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The first stages of DNA evolution

Scientists at the LMU investigated the first stages of molecular evolution inside dew water droplets, to mimic the early moments of the origin of life on Earth.

One fundamental question in the field of the Origin of Life is how the first molecules of DNA replicated and evolved on the primordial Earth, more than 4 billion years ago. Before the emergence of the first cells or any other form of compartmentalization, DNA and RNA molecules were likely dissolved into water ponds or into pores of rock filled with water and gas: ubiquitous conditions on a volcanic Earth. The high volcanic activity and the high temperatures were responsible for an atmosphere extremely rich in CO_2. The concentration of carbon dioxide was about 25,000 times higher than today.

These are the conditions that Prof. Dieter Braun and his research group at the faculty of physics (LMU) have been recreating: artificial "thermal traps" to mimic millimetric pores of rock filled with water and gaseous CO_2. Braun's team examined the replication and evolution of short DNA molecules under the most plausible primordial conditions.

The study highlights how local temperature differences can induce water cycles inside small pores of rock. The evaporation and condensation of water creates small dew droplets that acidify in the CO_2-rich atmosphere. The dew droplets were seen acting as primordial, membrane-less compartments that contain and concentrate DNA. The periodic condensation and evaporation of the dew droplets force the DNA molecules into cycles of neutral-acidic pH, high-low salts and wet-dry states.

Such fluctuations have a strong influence on the replication of short DNA strands. "We have found that dew droplets of acidic water in a primordial CO_2 atmosphere could enhance the replication of DNA molecules." says Alan Ianeselli, Ph.D. student and first author of the research. "Via salt, pH and wet-dry cycles, the dew promoted DNA mutations and recombinations, creating DNA strands up to 20 times longer than the initial ones."

During the replication cycles in the dew droplets, the initially short DNA molecules heavily mutate and become progressively longer, driven by the peculiar features of the millimetric water cycles. The physical conditions of the dew also induce a selection process on the DNA strands, creating DNA molecules enriched in specific sequence fingerprints.

These findings point towards the dew droplets as the first primordial compartments capable of hosting the replication and evolution of DNA molecules. The lab of Prof. Dieter Braun plans to characterize the effects of such dew cycles on a variety of prebiotic chemical reactions, from the abiotic synthesis of nucleotides to the assembly of large RNA complexes capable of self-replication.

More information: *Alan Ianeselli et al, Water cycles in a Hadean CO2 atmosphere drive the evolution of long DNA, Nature Physics (2022). DOI: 10.1038/s41567-022-01516-z*

https://bit.ly/35bKPiS

Saliva Testing for COVID-19 Is Quicker and Safer Than Nasal Swabs

Genetic testing of saliva samples identifies the SARS-CoV-2 virus more quickly than testing of nasal swabs.

The research is published today (March 21, 2022) in *Microbiology Spectrum*, a journal of the American Society for Microbiology.

“That is important because people can spread COVID-19 before they know that they have it,” said coauthor Donald K. Milton, M.D., DrPH, a professor of occupational and environmental health at the Institute for Applied Environmental Health, University of Maryland School of Public Health, College Park. “Earlier detection can reduce the disease’s spread.”

The research was motivated by the problem that early in the

pandemic, an urgent need to increase testing was accompanied by a shortage of supplies, notably nasal swabs, which were then the standard method for collecting samples for testing.

To identify people with COVID-19 the investigators began conducting weekly tests of saliva samples from healthy community volunteers in May 2020 and continued over the next 2 years. Of the asymptomatic volunteers who tested positive, Milton and his colleagues found that those patients would typically show symptoms a day or 2 later. "That made us wonder whether saliva was better for catching pre-symptomatic patients than the traditional nasal swabs," he said.

To answer that question, the researchers used data from a companion study of close contacts of people with confirmed cases of COVID-19. In the study, "We collected saliva and mid-turbinate [nasal] swab samples from contacts every 2 or 3 days during their quarantine period," said Milton. "All samples were tested using real-time reverse transcription polymerase chain reaction [RT-PCR] to detect SARS-CoV-2 and measure how much viral RNA was in the samples. We then analyzed how these results changed in the days before and after symptom onset."

"Early in the course of infection, saliva was significantly more sensitive than mid-turbinate nasal swabs," notably so before onset of symptoms, according to the study, which noted that previous studies had shown that pre-symptomatic transmission plays a greater role than symptomatic transmission of SARS-CoV-2.

The findings have implications for improving public acceptance of COVID-19 testing, reducing the cost of mass COVID-19 screening and improving the safety of healthcare workers who conduct testing. In the latter case, saliva self-testing avoids the close contact between patient and healthcare worker that nasal swabbing entails and avoids causing patients to cough and sneeze, thereby spreading virus particles as a result of swabbing the sensitive nasal passages, as well as discomfort to patients.

"Our research supports the use of saliva in large-scale screening in schools and workplaces, as a means of improving screening rates, as well as early detection," said Milton. "We expect that if rapid saliva tests become available, they could be a major advance from the current nasal swab-based rapid tests."

Reference: "Comparison of Saliva and Midturbinate Swabs for Detection of SARS-CoV-2" by Jianyu Lai, Jennifer German, Filbert Hong, S.-H. Sheldon Tai, Kathleen M. McPhaul and Donald K. Milton for the University of Maryland StopCOVID Research Group, 21 March 2022, Microbiology Spectrum. DOI: 10.1128/spectrum.00128-22

https://bit.ly/3NzBPFR

Bacteria-shredding insect wings inspire new antibacterial packaging

Inspired by the bacteria-killing wings of insects like cicadas, scientists have developed a natural antibacterial texture for use on food packaging to improve shelf life and reduce waste.

The lab-made nanotexture from an Australian-Japanese team of scientists kills up to 70% of bacteria and retains its effectiveness when transferred to plastic.

More than 30% of food produced for human consumption becomes waste, with entire shipments rejected if bacterial growth is detected. The research sets the scene for significantly reducing waste, particularly in meat and dairy exports, as well as extending the shelf life and improving the quality, safety and integrity of packaged food on an industrial scale.

Distinguished Professor Elena Ivanova of RMIT University said the research team had successfully applied a natural phenomenon to a synthetic material—plastic. "Eliminating bacterial contamination is a huge step in extending the shelf life of food," she said.

"We knew the wings of cicadas and dragonflies were highly-efficient bacteria killers and could help inspire a solution, but replicating nature is always a challenge. We have now created a nanotexturing that mimics the bacteria-destroying effect of insect

wings and retains its antibacterial power when printed on plastic. This is a big step towards a natural, non-chemical, antibacterial packaging solution for the food and manufacturing industry."

The research, published in *ACS Applied Nano Materials*, is a collaboration between RMIT, Tokyo Metropolitan University and Mitsubishi Chemical's The KAITEKI Institute. In 2015, Australia exported $US 3.1 billion of food and agricultural exports to Japan, making it the 5th largest exporter of such products to the country.

How it works

Dragonfly and cicada wings are covered by a vast array of nanopillars—blunted spikes of similar size to bacteria cells. When bacteria settle on a wing, the pattern of nanopillars pulls the cells apart, rupturing their membranes and killing them. "It's like stretching a latex glove," Ivanova said. "As it slowly stretches, the weakest point in the latex will become thinner and eventually tear."

Ivanova's team developed their nanotexture by replicating insects' nanopillars and developing nanopatterns of their own. To assess the pattern's antibacterial ability, bacteria cells were monitored at RMIT's world-class Microscopy and Microanalysis Facility. The best antibacterial patterns were shared with the Japan team, who developed a way to reproduce the patterns on plastic polymer.

Back in Australia, Ivanova's team tested the plastic nanopatterns and found the one which best replicated insect wings but is also easiest to fabricate and scale up. Ivanova said dealing with plastic was more difficult than other materials like silicon and metals, because of its flexibility. "The nanotexturing created in this study holds its own when used in rigid plastic. Our next challenge is adapting it for use on softer plastics," she said.

Since Ivanova and her colleagues discovered the bacteria killing nature of insect wings a decade ago, they've been working to design the optimal nanopattern to harness insects' bacteria-killing powers and use it on a range of materials. Until recently, it was difficult to find suitable technology to reproduce this nanotexturing on a scale suitable for manufacturing.

But now technology exists to scale up and apply antibacterial properties to packaging, among a range of other potential applications, like personal protective equipment.

Their new research builds on a 2020 study into using insect-inspired nanomaterials to fight superbugs. The team is keen to collaborate with potential partners in the next stage of the research—upscaling the technology and determining the best ways to mass manufacture the antibacterial packaging.

More information: *Denver P. Linklater et al, Nanopillar Polymer Films as Antibacterial Packaging Materials, ACS Applied Nano Materials (2022). DOI: 10.1021/acsanm.1c04251*

https://bit.ly/384AqPN

Genes Are Switched On in the Human Embryo From the Get-Go – Challenging the Way We Think About Our Developmental Origins

Challenges standard view that genes aren't active until embryos are made up of four-to-eight cells

The finding that some genes are active from the get-go challenges the textbook view that genes don't become active in human embryos until they are made up of four-to-eight cells, two or three days after fertilization.

The newly discovered activity begins at the one-cell stage – far sooner than previously thought – promising to change the way we think about our developmental origins.

The research, published recently in the journal *Cell Stem Cell*, was co-led by Professor Tony Perry at the University of Bath, Dr. Giles Yeo at the University of Cambridge, and Dr. Matthew VerMilyea at Ovation Fertility, US.

Using a method called RNA-sequencing, the team applied precision analysis to individual human eggs and one-cell embryos to make a

detailed inventory of tell-tale products of gene activity, called RNA transcripts.

It revealed that hundreds of genes awaken in human one-cell embryos. Because the gene activity starts small, previous techniques had not been sensitive enough to detect it. But state-of-the art RNA-sequencing used in this study was able to reveal even small changes.

"This is the first good look at the beginning of a biological process that we all go through – the transit through the one-cell embryo stage," said Professor Perry, from the Department of Biology and Biochemistry at Bath. "Without genome awakening, development fails, so it's a fundamental step."

The team found that many genes activated in one-cell embryos remain switched on until the four-to-eight cell stage, at which point they are switched off.

"It looks as if there is a sort of genetic shift-work in early embryos: the first shift starts soon after fertilization, in one-cell embryos, and a second shift takes over at the eight-cell stage," said Professor Perry.

What human genome awakening tells us

At the moment of human fertilization, sperm and egg genomes – the collection of all of their genes – are inactive: the sperm and egg rely on transcripts produced when they were being formed for instructions that regulate their characteristics.

Transcripts provide essential instructions in all cells, and embryo cells are no exception. This means that it is essential for parental (sperm and egg) genomes to awaken in the new embryo. But when and how does this happen?

Understanding the process of genome awakening is important: it is a key piece of the jigsaw of development that promises a better understanding of disease, inheritance and infertility. The scientists found some activated genes that might be expected to play roles in early embryos, but the roles of others were unknown and could point to embryonic events that we don't yet understand.

The team's findings also shine a light on how the genes are activated. "Although the trigger for activation is thought to come from the egg, it's not known how; now we know which genes are involved, we can locate their addresses and use molecular techniques to find out," said Professor Perry.

The link with cancer

Remarkably, candidates that might trigger gene activation include factors usually associated with cancer, such as some well-known oncogenes. This led the researchers to speculate that the natural, healthy role of factors that are known to misbehave in cancer, is to awaken genes in one-cell embryos. If this proves to be correct, the team's findings could illuminate events that initiate cancer, providing new diagnostic and preventive opportunities.

The findings also have clinical implications for the inheritance of acquired traits, such as obesity: parents who gain weight seem to pass the trait to their kids. It is not known how such acquired traits are transmitted, but altering gene activation after fertilisation is a possible mechanism.

As Dr Yeo from the Medical Research Council Metabolic Diseases Unit at Cambridge suggests, "If true, we should be able to see this altered gene activation signature at the one cell stage."

The team also looked at unhealthy one-cell embryos that do not go on to develop, and found that many of their genes fail to activate. Abnormal embryos have been used to evaluate methods of human heritable genome editing, but the new findings suggest they may be inappropriate as a reliable test system.

Reference: "Human embryonic genome activation initiates at the one-cell stage" by Maki Asami, Brian Y.H. Lam, Marcella K. Ma, Kara Rainbow, Stefanie Braun, Matthew D. VerMilyea, Giles S.H. Yeo and Anthony C.F. Perry, 21 December 2021, Cell Stem Cell.
DOI: 10.1016/j.stem.2021.11.012

https://bit.ly/36NSLHo

In a first, brain implant lets man with complete paralysis spell out thoughts: 'I love my cool son.'

Surgically placed electrodes enable person with late-stage ALS to communicate via neural signals

By Kelly Servick

In its final stages, the neurological disease amyotrophic lateral sclerosis (ALS) can bring extreme isolation. People lose control of their muscles, and communication may become impossible. But with the help of an implanted device that reads his brain signals, a man in this "complete" locked-in state could select letters and form sentences, researchers report this week.

"People have really doubted whether this was even feasible," says Mariska Vansteensel, a brain-computer interface researcher at the University Medical Center Utrecht who was not involved in the study, published in *Nature Communications*. If the new spelling system proves reliable for all people who are completely locked in—and if it can be made more efficient and affordable—it might allow thousands of people to reconnect to their families and care teams, says Reinhold Scherer, a neural engineer at the University of Essex.

ALS destroys the nerves that control movement, and most patients die within 5 years of diagnosis. When a person with ALS can no longer speak, they can use an eye-tracking camera to select letters on a screen. Later in the disease's progression, they can answer yes-or-no questions with subtle eye movements. But if a person chooses to prolong their life with a ventilator, they may spend months or years able to hear but not communicate.

In 2016, Vansteensel's team reported that a woman with ALS could spell out sentences with a brain implant that detected attempts to move her hand. But this person still had minimal control of some eye and mouth muscles. It wasn't clear whether a brain that has lost all control over the body can signal intended movements consistently enough to allow meaningful communication.

The participant in the new study, a man with ALS who is now 36, started to work with a research team at the University of Tübingen in 2018, when he could still move his eyes. He told the team he wanted an invasive implant to try to maintain communication with his family, including his young son. His wife and sister provided written consent for the surgery.

Consent for this type of study comes with ethical challenges, says Eran Klein, a neurologist and neuroethicist at the University of Washington, Seattle. This man wouldn't have been able to change his mind or opt out during the period after his last eye-movement communication.

Researchers inserted two square electrode arrays, 3.2 millimeters wide, into a part of the brain that controls movement. When they asked the man to try to move his hands, feet, head, and eyes, the neural signals weren't consistent enough to answer yes-or-no questions, says Ujwal Chaudhary, a biomedical engineer and neurotechnologist at the German nonprofit ALS Voice.

After nearly 3 months of unsuccessful efforts, the team tried neurofeedback, in which a person attempts to modify their brain signals while getting a real-time measure of whether they are succeeding. An audible tone got higher in pitch as the electrical firing of neurons near the implant sped up, lower as it slowed. Researchers asked the participant to change that pitch using any strategy. On the first day, he could move the tone, and by day 12, he could match it to a target pitch. "It was like music to the ear," Chaudhary recalls. The researchers tuned the system by searching for the most responsive neurons and determining how each changed with the participant's efforts.

By holding the tone high or low, the man could then indicate "yes" and "no" to groups of letters, and then individual letters. After

about 3 weeks with the system, he produced an intelligible sentence: a request for caregivers to reposition him. In the year that followed, he made dozens of sentences at a painstaking rate of about one character per minute: "Goulash soup and sweet pea soup." "I would like to listen to the album by Tool loud." "I love my cool son."

He eventually explained to the team that he modulated the tone by trying to move his eyes. But he did not always succeed. Only on 107 of 135 days reported in the study could he match a series of target tones with 80% accuracy, and only on 44 of those 107 could he produce an intelligible sentence.

"We can only speculate" about what happened on the other days, Vansteensel says. The participant may have been asleep or simply not in the mood. Maybe the brain signal was too weak or variable to optimally set the computer's decoding system, which required daily calibration. Relevant neurons may have drifted in and out of range of the electrodes, notes co-author Jonas Zimmermann, a neuroscientist at the Wyss Center for Bio and Neuroengineering.

Still, the study shows it's possible to maintain communication with a person as they become locked in by adapting an interface to their abilities, says Melanie Fried-Oken, who studies brain-computer interface at Oregon Health & Science University. "It's so cool." But hundreds of hours went into designing, testing, and maintaining the personalized system, she notes. "We're nowhere near getting this into an assistive technology state that could be purchased by a family."

The demonstration also raises ethical questions, Klein says. Discussing end-of-life care preferences is difficult enough for people who can speak, he notes. "Can you have one of those really complicated conversations with one of these devices that only allows you to say three sentences a day? You certainly don't want to misinterpret a word here or a word there." Zimmermann says the research team stipulated the participant's medical care shouldn't depend on the interface. "If the speller output were, 'unplug my ventilator,' we wouldn't." But, he adds, it's up to family members to interpret a patient's wishes as they see fit.

Chaudhary's foundation is seeking funding to give similar implants to several more people with ALS. He estimates the system would cost close to $500,000 over the first 2 years. Zimmermann and colleagues, meanwhile, are developing a signal processing device that attaches to the head via magnets rather than anchoring through the skin, which carries a risk of infection.

So far, devices that read signals from outside the skull haven't allowed spelling. In 2017, a team said it could classify with 70% accuracy yes-or-no answers from the brain of a completely locked-in participant using a noninvasive technology called functional near-infrared spectroscopy (fNIRS). Two co-authors on the new study, Chaudhary and University of Tübingen neuroscientist Niels Birbaumer, were part of that team. But other researchers have voiced concerns about the study's statistical analysis. Two investigations found misconduct in 2019, and two papers were retracted. The authors sued to challenge the misconduct findings, Chaudhary says. Scherer, who was skeptical of the fNIRS study, says the results with the invasive device are "definitely sounder."

Wyss Center researchers continue to work with this study participant, but his ability to spell has decreased, and he now mostly answers yes-or-no questions, Zimmermann says. Scar tissue around the implant is partly to blame because it obscures neural signals, he says. Cognitive factors could play a role, too: The participant's brain may be losing the ability to control the device after years of being unable to affect its environment. But the research team has committed to maintaining the device as long as he continues to use it, Zimmermann says. "There's this huge responsibility. We're quite aware of that."

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Cosmic Milestone: NASA Confirms 5,000 Exoplanets – "It Is Inevitable That We'll Find Some Kind of Life Somewhere"

The count of confirmed exoplanets just ticked past the 5,000 mark, representing a 30-year journey of discovery led by NASA space telescopes.

Not so long ago, we lived in a universe with only a small number of known planets, all of them orbiting our Sun. But a new raft of discoveries marks a scientific high point: More than 5,000 planets are now confirmed to exist beyond our solar system.

The planetary odometer turned on March 21, with the latest batch of 65 exoplanets – planets outside our immediate solar family – added to the NASA Exoplanet Archive. The archive records exoplanet discoveries that appear in peer-reviewed, scientific papers, and that have been confirmed using multiple detection methods or by analytical techniques.

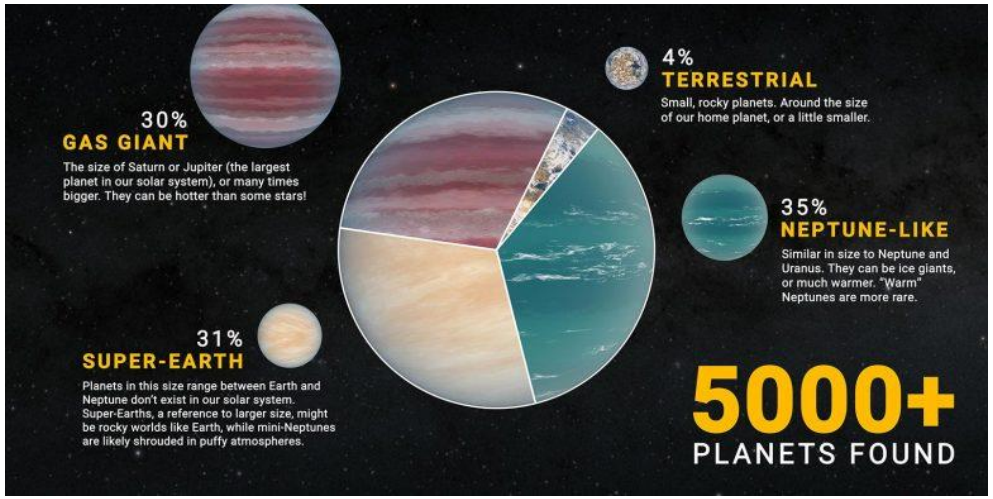
The 5,000-plus planets found so far include small, rocky worlds like Earth, gas giants many times larger than Jupiter, and "hot Jupiters" in scorchingly close orbits around their stars. There are "super-Earths," which are possible rocky worlds bigger than our own, and "mini-Neptunes," smaller versions of our system's Neptune. Add to the mix planets orbiting two stars at once and planets stubbornly orbiting the collapsed remnants of dead stars.

"It's not just a number," said Jessie Christiansen, science lead for the archive and a research scientist with the NASA Exoplanet Science Institute at Caltech in Pasadena. "Each one of them is a new world, a brand-new planet. I get excited about every one because we don't know anything about them."

We do know this: Our galaxy likely holds hundreds of billions of such planets. The steady drumbeat of discovery began in 1992 with strange new worlds orbiting an even stranger star. It was a type of neutron star known as a pulsar, a rapidly spinning stellar corpse that pulses with millisecond bursts of searing radiation. Measuring slight changes in the timing of the pulses allowed scientists to reveal planets in orbit around the pulsar.

Finding just three planets around this spinning star essentially opened the floodgates, said Alexander Wolszczan, the lead author on the paper that, 30 years ago, unveiled the first planets to be confirmed outside our solar system.

"If you can find planets around a neutron star, planets have to be basically everywhere," Wolszczan said. "The planet production process has to be very robust."



The more than 5,000 exoplanets confirmed in our galaxy so far include a variety of types – some that are similar to planets in our solar system, others vastly different. Among these are a mysterious variety known as "super-Earths" because they are larger than our world and possibly rocky. **Credit: NASA/JPL-Caltech**

Wolszczan, who still searches for exoplanets as a professor at Penn State, says we're opening an era of discovery that will go beyond simply adding new planets to the list. The Transiting Exoplanet Survey Satellite (TESS), launched in 2018, continues to make new

exoplanet discoveries. But soon powerful next-generation telescopes and their highly sensitive instruments, starting with the recently launched James Webb Space Telescope, will capture light from the atmospheres of exoplanets, reading which gases are present to potentially identify tell-tale signs of habitable conditions.

The Nancy Grace Roman Space Telescope, expected to launch in 2027, will make new exoplanet discoveries using a variety of methods. The ESA (European Space Agency) mission ARIEL, launching in 2029, will observe exoplanet atmospheres; a piece of NASA technology aboard, called CASE, will help zero in on exoplanet clouds and hazes.

"To my thinking, it is inevitable that we'll find some kind of life somewhere – most likely of some primitive kind," Wolszczan said. The close connection between the chemistry of life on Earth and chemistry found throughout the universe, as well as the detection of widespread organic molecules, suggests detection of life itself is only a matter of time, he added.

How to Find Other Worlds

The picture didn't always look so bright. The first planet detected around a Sun-like star, in 1995, turned out to be a hot Jupiter: a gas giant about half the mass of our own Jupiter in an extremely close, four-day orbit around its star. A year on this planet, in other words, lasts only four days.

More such planets appeared in the data from ground-based telescopes once astronomers learned to recognize them – first dozens, then hundreds. They were found using the "wobble" method: tracking slight back-and-forth motions of a star, caused by gravitational tugs from orbiting planets. But still, nothing looked likely to be habitable.

Finding small, rocky worlds more like our own required the next big leap in exoplanet-hunting technology: the "transit" method. Astronomer William Borucki came up with the idea of attaching extremely sensitive light detectors to a telescope, then launching it into space. The telescope would stare for years at a field of more than 170,000 stars, searching for tiny dips in starlight when a planet crossed a star's face.

That idea was realized in the Kepler Space Telescope.

Borucki, principal investigator of the now-retired Kepler mission, says its launch in 2009 opened a new window on the universe.

"I get a real feeling of satisfaction, and really of awe at what's out there," he said. "None of us expected this enormous variety of planetary systems and stars. It's just amazing."

https://wb.md/3qG68Rn

Ivermectin Did Not Reduce COVID Hospitalizations, Study Shows

The anti-parasitic drug ivermectin does not reduce hospitalizations of people infected with COVID-19, according to a large study conducted in Canada.

Ralph Ellis

Researchers at McMaster University in Ontario studied around 1,358 COVID patients who were at risk for severe disease because they had diabetes or other conditions, *The Wall Street Journal* reported. Half the patients were given a course of ivermectin pills for three days and the other half a placebo. Researchers then tracked the patients to see if any of them had been hospitalized.

"There was no indication that ivermectin is clinically useful," Edward Mills, one of the study's lead researchers and a professor of health sciences at McMaster University, told *The Wall Street Journal.*

The FDA has not approved any form of ivermectin to treat COVID-19. Several previous studies found ivermectin is ineffective against COVID, and last month a study published in JAMA Internal Medicine said it does not help treat mild to moderate COVID-19.

"This is the first large, prospective study that should really help put

to rest ivermectin and not give any credibility to the use of it for Covid-19," Peter Hotez, MD, dean of the National School of Tropical Medicine at Baylor College of Medicine, told *The Wall Street Journal.*

Still, some doctors prescribe ivermectin as a COVID treatment and some anti-vaccine advocates cite it as a useable alternative.

The FDA warns people not to confuse the ivermectin designed for humans and the ivermectin designed for animals.

The FDA says it approved tablets to treat people with intestinal strongyloidiasis and onchocerciasis, conditions caused by parasitic worms, and topical medications for head lice and skin conditions like rosacea. A different form of ivermectin is used to treat horses and cows for heartworm disease and parasites and is applied as pour-on, injectable, paste, or "drench."

Ivermectin products for animals are dangerous for humans, and the ivermectin tablets for humans are not effective against COVID, the FDA says.

Source *The Wall Street Journal: "Ivermectin Didn't Reduce Covid-19 Hospitalizations in Largest Trial to Date"*

https://bit.ly/36s3nfC

Researchers find humans have given wild animals their diseases nearly 100 times

An international research team led by scientists at Georgetown University has found that humans might give viruses back to animals more often than previously understood.

In a study published March 22 in *Ecology Letters* ("Assessing the risk of human-to-wildlife pathogen transmission for conservation and public health"), the authors describe nearly one hundred different cases where diseases have undergone "spillback" from humans back into wild animals, much like how SARS-CoV-2 has been able to spread in mink farms, zoo lions and tigers, and wild white-tailed deer.

"There has understandably been an enormous amount of interest in human-to-wild animal pathogen transmission in light of the pandemic," says Gregory Albery, Ph.D., a postdoctoral fellow in the Department of Biology at Georgetown University and the study's senior author. "To help guide conversations and policy surrounding spillback of our pathogens in the future, we went digging through the literature to see how the process has manifested in the past."

In their new study, Albery and colleagues found that almost half of the incidents identified occurred in captive settings like zoos, where veterinarians keep a close eye on animals' health and are more likely to notice when a virus makes the jump. Additionally, more than half of cases they found were human-to-primate transmission, an unsurprising result both because pathogens find it easier to jump between closely-related hosts, and because wild populations of endangered great apes are so carefully monitored.

"This supports the idea that we're more likely to detect pathogens in the places we spend a lot of time and effort looking, with a disproportionate number of studies focusing on charismatic animals at zoos or in close proximity to humans" says Anna Fagre, DVM, Ph.D., MPH, a virologist and wildlife veterinarian at Colorado State University who was lead author on the study, and has also published research on the risks of SARS-CoV-2 spillback using laboratory experiments with the North American deer mouse (*Peromyscus maniculatus*). "It brings into question which cross-species transmission events we may be missing, and what this might mean not only for public health, but for the health and conservation of the species being infected."

Disease spillback has recently attracted substantial attention due to the spread of SARS-CoV-2, the virus that causes COVID-19, in wild white-tailed deer in the United States and Canada. Some data suggest that deer have given the virus back to humans in at least

one case, and many scientists have expressed broader concerns that new animal reservoirs might give the virus extra chances to evolve new variants.

In their new study, Albery and colleagues find a sliver of good news: scientists can use artificial intelligence to anticipate which species might be at risk of contracting the virus. When the researchers compared species that have been infected with SARS-CoV-2 to predictions made by other researchers earlier in the pandemic, they found that scientists were able to guess correctly more often than not.

"It's quite satisfying to see that sequencing animal genomes and understanding their immune systems has paid off," says Colin Carlson, Ph.D., an assistant research professor in the Center for Global Health Science and Security at Georgetown University Medical Center and an author on the study. "The pandemic gave scientists a chance to test out some predictive tools, and it turns out we're more prepared than we thought."

The new study is part of a National Science Foundation-funded project called the Viral Emergence Research Initiative, or Verena. The Verena team uses data science and machine learning to study "the science of the host-virus network"—a new field that aims to predict which viruses can infect humans, which animals host them and where, when and why they might emerge. Those insights could be critical if scientists want to understand how and why humans share their diseases with animals.

Spillover may be predictable, the authors conclude, but the biggest problem is how little we know about wildlife disease. "We're watching SARS-CoV-2 more closely than any other virus on earth, so when spillback happens, we can catch it. It's still much harder to credibly assess risk in other cases where we're not able to operate with as much information," says Carlson. As a result, it's hard to measure how severe a risk spillback poses for human health or wildlife conservation, particularly for pathogens other than SARS-CoV-2.

"Long-term monitoring helps us establish baselines for wildlife health and disease prevalence, laying important groundwork for future studies," says Fagre. "If we're watching closely, we can spot these cross-species transmission events much faster, and act accordingly."

More information: *Assessing the risk of human-to-wildlife pathogen transmission for conservation and public health, Ecology Letters (2022).*

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

Morgue data hint at COVID's true toll in Africa

Around 90% of deceased people tested at a Lusaka facility during coronavirus surges were positive for SARS-CoV-2 infection, suggesting flaws in the idea of an 'African paradox'.

Freda Kreier

Almost one-third of more than 1,000 bodies taken to a morgue in Lusaka in 2020 and 2021 tested positive for SARS-CoV-2, implying that many more people died of COVID-19 in Zambia's capital than official numbers suggest[1]. Some scientists say that the findings further undermine the 'African paradox', a narrative that the pandemic was less severe in Africa than in other parts of the world.

This idea arose after health experts noticed that sub-Saharan nations were reporting lower case numbers and fewer COVID-19 deaths than might be expected. But researchers say that the findings from Zambia could reflect a broader truth — that a deficit of testing and strained medical infrastructure have masked COVID-19's true toll on the continent. The findings have not yet been peer reviewed.

Ignoring the true extent of COVID-19 in Lusaka and beyond "is so wrong. People were ill. They've had their families destroyed," says co-author Christopher Gill, a global-health specialist at Boston University in Massachusetts. One of his colleagues in Zambia died

of COVID-19 while working on the project.

"It's not hypothetical to me," says Gill.

Missing COVID cases

When SARS-CoV-2 began spreading globally, many health researchers worried that the virus would devastate sub-Saharan Africa. But the surprisingly low numbers of reported COVID-19 cases in the region led to the perception "that severe debilitation and deaths caused by COVID-19 were somehow less in Africa compared to other continents", says Yakubu Lawal, an endocrinologist at the Federal Medical Centre Azare in Nigeria.

Lawal and other scientists speculated[2] that the relative youth of Africa's population might have helped to spare the continent, but also suspected that official numbers were under-reported. The question was by how much.

Seeking answers, Gill and his colleagues in Zambia tested bodies in one of Lusaka's largest morgues for SARS-CoV-2 over several months in 2020 and 2021. Test positivity was 32% overall — and reached around 90% during the peak of the waves caused by the Beta and Delta variants. Moreover, only 10% of the people whose bodies were found to contain the virus after death had tested positive while still alive. Some had falsely tested negative, but most had never been tested at all.

Although Gill and his colleagues can't confirm that all of these people died of COVID-19, the results still stand in sharp contrast to official numbers. So far, there have been fewer than 4,000 confirmed COVID-19 deaths in Zambia, a country of around 19 million people. Separate findings published on 10 March suggest that Zambia's 'excess' deaths — those above what would usually be expected — from 1 January 2020 to the end of 2021 exceeded 80,000[3].

The Lusaka numbers mesh with statistics from South Africa, where a 2021 study found that only 4–6% of SARS-CoV-2 infections in two communities were officially documented[4]. Further study of the same communities showed that 62% of study participants had been infected at least once from July 2020 to August 2021[5]. Co-author Cheryl Cohen, an epidemiologist at the University of the Witwatersrand in Johannesburg, South Africa, says that many of these infections were asymptomatic, but that people with symptoms might also have gone undetected because of the cost and difficulty of getting tested.

Gill suspects that a major reason for the gap between his results and official counts is that most people in Zambia who die of COVID-19 do so outside medical care. Four out of five people tested in the study were never admitted to a hospital; the majority of unreported infections were in people living in Lusaka's lowest-income neighbourhoods. "Nobody's vaccinated. Nobody has masks. Nobody has access to the medical care they need," says Gill. "We're in a population that is already stressed and unhealthy, and then — bam! In comes COVID."

Vast variation

But not everyone is convinced that the Lusaka findings invalidate the idea of the African paradox. In Ethiopia, for instance, "our experience is people get infected with the virus, are asymptomatic or have mild symptoms, and recover", says Amare Abera Tareke, a physiologist at Wollo University in Dessie. "While it is difficult to ignore the current finding, we have to take it cautiously."

Gill worries that the idea that Africa was spared the worst of the pandemic might have led people to take unnecessary risks or contributed to "the lack of urgency" in supplying African nations with vaccines. "I suppose this could be unique to Lusaka," he says, "But boy, you'd really have to try hard to explain why."

doi: https://doi.org/10.1038/d41586-022-00842-9

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https://bit.ly/3iH7gzz

New Type of UV Light Makes Indoor Air As Safe as Outdoors – Variant Proof & Effective Against COVID, Flu

Using far-UVC light in places where people gather indoors could help prevent the next pandemic.

A new type of ultraviolet light that is safe for people took less than five minutes to reduce the level of indoor airborne microbes by more than 98%, a joint study by scientists at Columbia University Vagelos College of Physicians and Surgeons and in the U.K. has found. Even as microbes continued to be sprayed into the room, the level remained very low as long as the lights were on.

The study suggests that far-UVC light from lamps installed in the ceiling could be a highly effective passive technology for reducing person-to-person transmission of airborne-mediated diseases such as COVID and influenza indoors, and lowering the risk of the next pandemic.

"Far-UVC rapidly reduces the amount of active microbes in the indoor air to almost zero, making indoor air essentially as safe as outdoor air," says David Brenner, PhD, director of the Center for Radiological Research at Columbia University Vagelos College of Physicians and Surgeons and co-author of the study. "Using this technology in locations where people gather together indoors could prevent the next potential pandemic."

The study was published March 23 in the journal *Scientific Reports*, a *Nature* journal.

"Far-UVC light is simple to install, it's inexpensive, it doesn't need people to change their behavior, and above all it's a safe way to prevent the transmission of any virus, including the COVID virus and its variants, as well as influenza and also any potential future pandemic viruses," Brenner says.

What is far-UVC light?

Disinfecting indoor air with far-UVC light is a new approach to safely and efficiently destroy airborne viruses in occupied spaces, including the viruses that cause COVID and influenza.

Scientists have known for decades that a type of ultraviolet light known as UVC light rapidly kills microbes, including bacteria and viruses. But conventional germicidal UVC light cannot be used directly to destroy airborne viruses in occupied indoor spaces because it is a potential health hazard to the skin and eyes.

About a decade ago, Columbia University scientists proposed that a different type of UVC light, known as far-UVC light, would be just as efficient at destroying bacteria and viruses but without the safety concerns of conventional germicidal UVC.

Far-UVC light is safe for people because it has a shorter wavelength than conventional germicidal UVC, so it can't penetrate into living human skin cells or eye cells. But it is equally efficient at killing bacteria and viruses, which are much smaller than human cells.

In the past decade, many studies around the world have shown that far-UVC is both efficient at destroying airborne bacteria and viruses and safe for use around people. But until now these studies had only been conducted in small experimental chambers, not in full-sized rooms mimicking real-world conditions.

New study shows far-UVC is highly effective in real room environment

In the current study, scientists at the University of St. Andrews, University of Dundee, University of Leeds, and Columbia University tested the efficacy of far-UVC light in a large room-sized chamber with the same ventilation rate as a typical home or office (about three air changes per hour).

During the experiment, a sprayer continuously emitted an aerosol mist of *S. aureus* bacteria into the room. (This microbe was chosen because it is slightly less sensitive to far-UVC light than coronaviruses, providing the researchers with an appropriately conservative model.) When the concentration of microbes in the room stabilized, the researchers turned on commercially available overhead far-UVC lamps.

At an intensity based on the current regulatory limit on far-UVC light exposure, set by the American Conference of Governmental Industrial Hygienists, the far-UVC lamps inactivated more than 98% of the airborne microbes in just five minutes. The low level of viable microbes was maintained over time, even though microbes continued to be sprayed into the room.

The efficacy of different approaches to reducing indoor virus levels is usually measured in terms of equivalent air changes per hour. In this study, far-UVC lamps produced the equivalent of 184 equivalent air exchanges per hour. This surpasses any other approach to disinfecting occupied indoor spaces, where five to 20 equivalent air changes per hour is the best that can be achieved practically.

"Our trials produced spectacular results, far exceeding what is possible with ventilation alone," says Kenneth Wood, PhD, lecturer in the School of Physics and Astronomy at the University of St. Andrews and senior author of the study. "In terms of preventing airborne disease transmission, far-UVC lights could make indoor places as safe as being outside on the golf course on a breezy day at St. Andrews."

Far-UVC light is variant-proof

"Previous studies have shown that far-UVC light can kill the COVID virus, other human coronaviruses, influenza, and drug-resistant bacteria," Brenner says. "What's particularly attractive about far-UVC technology as a practical method of preventing indoor disease transmission is that it will be equally good at inactivating all future COVID variants, as well as new infectious viruses that have yet to emerge, while retaining efficacy against 'old fashioned' viruses like influenza and measles."

Finally, because of the way ultraviolet light kills microbes, viruses and bacteria cannot develop resistance as they do with vaccines and drug treatments.

More information *The study, titled "Far-UVC (222 nm) efficiently inactivates an airborne pathogen in a room-sized chamber," was published in Scientific Reports on March 23. The authors are Ewan Eadie (Ninewells Hospital, Dundee, Scotland), Waseem Hiwar (University of Leeds, England), Louise Fletcher (University of Leeds), Emma Tidswell (University of Leeds), Paul O'Mahoney (University of Dundee), Manuela Buonanno (Columbia University), David Welch (Columbia University), Catherine Adamson (St. Andrews University, Scotland), David Brenner (Columbia University), Catherine Noakes (University of Leeds), and Kenneth Woods (University of St. Andrews).*

The study was supported by grants from the U.K. Health Security Agency.

David J. Brenner and co-inventors have been granted a U.S. patent titled "Apparatus, method and system for selectively affecting and/or killing a virus" (US1078019B2). Columbia University has licensed aspects of filtered UV light technology to USHIO Inc. and has received a research gift from LumenLabs, a company producing far-UVC sources. Other disclosures are noted in the paper.

Reference: "Far-UVC (222 nm) efficiently inactivates an airborne pathogen in a room-sized chamber" 23 March 2022, Scientific Reports. DOI: 10.1038/s41598-022-08462-z

https://bit.ly/3qGi59H

Male Contraceptive Pill Found 99% Effective in Mice, With No Observable Side Effects

Findings mark a key step towards expanding birth control options – as well as responsibilities – for men

Issam Ahmed, AFP

A team of scientists said Wednesday they had developed a male oral contraceptive that was 99 percent effective in mice and didn't

cause observable side effects, with the drug expected to enter human trials by the end of this year. The findings will be presented at the American Chemical Society's spring meeting, and mark a key step towards expanding birth control options – as well as responsibilities – for men.

Ever since the female birth control pill was first approved in the 1960s, researchers have been interested in a male equivalent, Md Abdullah Al Noman, a graduate student at the University of Minnesota who will present the work, told AFP. "Multiple studies showed that men are interested in sharing the responsibility of birth control with their partners," he said – but until now, there have been only two effective options available: condoms or vasectomies.

Vasectomy reversal surgery is expensive and not always successful. The female pill uses hormones to disrupt the menstrual cycle, and historic efforts to develop a male equivalent targeted the male sex hormone testosterone. The problem with this approach, however, was that it caused side effects such as weight gain, depression, and increased levels of a cholesterol known as low-density lipoprotein, which increases heart disease risks.

The female pill also carries side effects, including blood-clotting risks – but since women face becoming pregnant in the absence of contraception, the risk calculation differs.

Non-hormonal

To develop a non-hormonal drug, Noman, who works in the lab of Professor Gunda Georg, targeted a protein called "retinoic acid receptor (RAR) alpha". Inside the body, vitamin A is converted into different forms, including retinoic acid, which plays important roles in cell growth, sperm formation, and embryo development.

Retinoic acid needs to interact with RAR-alpha to perform these functions, and lab experiments have shown mice without the gene that creates RAR-alpha are sterile.

For their work, Noman and Georg developed a compound that blocks the action of RAR-alpha. They identified the best molecular structure with the help of a computer model. "If we know what the keyhole looks like, then we can make a better key – that's where the computational model comes in," said Noman.

Their chemical, known as YCT529, was also designed to interact specifically with RAR-alpha, and not two other related receptors RAR-beta and RAR-gamma, in order to minimize potential side effects.

Five years to market?

When administered orally to male mice for four weeks, YCT529 drastically reduced sperm counts and was 99 percent effective in preventing pregnancy in a mating trial. The researchers monitored weight, appetite, and overall activity, finding no apparent adverse impacts, although mice of course can't report side effects like headaches or mood changes. Four to six weeks after they were taken off the drug, the mice could once more sire pups.

The team, which received funding from the National Institutes of Health and the Male Contraceptive Initiative, is working with a company called YourChoice Therapeutics to start human trials by the third or fourth quarter of 2022, said Georg.

"I'm optimistic this will move forward quickly," she said, envisaging a possible timeline to market in five years or under.

"There is no guarantee that it will work...but I would really be surprised if we didn't see an effect in humans as well," she added.

A persistent question about future male contraceptive pills has been whether women will trust men to use them. But surveys have shown that most women would in fact have faith in their partners, and significant numbers of men have indicated they would be open to the medication. "Male contraceptives will add to the method mix, providing new options that allow men and women to contribute in whatever way they deem appropriate to contraceptive use," argues the nonprofit Male Contraceptive Initiative, which engages in

fundraising and advocacy.

https://bit.ly/388tjxd

An AI Experiment Generated 40,000 Hypothetical Bioweapons in Just 6 Hours

New research emphasizes how easily AI models can be trained for malicious purposes as well as good

David Nield

The cutting-edge number-crunching capabilities of artificial intelligence mean that AI systems are able to spot diseases early, manage chemical reactions, and explain some of the mysteries of the Universe. But there's a downside to this incredible and virtually limitless artificial brainpower.

New research emphasizes how easily AI models can be trained for malicious purposes as well as good, specifically in this case to imagine the designs for hypothetical bioweapon agents. A trial run with an existing AI identified 40,000 such bioweapon chemicals in the space of only six hours.

In other words, while AI can be incredibly powerful – and much, much faster than humans – when it comes to spotting chemical combinations and drug compounds to improve our health, the same power can be used to dream up potentially very dangerous and deadly substances.

"We have spent decades using computers and AI to improve human health – not to degrade it," the researchers write in a new commentary. "We were naive in thinking about the potential misuse of our trade, as our aim had always been to avoid molecular features that could interfere with the many different classes of proteins essential to human life."

The team ran the trial at an international security conference, putting an AI system called MegaSyn to work – not in its normal mode of operation, which is to detect toxicity in molecules in order to avoid them, but to do the opposite.

In the experiment, the toxic molecules were kept rather than eliminated. What's more, the model was also trained to put these molecules together in combinations – which is how so many hypothetical bioweapons were generated in so short a time.

In particular, the researchers trained the AI with molecules in databases of drug-like molecules, instructing that they'd like something similar to the potent nerve agent VX.

As it turned out, a lot of the generated compounds were even more toxic than VX. As a result, the authors behind the new study are keeping some of the details of their research secret, and have seriously debated whether or not to make these results public at all.

"By inverting the use of our machine learning models, we had transformed our innocuous generative model from a helpful tool of medicine to a generator of likely deadly molecules," the researchers explain.

In an interview with The Verge, Fabio Urbina – lead author of the new paper and senior scientist at Collaborations Pharmaceuticals, where the research took place – explained that it doesn't take much to "flip the switch" from good AI to bad AI.

While none of the listed bioweapons were actually explored or put together in a lab, the researchers say their experiment serves as a warning of the dangers of artificial intelligence – and it's a warning that humanity would do well to heed. While some expertise is required to do what the team did here, a lot of the process is relatively straightforward and uses publicly available tools.

The researchers are now calling for a "fresh look" at how artificial intelligence systems can potentially be used for malevolent purposes. They say greater awareness, stronger guidelines, and tighter regulation in the research community could help us to avoid the perils of where these AI capabilities might otherwise lead.

"Our proof of concept thus highlights how a non-human autonomous creator of a deadly chemical weapon is entirely

feasible," the researchers explain.
"Without being overly alarmist, this should serve as a wake-up call for our colleagues in the 'AI in drug discovery' community."
The research has been published in *Nature Machine Intelligence*.

https://bbc.in/3ILeWeH

Persistent cough may be tuberculosis not Covid, doctor warns

The UK's top public health doctor says anyone with a persistent cough and fever should not dismiss it as Covid - and should consider other infectious illnesses like tuberculosis (TB).

Dr Jenny Harries' warning comes as provisional data shows there were 4,430 cases recorded in England in 2021, despite sharp declines in recent years. Charities are calling for more funding to tackle the disease around the world. They say the pandemic and conflicts have set back progress worldwide.
In 2020, global deaths because of tuberculosis ranked second to Covid for any infectious disease.

'Undetected cases'

The charity Stop TB Partnership warns the war in Ukraine could have "devastating impacts on health services", including the country's strong national TB treatment programme.
In 2021, Ukraine treated 24,000 people with TB including 5,000 with a drug-resistant form of the illness.
The country is among one of the 30 countries with highest rates of drug-resistant cases in the world.
The charity is urging all countries to put facilities in place urgently so refugees can be given the care they need.
In the UK a requirement for Ukrainians to take a TB test before arrival has been waived for those who are coming to the country on the family scheme visa. Refugees arriving on the scheme will get medical care and testing via GPs.
Meanwhile Dr Jenny Harries, chief executive of the UK Health Security Agency, said delayed diagnosis and treatment, particularly during the pandemic, will have increased the number of undetected cases in England.
She added: "It is important to remember not every persistent cough, along with fever, is Covid-19.
"A cough that usually has mucus and lasts longer than three weeks can be caused by a range of other issues, including tuberculosis."
Provisional UKHSA figures show:

**** There were 4,430 cases of TB recorded in England in 2021***
**** This compares to 4,125 in 2020 - but it is likely there were unrecorded cases during the pandemic***
**** There were 4,725 cases in 2019 after years of decline***
**** In 2011, cases peaked at 8,280***

Though sometimes life-threatening, the vast majority of TB cases can be treated successfully with six months of antibiotics.
But incomplete or inadequate treatment can lead to the development of drug resistance - meaning the bug can no longer be killed effectively by one or more medicines. Other combinations of drugs are then tried.
Drug-resistant TB is a particular problem - with 11.6% of cases in England in 2020 recorded as resistant to any drug and 2.4% resistant to both of the most frequently-used antibiotics.

https://wb.md/3qFVBoW

Experimental Device Would Give Oxygen by IV

Approach could prevent severe oxygen loss and lung injuries from ventilators

Donavyn Coffey

The human body needs a lot of oxygen: about a cup a minute, just to stay alive.
If we can't get the amount we need because of injury or disease, like COVID-19, our bodies quickly start to suffer from oxygen deprivation. After just a few minutes, abnormally low oxygen

levels in the blood can damage the brain and other organs, and even cause death.

Doctors have machines such as ventilators that can help people struggling to breathe get enough oxygen, but these have drawbacks and risks.

Now, researchers at Boston Children's Hospital have developed a device that can inject oxygen directly into the bloodstream through an IV. They haven't tested it in people yet, but a new study describes testing it out in rats. If the researchers eventually get it to work for people, the approach could prevent severe oxygen loss and lung injuries from ventilators, they say.

Though the technology is far from ready for testing in people, the test run with the rats "is a nice proof of concept," says John Kheir, MD, a doctor in the Cardiac Intensive Care Unit at Boston Children's Hospital who is leading the work on the new device.

Currently, patients who need help to breathe get oxygen through a nasal cannula, a ventilator, or, in the most severe cases, by ECMO, a machine that takes out a person's blood to pump carbon dioxide out and oxygen in before putting it back into their body.

While all these approaches save lives, ventilators can hurt the lungs if used for a long time, and ECMO has a high risk of infection. If doctors could put oxygen directly into a patient's blood through an IV, it could potentially reduce the need for other ways to give oxygen, or make them safer.

In the future, Kheir and his team hope this technology could be a way to give patients just enough oxygen to keep them going. "It gives patients more time and makes them more stable to go on ECMO," he says, which can take 15 minutes at the best hospitals to over an hour at others.

How It Works: Oxygen Emulsion

To prepare the oxygen to be injected into the bloodstream, the researchers put it into the device along with a fluid containing phospholipids, a type of fat found in your cell membranes.

The gas and fluid move through nozzles of decreasing size to create tiny nano-bubbles of oxygen with a phospholipid coating -- all smaller than a single red blood cell. The new emulsion, a fluid full of tiny bubbles, is then injected into the bloodstream.

The phospholipid packaging and tiny size of the bubbles are critical to giving the oxygen safely.

You can't just inject oxygen into the bloodstream directly because it will make an air bubble that could block a blood vessel, like what happens when divers get the bends after coming back to the surface too quickly after diving, says Peyman Benharash, MD, a heart surgeon and director of the Adult ECMO Program at UCLA.

With this new nanotechnology approach, "the balls of oxygen are trapped in fat and slowly released to prevent the bends from happening," he says.

The way the new technology works "is very straightforward, so it could be scalable," Benharash says.

Fewer than 5% of hospitals have ECMO machines, he says. Something easier to use, like this technology, could potentially offer life-saving oxygen to more people in more remote places.

While the therapy is interesting, Benharash says, "it's not ready by any means for prime time or use in patients." Next, he says, he'd like to see how the device works in larger animals for longer periods of time.

As the researchers keep working on their device, Kheir says, they need to scale it up to provide at least 10 times more oxygen, and make it more dependable.

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John Kheir, MD, doctor, Cardiac Intensive Care Unit, Boston Children's Hospital; professor of pediatrics, Harvard Medical School.

Peyman Benharash, MD, heart surgeon, associate professor of surgery and bioengineering, director, Adult ECMO Program, University of California, Los Angeles.

https://bit.ly/3tIsfbt

Tetanus Immunity Protects Mice Against Pancreatic Cancer

Because most people are vaccinated against tetanus as children, delivering benign bacteria carrying a tetanus antigen into pancreatic tumors makes them visible to memory cells in the immune system, researchers report.

Amanda Heidt

Researchers have leveraged childhood immunity to tetanus in order to target treatment-resistant pancreatic cancer, according to a new study published this week (March 23) in *Science Translational Medicine*. Using an inert, nontoxic species of *Listeria* bacteria, scientists were able to deliver benign tetanus proteins into pancreatic tumor cells in mice, thereby flagging them as foreign to circulating memory immune cells. Following the treatment, both the original tumor and those that had metastasized shrank significantly, and the mice lived longer as a result.

"I'm extremely excited. [The result] feels terrific. We're very close to a clinical trial," Claudia Gravekamp, an immunologist and microbiologist at the Albert Einstein College of Medicine who led the study, tells *STAT News*.

Pancreatic cancer is difficult to treat for several reasons. The cancerous cells often lack the mutational vulnerabilities exploited by current pharmaceutical therapies. Tumors also often grow and metastasize before the onset of symptoms. And as they grow, they secrete molecules that dampen the local immune response while also coating themselves in thick, fibrous myeloid-derived cells that physically shield the tumor. "Pancreas cancer goes cloaked," Gregory Beatty, an immunologist at the University of Pennsylvania who studies pancreatic cancer but was not involved in the study, tells *STAT*. As a result, only 10 percent of patients live for more than five years after diagnosis.

Gravekamp and her colleagues used *Listeria*, the bacteria behind most cases of food poisoning, as a means to circumvent pancreatic cancer's many tricks. *Listeria* preferentially infects cancerous and tumor-associated cells, and the form that Gravekamp used was genetically modified to bear proteins from the bacteria that causes tetanus. Because most people are immunized against tetanus as children, the body's memory T cells continue to recognize tetanus antigens throughout life, even if cancer-spotting T cells fail to recognize pancreatic cancer. The researchers hypothesized that if the tetanus look-alike were to build up within tumor cells, its antigens would end up displayed on the surface of the tumor, and that could trigger an immune response. "Essentially, our new therapy makes immunologically 'cold' tumors hot enough for the immune system to attack and destroy them," Gravekamp says in a press release.

To test the method in vivo, Gravekamp and her colleagues inoculated young mice engineered to develop pancreatic cancer as they aged with a standard tetanus vaccine. Then, once the mice had advanced cancer, the scientists injected tetanus-bearing *Listeria* into their abdomens, and a subset also received a dose of a chemotherapy drug to test the two treatments in combination. The bacteria were quickly swarmed by myeloid-derived immune cells, which ended up being infected by the bacteria and shuttling them to the tumors. "Ironically, the tumor attracts these same myeloid-derived cells because they help the tumor grow and metastasize," Gravekamp tells *STAT*. "So, they bring the *Listeria* as a Trojan horse to the tumor."

Shortly after, the researchers report in their paper, the body's T cells began attacking the tumors. This happened even in the absence of the chemotherapy drug, but mice that received both treatments received the largest benefit. These mice saw their pancreatic tumors shrink by an average of 80 percent and their metastases by 87

percent compared to untreated controls and also lived roughly 40 percent longer, amounting to several months.

Beatty calls the team's method "a unique spin on this particular approach [in using *Listeria*]" to treat cancer, adding that "I think it has a path forward" in clinical trials. While it's unknown how well this method might work in people—plenty of techniques that worked well in mice go on to flop in humans, and the heterogeneous nature of the human tumor microenvironment presents a consistent challenge—Beatty tells *STAT* that he can see *Listeria* being added to the standard of care in addition to things like surgery and chemotherapy. "Surgery is the best chance for a 'cure,'" Beatty says. "Incorporating [the therapy] in that setting is attractive, and maybe you could improve the number of patients [healed]."

Moving forward, the researchers plan to test the new technique in humans. Gravekamp tells *STAT* that a patent for the therapy has already been licensed to New York-based biotech company Loki Therapeutics and, speaking to *New Scientist*, she adds that they are currently organizing a clinical trial to assess the safety of injecting the bacteria into the abdomens of healthy patients before moving on to those with pancreatic cancers. In the meantime, Gravekamp has also applied the tetanus-containing *Listeria* to murine models of ovarian cancer, with "very, very promising results," and will be targeting bowel and brain cancers next.

https://bit.ly/3uBleZk

Quake-Ception – Groundbreaking Earthquake Discovery: Risk Models Overlook an Important Element

In a new study, researchers demonstrate that the behaviour of tectonic plates can change following an earthquake

Earthquakes themselves affect the movement of Earth's tectonic plates, which in turn could impact on future earthquakes, according to new research from the University of Copenhagen. This new knowledge should be incorporated in computer models used to gauge earthquake risk, according to the researchers behind the study.

Like a gigantic puzzle, Earth's tectonic plates divide the surface of our planet into larger and smaller pieces. These pieces are in constant motion due to the fluid-like part of Earth's mantle, upon which they slowly sail. These movements regularly trigger earthquakes, some of which can devastate cities and cost thousands of lives. In 1999, the strongest European earthquake in recent years struck the town of İzmit, Turkey – taking the lives of 17,000 of its residents.

Among researchers and earthquake experts, it is well accepted that earthquakes are caused by a one-way mechanism: as plates move against one another, energy is slowly accrued along plate margins, and then suddenly released via earthquakes. This happens time and again over decades- or century-long intervals, in a constant stick-slip motion.

But in a new study, researchers from the Geology Section at the University of Copenhagen's Department of Geosciences and Natural Resource Management demonstrate that the behaviour of tectonic plates can change following an earthquake.

Using extensive GPS data and analysis of the 1999 İzmit earthquake, the researchers have been able to conclude that the Anatolian continental plate that Turkey sits upon has changed direction since the earthquake. Data also show that this influenced the frequency of quakes around Turkey after 1999.

"It appears that the link between plate motion – earthquake occurrence is not a one-way street. Earthquakes themselves feed back, as they can cause plates to move differently afterwards," explains the study's lead author, postdoc Juan Martin De Blas, who

adds:

"As the plate movements change, it somewhat affects the pattern of the later earthquakes. If a tectonic plate shifts direction or moves at a different rate than before, this potentially impacts onto the seismicity of its margins with neighboring plates."

Quake models can be improved

According to the researchers, the new findings provide a clear basis for reevaluating the risk models that interpret data gathered from the monitoring of tectonic plate movements. This data is used to assess the risk of future earthquakes in terms of probability, somehow like the nice/bad weather forecast.

"An important aspect of these models is that they operate under the assumption that plate movements remain constant. With this study, we can see that this isn't the case. Therefore, the models can now be further evolved so they take the feedback mechanism that occurs following an earthquake into account, where plates shift direction and speed," says Associate Professor Giampiero Iaffaldano, the study's co-author.

The assumption that plate movements are constant has largely been a "necessary" assumption according to the researchers, because monitoring plate motions over period of few years was once impossible. But with the advent of geodesy in Geosciences, and the extensive and ever-growing use of GPS devices over the last 20 years, we can track plate motion changes over year-long periods.

Could make us better at assessing risk

How tectonic plates are monitored varies greatly from place to place. Often GPS transmitters are positioned preferentially near the edges of a tectonic plate. This allows public agencies and researchers to track the movement of plate boundaries. But according to the researchers, we can also benefit from even more GPS devices continuously monitoring plate interiors, away from their margins.

"Plate boundaries undergo constant deformation and poorly represent the movement of plates as a whole. Therefore, GPS data from monitors positioned farther away from the plate boundaries should be used to a much greater degree. This can better inform us weather plates are changing motion and how, and provide information useful for assessing the risk of future events somewhere other than the known hot-spots," says Giampiero Iaffaldano.

The researchers point out that their study is limited to the Anatolian continental plate, as the İzmit earthquake is one of the few event for which a combination of sufficient seismic and GPS data is available. However, they expect that the picture is the same for other tectonic plates around the planet.

Reference: "Have the 1999 Izmit–Düzce earthquakes influenced the motion and seismicity of the Anatolian microplate?" by J Martin de Blas, G Iaffaldano and E Calais, 20 January 2022, Geophysical Journal International. DOI: 10.1093/gji/ggac020

https://bit.ly/36TZmQD

Astronomers Have Detected a Curious Dust Cloud 330 Light-Years Away

Astronomers have detected a cloud of dust the size of a whole star, 330 light-years away. Its cause? A colossal smash-up between two exoplanets that were still just forming.

Michelle Starr

We know this because astronomers have analyzed the infrared glow of said dust cloud, along with changes in the light of the host star, periodically blotted out by the debris in orbit around it. With these data, we now know the size of the objects involved, and other key details about the collision.

This could provide insight into the formation of our own Solar System – and perhaps even shed light on stars with peculiar dimming patterns, such as KIC 8462852 or Boyajian's Star, by providing more information on how rapidly such debris clouds

disperse.

"For the first time," said astronomer Everett Schlawin of the University of Arizona's Steward Observatory, "we captured both the infrared glow of the dust and the haziness that dust introduces when the cloud passes in front of the star."

The star in question is a wee ickle baby, just 10 million years old, named HD 166191. Because it formed so recently, it is still surrounded by quite a bit of material, leftover from the formation process.

Stars form from a dense knot in a cloud of gas that collapses under its own mass; spinning, the star grows by accreting more material from the surrounding cloud, as the latter arranges into a disk feeding into the star, like water going down a drain.

Once the star has finished forming, whatever is left in the disk can go on to form the other elements of a planetary system. Clumps of material stick together, first attracted electrostatically, then gravitationally.

As you can imagine, this is a messy process, with lots of collisions. Eventually, enough material sticks together to form, first a planet seed, or planetesimal, then eventually a planet.

Collisions between bodies can guide the process. It's thought that our Moon formed when another planetary body slammed into Earth during the Solar System's youth, for example. But it's not a given that every collision will leave survivors.

Led by astronomer Kate Su of Steward Observatory, a team of researchers used the now-retired Spitzer Space Telescope to make infrared observations of HD 166191. These wavelengths can penetrate dust clouds to see what processes are taking place in heavily shrouded environments. In addition, starlight absorbed and re-emitted by dust glows brightly in infrared.

Between 2015 and 2019, the researchers collected 126 datasets from the star, looking specifically for orbiting clouds of dust that may be the result of a planetesimal collision.

In 2018, the signal they had been looking for showed up: an infrared brightening, suggesting an increase in dust, and a dimming, suggesting that the light of the star was being blocked. The same dimming event was captured by a ground-based telescope in optical wavelengths – and a similar dimming 142 days earlier, during a gap in the Spitzer observations.

Multi-wavelength transit data confirmed it: The signal was generated by the guts of two planetesimals that smacked into each other and spewed dust everywhere. The earlier observation from the ground-based telescope suggested an orbital period of 142 days, which gave an orbital distance from the star of 0.62 astronomical units. That's the distance at which rocky planets are expected to form.

Having data from multiple transits also allowed the team to observe the evolution of the cloud. It changed rapidly from the first to the second transit, ballooning out, growing wider and more opaque and elongated, covering an area at least three times that of the star.

But Spitzer data suggests that just a small portion of the cloud passed between us and the star. That suggests that the actual cloud was much, much bigger, perhaps hundreds of times bigger than the star.

To produce so much dust, the team calculated the collision had to have been between two bodies that were dwarf-planet sized, around 400 to 600 kilometers (around 250 to 470 miles) in diameter. The initial collision would have generated so much heat that some of the material vaporized; the remainder would have flown into fragments that continued to ricochet around and collide with each other, as well as other rocks in the vicinity, to create even more dust.

By the time the third transit was due to roll around, very little trace of the original cloud remained. However, the environment around the star had grown twice as dusty as it was before the collision. This

suggests that the debris from the collision dispersed quite rapidly throughout the protoplanetary disk around the star.

Not only does this suggest that clumpy dust clouds may not be a good fit for explaining peculiarly dimming stars, but it can also help elucidate the processes that go into forming a full planetary system, including ours.

"By looking at dusty debris disks around young stars, we can essentially look back in time and see the processes that may have shaped our own Solar System," Su said.

"Learning about the outcome of collisions in these systems, we may also get a better idea of how frequently rocky planets form around other stars."

The team will continue to monitor HD 166191 to see if they can spot any more fascinating changes in its dusty shroud.

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

https://bit.ly/3NqIPoc

Large-Scale Study Reveals Strange Link Between Antibiotics And Cognitive Decline

A study involving a total of 14,542 women has found an as-yet-unexplained link between taking antibiotics for at least two months in midlife, and a dip in cognitive score assessments taken several years later.

David Nield

The team behind the research, led by epidemiologists from Harvard Medical School in Massachusetts, says it shows how important it is to carefully monitor antibiotic use – and also how important it is that we understand the link between what's going on in our guts (which antibiotics can affect) and what's happening in our brains.

Plenty of previous studies have highlighted the link between the gut microbiome and the brain, but it's not clear exactly what the relationship might be. This new research adds more data points in a much-needed field of study.

"In a cohort of over 14,000 women, we observed that antibiotic use in midlife was significantly associated with subsequent poorer scores for global cognition, learning, and working memory, and psychomotor speed and attention," write the researchers in their paper.

"To our knowledge, our study represents the first large study of chronic long-term use of antibiotics and subsequent cognition."

The women in the cohort (a long-term chronic disease research project called Nurses' Health Study) had taken antibiotic drugs for a variety of reasons, including for respiratory infections, dental problems, acne, and urinary tract infections.

For those on antibiotics, the resulting drop in brain power across the various categories of learning, response, and memory was the equivalent of about three or four years of normal aging, according to the data.

Cognitive ability was assessed an average of seven years after the antibiotic use began, through an online test the participants completed at home. The test includes four different tasks in total, designed to measure different aspects of cognitive performance.

"This relationship was associated with longer duration of antibiotic use and persisted after adjustment for many potential confounding factors," write the researchers.

As usual with studies such as this, the link isn't enough to prove causation – that is, the data don't show it's definitely antibiotic use that's leading to a drop in cognition. It's possible that the conditions the antibiotics were intended to treat, rather than the antibiotics themselves, caused this small drop in cognition, for example.

However, there is enough here to suggest that more research is definitely warranted. The limitations of this study are that it didn't look at any particular type of antibiotic and that it relied on self-reporting for antibiotic use. However, the large sample size and the factoring in of other variables, including diet and other medications,

increase its value.

Investigations into the link between antibiotics, gut microbiome, and brain function will continue, but to date, this is one of the best studies we've got looking at the potential long-term effects in adult human beings.

"Given the profound effect of antibiotic use on the gut microbiome – with prior studies showing alterations in functional potential at two and four years after antibiotic exposure – the gut-brain axis could be a possible mechanism for linking antibiotics to cognitive function," write the researchers.

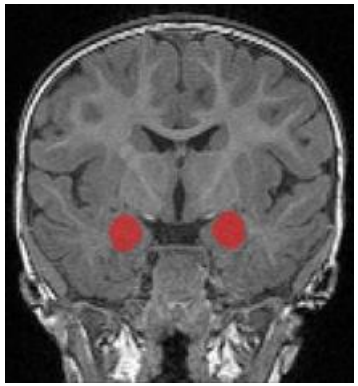
The research has been published in *PLOS One*.

https://bit.ly/3tGNASO

Overgrowth of Key Brain Structure Identified in Babies Who Later Develop Autism

First research to demonstrate overgrowth of the amygdala in the first year of life

Research led by Mark Shen, PhD, Heather Hazlett , PhD, and Joseph Piven, MD, from UNC-Chapel Hill is the first to demonstrate overgrowth of the amygdala in the first year of life, before babies show most of the behavioral symptoms that later consolidate into a diagnosis of autism. This overgrowth may be unique to autism, as babies with fragile X syndrome show a different brain growth pattern.



The amygdala (in red) grows too rapidly in babies (6-12 months) who later develop autism as toddlers. **Credit: CIDD at UNC-CH**

The amygdala is a small structure deep in the brain important for interpreting the social and emotional meaning of sensory input – from recognizing emotion in faces to interpreting fearful images that inform us about potential dangers in our surroundings. Historically the amygdala has been thought to play a prominent role in the difficulties with social behavior that are central to autism.

Researchers have long known the amygdala is abnormally large in school-age children with autism, but it was unknown precisely when that enlargement occurs. Now, for the first time, researchers from the Infant Brain Imaging Study (IBIS) Network, used magnetic resonance imaging (MRI) to demonstrate that the amygdala grows too rapidly in infancy. Overgrowth begins between six and 12 months of age, prior to the age when the hallmark behaviors of autism fully emerge, enabling the earliest diagnosis of this condition. Increased growth of the amygdala in infants who were later diagnosed with autism differed markedly from brain-growth patterns in babies with another neurodevelopmental disorder, fragile X syndrome, where no differences in amygdala growth were observed.

Published in the *American Journal of Psychiatry*, the official journal of the American Psychiatric Association, this research demonstrated that infants with fragile X syndrome already exhibit cognitive delays at six months of age, whereas infants who will later be diagnosed with autism do not show any deficits in cognitive ability at six months of age, but have a gradual decline in cognitive ability between six and 24 months of age, the age when they were diagnosed with Autism Spectrum Disorder in this study. Babies who go on to develop autism show no difference in the size of their amygdala at six months. However, their amygdala begins growing faster than other babies (including those with fragile X syndrome and those who do not develop autism), between six and 12 months of age, and is significantly enlarged by 12 months. This amygdala enlargement continues through 24 months, an age when behaviors are often sufficiently evident to warrant a diagnosis of autism.

“We also found that the rate of amygdala overgrowth in the first year is linked to the child’s social deficits at age two,” said first

author Mark Shen, PhD, Assistant Professor of Psychiatry and Neuroscience at UNC Chapel Hill and faculty of the Carolina Institute for Developmental Disabilities (CIDD). "The faster the amygdala grew in infancy, the more social difficulties the child showed when diagnosed with autism a year later."

This research – the first to document amygdala overgrowth before symptoms of autism appear – was conducted through The Infant Brain Imaging Study (IBIS) Network, a consortium of 10 universities in the United States and Canada funded through a National Institutes of Health Autism Center of Excellence Network grant.

The researchers enrolled a total of 408 infants, including 58 infants at increased likelihood of developing autism (due to having an older sibling with autism) who were later diagnosed with autism, 212 infants at increased likelihood of autism but who did not develop autism, 109 typically developing controls, and 29 infants with fragile X syndrome. More than 1,000 MRI scans were obtained during natural sleep at six, 12, and 24 months of age.

So, what might be happening in the brains of these children to trigger this overgrowth and then the later development of autism? Scientists are starting to fit the pieces of that puzzle together.

Earlier studies by the IBIS team and others have revealed that while the social deficits that are a hallmark of autism are not present at six months of age, infants who go on to develop autism have problems as babies with how they attend to visual stimuli in their surroundings. The authors hypothesize that these early problems with processing visual and sensory information may place increased stress on the amygdala, leading to overgrowth of the amygdala.

Amygdala overgrowth has been linked to chronic stress in studies of other psychiatric conditions (e.g., depression and anxiety) and may provide a clue to understanding this observation in infants who later develop autism.

Senior author Joseph Piven, M.D., Professor of Psychiatry and Pediatrics at the University of North Carolina at Chapel Hill added, "Our research suggests an optimal time to start interventions and support children who are at highest likelihood of developing autism may be during the first year of life. The focus of a pre-symptomatic intervention might be to improve visual and other sensory processing in babies before social symptoms even appear."

Reference: "Subcortical Brain Development in Autism and Fragile X Syndrome: Evidence for Dynamic, Age- and Disorder-Specific Trajectories in Infancy" by Mark D. Shen, Ph.D., Meghan R. Swanson, Ph.D., Jason J. Wolff, Ph.D., Jed T. Elison, Ph.D., Jessica B. Girault, Ph.D., Sun Hyung Kim, Ph.D., Rachel G. Smith, B.A., Michael M. Graves, M.S., Leigh Anne H. Weisenfeld, M.S.W., Lisa Flake, M.S.W., Leigh MacIntyre, M.S., Julia L. Gross, B.S., Catherine A. Burrows, Ph.D., Vladimir S. Fonov, Ph.D., D. Louis Collins, Ph.D., Alan C. Evans, Ph.D., Guido Gerig, Ph.D., Robert C. McKinstry, M.D., Ph.D., Juhi Pandey, Ph.D., Tanya St. John, Ph.D., Lonnie Zwaigenbaum, M.D., Annette M. Estes, Ph.D., Stephen R. Dager, M.D., Robert T. Schultz, Ph.D., Martin A. Styner, Ph.D., Kelly N. Botteron, M.D., Heather C. Hazlett, Ph.D. and Joseph Piven, M.D. for the IBIS Network, 25 March 2022, American Journal of Psychiatry.

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