one resumption of heartbeat. Seven had heartbeats that stopped and started more than once.

Most of these resurgences in heart activity occurred between 1 or 2 minutes after the heart had stopped. They were usually only a single heartbeat long, or less than 5 seconds in duration.

The study suggests that protocols around organ donation should stick to the 5-minute convention, given that no one's heart restarted again after a gap longer than 4 minutes and 20 seconds, Dhanani said. Transplant teams should be prepared for the possibility that they might have to adjust their timing if a patient's heart does restart. Ultimately, he said, the research should help standardize organ donation processes internationally. "I think our work will inform national and international guidelines," he said.

http://lat.ms/3ctqqqN

Dangerous new coronavirus strains may incubate in COVID-19's sickest

Scientists are turning to the case of a 45-year-old COVID-19 patient to understand how the virus is able to outwit humans.

By Melissa HealyStaff Writer

Among the 100 million people around the world who have battled coronavirus infections, scientists are turning to the case of a 45-year-old COVID-19 patient in Boston to understand how the virus is able to outwit humans.

During his 154-day illness — one of the longest on record — the patient's body became a crucible of riotous viral mutation. He offered the world one of the first sightings of a key mutation in the virus' spike protein that set off alarm bells when it was later found in strains in the United Kingdom, South Africa and Brazil.

In the U.K. strain, the genetic change known as N501Y is thought to help enhance the virus' transmissibility by about 50%. In the South Africa strain, it may reduce the effectiveness of COVID-19 vaccines and treatments. Tests of its effect on the Brazil variant are still in progress.

The Boston patient is now being viewed as an important harbinger of the coronavirus' ability to spin off new and more dangerous versions of itself. Though he died over the summer, the medical file he left behind is helping experts anticipate the emergence of new strains by focusing on the role of a growing population of patients with compromised immune systems who battle the virus for months. Among the sickest of COVID-19 patients, this population of "long haulers" appears to play a key role in incubating new variants of the coronavirus, some of which could change the trajectory of the pandemic.

The mutations that arose from this single patient are "a microcosm of the viral evolution we're seeing globally," said Dr. Jonathan Z. Li, an infectious-disease specialist at Brigham and Women's Hospital in Boston who treated him. "He showed us what could happen" when a germ with a knack for genetic shape-shifting stumbles upon conditions that reward it for doing so.

Indeed, situations in which patients can't clear a viral infection are "the worst possible scenario for developing mutations," said Dr. Bruce Walker, an immunologist and founding director of the Ragon Institute in Boston.

As weeks of illness turn into months, a virus copies itself millions of times. Each copy is an opportunity to make random mistakes. As it spins off new mutations, the virus may happen upon ones that help it resist medications, evade the immune system and come back stronger.

SARS-CoV-2, the coronavirus that causes COVID-19, has been an unpredictable adversary. The chance to witness its transformation in near-real time, and see where and how it mutates in a single host, can guide the design of vaccines and medications that don't lose their effectiveness over time, Walker said.

COVID-19 patients were just beginning to fill the beds of Brigham and Women's Hospital in the spring of 2020, when the Boston patient was first admitted. He had a fever, nausea, and a CT of his lungs that bore the hallmark "ground glass" appearance of the new disease, said Li, who was part of a team that detailed the man's case in the New England Journal of Medicine.

But COVID-19 was just one of his challenges. For 22 years, he suffered from a rare disorder called antiphospholipid syndrome, which caused his immune system to attack his own organs and spawn dangerous blood clots throughout his body.

To keep his rogue immune system from killing him, the patient required an arsenal of immunosuppressive drugs. But in his fight against the coronavirus, those medicines kept the patient's punching arm tied behind his back.

The Boston patient tested positive for SARS-CoV2 infections four separate times over 22 weeks. He was admitted to the hospital six times, including stints in intensive care. Doctors treated him with three courses of the antiviral medication remdesivir and once with Regeneron's experimental cocktail of monoclonal antibodies.

Swabs taken from his nose and throat during his second hospital stay provided the first hint of the virus' startling pace of genetic transformation: Compared with a sample taken during his first hospitalization, 11 letters in the coronavirus' 30,000-letter sequence had flipped, and nine such nucleotides had dropped out.

His next trip to the hospital landed him in the ICU. Tests revealed that 10 more letters in the virus' genetic code had changed and that one more had been deleted in a period of just five weeks. Three weeks later, after he had seemed to recover, he tested positive again and was put on a mechanical ventilator to help him breathe. This time, researchers found 11 more letter changes and 24 more deletions in the virus' genome.

Scientists couldn't say whether the Boston patient was failing to kick the virus or whether it was changing so completely that his immune system couldn't recognize it.

One thing was clear: More than half of the alterations occurred in a stretch of genetic code that dictates the structure of the virus' spike protein, the protuberance that latches onto human cells and initiates an infection. The virus' "receptor binding domain" — essentially the key that picks the lock on a human cell — accounts for only 2% of the virus' genetic code. But 38% of the mutations spun off during the Boston patient's prolonged illness were concentrated in just that spot.

In late December, British scientists speculated that just such a scenario involving an immunocompromised patient somewhere in England may have spawned the mutations that distinguish the U.K. strain.

Walker said he fears there are many more such patients out there, including people with untreated HIV infections. Immunocompromised by HIV, sick with COVID-19 and given drugs that reward SARS-CoV-2 for devising "escape" mutations, such people could become crucibles of viral mutation.

Scientists in South Africa share that anxiety.

"In South Africa, the country with the world's biggest HIV epidemic, one concern has been the prolonged viral replication and

intra-host evolution in the context of HIV infection," wrote the authors of a preliminary study that alerted the world to the new variant in early December.

So far, there's no evidence that patients with HIV are more prone to long-lasting cases of COVID-19. And even if they were, a lengthy chain of immunocompromised patients probably would have been necessary to generate the numerous mutations that distinguish the South Africa strain, its discoverers said.

Scientists are still trying to understand how certain mutations like N501Y have cropped up in so many places at once. Has the mushrooming scale of the pandemic given the virus too many opportunities to alter itself? Or are these mutations arising in a small number of people, like the Boston patient, and then somehow hitching a ride around the world?

Both factors are probably at work, and the longer and hotter the pandemic rages, the more chances the virus will have to devise random mutations.

The Boston patient shows why that can be so dangerous. In his case, the stretches of genetic code that were most prone to change affected structures that COVID-19 vaccines and drugs are designed to recognize. Now there are hints that the changes could undermine the value of those remedies.

Tulio de Oliveira, an infectious-disease researcher at South Africa's University of KwaZulu-Natal, sees a pattern in which uncontrolled spread and long-haul infections work in tandem to fuel coronavirus mutations.

Many of the places where new variants have been identified — including South Africa, Britain and California — experienced two waves of outbreaks divided by just a few months. That, De Oliveira suspects, is no mere coincidence.

In the first wave, he said, the proliferation of infections gives the virus ample opportunity to take on genetic changes that may live on in bodies of immunocompromised patients. By the time a second wave begins, novel variants that were incubating in these long-haulers have also begun to circulate. When they encounter vast numbers of new hosts, the result is a fertile environment for strains to establish themselves — if their genetic modifications confer some advantage.

The best way to prevent the emergence of more mutations is to both expand vaccinations and do more to protect people with compromised immune systems, De Oliveira said.

"If we keep the virus around for a long time, we will be giving it more opportunities to outsmart us," he said.

http://bit.ly/39B3aoY

Doctors must now prescribe drugs using their chemical name, not brand names. That's good news for patients

This national legislation change, called active ingredient prescribing, is long overdue for Australian health care.

Matthew Grant*

From today (February 1), when you receive a prescription in Australia, it will list the name of the medication's active ingredient rather than the brand name. So, for example, instead of receiving a prescription for Ventolin, your script will say "salbutamol".

Using the name of the drug — instead of the brand name, of which there are often many — will simplify how we talk about and use medications. This could have a range of benefits, including fewer medication errors by both doctors and patients.

What is an active ingredient?

The active ingredient describes the main chemical compound in the medicine that affects your body. It's the ingredient that helps control your asthma or headache, for example.

Drugs are tested to ensure they contain exactly the same active ingredients regardless of which brand you buy.

There's only one active ingredient name for each type of medical

compound, although they may come in different strengths. Some types of medications may contain multiple active ingredients, such as Panadeine Forte, which contains both paracetamol and codeine.

There can be several brand names

Until now, doctors and other prescribers have used a mixture of brand and active ingredient names when prescribing medicines. An Australian study found doctors used brand names for 80.5% of prescriptions.

Different brands are available for most medications — up to 12 for some. Combined with active ingredient names, this equates to thousands of different names — too many for any patient, doctor, nurse or pharmacist to remember.

Here's an example of the problem.

I ask John, a patient whom I've just met, whether he takes cholesterol medications, commonly called statins. The active ingredient names for this group of medications all end in "statin" (for example, pravastatin, simvastatin).

"Ummm, I'm not sure, is it a blue pill?" John asks.

"It could come in many colours. It might be called atorvastatin, or Lipitor," I reply. "Perhaps rosuvastatin, or Crestor, or Zocor?"

"Ah yes, Crestor, I am taking that," John exclaims, after deliberating for some time.

This is a common and important conversation, but could be simpler for both of us if John was familiar with the active ingredient name.

And while we did eventually come to the answer, this medication could have easily been overlooked, by both John and myself. This may have significant implications and interact with other medicines I might prescribe.

Cause for confusion

The main problem with using brand names for medications is the potential for confusion, as we see with John.

A prescription written using a brand name doesn't mean you can't buy other brands. And your pharmacist may offer to substitute the brand specified for an equivalent generic drug. So, people often leave the pharmacy with a medication name or package that bears no resemblance to the prescription.

When the terms we use to describe medicines in conversation, on prescriptions and what's written on the medication packet can all be different, patients might not understand which medications they're taking, or why.

This often leads to doubling up (taking two brands of the same medication), or forgetting to take a certain medication because the name on the package doesn't match what's written on your medication list or prescription.

Confusion resulting from using brand names has been associated with serious medication errors, including overdoses. Elderly people are the most susceptible, as they're most likely to take multiple medications.

Even when the confusion doesn't cause harm, it can be problematic in other ways. If patients don't understand their medicines, they may be less likely to be proactive in making decisions with their doctor or pharmacist about their health care.

Health professionals can also get confused, potentially leading to prescribing errors.

What are the benefits of active ingredient prescribing?

The main benefit of the switch is to simplify the language around medications. Once we become accustomed to using one standardised name for each medicine, it will be easier to talk about medicines, whether with a family member, pharmacist or doctor.

The better we understand the medications we're using, the fewer errors we make, and the more control we can take over our medication use and decisions.

This change will also serve to promote choice.

When you're prescribed a medicine with a certain name, you're

more likely to buy that brand. In some cases there may be generic medicines that are cheaper and just as effective. Or there may be other forms of the medication that better suit your needs, such as a capsule only available in another brand.

Not too much will change

This new rule is not expected to lead to extra work for doctors, pharmacists or other health professionals who prescribe medicines, as most clinical software will make the transition automatically.

Doctors can elect to still include the brand name on the prescription, if they feel it's important for the patient. But aside from some limited exceptions, the active ingredient name will need to be listed, and will be listed first.

Some active ingredient names may be a bit longer and more complex than certain brand names, so there might be a period of adjustment for consumers. But in the long term, this change will streamline terminology around medicines and make things easier, and hopefully safer, for everyone.

Next time you receive your prescription, have a look at the name of the active ingredient. Remember it, and use that name when you talk to your family, doctor and pharmacist.

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Disclosure statement

Matthew Grant received funding from the National Health and Medical Research Council.