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Soil in wounds can help stem deadly bleeding

New UBC research shows for the first time that soil silicates--the most abundant material on the Earth's crust--play a key role in blood clotting.

"Soil is not simply our matrix for growing food and for building materials. Here we discovered that soil can actually help control bleeding after injury by triggering clotting," says the study's senior author Christian Kastrup, associate professor in the faculty of medicine's department of biochemistry and molecular biology and a scientist in UBC's Michael Smith Laboratories and Centre for Blood Research.

The study, published today in *Blood Advances*, found that the presence of soil in wounds helps activate a blood protein, known as coagulation Factor XII. Once activated, the protein kicks off a rapid chain reaction that helps leads to the formation of a plug, sealing the wound and limiting blood loss.

While the researchers caution that there is a high risk of infection from unsterilized dirt, they say their findings may have implications for the future development of novel strategies using sterilized dirt to help manage bleeding and potentially understand infection after trauma.

"Excessive bleeding is responsible for up to 40 per cent of mortality in trauma patients. In extreme cases and in remote areas without access to healthcare and wound sealing products, like sponges and sealants, sterilized soil could potentially be used to stem deadly bleeding following injuries," says Kastrup.

The study also uncovered that the mechanism by which soil silicates activate Factor XII and promote faster clotting is unique to terrestrial mammals, or those that live predominantly or entirely on land.

"This finding demonstrates how terrestrial mammals, ranging from mice to humans, evolved to naturally use silicates as a specific signal to Factor XII to trigger blood clotting," says Lih Jiin Juang, the study's first author and UBC PhD student in the department of biochemistry and molecular biology. "These results will have a profound impact on the way we view our relationship with our environment."

The scientists' next plan includes testing if the response of blood to silicates helps prevent infection from microbes in soil. They will also look to test if silicates from the moon's surface are able to active Factor XII and stop bleeding.

"If moon silicates activate Factor XII, this discovery could prove useful in preventing death among people visiting or colonizing the moon, and it would provide further insight to identifying materials that may halt bleeding in very remote environments with limited resources and medical supplies," says Kastrup.

https://go.nature.com/2YhB3FY

Cells edited with CRISPR prove safe in humans

People with cancer show no serious side effects after treatment with gene-edited immune cells.

The first human trial of cells modified with CRISPR gene-editing technology shows that the treatment is safe and lasting.

A team led by You Lu at the West China Hospital in Chengdu took immune cells from people with aggressive lung cancer and applied CRISPR to them to disable a gene called *PD-1*. Usually, the PD-1 protein sends signals that keep immune cells from mounting an attack against the body’s own tissues, but active *PD-1* can open the door to the spread of cancer.

The team injected each study participant with edited versions of their own immune cells. Participants experienced only mild side effects, and potentially dangerous mutations caused by gene editing — the researcher’s main fear — were limited.

The modified cells remained in the blood for at least four weeks, showing that the strategy could have a lasting effect. This experiment, however, involved only 12 people with cancer, and did not lengthen participants' lives. The authors call for a larger study with newer gene-editing systems.

The experiment ushered in a slew of CRISPR-based trials, some of which have already been reported. *Nat. Med.* (2020)

https://nyti.ms/35j4zwx

Can Estrogen and Other Sex Hormones Help Men Survive Covid-19?

Men are more likely than women to die of the coronavirus, so scientists are treating them with something women have more of: female sex hormones.

By Roni Caryn Rabin

As the novel coronavirus swept through communities around the world, preying disproportionately on the poor and the vulnerable, one disadvantaged group has demonstrated a remarkable resistance. Women, whether from China, Italy or the U.S., have been less likely to become acutely ill — and far more likely to survive.

Which has made doctors wonder: Could hormones produced in greater quantities by women be at work?

Now scientists on two coasts, acting quickly on their hunches in an effort to save men's lives, are testing the hypothesis. The two clinical trials will each dose men with the sex hormones for limited durations.

Last week, doctors on Long Island in New York started treating Covid-19 patients with estrogen in an effort to increase their immune systems, and next week, physicians in Los Angeles will start treating male patients with another hormone that is predominantly found in women, progesterone, which has anti-inflammatory properties and can potentially prevent harmful overreactions of the immune system.

"There's a striking difference between the number of men and women in the intensive care unit, and men are clearly doing worse," said Dr. Sara Ghandehari, a pulmonologist and intensive care physician at Cedars-Sinai in Los Angeles who is the principal investigator for the progesterone study. She said 75 percent of the hospital's intensive care patients and those on ventilators are men.

And pregnant women, who are usually immunocompromised but have high levels of estrogen and progesterone, tend to have mild courses of the disease. "So something about being a woman is protective, and something about pregnancy is protective, and that makes us think about hormones," Dr. Ghandehari said.

Some experts who study sex differences in immunity, however, warned that hormones may fail to be the magic bullet that some are hoping for; even elderly women with Covid-19 are outliving their male peers, and there is a drastic reduction in levels of hormones for women after menopause.

The genesis of the estrogen trial at the Renaissance School of Medicine at Stony Brook University on Long Island stemmed from a similar observation, said Dr. Sharon Nachman, the trial's principal investigator, who credited a Stony Brook surgeon, Dr. Antonios Gasparis, with the idea.

The trial enrolled its first patient this past week, and preliminary results could be available in a few months, she said.

"It's totally out of the box, which is how good ideas often start," said Dr. Nachman, associate dean for research at the Renaissance School, which is part of the State University of New York.

The gender gap in coronavirus survival became apparent early in the pandemic. Reports from China indicated men were dying at higher rates, but the disparity was attributed to higher smoking rates. But the outcomes were consistent in other countries, with men in Italy dying at higher rates than women, and men in New York City dying at nearly double the rate of women.

Scientists who study sex differences say that both biological differences in immunity, as well as behavioral factors are at play. Men smoke more almost everywhere, they say; men also wash their hands less. While women appear to have more robust immune systems, these experts say, the causes are complex and multifactorial, and hormones are only part of the picture.

If such sex hormones were the primary protective factor for women, then elderly women with Covid-19 would fare as poorly as elderly men, because women's reproductive hormones plummet after menopause, said Sabra Klein, a scientist who studies sex differences in viral infections and vaccination responses at the Johns Hopkins Bloomberg School of Public Health.

But that's not the case, she said.

"We see this bias across the life course," Dr. Klein said. "Older men are still disproportionately affected, and that suggests to me it's got to be something genetic, or something else, that's not just hormonal." "Estrogen has immune modulatory properties — don't get me wrong," she continued. "You could get a beneficial effect in both men and women. But if women are better at recovery at 93 years old, I doubt it's hormones."

Research has shown estrogen may have an effect on a protein known as angiotensin-converting enzyme 2 (ACE2), for example. The coronavirus uses ACE2 receptors on the surfaces of cells as an entry route, and ACE2 is regulated differently in men and women, said Kathryn Sandberg, director of the Center for the Study of Sex Differences in Health, Aging and Disease at Georgetown University. In studies with rats, Dr. Sandberg and her colleagues have shown that estrogen can reduce ACE2 protein expression in their kidneys, so it is possible the hormone may reduce ACE2 expression in men as well.

Dr. Nachman said, "We may not understand exactly how estrogen works, but maybe we can see how the patient does," adding that estrogen plays a complex role, both in the early immune response that can help clear a viral infection, as well as in a secondary clean up or repair response, which can evolve into a cytokine storm.

"While we see women do get infected, their responses are different," Dr. Nachman said. "We see fewer of them having the second, disregulated immune response."

The Stony Brook estrogen trial is recruiting 110 patients who come to the hospital's emergency room with symptoms like fever, cough, shortness of breath or pneumonia, and who have either tested positive for Covid-19 or are presumed to have the illness, as long as they do not require intubation.

The trial is open to adult men as well as to women aged 55 and older, since they have low levels of estrogen. Half of the participants will be given an estradiol patch for one week, while the other half will serve as a control group, and researchers will follow them to see whether estrogen reduces the severity of their disease.

The Cedars-Sinai study is smaller, with only 40 subjects, all men, half of whom will be a control group. Only hospital inpatients with mild to moderate disease who have tested positive for Covid-19 can participate. (Patients with certain conditions, like a history of blood clots, are excluded for safety reasons.)

The patients will get two shots of progesterone a day for five days.

They will be monitored to see if their status is improving, how their needs for oxygen change and whether they go on to require intensive care or mechanical ventilation; their progress will be compared to patients in the control group.

The researchers in Los Angeles are pinning their hopes on progesterone rather than estrogen because research has shown that the hormone reduces pro-inflammatory immune cells, and supports those that fight inflammation, Dr. Ghandehari said. The hypothesis is that progesterone will prevent or dampen a harmful overreaction of the immune system, called a cytokine storm, and will reduce the

likelihood of acute respiratory distress syndrome. Both hormones are believed to be safe, especially when used for short durations. Participants will be warned of possible side effects that may be a first for many men, like tenderness in the breast and hot flashes.

https://bit.ly/2SndNTo

Breastfeeding moms' exposure to nicotine linked to infant skull defect

Vaping, nicotine patches may be as dangerous as cigarettes, study in mice suggests

COLUMBUS, Ohio - Lactating mothers who use e-cigarettes or nicotine replacement therapies may be putting their breastfed babies at risk for skull defects, a new study in animals suggests.

Cigarette smoking has already been linked to increased risk for these abnormalities in previous research. This study tested the effects of nicotine alone on head and face development.

Researchers added nicotine to the drinking water of adult female mice that were nursing litters of newborn pups. The nicotine exposure was the equivalent of about one-half to a full pack of cigarettes per day.

Scientists found in 15-day-old pups that the skull joints across the top of their heads were narrowed, putting them on a path to fuse earlier than normal. Because mouse pups at this age don't drink water, breast milk was the only possible source of their nicotine exposure. In human babies, this skull abnormality not only changes the shape of the head but can require neurosurgery to make room for the brain to grow.

The study builds upon previous work by the Ohio State University researchers that showed in mice that nicotine exposure during pregnancy altered offspring's craniofacial growth and development.

"We knew based on previous data in pregnancy that we'd see some changes, but we were a bit taken aback to find there were discernible differences when the nicotine exposure was occurring only during lactation," said James Cray, associate professor of anatomy in Ohio State's College of Medicine and senior author of the study.

"Our data suggest that nicotine alone can alter development of the head and face. That means mothers who vape are likely exposing their unborn children or infants to an amount of nicotine and its metabolites that can disturb growth in the same way cigarettes can."

The research was scheduled to be presented at the April 2020 American Association for Anatomy meeting held as part of the Experimental Biology conference, which was canceled because of the COVID-19 pandemic. In lieu of that presentation, the abstract was published in *The FASEB Journal*.

The disorder seen in these studies is called craniosynostosis, which results from the premature closure of joints, or sutures, that connect sections of the skull and remain flexible early in life as the brain continues to grow. One or more of the sutures can be affected.

"Where there is supposed to be a growth site to allow for expansion of the brain, the joints are locked together. The brain can't push those skull sections apart, so it grows in other directions," Cray explained.

The Centers for Disease Control and Prevention estimates that 1 in every 2,500 babies is born with craniosynostosis. A definitive cause is unknown, but the disorder has been linked in studies to genetic mutations and mothers' use of certain medications.

Craniosynostosis can alter the shape of the head and impair the development of the eyes and vital organs and, if not repaired in surgery, may lead to developmental delays. Symptoms include altered head shape, projectile vomiting, poor feeding, high-pitched crying and sleepiness caused by increased pressure on the brain. Children with the disorder who don't need surgery live normal lives with uncorrected abnormalities.

Based on previous work, Cray and colleagues targeted the nicotine dose in this study at 100 micrograms per milliliter, expecting mice to drink 3 to 5 milliliters of water per day. The researchers confirmed the mouse moms' level of exposure by measuring chemicals that are metabolites of nicotine in their blood.

When the pups were 15 days old, which roughly equates to age 1-2 years in humans, the scientists used micro-CT scanning to measure their heads. They found abnormalities in development of the pups' coronal sutures, joints that span the top of the head from ear to ear.

Cray is continuing this work, next planning to vaporize nicotine in mouse studies to mimic the effects of e-cigarettes on head and face development in offspring. His lab is also studying nicotine's effects on bone cells, looking for potential mechanisms to explain the damage. Early results suggest nicotine increases cell division and also puts so much stress on cells in the skull that they prematurely discard components that contribute to their normal function.

"The broader implication of this work, simply put, is that nicotine cannot be viewed as a relatively safe chemical that acts only on addiction," Cray said. "We know a lot as a scientific community about cigarettes. But we don't know as much about the components in cigarettes. The need to better understand the effects of nicotine alone is our specific aim."

This work is supported by the National Institute of Dental and Craniofacial Research.

The study was led by first author Amr Mohi, a graduate student in Cray's lab, and also co-authored by Rajiv Kishinchand and Emily Durham.

https://bit.ly/2WhhCuh

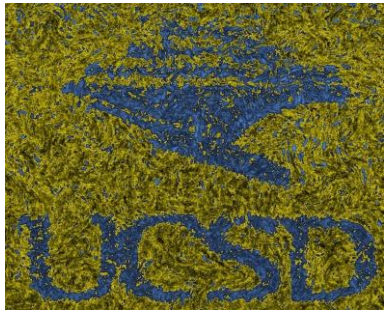
Bacteria with robust memories

Researchers draw parallels to sophisticated neurons.

By Nick Carne

Bacteria may not be the simple organisms we take them for. US biologists have found that bacterial cells stimulated with light remember the exposure hours after the initial stimulus. The team from the University of California San Diego says it was even able to manipulate the process so that memory patterns emerged.

The findings reveal surprising parallels between low-level single-cell organisms and sophisticated neurons that process memory in the human brain, the researchers say, and provide a starting point for scientists to one day design basic computing systems with living organisms such as bacteria.



Researchers used light exposure to impress a logo across an area slightly smaller than the thickness of a human hair onto a biofilm community made up of hundreds of bacteria. **Süel Lab, UC San Diego**

The research, which was led by Chih-Yu Yang, Maja Bialecka-Fornal, is described in a paper in the journal *Cell Systems*.

"Even just a few years ago people didn't think bacterial cells and neurons were anything alike because they are such different cells. This finding in bacteria provides clues and a chance to understand some key features of the brain in a simpler system," says co-author Gürol Süel. "If we understand how something as sophisticated as a neuron came to be – its ancient roots – we have a better chance of understanding how and why it works a certain way."

Previous research by Süel and others has shown that bacteria use ion channels to communicate and suggested they might also have the ability to store information about their past states.

In the new study, the researchers were able to encode complex memory patterns in bacterial biofilms with light-induced changes in the cell membrane potential of Bacillus subtilis bacteria.

The optical imprints, they found, lasted for hours after the initial stimulus, leading to a direct, controllable single-cell resolution depiction of memory.

"When we perturbed these bacteria with light they remembered and responded differently from that point on," says Süel. "So for the first time we can directly visualise which cells have the memory. That's something we can't visualise in the human brain."

The ability to encode memory in bacterial communities, the researchers say, could enable future biological computation through the imprinting of complex spatial memory patterns in biofilms.

"Being able to write memory into a bacterial system and do it in a complex way is one of the first requirements for being able to do computations using bacterial communities," says Süel.

It may thus be possible, the researchers note in their paper, to imprint synthetic circuits in bacterial biofilms by activating different kinds of computations in separate areas of the biofilm.

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Offspring may inherit legacy of their father's Toxoplasma infection

Australian researchers have revealed for the first time that males infected with the Toxoplasma parasite can impact their offspring's brain health and behaviour.

Studying mice infected with the common parasite *Toxoplasma*, the team discovered that sperm of infected fathers carried an altered 'epigenetic' signature which impacted the brains of resulting offspring. Molecules in the sperm called 'small RNA' appeared to influence the offspring's brain development and behaviour.

'Intergenerational inheritance' of similar epigenetic changes from men exposed to extreme trauma has been well documented. This latest research, published in Cell Reports, has raised the question of whether *Toxoplasma* infections - or even possibly other infections - in men before conception could impact the health of subsequent generations.

The research was led by Walter and Eliza Hall Institute researchers Dr Shiraz Tyebji and Associate Professor Chris Tonkin, in collaboration with Professor Anthony Hannan at the Florey Institute of Neuroscience and Mental Health.

Infectious inheritance

Toxoplasma is one of the world's most common parasites, estimated to be carried by between 25 and 80 per cent of the global population. *Toxoplasma* infection can cause an initial mild illness in most people, however, pregnant women, babies and people with weakened immunity experience more severe infections.

Associate Professor Tonkin said people could carry the dormant *Toxoplasma* parasite for decades, and that this had been associated with the appearance of symptoms of mental disorders such as schizophrenia and bipolar disorder.

"*Toxoplasma* infections have been shown to cause long-term epigenetic changes in a range of cells around our body. These are changes that do not alter the genetic sequence of DNA, but influence gene expression - that is, which genes are switched on or off," he said.

"As other epigenetic changes in fathers - such as those caused by trauma or smoking - can influence their children, we decided to look at whether the effects of epigenetic changes caused by *Toxoplasma* infection could also be passed between generations."

By studying male mice infected with *Toxoplasma*, the researchers were able to narrow their investigations down to the transmission of epigenetic information through sperm, Dr Tyebji said.

"We discovered that *Toxoplasma* infection alters levels of DNA-like molecules, called small RNA, that are carried by sperm," he said. "These changes in small RNA levels affect gene expression, and so could potentially influence brain development and behaviour of offspring. "We were stunned to see that even the next generation - the 'grandchildren' of the original infected male - displayed changes in their behaviour," Dr Tyebji said.

Impacts for public health

Professor Hannan said this was the first time it had been shown that an infection in a male can result in epigenetic changes being transmitted to subsequent generations. "While our studies were in mice, it raises an important question about whether infections in human fathers before conception also impact their children," he said. "We normally think more about how infectious diseases in women affect the developing fetus, but perhaps certain infections in men could have long-term impacts on subsequent generations' health.

"This is certainly something we are following up, both looking at what is happening in humans, as well as investigating infections other than *Toxoplasma*, including animal models of infection with the SARS-CoV-2 virus which causes COVID-19," Professor Hannan said.

Associate Professor Tonkin said the study was an outstanding example of how collaboration enhanced medical research. "We have combined more than a decade of research in my laboratory into *Toxoplasma* infections and their impact on brain development with the expertise Professor Hannan's team has established in understanding the role of epigenetics in brain development and behaviour," Associate Professor Tonkin said.

The research was supported by The David Winston Turner Endowment, the DHB Foundation (Equity Trustees), the National Health and Medical Research Council and the Victorian Government.

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Major trial shows breast cancer drug can hit prostate cancer Achilles heel

A drug already licensed for the treatment of breast and ovarian cancers is more effective than targeted hormone therapy at keeping cancer in check in some men with advanced prostate cancer, a major clinical trial reports.

Olaparib, a pill lacking the side effects of chemotherapy, can target an Achilles heel in prostate cancers with a weakness in their ability to repair damaged DNA. It is now on the verge of becoming approved as the first genetically targeted treatment for prostate cancer.

This precision medicine drug, a type of treatment called a PARP inhibitor which specifically targets cancer cells with faulty DNA repair genes, blocked prostate cancer growth more effectively than the modern targeted hormone treatments abiraterone and enzalutamide.

The final results from the PROfound trial, published in the prestigious journal the *New England Journal of Medicine* today (Tuesday), are set to herald the landmark approval of olaparib in prostate cancer in the US and Europe this year. The study was funded by AstraZeneca.

A team from The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, alongside colleagues from all around the world including Northwestern University in Chicago, US, studied 387 men with advanced prostate cancer who had alterations in one or more of 15 DNA repair genes. The researchers found that using olaparib in this group of men with faulty DNA repair genes significantly delayed disease progression.

Men with prostate cancers that had faulty BRCA1, BRCA2 or ATM genes benefited the most from receiving olaparib - with their disease taking 7.4 months before it progressed, compared with 3.6 months for those who received enzalutamide and abiraterone.

Men with an alteration in any of the other 12 pre-selected DNA repair genes also benefitted from receiving olaparib.

Overall, for men with any of the 15 faulty DNA repair genes who were given olaparib, the length of time before their cancer got worse was 5.8 months on average, compared with 3.5 months with targeted hormonal treatment.

The discovery of abiraterone by The Institute of Cancer Research (ICR), and its development by the ICR and The Royal Marsden, has transformed treatment for men with advanced prostate cancer.

Researchers are excited at the prospect that olaparib - which the ICR discovered how to genetically target - could be even more effective than abiraterone in selected men with DNA repair mutations.

The overall survival of men with faulty BRCA1, BRCA2 or ATM genes was 19 months on average for those who received olaparib, compared with 15 months for those who received abiraterone or enzalutamide - despite more than 80 per cent of the men who received the targeted hormone treatments switching to olaparib when their cancer progressed and spread. However, longer follow-up will be needed to show a survival improvement conclusively.

The most frequent adverse effects were anaemia and nausea, which have been associated with olaparib in the past. But overall olaparib is a well-tolerated treatment, and much kinder on patients than chemotherapy.

PROfound is the first trial to show how crucial it is to carry out genomic testing in prostate cancer patients. It is vital to identify different patient groups based on their genetics and to tailor treatment accordingly. Researchers are now hoping to see olaparib become available on the NHS for patients with advanced prostate cancer and faulty DNA repair genes within the next two years.

Next, they will look at combining olaparib with other treatments, with the aim of improving outcomes even further.

Study co-leader Professor Johann de Bono, Professor of Experimental Cancer Medicine at The Institute of Cancer Research, London, and Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust, said:

"Our findings show that olaparib - a drug which targets an Achilles heel in cancer cells while sparing normal, healthy cells - can outperform targeted hormone treatments in some men with advanced prostate cancer.

"It's exciting to see a drug which is already extending the lives of many women with ovarian and breast cancer now showing such clear benefits in prostate cancer too. I can't wait to see this drug start reaching men who could benefit from it on the NHS - hopefully in the next couple of years.

"Next, we will be assessing how we can combine olaparib with other treatments, which could help men with prostate cancer and faulty DNA repair genes live even longer."

Peter Isard, 59, a patient at The Royal Marsden, said:

"Initially after diagnosis I went onto hormone therapy and then chemotherapy. Six months after finishing chemotherapy, my PSA rose rapidly and I was told my chance of living for two years would be quite low. I came to The Royal Marsden for a second opinion and Prof de Bono found I had a genetic mutation that would make me suitable for an olaparib trial. I've been on the drug for almost two years now. I had a number of tumours in my lymph nodes, but now there is only one that is visible and I feel incredibly lucky not to have experienced any side-effects whatsoever."

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said:

"It is great to see that this treatment, which we learned how to genetically targeted at the ICR, can successfully hit an Achilles heel in some men with advanced prostate cancer. These landmark findings mean that olaparib is now set to become the first ever genetically targeted drug for the disease.

"The next step will be to find new ways to combine olaparib with other treatments in order to prevent or overcome drug resistance. It is this kind of research, which aims to target cancer's lethal ability to adapt and evolve, which we will be conducting in our pioneering Centre for Cancer Drug Discovery once it opens later this year."

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Coronavirus triggered a 'ruptured heart' in first reported US COVID-19 death

Autopsy of the first known COVID-19 death in the U.S. reveals odd cause of death.

By Rachael Rettner - Senior Writer

An autopsy of the remains from the first known COVID-19 death in the U.S. has revealed that the person died from a ruptured heart triggered by the virus's attack, according to news reports.

The 57-year-old woman, Patricia Dowd of San Jose, California, died at home on Feb. 6 after experiencing flu-like symptoms, according to The Mercury News. Recently, an investigation into her death found that Dowd was actually infected with the new coronavirus, meaning that U.S. COVID-19 deaths had occurred weeks earlier than thought.

Dowd's death was initially thought to be the result of a heart attack. But now, an autopsy report shows that the virus had spread to Dowd's heart muscle, and the viral infection caused a valve in her heart to rupture, The Mercury News reported.

"The immune system was attacking the virus and in attacking the virus, it damaged the heart and then the heart basically burst," Dr. Judy Melinek, a forensic pathologist who was not involved with Dowd's case, told The Mercury News.

This type of heart rupture occurs more typically in people with high cholesterol levels or abnormalities in the heart muscle, Melinek said. But Dowd's case was very unusual because her heart was a normal size and weight, she said.

"There's something abnormal about the fact that a perfectly normal heart has burst open," Melinek told The San Francisco Chronicle. "Normal hearts don't rupture."

Dowd was reportedly in good health and exercised regularly before she fell sick.

Previous studies have noted a connection between COVID-19 and the heart, with one small study in China finding that more than 1 in 5 COVID-19 patients develop heart damage as a result of the infection, Live Science previously reported.

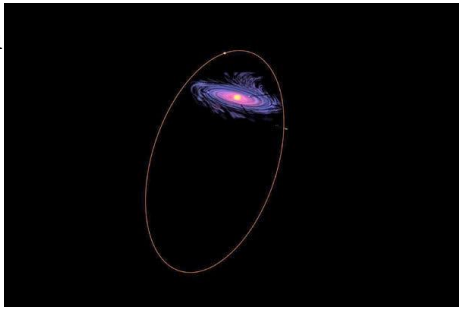
https://nyti.ms/3f8wNPd

A Nest of Alien Asteroids Orbits Our Sun

Astronomers say they have found orphan rocks from another star, or stars, stashed in the outer solar system.

By Dennis Overbye

A pair of astronomers announced last week that they had identified 19 alien asteroids circling our sun.



The rocks were probably stolen from other nearby stars 4.5 billion years ago, during the birth throes of the sun. Today they mingle in the sky with a class of asteroids called Centaurs that inhabit outer realms of the solar system between Jupiter and Neptune.

An illustration of the orbit of a Centaur asteroid **Namouni and Morais, NASA**

But unlike the rest of the Centaurs, the aliens' orbits take them far out of the plane in which the planets go around the sun, suggesting that they were once circling other stars.

Fathi Namouni, of France's Observatoire de la Côte d'Azur, and Maria Helena Morais, of Brazil's Universidade Estadual Paulista, published their results last week in the Monthly Notices of the Royal Astronomical Society.

In a statement from the Royal Astronomical Society, Dr. Morais said studying these oddball asteroids "will give us clues about the sun's early birth cluster, how interstellar asteroid capture occurred, and the role that interstellar matter had in chemically enriching the solar system and shaping its evolution."

The new work follows on a rash of discoveries of outsider rocks and comets invading or even occupying our space, more evidence that seemingly disparate and isolated realms of the universe are in fact mixing it up over the vast span of cosmic time.

First came Oumuamua, a barren cigar-shaped rock later identified as a mostly inert comet, found sailing past the planets in 2017.

Last year brought a more familiar looking comet, 2I/Borisov, of interstellar origin to our neighborhood. It now seems to be breaking into pieces as it attempts to escape our corner of the Milky Way.

Those were only temporary invaders. But two years ago, Dr. Namouni and Dr. Marais first identified an alien with permanent residency status, circling the sun near Jupiter, but in the opposite direction.

At the time, they suggested that there were probably other "extrasolar" occupants out there, most likely in orbits that take them over the poles of the sun. That is what they say they have now confirmed, using computer simulations to rewind the cosmic clock back to the beginning of the solar system.

"We chose them because they were unusual in the first place," Dr. Namouni said by email, explaining that their orbits took them far out of the ecliptic, the tilted plane along which the planets travel around the sun. "They're known as high-inclination asteroids," he explained.

Astronomers believe that the sun and other stars were born when a dense cloud of proto-stellar material, gas and dust, collapsed some 4.5 billion years ago, perhaps as a result of a nearby supernova explosion.

When the sun formed it was already accompanied by a swirl of gas and dust orbiting in that ecliptic plane that the planets and most asteroids would eventually occupy. But the 19 asteroids that the astronomers tracked were not part of that disc back then. They were in fact orbiting in a plane perpendicular to the sun's system, and in orbits that took them much farther from the sun than the other objects that would become our planets.

They probably belonged to other stars, each of which would have been born with its own retinue of worldly crumbs of planets and asteroids and comets.

In the close quarters of the birth cluster, however, it was easy for stars to steal wandering asteroids from one another. Any more details of this cosmic history are lost for now.

"We can't say they were snatched from a single star," Dr. Namouni said. "They could have been snatched from different stars at different times." He said their next research goal is see if they can distinguish families in the asteroids, indicating that some of them were captured in the same event.

We were once all brothers in the same nebula, as the late astronomer and cosmologist Allan Sandage of Carnegie Observatories liked to say. Some of our cousins got to come home and live with us.

https://bit.ly/2Ssvr8l

4-billion-year-old nitrogen-containing organic molecules discovered in Martian meteorites

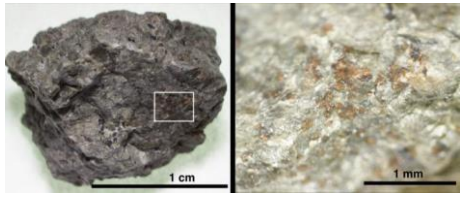
Using advanced techniques, scientists have detected organic compounds containing nitrogen in Martian meteorites which were ejected from Mars' surface ~ 15 million years ago, proving that evidence for early life can be preserved and detected today

A research team including research scientist Atsuko Kobayashi from the Earth-Life Science Institute (ELSI) at Tokyo Institute of Technology, Japan and research scientist Mizuho Koike from the Institute of Space and Astronautical Science at Japan Aerospace Exploration Agency, have found nitrogen-bearing organic material in carbonate minerals in a Martian meteorite. This organic material has most likely been preserved for 4 billion years since Mars' Noachian age. Because carbonate minerals typically precipitate

from the groundwater, this finding suggests a wet and organic-rich early Mars, which could have been habitable and favourable for life to start.

For decades, scientists have tried to understand whether there are organic compounds on Mars and if so, what their source is.

Although recent studies from rover-based Mars exploration have detected strong evidence for Martian organics, little is known about where they came from, how old they are, how widely distributed and preserved they may be, or what their possible relationship with biochemical activity could be.



A rock fragment of Martian meteorite ALH 84001 (left). An enlarged area (right) shows the orange-coloured carbonate grains on the host orthopyroxene rock. **Koike et al. (2020) Nature Communications.**

Martian meteorites are pieces of Mars' surface that were themselves blasted into space by meteor impacts, and which ultimately landed on Earth. They provide important insights into Martian history. One meteorite in particular, named Allan Hills (ALH) 84001, named for the region in Antarctica it was found in 1984, is especially important. It contains orange-coloured carbonate minerals, which precipitated from salty liquid water on Mars' near-surface 4 billion years ago. As these minerals record Mars' early aqueous environment, many studies have tried to understand their unique chemistry and whether they might provide evidence for ancient life on Mars. However, previous analyses suffered from contamination with terrestrial material from Antarctic snow and ice, making it difficult to say how much of the organic material in the meteorite were truly Martian. In addition to carbon, nitrogen (N) is an essential element for terrestrial life and a useful tracer for planetary system evolution. However, due to previous technical limitations, nitrogen had not yet been measured in ALH84001.

This new research conducted by the joint ELSI-JAXA team used state-of-the-art analytical techniques to study the nitrogen content of the ALH84001 carbonates, and the team is now confident they have found the first solid evidence for 4-billion-year-old Martian organics containing nitrogen.

Terrestrial contamination is a serious problem for studies of extraterrestrial materials. To avoid such contamination, the team developed new techniques to prepare the samples with. For example, they used silver tape in an ELSI clean lab to pluck off the tiny carbonate grains, which are about the width of a human hair, from the host meteorite. The team then prepared these grains further to remove possible surface contaminants with a scanning electron microscope-focused ion beam instrument at JAXA. They also used a technique called Nitrogen K-edge micro X-ray Absorption Near Edge Structure (μ-XANES) spectroscopy, which allowed them to detect nitrogen present in very small amounts and to determine what chemical form that nitrogen was in. Control samples from nearby igneous minerals gave no detectable nitrogen, showing the organic molecules were only in the carbonate.

After the careful contamination checks, the team determined the detected organics were most likely truly Martian. They also determined the contribution of nitrogen in the form of nitrate, one of the strong oxidants on current Mars, was insignificant, suggesting the early Mars probably did not contain strong oxidants, and as scientists have suspected, it was less-oxidizing than it is today.

Mars' present surface is too harsh for most organics to survive. However, scientists predict that organic compounds could be preserved in near-surface settings for billions of years. This seems to be the case for the nitrogen-bearing organic compounds the team found in the ALH84001 carbonates, which appear to have been

trapped in the minerals 4 billion years ago and preserved for long periods before finally being delivered to Earth.

The team agrees that there are many important open questions, such as where did these nitrogen-containing organics come from? Kobayashi explains, 'There are two main possibilities: either they came from outside Mars, or they formed on Mars. Early in the Solar System's history, Mars was likely showered with significant amounts of organic matter, for example from carbon-rich meteorites, comets and dust particles. Some of them may have dissolved in the brine and been trapped inside the carbonates.'

The research team lead, Koike adds that alternatively, chemical reactions on early Mars may have produced the N-bearing organics on-site. Either way, they say, these findings show there was organic nitrogen on Mars before it became the red planet we know today; early Mars may have been more 'Earth-like', less oxidising, wetter, and organic-rich. Perhaps it was 'blue.'

Reference

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https://bit.ly/3bTvZvr

Arteries respond in opposite ways for males and females

UC Davis Health researchers lead the way toward sex-specific hypertension treatment

A protein known to expand blood vessels -- key to controlling conditions like high blood pressure -- actually has different functions in males and females, new UC Davis Health research shows.

Conducted using arterial cells from mice, the study is the first to identify sex-based distinctions in how the protein --Kv2.1 -- works.

Kv2.1 is generally known to form calcium channels that dilate blood vessels. In arterial cells from female mice, however, it contracted blood vessels. The research was led by Luis Fernando Santana, professor and chair of physiology and membrane biology, and graduate student Samantha O'Dwyer. It is published in the Proceedings of the National Academy of Sciences.

"We were shocked at the difference and the strength of that difference," Santana said. "We think we've found the physiological explanation for what some of our clinical colleagues are seeing in patients - some high blood pressure medications tend to work better for men, while others work better for women."

Santana and his team study calcium channels, their effects on heart muscle cells and how to alter that process to improve treatments for cardiovascular disease. They are especially interested in finding new treatments for hypertension, because it affects 45% of adults in the U.S. and is linked with serious conditions such as stroke, heart failure and aneurysm.

The current study focused on how Kv2.1 changes calcium channel organization and function. The investigators found that Kv2.1 promotes tight clustering of calcium channels. Kv2.1 expression is higher in cells from female mice, leading to larger clusters. This

caused higher calcium levels in arterial cells and vasoconstriction. In arterial cells from male mice, Kv2.1 expression was not as high and calcium channel clusters were much smaller, causing vasodilation. "This difference can only be attributed to the sex of the research mice," Santana said.

The next step, Santana said, is to determine what causes the different roles of Kv2.1. He plans to investigate the potential that sex hormones regulate the protein in arterial cells. His ultimate goal is tailored treatment strategies for hypertension for men and women. "Until recently, the research community only used male mice to investigate heart disease," Santana said. "Our study proves what a major oversight that has been."

Other researchers on the study were Stephanie Palacio, Collin Matsumoto, Laura Guarina, Nicholas Klug, Sendoa Tajada, Barbara Rosati, David McKinnon and James Trimmer, all of UC Davis. Rosati also is affiliated with the State University of New York.

The study was supported by grants from the National Institutes of Health (grant numbers 5R01HL085686, 1R01HL144071, 1OT2OD026580 and T32HL086350) and the American Heart Association.

"Kv2.1 Channels Play Opposing Roles in Regulating Membrane Potential, Ca2+ Channel Function, and Myogenic Tone in Arterial Smooth Muscle" is available online.

https://wb.md/3d0qwmS

German Physician Explains His Alternative Ventilation Strategy for COVID-19

Regimen runs in direct contrast with widely held ventilation strategies and current guidance on COVID-19 treatment

Over 48 hours, eight patients arrived at the COVID-19 unit in Neustadt, Germany — four from an overwhelmed hospital in Strasbourg, France, and four who were transferred from other hospitals across Germany. All were critically ill, deeply sedated, and receiving lung-protective ventilation. It was clear to Gerhard Laier-Groeneveld, MD, a pulmonologist specializing in respiratory failure, that for all eight of his new patients, the long-trusted ventilation protocol wasn't working. So, he made a controversial call.

He ordered that positive end-expiratory pressure (PEEP) be set to zero, inspiratory time to 1.4 seconds, pCO2 to less than 35 mmHg, and that tidal volume be increased to at least 800 mL. The regimen runs in direct contrast with widely held ventilation strategies and current guidance on COVID-19 treatment.

Within 20 hours of passive ventilation, one of the French patients, a woman who had been intubated for 14 days, was able to be extubated. Another was extubated on the second day. The remaining six are doing well in the ICU but are too weak to breathe on their own for more than a few hours, owing to the fact that they arrived under such heavy sedation. After 2½ weeks without any deaths, Groeneveld decided to share his strategy via Medscape Consult, a crowdsourced social media platform where clinicians share and discuss real cases.

"COVID-19 is not ARDS [acute respiratory distress syndrome]," Groeneveld posted. "And it does need a different strategy of ventilation," he added later in an interview with *Medscape Medical News*. Although his patients were hypoxemic, CT scans showed pneumonia "with some homogeneous air space consolidation that does not respond to PEEP or prone positioning," he wrote. Physicians from all over the world responded, thanking him for his advice and asking for clarifications.

It's now been 4 weeks since the first patients arrived from France, and still there there have been no mortalities at the Neustadt COVID-19 unit. But many physicians are wary of abandoning decades of research-backed practices for this new approach in the face of a little-known virus. Still, Groeneveld insists the current protocols are inadequate, even dangerous, for treating COVID-19. And he's not alone.

Groeneveld posted to Consult just days after Luciano Gattinoni, MD, and his colleagues wrote an editorial arguing that COVID-19 has two distinct phenotypes, type L and type H. Type H, which is

similar in pathology and treatment to ARDS, was only present in 20% to 30% of their 150 patients. Gattinoni argues that for the remaining 70% with type L, standard ventilation protocols are not productive and may even create injuries that cause COVID-19 to progress. The difference, Groeneveld says, between Gattinoni's approach, detailed in a recent *JAMA* editorial, and his own is that Groeneveld believes passive ventilation is the best course of treatment for all patients, even ARDS-like type H.

A physician on the front line in New York City has also questioned ventilation protocols because he found that COVID-19 symptoms could often present more like high-altitude pulmonary edema (HAPE) than ARDS. However, clinicians with experience treating both HAPE and COVID-19 have pushed back on this observation and have argued that the comparison between the diseases is potentially risky.

Other experts say it's too soon to abandon ventilation strategies that have been established through years of clinical trials. "Regardless of whether COVID-19 behaves like ARDS or not, we as physicians have been thinking about judicious use of mechanical ventilation for several decades," William Checkley, MD, PhD, a pulmonologist and critical care specialist at Johns Hopkins, told Medscape. "I don't think we should stray away from some principles of mechanical ventilation."

The Case for Passive Ventilation

Since 2011, Groeneveld has been researching an alternative to lung-protective ventilation — a way to relieve pressure on the respiratory muscles and avoid sedation using noninvasive oxygen therapies. Long before the current pandemic, he regarded the mortality rates among ARDS patients who undergo lung-protective ventilation — 35% to 50% — as unacceptable.

Now with COVID-19, the mortality rates are far worse. The UK's Intensive Care National Audit and Research Center (ICNARC) reported higher than normal mortalities: more than two thirds of 1053 COVID-19 patients who underwent mechanical ventilation died. This is almost twice the mortality rate of patients who received mechanical ventilation for viral pneumonia between 2017 and 2019. "If we are to believe our colleagues in New York, 80% of the patients die on ventilator therapy. We have to change this therapy right now," Groeneveld told Medscape.

He's been testing passive ventilation without sedation in patients with respiratory failure for almost a decade and says he has achieved mortality rates as low as 2% to 8%. So when the pandemic hit Europe, he suspected his treatment approach could help. He left his job and home in Oberhausen, Germany, because the hospital there wouldn't admit foreign COVID-19 patients. In Neustadt, he could treat patients coming in from overwhelmed hospitals in Italy, Spain, and France.

Patients who arrive at Neustadt for COVID-19 are "treated with oxygen, mask ventilation, and high tidal volumes to meet respiratory drive," he said. Groeneveld and his team avoid intubation, regardless of saturated oxygen levels, until mental function is compromised. "We are sure that noninvasive ventilation is very effective and many people do not need intubation and sedatives," he said.

Still, many physicians, such as Johns Hopkins' Checkley, are resistant to forgo ARDS protocols. "The importance of limiting tidal volumes in mechanically ventilated patients," Checkley said, "is to avoid creating volume trauma — same goes with pressure. The risk of liberalizing the amount of tidal volume delivered could be problematic in the sense that you could induce injury." For patients with adequate respiratory system compliance, Checkley doesn't think physicians should increase tidal volumes above 8 mL/kg of predicted body weight.

Todd Rice, MD, a pulmonologist and critical care specialist at Vanderbilt University, is more skeptical. "To me, in my hospital it doesn't matter if you have ARDS. We do lung-protective ventilation on everybody because that's what the research supports," he said in an interview. In lung-protective studies, high tidal volume is often the control arm, Rice said. "High tidal volumes look better, their oxygen and CO_2 levels are often better. But when the studies were done, we saw they died more often," he said.

It's true that studies from the ARDS Network show a higher mortality rate with tidal volume at 12 mL/kg of body weight, but Groeneveld argues that the high tidal volumes used in these studies are not a proxy for his strategy. In these studies, all patients were sedated and were receiving excessive fluids, and no one was extubated early. His approach uses highly individualized tidal volumes (usually >800 mL) determined on the basis of the disease, not body weight. The priority is to keep patients awake and passively ventilated so they aren't breathing on their own and to extubate as soon as possible.

Despite controversy around the elevated tidal volume and low PEEP associated with Groeneveld's approach, most physicians agree that limiting sedation as much as possible and delaying intubation is best for the patient.

For Groeneveld's patients still in the ICU, daily T-piece trials are being conducted, and when the trials are successful, they proceed with extubation. There are now seven patients in the ICU. All underwent intubation before arriving at Neustadt, and there still have been no mortalities. But this victory isn't enough to change the scientific community's opinion, Groeneveld acknowledges. There needs to be a direct comparison between the two ventilation protocols. So, on May 1, he's again moving, this time to the University of Göttingen, where there are more COVID-19 patients and he can compare the two protocols in the same disease. If the medical community doesn't adjust now, Groeneveld says, "will we repeat this disaster every couple of years when a new virus arrives?"

https://bbc.in/3b38qPT

Kawasaki-like disease: Coronavirus risks for children

There are concerns about a severe inflammatory symptoms in children that could be linked to coronavirus.

By Rachel Schraer Health reporter

So what does this mean for how we understand the risks of coronavirus in young people?

What were the concerns?

An urgent alert was issued to GPs after several children presented with symptoms similar to Kawasaki disease - a potentially fatal syndrome that affects blood vessels - including a high temperature, low blood pressure, a rash and difficulty breathing.

The syndrome appeared to be similar to the over-active immune response, known as a "cytokine storm", seen in adults with Covid-19. In many cases it seems it's the body's immune response rather than the virus itself that proves life-threatening.

But these symptoms identified in children are rare events - known to affect about 20 children so far - and not all of them tested positive for Covid-19.

It remains the case that, overall, older people are at higher risk from coronavirus. It's far rarer for children to have severe symptoms.

Although extremely rare, there have been a small number cases of children who have become very ill and died.

The risk at different ages

The average age of people being admitted to critical care units in England, Wales and Northern Ireland was 60 as of 24 April, an audit by a research charity suggested.

Meanwhile, data from the US's Centers for Disease Control and Prevention (CDC) suggested over 65s were twice as likely to be

hospitalised with coronavirus than 50-64-year-olds - who in turn were more than three times as likely to be hospitalised than 18-49-year-olds. Under-18s were the least effected group.

"Children have so far accounted for between 1% and 5% of diagnosed Covid-19 cases, have often milder disease than adults and deaths have been extremely rare," according to Prof Adilia Warris, a paediatric infectious diseases specialist at the University of Exeter.

But, Prof Rosalind Smyth, a consultant in paediatric respiratory medicine at Great Ormond Street Hospital points out, "our understanding of this condition in children is limited.

"We should investigate fully these children, with SARS-CoV-2, who present with a multi-system inflammatory disease to assess whether this is a presentation of Covid-19," she says.

When to seek help

Whilst coronavirus is infectious to children, it is rarely serious. If your child is unwell it is likely to be a non-coronavirus illness, rather than coronavirus itself.

The Royal College of Paediatrics and Child Health advises parents seek urgent help (call 999 or go to A&E) if their child is:

Becoming pale, mottled and feeling abnormally cold to the touch

Has pauses in their breathing (apnoeas), has an irregular breathing pattern or starts grunting

Has severe difficulty in breathing becoming agitated or unresponsive

Is going blue round the lips

Has a fit/seizure

Becomes extremely distressed (crying inconsolably despite distraction), confused, very lethargic (difficult to wake) or unresponsive

Develops a rash that does not disappear with pressure (the 'Glass test')

Has testicular pain, especially in teenage boys

Can children be spreaders?

Just because most children won't develop severe symptoms, doesn't mean they can't carry the virus and spread it to others through coughs and sneezes.

But we still have a lot to learn about how infectious people with no symptoms, or only very mild ones, actually are to others.

"One of the many unknowns with the current coronavirus outbreak is how many children are being infected and potentially passing on infection to others," says Prof Matthew Snape at the University of Oxford. He is about to begin research into how many children and teenagers have been infected and developed immunity.

"Understanding this is vital to understanding how to manage the outbreak response, including decisions about when to re-open schools," he says. Early modelling, and a more recent study by researchers at the University College London, suggested the negative effects of school closures may outweigh any benefits of slowing the spread of the virus.

Pre-existing conditions

Underlying health conditions also play a role, regardless of age.

For example, there are about five-and-a-half million people in the UK of all ages who have asthma - and this puts you at higher risk of severe illness if you contract coronavirus.

Some may have undiagnosed conditions which may not be discovered until a coroner investigates.

https://bit.ly/2zR8Sni

Machine That Keeps Livers Alive for a Week Can Repair Damaged Organs

A new device could ultimately increase the number of usable livers for transplants and could perhaps preserve other types of organs

By Tanya Lewis

More than 1,000 people in the U.S. died while waiting for a liver transplant in 2018, partly because standard preservation methods can keep a donor liver alive outside the body for only about 24 hours. But now, in a feat of medical engineering, scientists have developed a machine that can keep a liver functional for a week or more. It has not yet been used for human transplants, but the technology represents a leap forward in the field of organ preservation.

Many donor livers do not meet the criteria for transplantation, because they are too old, contain too much fat or have been damaged (by cardiac arrest, for example). Researchers say the new device could keep livers alive long enough to repair themselves—something they can do to some extent in the body—and give doctors time to better assess the organs' condition. “We decided to [study the livers] for one week because this is the amount of time you need for a liver to regenerate” in patients who have had part of the organ removed, says Pierre-Alain Clavien, head of surgery and transplantation at University Hospital Zurich and senior author on a paper describing the research. He says this preservation technique could especially benefit some liver cancer patients, who could have noncancerous portions of their own livers kept alive for later reimplantation to circumvent problems related to tissue rejection.

The standard method for preserving donor livers is flushing them with a cold solution and putting them on ice, where they can remain viable for 12 to 18 hours. Recently scientists developed a method of cooling livers without freezing them, which can extend that time to 27 hours. But this is still not long enough for an injured liver to repair itself, Clavien says.

The new machine buys crucial time by mimicking key features of the human body. The setup pumps blood through the organ—a process called perfusion—at carefully controlled pressures and oxygen levels. A sugar solution provides energy to red blood cells going through the liver, and the hormones insulin and glucagon are injected to maintain glucose levels. A dialysis unit removes wastes and keeps electrolytes in balance. And an inflatable balloon positioned under the liver replicates the movement of the diaphragm during breathing, which prevents tissue damage from constant pressure on the organ.

The researchers developed and refined their device using pig livers before trying it with human ones. They managed to preserve a total of eight healthy pig livers for one week and successfully transplanted three into live pigs, which survived the surgery. After transplantation the perfused livers showed levels of injury markers comparable to those of five livers that had instead been stored on ice for several hours before transplantation.

The team then tested the machine with 10 human livers that multiple European transplant centers had rejected because of the organs' poor quality. Liver damage can be measured by an increase in proteins called damage-associated molecular patterns (DAMPs); of the 10 livers in the experiment, six showed a decrease in DAMPs and other signs of damage after time in the machine. “We can now consider injured human livers for transplantation without endangering a patient life,” Clavien says. He and his colleagues described their work this past January in *Nature Biotechnology*.

“It's a very well-done study,” says Korkut Uygun, a surgeon and bioengineer at Harvard Medical School, who was not involved in the new research. “From a clinical perspective, [keeping livers alive] just a few extra hours will help.” The study's biggest limitation, Uygun says, is that only 60 percent of the livers remained stable after a week on the machine— if they were healthy livers, “a 40 percent failure rate is not acceptable in the world of transplantation.” Uygun is also not convinced the machine can actually enable liver regeneration as opposed to just preserving

them. “Regeneration is a tough thing,” he says. “The potential is incredible, but we need more time to show this.”

The significance of the new findings can be summarized in one word: time, says Stefan Schneeberger, head of transplant and hepatobiliary surgery at Innsbruck Medical University in Austria. “It's the first example of technology allowing for preservation of an organ for a week. That is kind of a milestone,” says Schneeberger, who was not involved in the study. He says there is not much evidence that the machine can improve the quality of the livers, and actual “regeneration” is likely further off—but it remains the ultimate goal.

Although the results are promising, the researchers have yet to demonstrate the preserved livers' long-term functionality. The next step is to perform transplant survival experiments in large animals, Schneeberger says. If those experiments are successful, they will make more livers usable for transplant into human patients who have low priority on waiting lists—and Clavien says this could happen as early as this year. In the future, he adds, the new machine could theoretically be used to preserve other organs such as hearts or kidneys.

https://bit.ly/3d9nuq5

Coronavirus vaccine developed in the UK could be ready by fall, if it works

It worked in monkeys. Now they are testing the vaccine in humans.

By Yasemin Saplakoglu - Staff Writer

Scientists at Oxford University have begun clinical trials of a coronavirus vaccine that has shown promise in rhesus monkeys, according to news reports.

If the vaccine can effectively protect humans against the novel coronavirus, known as SARS-CoV-2, the first doses could potentially be administered by the autumn, according to a blog post on the official trial's web page.

The vaccine is made up of a weakened version of a common cold virus called an adenovirus that causes infections in chimpanzees. But the virus has been genetically altered to make it "impossible" for the virus to grow in humans, according to a statement. Then, they combined the weakened adenovirus with genes that code for the coronavirus "spike" protein that SARS-CoV-2 uses to infect human cells.

In theory, the vaccine will train the body to recognize and develop an immune response to the spike protein, thereby preventing SARS-CoV-2 virus from entering human cells, according to the statement.

Similar vaccines — made from the same backbone, the weakened version of the chimpanzee adenovirus — have been given to more than 320 people to date and have been shown to "be safe and well tolerated," aside from temporary side effects such as fever, headache and a sore arm, according to the statement.

The trials began on April 23, and up to 1,102 healthy participants will eventually be recruited in Oxford, Southampton, London and Bristol to take part. Half of the participants will receive the novel vaccine; most of those people will receive one dose of the vaccine, but 10 of those people will receive a second dose a month later. The other half of the participants will receive a "control" vaccine — already approved and given routinely to teenagers since 2015 — which protects against meningitis and sepsis.

The reason the researchers decided to use this control vaccine and not just a saltwater solution is so that participants won't be able to guess whether they received the actual vaccine. The researchers expect the novel coronavirus vaccine to cause temporary side effects such as sore arm, headache and fever, side effects that are also expected from the control vaccine but that wouldn't be expected from a saltwater solution.

The trial will last up to six months, with an optional visit one year after vaccination. "The best-case scenario is that by the autumn of 2020, we could have an efficacy result from the phase III trial to show that the vaccine protects against the virus, alongside the ability to manufacture large amounts of the vaccine; but these best-case time frames are highly ambitious and subject to change," the researchers wrote in the blog post.

Of course, it's too early to tell whether or not the vaccine will work, but it has shown promise in rhesus monkeys, according to The New York Times. Researchers gave the vaccine to six rhesus macaque monkeys at the National Institutes of Health's Rocky Mountain Laboratory in Montana. Researchers then exposed them to high amounts of the coronavirus, according to the Times. More than 28 days later, all six monkeys were healthy.

Another vaccine, this one made from an inactivated form of the coronavirus, has also shown promise in monkeys in China, according to a previous Live Science report. Researchers in China are now testing that vaccine on humans in clinical trials. More than 70 other vaccines are under development worldwide, according to the World Health Organization.

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Is remdesivir a miracle drug to cure coronavirus?

Don't get your hopes up yet

The race is on to find a drug that is both effective and safe for treating COVID-19, which has spread to 3.1 million infections and caused 220,000 deaths worldwide.

Nial Wheate * Andrew Bartlett **

This week, the US National Institute of Allergy and Infectious Diseases released findings of a clinical trial of the experimental antiviral drug remdesivir. This showed COVID-19 patients recovered more quickly and had an improved survival rate when taking the drug, compared with those given a placebo and standard care.

But these are just the preliminary results of one study. Other human trials have not shown similar results. Further trials are under way and will more definitively show whether remdesivir is a suitable and effective treatment for COVID-19.

What is remdesivir?

Remdesivir is an experimental antiviral drug being developed by Gilead Sciences. Originally it was being developed as a treatment for Ebola, a viral infection that causes severe internal bleeding. But researchers are now interested in its potential to treat patients with COVID-19.

Remdesivir mimics a natural ingredient called adenosine of DNA and RNA, the latter being a molecule similar to DNA that is used to carry the genetic information of viruses. After the drug is activated in the body, it works by blocking a type of enzyme called a polymerase, which is needed to make DNA and RNA.

When you block the enzyme, the virus can't make copies of itself, limiting the development of symptoms and spread of the disease.

It should be noted that no drug is perfectly safe, and remdesivir is no different. Studies undertaken so far suggest the drug may damage the liver and cause other short-term side effects such as nausea and vomiting.

These side effects need to be taken into consideration when treating COVID-19 patients who have other underlying conditions.

Clinical trials in US positive but only preliminary

This week the National Institute of Allergy and Infectious Diseases (NIAID) released the results of its trial using remdesivir for COVID-19 patients. They studied the effects of the drug on patients who were already infected with COVID-19 to see whether it helped them recover faster and improve their survival rate.

Adult patients hospitalised with COVID-19 were given daily injections of remdesivir. They were found to recover four days faster, an improvement of 31%, when compared with other patients who only received standard care and placebo. The results also indicated that more patients survived the infection with remdesivir treatment, with the death rate dropping from 11.6% to 8%.

The results are significant enough that director of NIAID Anthony Fauci said it was an "ethical responsibility" for the remaining trial patients who were taking the placebo to be switched to the active drug. But we need to treat the results of this trial with caution; for the moment they are only preliminary.

A data and safety panel has looked at the initial results, but they haven't been peer-reviewed. During peer review, independent experts from the scientific community scrutinise the study design, methods, data produced, and the conclusions before the study is published in a medical journal.

How does it compare with other studies?

The results of other trials, such as one undertaken in China, have not shown the same promising results.

The Chinese study was published in the Lancet, considered one of the most influential medical journals in the world. This trial was a randomised, double-blind, placebo-controlled study which means that neither the researchers nor the patients knew if they'd been given the active drug or a placebo.

These types of studies can reduce some biases that can influence studies, but also help quantify the effectiveness of the drug.

But the study also had limitations that need to be recognised. The patients were not as seriously ill as those in the NIAID trial, and the study was terminated early because the outbreak in China was easing.

In the end, the study only collected data on 237 patients, compared with 1,063 patients in the NIAID trial. The authors acknowledge further study is needed in more seriously ill patients and with a larger sample size.

Currently there are more than a dozen other clinical trials of remdesivir and COVID-19 being undertaken throughout the world. We need to await the data to know for sure whether the drug is as effective as we need it to be.

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Disclosure statement

Associate Professor Wheate in the past has received funding from the ACT Cancer Council, Tenovus Scotland, Medical Research Scotland, Scottish Crucible, and the Scottish Universities Life Sciences Alliance. He is Fellow of the Royal Australian Chemical Institute and a member of the Australasian Pharmaceutical Science Association. Nial is also a director of the medicinal cannabis company Canngea Pty Ltd and a Standards Australia committee member for sunscreen agents.

Andrew Bartlett is a Pharmacist and lecturer in Pharmacy practice at Sydney University and is a member of the Australian College of Pharmacists.

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https://bit.ly/3aNItDK

Link identified between dietary selenium and outcome of COVID-19 disease

Link identified between the COVID-19 cure rate and regional selenium status

An international team of researchers, led by Professor Margaret Rayman at the University of Surrey, has identified a link between the COVID-19 cure rate and regional selenium status in China.

Publishing their findings in the *American Journal of Clinical Nutrition*, researchers using data (up to 18 February), investigated possible links between selenium levels in the body and cure or death rates of those with the COVID-19 virus in China.

Selenium is an essential trace element obtained from the diet (i.e. fish, meat and cereals) which has been found to affect the severity of a number of viral diseases in animals and humans. For example selenium status in those with HIV has been shown to be an

important factor in the progression of the virus to AIDs and death from the condition. China is known to have populations that have both the lowest and highest selenium status in the world, due to geographical differences in the soil which affects how much of the trace element gets into the food chain.

Margaret Rayman, Professor of Nutritional Medicine at the University of Surrey, said; "Given the history of viral infections associated with selenium deficiency, we wondered whether the appearance of COVID-19 in China could possibly be linked to the belt of selenium deficiency that runs from the north-east to the south-west of the country."

Examining data from provinces and municipalities with more than 200 cases and cities with more than 40 cases, researchers found that areas with high levels of selenium were more likely to recover from the virus. For example, in the city of Enshi in Hubei Province, which has the highest selenium intake in China, the cure rate (percentage of COVID-19 patients declared 'cured') was almost three-times higher than the average for all the other cities in Hubei Province. By contrast, in Heilongjiang Province, where selenium intake is among the lowest in the world, the death rate from COVID-19 was almost five-times as high as the average of all the other provinces outside of Hubei.

Most convincingly, the researchers found that the COVID-19 cure rate was significantly associated with selenium status, as measured by the amount of selenium in hair, in 17 cities outside of Hubei.

Kate Bennett, a medical statistician at the University of Surrey, said; "There is a significant link between selenium status and COVID-19 cure rate, however it is important not to overstate this finding; we have not been able to work with individual level data and have not been able to take account of other possible factors such as age and underlying disease."

Ramy Saad, a doctor at Royal Sussex County Hospital, Brighton, currently taking an MSc degree in Nutritional Medicine at the Department of Nutritional Sciences at Surrey, commented; "The correlation we have identified is compelling, particularly given previous research on selenium and infectious diseases. As such, a careful and thorough assessment of the role selenium may play in COVID-19 is certainly justified and may help to guide ongoing public-health decisions".

Notes to editors

[1] Data was obtained from the Baidu website, a nongovernmental website that provides daily updates of the reports of the health commissions of each province, municipality, or city on numbers of COVID- 19 confirmed cases, numbers cured, and numbers who died.

https://bit.ly/35uFPSm

Reduced obesity for weighted-vest wearers

Akin to built-in a bathroom scale that contributes to keeping our body weight and fat mass constant

Scientists from the University of Gothenburg, Sweden, have found a new method of reducing human body weight and fat mass using weighted vests. The new study indicates that there is something comparable to built-in bathroom scales that contributes to keeping our body weight and, by the same token, fat mass constant.

The researchers hypothesized that loading the vests with weights would result in a compensatory body-weight decrease. Sixty-nine people with a body mass index (BMI) of 30-35, the lowest obesity category, took part in the clinical study. Their instructions were to wear a weighted vest eight hours a day for three weeks, and otherwise live as usual.

All the study participants wore weighted vests but, by drawing of lots, they were assigned to one of two groups. The control group wore only light vests weighing 1 kg, while the treatment group wore heavy vests weighing some 11 kg. When the three weeks had passed, the experimental subjects who wore the heavier vests had lost 1.6 kg in weight, while those wearing the light vests had lost

0.3 kg. "We think it's very interesting that the treatment with the heavier weighted vests reduced fat mass while muscle mass simultaneously remained intact," says Professor Claes Ohlsson of Sahlgrenska Academy, University of Gothenburg.

"The effect on fat mass we found, from this short experiment, exceeded what's usually observed after various forms of physical training. But we weren't able to determine whether the reduction was in subcutaneous fat (just under the skin) or the dangerous visceral kind (belly fat) in the abdominal cavity that's most strongly associated with cardiovascular diseases and diabetes," says Professor John-Olov Jansson of Sahlgrenska Academy, University of Gothenburg.

In previous animal studies published in 2018, the scientists showed that there is an energy balance system that endeavors to keep body weight constant: the "gravitostat," as they have dubbed it. In mice, this regulation takes place partly by influencing appetite. To work, the system must contain a kind of personal weighing machine. The researchers' new clinical study shows that similar built-in scales exists in humans as well.

If people do a lot of sitting, what seems to happen is that the reading on our personal scales falls too low. This may explain why sitting is so clearly associated with obesity and ill-health. Weighted vests can raise the reading on the scales, resulting in weight loss.

Many questions about how the gravitostat works remain for the researchers to answer. Aspects they want to study include whether, in wearers of weighted vests, changed energy expenditure, appetite and mobility help them to lose weight. The scientists also want to see whether the weight reduction continues for the vest wearers over periods longer than three weeks, and whether the dangerous visceral fat is reduced by the treatment.

Increased Weight Loading Reduces Body Weight and Body Fat in Obese Subjects - A Proof of concept randomized clinical trial; https://doi.org/10.1016/j.eclinm.2020.100338

https://bit.ly/2z8pGpe

Plant extract combo may relieve hangover symptoms

But popular beliefs around dehydration and mineral depletion linked to too much alcohol may be misguided

A plant extract combination of fruits, leaves, and roots may help to relieve hangover symptoms, reveals research published online in *BMJ Nutrition Prevention & Health*.

And received wisdom that it's the dehydrating effects of alcohol and the associated loss of electrolytes--electrically charged minerals in the body that help balance water content and acid levels--which are largely responsible for some of the most common hangover symptoms, may be wrong, the findings indicate.

Various natural remedies have been recommended to ease hangover symptoms, but there is as yet no strong scientific evidence for their use. In a bid to address that, the researchers assessed the potential of specific plant extracts, vitamins and minerals, and antioxidant compounds to ease a range of recognised physical and psychological symptoms associated with drinking alcohol.

The plant extracts included Barbados cherry (Acerola), prickly pear, ginkgo biloba, willow and ginger root. The vitamins and minerals included magnesium, potassium, sodium bicarbonate, zinc, riboflavin, thiamin and folic acid.

Some 214 healthy 18-65 year olds were randomly split into three groups and given a 7.5 g flavoured, water soluble supplement 45 minutes before, and immediately after they stopped drinking any of beer, white wine, or white wine spritzer.

The first group (69) were given a supplement containing the plant extracts, vitamins and minerals, and additional antioxidant compounds--steviol glycosides and inulin. The second group (76) were given a supplement minus the plant extracts, while the third group (69) were given glucose alone (placebo).

The number and type of drinks consumed was recorded as was how many times they emptied their bladder between 1700 and 2100 hours. Blood and urine samples and blood pressure measurements were taken before and after the start of this four-hour period, after which the participants were sent home to sober up.

Twelve hours later the same samples and blood pressure measurements were taken, and participants filled in a questionnaire about the type and intensity of perceived hangover symptoms, which were ranked on a zero to 10 scale. The average amount of alcohol consumed was virtually the same in all three groups: 0.62 ml/minute. Analysis of all the data showed that symptom intensity varied widely among the participants.

But compared with the glucose only supplement, those taking the full supplement of plant extracts, minerals/vitamins, and antioxidants reported less severe symptoms.

Average headache intensity was 34% less, nausea 42% less, while feelings of indifference fell by an average of 27% and restlessness by 41%. No significant differences or reductions were reported for any of the other symptoms.

Polyphenol and flavonoid compounds in each of the five plant extracts have been associated with curbing the physiological impact of alcohol in previously published experimental studies, explain the researchers. But it's not clear how.

"The underlying mechanisms remain to be unravelled and surely need further investigation," they suggest.

No significant difference in any symptom was reported by those taking the supplement minus the plant extracts, suggesting that plant extracts were largely responsible for the observed changes, say the researchers.

And the absence of any observed impact for vitamins and minerals on their own suggests that alcohol might not affect electrolyte and mineral balance, as is commonly thought, they add.

Their analysis also showed levels of water content in the body weren't significantly associated with the amount of alcohol drunk. "Our results suggest that alcohol-induced increased fluid excretion does not necessarily lead to a significant dehydration process," they write. "It seems to be clear that hangover symptoms are predominantly caused by alcohol and its metabolites," they conclude.

Peer reviewed? Yes
Evidence type: Double blind randomised controlled trial
Subjects: People

https://bit.ly/2WiLqQ5

New discovery explains how the prostate gland regenerates itself

It is not what the scientists initially expected

The standard treatment for men with advanced prostate cancer is androgen-deprivation therapy. Androgens are hormones that fuel prostate cell growth; removing them with either drugs or surgery causes the prostate gland to shrink by 90%.

Nevertheless, the cells that remain can eventually regrow a tumor, and when they do, the tumor is usually resistant to further hormone therapy. It is also more likely to spread to other organs (metastasize).

A new study from researchers at Memorial Sloan Kettering provides insight into how the prostate is able to regrow so swiftly. And it is not what the scientists initially expected.

"Most people, including me, expected to find a rare population of stem cells that is responsible for regenerating the gland," says Charles Sawyers, Chair of the Human Oncology and Pathogenesis Program at MSK and the corresponding author on the paper, published May 1 in the journal *Science*. "But this is not the case."

Instead, he says, nearly all of the cells that persisted after hormone-deprivation therapy contributed to the regeneration of the prostate

gland. Most of these were luminal cells, which form the inside of the hollow organ. The findings have implications for how doctors think about prostate cancer treatment.

A Cellular Atlas of the Prostate

The investigators made their discovery with the help of a powerful technique called single-cell RNA sequencing (scRNA seq). This method of analysis allows scientists to identify which genes are turned on in many individual cells in a tissue at once. Collaborating with scientists from the Dana Pe'er lab in the Sloan Kettering Institute and Aviv Regev's lab at the Broad Institute, the team performed scRNA seq on nearly 14,000 cells in the mouse prostate gland. From these data, they were able to completely map out the cell types found in a normal mouse prostate.

With the information, they could then determine which cell types remained in the prostate after the mice received androgen-deprivation therapy, and which divided to regrow the gland when androgen was restored.

From these analyses, it was clear that nearly all the luminal cells in the prostate were dividing, rather than just a subset -- as would be expected if a stem cell population were mainly responsible for regenerating the gland. What's more, the luminal cells (whose typical function is to secrete fluids) had clearly acquired abilities they don't usually have in a hormonally intact animal.

"They became much more stemlike," says Wouter Karthaus, a senior postdoctoral fellow in the Sawyers lab and the paper's first author. "Without androgens influencing their gene expression, they were free to turn on other genes and acquire regenerative properties." In addition to the mouse work, the investigators performed scRNA seq on prostate tissue taken from men who had been treated for prostate cancer. They found a similar pattern of luminal prostate cells that had acquired the attributes of stem cells. This implies that what is true of mice may also be true of men.

Plastic Identities

The study's findings contradict a classic model of how stem cells regenerate and repair tissue. By that way of thinking, stem cells are a rare and special type of cell that can give rise to many cell types yet retain a proliferative capacity. But recent studies -- including, now, this one -- have questioned how broadly this model applies across different organs. At least in the prostate, fully differentiated cells can become stem cells under the right conditions, this study suggests.

Prior work from the Sawyers lab showed that some prostate cancer cells possess an ability to change their identity. This is called lineage plasticity. They can, for example, reprogram themselves to become a type of prostate cell that does not require androgen to survive. Lineage plasticity is an important way that prostate cancer cells eventually develop resistance to hormone-blocking therapies.

What the latest findings mean for treatment is an open question, but there could be significant implications. "Androgen-deprivation therapy may be a double-edged sword," Dr. Sawyers says. "Lots of cells die, but the ones that persist acquire this stemlike property."

"It is likely that we push prostate cancer to have a more progenitor-like state during therapy," Dr. Karthaus adds. The team's next effort will be to identify the molecular and cellular cues that control this switch in the hope of developing ways to turn it off.

https://bit.ly/3dbeyqG

Naked mole-rats need carbon dioxide to avoid seizures and here's why

Researchers may have found the mole-rats' kryptonite: they need high levels of carbon dioxide to function.

African naked mole-rats are sometimes referred to as animal superheroes. They resist cancer, tolerate pain, and live a remarkably long time. They're also known for their ability to handle high levels of carbon dioxide and can go for several minutes without oxygen.

But researchers reporting in *Current Biology* on April 30 say they may have found the mole-rats' kryptonite: they need high levels of carbon dioxide to function.

"While they thrive in their cramped nest quarters, the air composition just above the surface of their burrows in East Africa makes them vulnerable to seizures," said Dan McCloskey of The City University of New York. "Because that's what happens when naked mole-rats lose carbon dioxide."

An African naked mole-rat. **Roland Gockel**

In other words, the mole-rats don't just tolerate high levels of carbon dioxide in their crowded nests; it appears that they actually require it. When they reach the hot surface and start heat-induced hyperventilation in the fresh air, it sends them into seizures. In the study now reported, the researchers found that this curious need for carbon dioxide is explained by the presence of a missense mutation in a gene that encodes the major neuronal chloride transporter known as KCC2.

The researchers came to this discovery in an unexpected way. Naked mole-rats have little control over their body temperature and also are prone to seizing in response to heat, they knew. McCloskey and first author of the new study Michael Zions had been exploring this susceptibility to fever-like conditions as a model for fever-induced (febrile) seizures in human children.

The team joined forces with Kai Kaila and Martin Puskarjov, University of Helsinki, Finland. Kaila, an expert in febrile seizures, and Puskarjov had earlier found a mutation affecting KCC2 in families of people prone to them. What they now know is that mole-rats and those families with a genetic predisposition for febrile seizures carry the very same genetic change.

"We knew there was some value in the line of inquiry, but we had no idea that the similarities would go all the way down to the genetic level," Kaila said.

"The identification of the genetic polymorphism in the naked mole-rat KCC2 was a surprise," Puskarjov added. "Aside from a small subset of humans, naked mole-rats are now the only other mammals known to harbor this variant."

Further study yielded more surprises. When the researchers gave a naked mole-rat the anti-seizure drug diazepam, the drug triggered a seizure rather than preventing one. While the result was unexpected, it helped them make sense of years of unusual behavioral and electrophysiological data: the naked mole-rats were relying on carbon dioxide to help them compensate for deficiencies in their brain's inhibitory GABAergic system.

KCC2 is a chloride transporter: its normal job is to control the amount of chloride inside of neurons. In a typical adult mammal, chloride levels in central neurons are kept low. When the neurotransmitter GABA binds to a neuron, chloride enters and blocks the activity of the neuron. This ability to reduce neural activity is essential for many thousands of neurons to work together in coordinated fashion and avoid becoming overexcited. In the naked mole-rat and people with the mutation, KCC2 doesn't clear chloride from neurons as effectively. As a result, this inhibitory cascade doesn't work as well.

"Naked mole-rat brains lack some of the inhibition that a mammal needs. Instead, they're using the carbon dioxide to get back to where they have to be," Zions said. "They prefer CO_2 levels that would panic a person, but are troubled by fresh air. They've leveraged a liability to literally dig themselves a niche."

As the researchers explain, an inhibition-impaired brain would normally be a handicap as it is in people prone to febrile seizures. It works for naked mole-rats because they rely on their carbon

dioxide-rich environments to help keep their brain within normal parameters. "We believe they are utilizing nest carbon dioxide to offset their impoverished GABA system," Kaila said.

African naked mole-rats in a colony nest. **Roland Gockel**

The researchers think the findings may provide an essential clue as to why the naked mole-rats are one of only two mammalian species to evolve eusociality, living together in highly cooperative colonies. "Low carbon dioxide areas may cause hyperexcitability and overstimulation or anxiety. Their brain physiology urges them to go back to the nest rather than set out on their own," McCloskey said. Support for this idea comes from the researchers' discovery that the only other eusocial mammal, the Damaraland mole-rat, has a slightly different mutation in the exact same location on the KCC2 gene as the naked mole-rat.

In addition to the insights into mole-rat evolution, the findings may also have implications for people who carry the KCC2 variant, including those prone to febrile seizures and people with idiopathic generalized epilepsy, schizophrenia, or autism who in some cases also have the variant, according to the researchers. "The breathing patterns and carbon dioxide needs of these individuals is something to consider," Kaila said.

More information: *Current Biology, Zions et al.: "Nest carbon dioxide masks GABA-dependent seizure susceptibility in the naked mole-rat" www.cell.com/current-biology/f … 0960-9822(20)30478-4 , DOI: 10.1016/j.cub.2020.03.071*

https://bit.ly/2xrKiIQ

Are 'covid toes' a real symptom of the coronavirus?

A frostbite-like rash on a person's toes might be a symptom of the new coronavirus, according to anecdotal evidence from dermatologists around the world.

However, research is needed to determine whether this peculiar rash is truly caused by COVID-19.

The pinkish-reddish rash can turn purple over time, and causes a burning sensation in some people, Dr. Esther Freeman, a dermatologist at Massachusetts General Hospital in Boston, told The Washington Post. But the inflammation tends to disappear without treatment in two to three weeks, Freeman said.

So far, data shows that most people with so-called "covid toes" are asymptomatic or have mild cases of the disease, Freeman told the Post. Moreover, this strange rash tends to affect the younger crowd, including children and adults in their 20s or 30s, she said.

"Most of the patients were young, healthy and had a benign clinical course," she told the Post.

"I don't want people to think if they are having purple spots on their toes that they are going to end up on a ventilator in the ICU. That is not what we are seeing in the data."

A series of images of covid toes, photographed by Italian dermatologist Andrea Bassi and posted on Twitter show the range of appearances this rash can take.

But there is still much to learn, so Freeman and colleagues who are part of an American Academy of Dermatology task force created an online COVID-19 dermatology registry, where health care workers can

report skin-related issues that seem to be linked to COVID-19, including the frostbite-like toe rashes.

The researchers hope that the database will help doctors "understand the relationship between the virus and skin" and determine whether any of these skin problems can help with early disease detection, the team wrote in a report in the Journal of the American Academy of Dermatology.

So far, roughly half of the more than 300 database entries include covid toes, USA Today reported on April 27.

Freeman noted that these toe rashes include skin sores or bumps known as pernio or chilblains, which usually occur when a person's foot has been exposed to extremely cold temperatures.

However, because these rashes are happening in spring and in COVID-19 patients, cold temperatures are unlikely to be the cause.

Instead, dermatologists say it's possible that inflammation in the toes is causing the rash, Freeman told USA Today.

Other ideas are that small blood clots in the toe's blood vessels may lead to the rash, or that the blood vessel walls are inflamed due to a condition known as vasculitis.

One of the first mentions of covid toes appeared in early April, when French doctors noted that the rash had an "appearance of pseudo-frostbite" and "persistent, sometimes painful redness, and transient hive lesions." (Translated with Google Translate.)

Mention of the toes surfaced again on April 18 in a Journal of the American Academy of Dermatology case report. In the case report, the researchers described a 23-year-old student in Belgium who had "COVID-19 infection–induced chilblains."

It's not uncommon for viruses to cause rashes. Measles, for instance, can cause itchy flat spots, while coxsackie can lead to painful sores in the hands, feet and mouth, the Post reported.

https://bit.ly/3daFBlJ

Recovered patients who tested positive for COVID-19 likely not reinfected

This phenomenon is likely due to the shortcomings of the coronavirus test, experts say

By Yasemin Saplakoglu - Staff Writer

More than 260 COVID-19 patients in South Korea tested positive for the coronavirus after having recovered, raising alarm that the virus might be capable of "reactivating" or infecting people more than once. But infectious disease experts now say both are unlikely.

Rather, the method used to detect the coronavirus, called polymerase chain reaction (PCR), cannot distinguish between genetic material (RNA or DNA) from infectious virus and the "dead" virus fragments that can linger in the body long after a person recovers, Dr. Oh Myoung-don, a Seoul National University Hospital doctor, said at a news briefing Thursday (April 30), according to The Korea Herald.

These tests "are very simple," said Carol Shoshkes Reiss, a professor of Biology and Neural Science at New York University, who was not involved in the testing. "Although somebody can recover and no longer be infectious, they may still have these little fragments of [inactive] viral RNA which turn out positive on those tests."

That's because once the virus has been vanquished, there is "all this garbage of broken-down cells that needs to be cleaned up," Reiss told Live Science, referring to the cellular corpses that were killed by the virus. Within that garbage are the fragmented remains of now non-infectious viral particles.

To determine whether or not someone is harboring infectious virus or has been reinfected with the virus, a completely different type of test would be needed, one that is not typically performed, Reiss said. Instead of testing the virus as it is, lab technicians would have to

culture it, or place that virus in a lab dish under ideal conditions and see if it was capable of growing.

Patients in South Korea who re-tested positive had very little to no ability to spread the virus, according to the Korea Centers for Disease Control and Prevention, the Korea Herald reported.

Reports of patients testing positive twice aren't limited to South Korea; they have also poured in from other countries, including China and Japan. But the general consensus in the scientific community — with all the information available to date on the new coronavirus — is that people aren't being reinfected, but rather falsely testing positive, Reiss said.

What's more, "the process in which COVID-19 produces a new virus takes place only in host cells and does not infiltrate the nucleus," or the very core of the cell, Oh said during the briefing, the Herald reported. Here's why: Some viruses, such as the human immunodeficiency virus (HIV) and the chickenpox virus, can integrate themselves into the host genome by making their way into the nucleus of human cells, where they can stay latent for years and then "reactivate." But the coronavirus is not one of those viruses and instead it stays outside of the host cell's nucleus, before quickly bursting out and infiltrating the next cell, Reiss said.

"This means it does not cause chronic infection or recurrence," Oh said. In other words, it's highly unlikely that the coronavirus would reactivate in the body soon after infection, Reiss said. But reinfection at some point is a theoretical possibility. "We don't know what's going to happen a year from now, nobody has that kind of crystal ball," Reiss said.

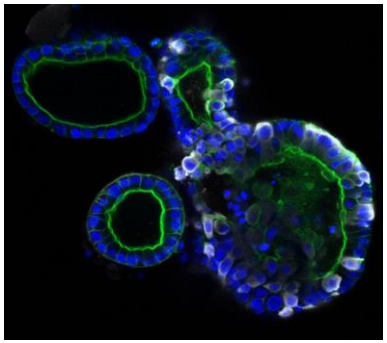
Reassuringly, the virus is currently undergoing very small genetic changes that are "too tiny" to evade the immune systems of people who have already been infected. The genetic changes would have to be substantial enough that a person's existing antibodies to SARS-CoV-2 would no longer work against a new strain. So far, that seems unlikely. "If this virus remains as it is [with] really tiny changes … then it's highly unlikely" that a person would be reinfected next year, Reiss added.

In the best-case scenario, which Reiss thinks is likely, the virus will behave like the virus that causes chickenpox, "imprinting" on the host immune memory. Then, even if antibody levels drop over time, people will retain a population of memory cells that can rapidly boost production of more antibodies if they are exposed to the virus again, Reiss said. Of course, this is still an "assumption," and it will be some time before we can fully understand the strength of the army the immune system creates against this virus — and whether that army's protection is long-lasting.

https://bit.ly/2KRUkGc

Coronavirus SARS-CoV-2 infects cells of the intestine

1/3 of COVID-19 patients experience gastrointestinal symptoms such as diarrhea, virus often can be detected in stool samples



Intestinal organoids, the right one infected with coronavirus SARS-CoV-2. The coronavirus is colored white, the organoids themselves are colored blue and green. **Joep Beumer, copyright Hubrecht Institue**

Researchers from the Hubrecht Institute in Utrecht, Erasmus MC University Medical Center Rotterdam, and Maastricht University in the Netherlands have found that the coronavirus SARS-CoV-2, which causes COVID-19, can infect cells of the intestine and multiply there.

Using state-of-the-art cell culture models of the human intestine, the researchers have successfully propagated the virus in vitro, and monitored the response of the cells to the virus, providing a new cell culture model for the study of COVID-19. These findings could explain the observation that approximately one third of COVID-19

patients experience gastrointestinal symptoms such as diarrhea, and the fact that the virus often can be detected in stool samples. The results of this study were published in the scientific journal *Science* on the 1st of May 2020.

Patients with COVID-19 show a variety of symptoms associated with respiratory organs - such as coughing, sneezing, shortness of breath, and fever - and the disease is transmitted via tiny droplets that are spread mainly through coughing and sneezing. One third of the patients however also have gastrointestinal symptoms, such as nausea and diarrhea. In addition, the virus can be detected in human stool long after the respiratory symptoms have been resolved. This suggests that the virus can also spread via so-called "fecal-oral transmission".

Though the respiratory and gastrointestinal organs may seem very different, there are some key similarities. A particularly interesting similarity is the presence of the ACE2 receptor, the receptor through which the COVID-19 causing SARS-CoV-2 virus can enter the cells. The inside of the intestine is loaded with ACE2 receptors. However, until now it was unknown whether intestinal cells could actually get infected and produce virus particles.

Intestinal organoids

Researchers from the Hubrecht Institute, Erasmus MC and Maastricht University set out to determine whether the SARS-CoV-2 virus can directly infect the cells of the intestine, and if so, whether it can replicate there as well. They used human intestinal organoids: tiny versions of the human intestine that can be grown in the lab. Hans Clevers (Hubrecht Institute): "These organoids contain the cells of the human intestinal lining, making them a compelling model to investigate infection by SARS-CoV-2."

Infection of intestinal cells

When the researchers added the virus to the organoids, they were rapidly infected. The virus enters a subset of the cells in the intestinal organoids, and the number of cells that are infected increases over time. Using electron microscopy, an advanced way to visualize different components of the cell in great detail, the researchers found virus particles inside and outside the cells of the organoids. Peter Peters (Maastricht University): "Due to the lockdown, we all studied virtual slides of the infected organoids remotely from home."

The researchers investigated the response of the intestinal cells to the virus with RNA sequencing, a method to study which genes are active in the cells. This revealed that so-called interferon stimulated genes are activated. These genes are known to combat viral infection. Future work will focus on these genes more carefully, and on how they could be used to develop new treatments.

The researchers also cultured the organoids in different conditions that result in cells with higher and lower levels of the ACE2 receptor, through which SARS-CoV-2 can enter the cells. To their surprise, they found that the virus infected cells with both high and low levels of the ACE2 receptor. Ultimately, these studies may lead to new ways to block the entry of the virus into our cells.

Implications

Bart Haagmans (Erasmus MC): "The observations made in this study provide definite proof that SARS-CoV-2 can multiply in cells of the gastrointestinal tract. However, we don't yet know whether SARS-CoV-2, present in the intestines of COVID-19 patients, plays a significant role in transmission. Our findings indicate that we should look into this possibility more closely." The current study is in line with other recent studies that identified gastrointestinal symptoms in a large fraction of COVID-19 patients and virus in the stool of patients free of respiratory symptoms. Special attention may be needed for those patients with gastrointestinal symptoms. More extensive testing using not only nose and throat swabs, but also rectal swabs or stool samples may thus be needed.

In the meantime, the researchers are continuing their collaboration to learn more about COVID-19. They are studying the differences between infections in the lung and the intestine by comparing lung and intestinal organoids infected with SARS-CoV-2.

Publication

SARS-CoV-2 productively Infects Human Gut Enterocytes. Mart M. Lamers, Joep Beumer*, Jelte van der Vaart*, Kèvin Knoops, Jens Puschhof, Tim I. Breugem, Raimond B.G. Ravelli, J. Paul van Schayck, Anna Z. Mykytyn, Hans Q. Duimel, Elly van Donselaar, Samra Riesebosch, Helma J.H. Kuijpers, Debby Schipper, Willine J. van de Wetering, Miranda de Graaf, Marion Koopmans, Edwin Cuppen, Peter J. Peters, Bart L. Haagmans† and Hans Clevers†. Science 2020. DOI * Equal contribution, † equal contribution.*

This study was a collaboration between the Hubrecht Institute in Utrecht, the Erasmus MC University Medical Center Rotterdam, Maastricht University, the UMC Utrecht and Single Cell Discoveries in the Netherlands. The microscopy data are publicly available via the Image Data Resource (idr0083, https://idr.openmicroscopy.org - with help from the University of Dundee and the European Bioinformatics Institute) and the genomic data are publicly available via the Gene Expression Omnibus (GSE149312, https://www.ncbi.nlm.nih.gov/geo), to ensure efficient sharing of data related to COVID-19 between researchers all across the world.

Hans Clevers is principal investigator at the Hubrecht Institute and the Princess Máxima Center for Pediatric Oncology, professor of Molecular Genetics at the UMC Utrecht and Utrecht University, and Oncode Investigator. Bart Haagmans is a principal investigator at the Viroscience department at the Erasmus MC University Medical Center Rotterdam. Peter Peters is director and principal investigator at the Maastricht Multimodal Molecular Imaging Institute (M4i) and professor of Nano Biology at the Maastricht University and Maastricht University Medical Center.

https://bit.ly/35rJqjT

COVID-19 Deaths Are Being Linked to Vitamin D Deficiency. Here's What That Means

A vitamin commonly produced by sun-exposed skin cells might play a role in preventing death by the coronavirus SARS-CoV-2, according to new research.

Mike McRae

Preliminary results from a yet-to-be-peer-reviewed study carried out by scientists from the Queen Elizabeth Hospital Foundation Trust and the University of East Anglia have linked low levels of the hormone vitamin D with COVID-19 mortality rates across Europe.

It's a study that certainly deserves some attention as a potential piece of the coronavirus puzzle, reminding us that health and disease can be a complex affair involving a variety of lifestyle factors.

But it's also important to interpret evidence like this as part of a bigger scientific conversation, meaning it would be premature to make any recommendations and *certainly* way too premature to hit the supplement aisle before further evidence arrives.

The researchers dug through existing health literature to catalogue the average levels of vitamin D among the citizens of 20 European countries, and then compared the figures with the relative numbers of COVID-19 deaths in each country.

A simple statistical test showed there was a pretty convincing correlation between the figures, where populations with lower than average concentrations of the vitamin also featured more deaths from SARS-CoV-2. "The most vulnerable group of population for COVID-19 is also the one that has the most deficit in vitamin D," the researchers conclude in their preliminary report.

Cross-sectional reports like these aren't without their problems, doing little more than suggesting some kind of relationship might exist. People who tend to have higher vitamin D levels in their body might be doing something else that helps limit destruction caused by the virus, for example.

But the results aren't surprising either, falling in line with previous, more robust studies that also suggest healthy vitamin D levels can reduce the risk of respiratory infections such as influenza and tuberculosis, as well as childhood asthma.

Vitamin D is a fat-soluble compound we can either get as a nutrient from foods like mushrooms or fish, or produced in our skin when a form of cholesterol reacts to UV light.

Commonly known for its role in maintaining calcium levels in our bones, deficiency in this vitamin is responsible for skeletal

deformities such as rickets as well as an increased risk of bone degeneration behind conditions such as osteoporosis.

Researchers are gradually piecing together the vitamin's functions in the immune system as well, noting its relationship with autoimmune conditions and the discovery of receptors for the chemical on various immune cells.

Just how it might combat coronavirus infections – if at all – is sure to be a popular subject in future studies. Meanwhile, as uncontroversial as the results might be, a single study ahead of peer review shouldn't be the basis for medical advice. Science just doesn't support making the leap between reading about healthy amounts of vitamin D in the blood and popping a supplement.

In 2017, medical researchers Mark J Bolland from the University of Auckland in New Zealand and Alison Avenell from the University of Aberdeen in the UK argued the need for caution over how we interpret studies not unlike this one. "Vitamin D supplementation is a hot topic, provoking passionate arguments for and against widespread supplementation," they write in an editorial on the diverse array of studies on the subject in the past decade.

Results might look positive, but there's just no way to turn a jumble of statistics into precise recommendations that can be tailored for individual needs. Even the World Health Organisation is tentative about using past research as the basis of specific recommendations.

"We think that they should be viewed as hypothesis generating only, requiring confirmation in well-designed, adequately powered randomised controlled trials," Bolland and Avenell write.

Research that speculates a single, commonly available vitamin might make the difference between life and death can seem like a potential life raft in choppy waters, but we need more research to tell us just how and why these patterns exist for us to balance the risks that come with vitamin supplements.

In the midst of a pandemic that has the potential to claim thousands of lives around the world every week, science feels painstakingly slow. But it's always worth the wait.

The paper is available as a pre-print on Research Square.

https://bit.ly/2xytYWO

Timing of immune response to COVID-19 may contribute to disease severity

The interaction between the innate and the adaptive immune responses to COVID-19 may be impacting disease progression, according to a new study from the Keck School of Medicine of USC

A new USC study suggests that temporarily suppressing the body's immune system during the early stages of COVID-19 could help a patient avoid severe symptoms.

That's because the research, just published online in the *Journal of Medical Virology*, shows that an interaction between the body's two main lines of defense may be causing the immune system to go into overdrive in some patients.

The body's first line of defense, the innate immune response, starts right after an infection, like an infantry going after a foreign invader, killing the virus and any cells damaged by it. The second line of defense, the adaptive immune response, kicks in days later if any virus remains, employing what it has learned about the virus to mobilize a variety of special forces such as T cells and B cells.

Using the "target cell-limited model," a common mathematical model developed to understand the dynamics of viral infections, the researchers examined how the two immune responses work in COVID-19 patients compared to patients who have the flu.

The flu is a fast-moving infection that attacks certain target cells on the surface of the upper respiratory system and kills almost all of the target cells within two to three days. The death of these cells deprives the virus of more targets to infect and allows the innate

immune response time to clear the body of almost all of the virus before the adaptive system comes into play.

Adaptive immune response kicking in too soon

But COVID-19, which targets surface cells throughout the respiratory system including in the lungs, has an average incubation of six days and a much slower disease progression. Mathematical modeling suggests that the adaptive immune response may kick in before the target cells are depleted, slowing down the infection and interfering with the innate immune response's ability to kill off most of the virus quickly.

"The danger is, as the infection keeps going on, it will mobilize the whole of the adaptive immune response with its multiple layers," said Weiming Yuan, associate professor in the Department of Molecular Microbiology and Immunology at the Keck School of Medicine of USC, and co-corresponding author of the study. "This longer duration of viral activity may lead to an overreaction of the immune system, called a cytokine storm, which kills healthy cells, causing tissue damage."

The interaction of the innate and the adaptive immune responses might also explain why some COVID-19 patients experience two waves of the disease, appearing to get better before eventually getting much worse. "Some COVID-19 patients may experience a resurgence of the disease after an apparent easing of symptoms," said Sean Du, adjunct researcher and lead author of the study. "It's possible that the combined effect of the adaptive and the innate immune responses may reduce the virus to a low level temporarily. However, if the virus is not completely cleared, and the target cells regenerate, the virus can take hold again and reach another peak."

Counterintuitive treatment

The most provocative result of the research is the kind of treatment it suggests to prevent this interaction between the two immune responses.

"Based on the results of the mathematical modeling, we proposed a counterintuitive idea that a short regimen of a proper immunosuppressant drug applied early in the disease process may improve a patient's outcome," said Du. "With the right suppressive agent, we may be able to delay the adaptive immune response and prevent it from interfering with the innate immune response, which enables faster elimination of the virus and the infected cells."

Small studies out of China, including a recent one of COVID-19 patients and one of SARS patients in 2003 show patients who received immunosuppressants such as corticosteroids had better results than those who did not.

The researchers said a possible next step could be to take daily measurements of viral loads and other biomarkers in COVID-19 patients, to see if the data validates the mathematical modeling. More preclinical studies including experiments in animal models will also be needed to prove the efficacy of an early immune suppressing treatment.

About this study

This study was supported by the National Institute of Allergy and Infectious Diseases (R21AI149365) and partially supported by a National Institutes of Health (P30CA014089) grant to the University of Southern California Norris Comprehensive Cancer Center.

https://bit.ly/2SydLrS

The Before Times of a Solar System

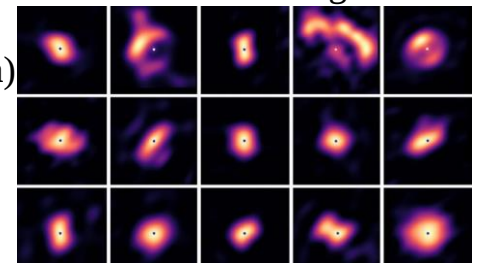
New observations of young stars capture the cosmic forces that can transform tiny particles into colossal worlds.

Marina Koren

Many moons ago, before the pandemic—before we even *had* moons—our home in the universe was a ring of glowing material, with the young sun in the center, like a donut sprinkled with cosmic dust and gas. Round and round the disk went, whisking particles around, until the material began to stick together in clumps. After millions of years, the clumps curved into the planets and the moons as we know them today, a rich assortment of worlds.

This is our story, but it has happened—*is* happening—countless times across the cosmos, around other stars. Astronomers have long known about such swirling structures, known as protoplanetary disks, which are the leftovers from the fiery birth of new suns.

Telescopes have even managed to observe them in stunning detail (well, as stunningly detailed as you can get many light-years from Earth) The latest batch of images, released this week, offers one of the highest-resolution views of these planetary nurseries yet.



Jacques Kluska, et al

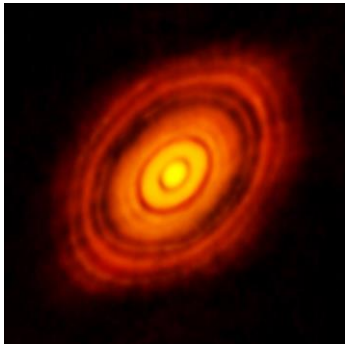
An international team of astronomers has captured images of the innermost rings of disks swirling around 15 stars, many hundreds of light-years away. Previous observations have never glimpsed this part of a protoplanetary disk, quite close to the parent star, this deeply before. To the untrained eye, the disks, shown at the top of this article, might look like bright splotches of oranges and purples. But to astronomers, they are *tantalizing* splotches of oranges and purples; there, in those blurry pixels close to the star, is where cosmic forces can transform tiny particles into colossal worlds—especially rocky planets like our own.

"It's an unexplored area," says Johanna Teske, an astronomer at the Carnegie Institution for Science, who was not involved in the new research.

According to theories of planet formation, a baby planet's position inside a protoplanetary disk dictates what kind of world it turns out to be. Gaseous worlds—like Jupiter and Saturn—arise farther out from their star, where it's cold enough for molecules to condense into ice and stay that way. Rocky worlds—like Earth and Mars—coalesce closer in, where the warmth of the star tends to evaporate icy material, but spares bits of rock. The thought of peering into these inner regions and searching for rocky planets, the only planets on which we know that life can arise, is a tantalizing one indeed.

None are visible in these images, mind you, but there are a few hints. Growing baby planets can perturb nearby matter in these disks, twisting and bending it. The indentations in some of the disks could be signs of material gathering in little whirlpools and sticking together, forming clumps with enough gravity of their own to tug at their surroundings.

Astronomers have found similar hints in other, more zoomed-out observations of protoplanetary disks. The rings in images like this one, for example, are likely the result of lurking planets carving a path through the dust and gas as they circle their star.



***ALMA* (ESO/NAOJ/NRAO)**

In 2018, astronomers even captured photographic evidence of a planet bending clouds of dust and gas around its young star, known as HL Tauri, as it swirled into being. They scrutinized the faint light emanating from the planet and discovered that it is an extremely hot, gaseous planet several times the mass of Jupiter. Perhaps another blood-orange-ish splotch to the rest of us, but a momentous discovery to researchers.

The newly released images are not quite photographs, at least not like the one above is. To observe the inner edges of these disks, astronomers blended together starlight absorbed by four different ground-based telescopes. This is a delightful hack in astronomy work: If a telescope isn't powerful enough to see a target, make a bigger one by syncing a bunch of small telescopes so that they scan the skies as one. (This is the same technique that produced the first-ever image of a black hole, which took 10 telescopes across four continents.)

The researchers then combined those data with mathematical models to reconstruct the finer details of the disks. The final result is a reconstruction of the real thing, though several astronomers who weren't involved in the research tell me it's a very good one. According to Jacques Kluska, the lead author of the research and an astronomer at KU Leuven, a university in Belgium, the views of the inner disks would amount to only a few pixels in a direct image from a single, powerful telescope. "These are pretty unprecedented physical scales," says Kate Folette, an astronomer at Amherst College who uses ground-based telescopes to search for planets around young stars, and wasn't involved in the latest work.

To peer much deeper into these disks of new beginnings, astronomers would need to use dozens of telescopes to simulate the resolution of an observatory much larger than anything currently in existence. Closer in, they could detect movements, patterns, orbits. They might even discover, in the cosmic fog, a rocky planet gliding at an Earth-like distance from its star. The view would present a perspective equally forward-looking and nostalgic: There would be the thrill of finding a world that might resemble ours, even though we cannot cross the unfathomable expanse to reach it. And there would be the realization of seeing the beginnings of our planet's own story, like uncovering a photograph from a past we don't remember. Until then, there is plenty to marvel at in our cosmic neighborhood, all grown up.

https://bbc.in/3deRbwq

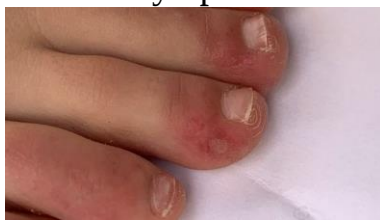
Coronavirus: 'Covid toe' and other rashes puzzle doctors

Five rashes, including Covid toe, are affecting some hospital patients diagnosed with Covid-19, a small study by Spanish doctors has found.

By Zoe Kleinman Reporter, BBC News

The rashes tended to appear in younger people and lasted several days. It is not uncommon for a rash to be a symptom of a virus, such as the spots that indicate chicken pox. But the researchers said they were surprised to see so many varieties of rash with Covid-19. Rashes are not currently included in the list of symptoms of the illness.

There have been many reports about "Covid toe" - a rash appearing on Covid patients' feet even in the absence of other symptoms - but lead researcher Dr Ignacio Garcia-Doval said the most common form of rash in the study was maculopapules - small, flat and raised red bumps that tend to appear on the torso.



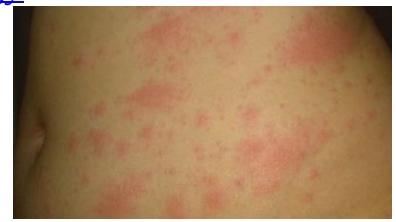
"Covid toe" is a rash that can look like chilblains **COVID-piel study**

"It is strange to see several different rashes - and some of them are quite specific," Dr Garcia-Doval told the BBC.

"It usually appears later on, after the respiratory manifestation of the disease - so it's not good for diagnosing patients," he added.

All the patients in the study were already in hospital and had respiratory symptoms. The peer-reviewed paper was published this week in the British Journal of Dermatology.

All dermatologists in Spain were asked to share details of Covid patients they had seen who had developed rashes in the previous two weeks. There were 375 in total.



The most commonly seen rash in the study affected nearly half of the patients **COVID-piel study**

The five rashes were:

Asymmetrical, chilblain-like lesions around the hands and feet, which could be itchy or painful. Generally found in younger patients, lasted on average 12 days, appeared later on in the course of the

disease, and were associated with mild infections. Accounted for 19% of cases.

Outbreaks of small blisters, often itchy, found on the trunk and limbs. These were found in middle-aged patients, lasted around 10 days, and appeared before other symptoms. (9%)

Pink or white raised areas of skin that looked like nettle rash, and often itchy. Mostly on the body but sometimes on the palms of the hands. (19%)

Maculopapules - small, flat and raised red bumps. These accounted for 47% of cases. They lasted around seven days and appeared at the same time as other symptoms but tended to be seen in patients with more severe infections.

Livedo (also known as necrosis) was present in 6% of cases. The skin looked blotchy red or blue, with a net-like pattern. It's a sign of poor blood circulation. This appeared in older patients with severe illness.

However, the researchers stressed that rashes can have many causes, and it can be difficult to differentiate between them without medical expertise.

"The relevance of this study is not so much in helping people self-diagnose, but rather to help build our wider understanding of how the infection can affect people," said Dr Ruth Murphy, president of the British Association of Dermatologists.

Dr Michael Head at the University of Southampton said that rashes were a well-known side effect of many viral infections, including pneumonia.

"With Covid-19, rashes and skin ulcers have been noted in a few per cent of hospitalised patients. We don't yet know the extent of these links, or precisely why this inflammation occurs in some patients but not others."

The American Academy of Determatology is also compiling a register of skin symptoms seen by its members.

https://bit.ly/2L1af4U

Researchers report discovery of antibody that blocks infection by the SARS-CoV-2 in cells

Utrecht University, Erasmus Medical Center and Harbour BioMed researchers report discovery of antibody that blocks infection by the novel coronavirus SARS-CoV-2 in cells

Researchers at Utrecht University, Erasmus Medical Center and Harbour BioMed (HBM) today reported that they have identified a fully human monoclonal antibody that prevents the SARS-CoV-2 (COVID-19) virus from infecting cultured cells. The discovery, published online today in *Nature Communications*, is an initial step towards developing a fully human antibody to treat or prevent the respiratory disease COVID-19 caused by the novel coronavirus SARS-CoV-2.

The COVID-19 pandemic has spread rapidly across the globe infecting more than 3.3M people worldwide and killing more than 235,000 people so far.

"This research builds on the work our groups have done in the past on antibodies targeting the SARS-CoV that emerged in 2002/2003," said Berend-Jan Bosch, Associate Professor, Research leader at Utrecht University, and co-lead author of the *Nature Communications* study. "Using this collection of SARS-CoV antibodies, we identified an antibody that also neutralizes infection of SARS-CoV-2 in cultured cells. Such a neutralizing antibody has potential to alter the course of infection in the infected host, support virus clearance or protect an uninfected individual that is exposed to the virus."

Dr. Bosch noted that the antibody binds to a domain that is conserved in both SARS-CoV and SARS-CoV-2, explaining its ability to neutralize both viruses. "This cross-neutralizing feature of the antibody is very interesting and suggests it may have potential

in mitigation of diseases caused by future-emerging related coronaviruses."

"This discovery provides a strong foundation for additional research to characterize this antibody and begin development as a potential COVID-19 treatment," said Frank Grosveld, PhD. co-lead author on the study, Academy Professor of Cell Biology, Erasmus Medical Center, Rotterdam and Founding Chief Scientific Officer at Harbour BioMed. "The antibody used in this work is 'fully human,' allowing development to proceed more rapidly and reducing the potential for immune-related side effects." Conventional therapeutic antibodies are first developed in other species and then must undergo additional work to 'humanize' them. The antibody was generated using Harbour BioMed's H2L2 transgenic mouse technology.

"This is groundbreaking research," said Dr. Jingsong Wang, Founder, Chairman & Chief Executive Officer of HBM. "Much more work is needed to assess whether this antibody can protect or reduce the severity of disease in humans. We expect to advance development of the antibody with partners. We believe our technology can contribute to addressing this most urgent public health need and we are pursuing several other research avenues."

The paper is titled, "A human monoclonal antibody blocking SARS-VoV-2 Infection. In addition to Drs. Bosch and Grosveld, authors on the paper included: Chunyan Wang, Wentao Li and Frank van Kuppeveld of Utrecht University; Nisreen Okba and Bart Haagmans of Erasmus Medical Center (Rotterdam); Dubravka Drabek and Rien van Haperen of Erasmus Medical Center and Harbour Antibodies; and Albert Osterhaus of the University of Veterinary Medicine (Hannover, Germany).

https://www.nature.com/articles/s41467-020-16256-y