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A Combination of Three Simple Treatments May Reduce Risk of Invasive Cancer by 61%

A combination of three simple treatments may reduce invasive cancer risk by 61% among adults aged 70+.

New research published in the journal *Frontiers in Aging* found that a combination of high-dose vitamin D, omega-3 fatty acids, and a simple home strength exercise program (SHEP) reduced cancer risk by 61 percent in healthy persons aged 70 and older. It is the first study to look at the combined benefit of three low-cost public health interventions for the prevention of invasive cancers. Following future studies, the results may influence the future of cancer prevention in older adults.

Cancer is regarded as a major age-related disease in Europe and the US. It is the second leading cause of death in older adults, and the risk of developing most cancers increases with age.

Apart from preventative recommendations such as not smoking and sun protection, public health efforts that focus on cancer prevention are limited, according to Dr Heike Bischoff-Ferrari of the University Hospital Zurich: "Preventive efforts in middle-aged and older adults today are largely limited to screening and vaccination efforts."

Vitamin D, omega-3, and exercise

Mechanistic studies have shown that vitamin D inhibits the growth of cancer cells. Similarly, omega-3 may inhibit the transformation of normal cells into cancer cells, and exercise has been shown to improve immune function and decrease inflammation, which may help in the prevention of cancer.

However, there was a lack of robust clinical studies proving the effectiveness of these three simple interventions, alone or combined. Bischoff-Ferrari and her colleagues wanted to fill these knowledge gaps by testing the effect of daily high-dose vitamin D3 (one form of vitamin D supplements), daily supplemental omega-3s, and a simple home exercise program, alone and in combination, on the risk of invasive cancer among adults aged 70 or older.

A combination of simple treatments

To do so, the researchers conducted the DO-HEALTH trial: a three-year trial in five European countries (Switzerland, France, Germany, Austria, and Portugal) with 2,157 participants.

"In DO-HEALTH, our aim was to test promising combined interventions for cancer prevention taking advantage of potentially small additive benefits from several public health strategies," explained Bischoff-Ferrari. "In fact, novel cancer treatments aim to block multiple pathways for cancer development by combining several agents. We translated this concept into cancer prevention."

The participants were randomized into eight different groups to test the individual and combined benefit of the interventions: group one received 2,000 IU per day of Vitamin D3 (equivalent to > 200% the amount of current recommendations for older adults, which is 800 IU per day), 1g per day of omega-3s, and three times per week SHEP; group two vitamin D3 and omega-3s; group three vitamin D3 and SHEP; group four omega-3s and SHEP; group five vitamin D3 alone; group six omega-3s alone; group seven SHEP alone; and the last group received a placebo.

Participants received check-up phone calls every three months and had standardized examinations of health and function in the trial centers at baseline, year 1, year 2, and year 3.

Preventing invasive cancer

The results show that all three treatments (vitamin D3, omega-3s, and SHEP) had cumulative benefits on the risk of invasive cancers.

Each of the treatments had a small individual benefit but when all three treatments were combined, the benefits became statistically significant, and the researchers saw an overall reduction in cancer risk by 61%.

"This is the first randomized controlled trial to show that the combination daily vitamin D3, supplemental marine omega-3s, and a simple home exercise program may be effective in the prevention of invasive cancer among generally healthy and active adults aged 70 and older," Bischoff-Ferrari commented.

The results may impact the future of invasive cancer prevention in older adults. Bischoff-Ferrari concluded: "Our results, although based on multiple comparisons and requiring replication, may prove to be beneficial for reducing the burden of cancer."

"Future studies should verify the benefit of combined treatments in the prevention of cancer, also extending to longer follow-ups beyond the three-year duration assessed in this trial."

Reference: "Combined Vitamin D, Omega-3 Fatty Acids, and a Simple Home Exercise Program May Reduce Cancer Risk Among Active Adults Aged 70 and Older: A Randomized Clinical Trial" by Heike A. Bischoff-Ferrari, Walter C. Willett, JoAnn E. Manson, Bess Dawson-Hughes, Markus G. Manz, Robert Theiler, Kilian Braendle, Bruno Vellas, René Rizzoli, Reto W. Kressig, Hannes B. Staehelin, José A. P. Da Silva, Gabriele Armbrecht, Andreas Egli, John A. Kanis, Endel J. Orav and Stephanie Gaengler, DO-HEALTH Research Group, 25 April 2022, Frontiers in Aging.
DOI: 10.3389/fragi.2022.852643

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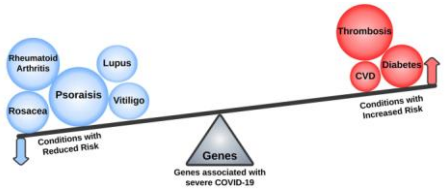
Genetic Links Revealed Between Severe COVID-19 and Other Medical Conditions

Large-scale study could help inform novel COVID-19 treatment strategies.

A new analysis of data from the Veterans Affairs Million Veteran Program has uncovered genetic links between COVID-19 severity and various medical conditions that are known risk factors for severe COVID-19. Anurag Verma of the Corporal Michael Crescenz VA Medical Center in Philadelphia, Pennsylvania, US, and colleagues published these findings on April 28th, 2022, in the open-access journal *PLOS Genetics*.

Some patients with COVID-19 have a more severe case of the disease than others. Previous research has found certain variants in specific human genes that are linked with a person experiencing more severe COVID-19. Some of these variations may also be associated with other medical conditions that may already be well understood; discovering these shared variants could increase understanding of COVID-19 and reveal potential new paths for treatment.



While genes linked to severe COVID-19 were associated with established risk factors and adverse outcomes, including deep vein thrombosis, a significant subset of these genes had opposite associations with reduced risk of immune-mediated disorders such as psoriasis, lupus, and rheumatoid arthritis. **Credit: Anurag Verma, Katherine Liao, and Scott Damrauer (CC-BY 4.0)**

To identify shared variants, Verma and colleagues used an unprecedented dataset of genotypic information linked to electronic health record data (EHR) for more than 650,000 U.S. veterans. They conducted a type of analysis known as a phenome-wide association study (PheWAS) to examine links between variants often found in Veterans who experienced severe COVID-19 and variants associated with a broad selection of medical conditions.

The analysis revealed that certain variants associated with COVID-19 are also associated with known risk factors for COVID-19. Particularly strong links were found for variants associated with venous embolism and thrombosis, as well as type 2 diabetes and ischemic heart disease—two known COVID-19 risk factors.

The analysis also found genetic links between severe COVID-19 and neutropenia for Veterans of African and Hispanic ancestry; these links did not appear for those of European ancestry.

Among respiratory conditions, idiopathic pulmonary fibrosis and chronic alveolar lung disease shared genetic links with severe COVID-19, but other respiratory infections and chronic obstructive pulmonary disease (COPD) did not. Some variants associated with severe COVID-19 were also associated with reduced risk of

autoimmune conditions, such as psoriasis and lupus. These findings highlight the need to carefully weigh various aspects of the immune system when developing new treatments.

Despite some limitations of the PheWAS method, these findings could help deepen understanding of COVID-19 and guide development of new treatments.

Verma concludes, "The study demonstrates the value and impact of large biobanks linking genetic variations with EHR data in public health response to the current and future pandemics. MVP is one of the most diverse cohorts in the US. We had a unique opportunity to scan thousands of conditions documented before the COVID-19 pandemic. We gained insights into the genetic architecture of COVID-19 risk factors and disease complication."

"One thing that stood out to us was the high number of immune-mediated conditions that shared genetic architecture with severe manifestations of COVID-19," coauthor Katherine Liao adds. "The nature of the associations brought to light how the SARS-CoV2 virus pushes on a pressure point in the human immune system and its constant balancing act of fighting infection while maintaining enough control so that it does not also become an autoimmune process, attacking self."

Reference: "A Phenome-Wide Association Study of genes associated with COVID-19 severity reveals shared genetics with complex diseases in the Million Veteran Program" by Anurag Verma, Noah L. Tsao, Lauren O. Thomann, Yuk-Lam Ho, Sudha K. Iyengar, Shiuh-Wen Luoh, Rotonya Carr, Dana C. Crawford, Jimmy T. Efird, Jennifer E. Huffman, Adriana Hung, Kerry L. Ivey, Michael G. Levin, Julie Lynch, Pradeep Natarajan, Saiju Pyarajan, Alexander G. Bick, Lauren Costa, Giulio Genovese, Richard Hauger, Ravi Madduri, Gita A. Pathak, Renato Polimanti, Benjamin Voight, Marijana Vujkovic, Seyedeh Maryam Zekavat, Hongyu Zhao, Marylyn D. Ritchie, VA Million Veteran Program COVID-19 Science Initiative, Kyong-Mi Chang, Kelly Cho, Juan P. Casas, Philip S. Tsao, J. Michael Gaziano, Christopher O'Donnell, Scott M. Damrauer and Katherine P. Liao, 28 April 2022, PLOS Genetics. DOI: 10.1371/journal.pgen.1010113

Funding: This research is based on data from the Million Veteran Program, Office of Research and Development, Veterans Health Administration, and was supported by award MVP035. S.M.D. is supported by US Department of Veterans Affairs (IK2-CX001780). R.C. is supported by NIH grants R01 AA026302 and P30 DK0503060. K.P.L. is supported by NIH P30 AR072577, and the Harold and Duval Bowen Fund. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Unlocking the Mystery of Why a Plant Virus Is So Powerful at Fighting Cancer – Even Metastatic Cancer

When cowpea mosaic virus, a plant virus that infects legumes, is injected into a tumor, it activates the immune system to treat the cancer—even metastatic cancer—and prevent it from returning.

Cowpea mosaic virus, a plant virus that infects legumes, has a special power that you may not be aware of: when injected into a tumor, it activates the immune system to treat the cancer—even metastatic cancer—and prevent it from returning.

Researchers at the University of California San Diego and Dartmouth College have spent the last seven years studying and testing cowpea mosaic virus—in the form of nanoparticles—as a cancer immunotherapy and have reported encouraging results in lab mice and companion dog patients. Its effectiveness has been unrivaled by other cancer-fighting techniques examined by the researchers. However, the precise reasons for its effectiveness have remained a mystery.

In a recent research study published in the journal *Molecular Pharmaceutics*, the researchers uncover details that explain why cowpea mosaic virus in particular is extraordinarily effective against cancer.

The work was led by Nicole Steinmetz, a professor of nanoengineering at the UC San Diego Jacobs School of Engineering, and Steven Fiering, a professor of microbiology and immunology at the Geisel School of Medicine at Dartmouth. Steinmetz and Fiering are co-founders of a biotechnology startup, called Mosaic ImmunoEngineering Inc., which has licensed the cowpea mosaic virus nanotechnology and is working to translate it

into the clinic as a cancer immunotherapy.

"This study helps validate the cowpea mosaic plant virus nanoparticle as our lead cancer immunotherapy candidate," said Steinmetz, who also serves as the director of the Center for NanoImmunoEngineering at UC San Diego. "Now we have mechanistic data to explain why it is the most potent candidate, which further de-risks it for clinical translation."

Up until now, Steinmetz, Fiering and their teams had a general idea of how their lead candidate worked. The cowpea mosaic virus nanoparticles, which are infectious in plants but not in mammals, are injected directly inside a tumor to serve as immune system bait. The body's immune cells recognize the virus nanoparticles as foreign agents and get fired up to attack. When the immune cells see that the virus nanoparticles are inside a tumor, they go after the cancerous cells.

The beauty of this approach, noted Steinmetz, is that it not only takes care of that one tumor, but it also launches a systemic immune response against any metastatic and future tumors. The researchers have seen it work in mouse models of melanoma, ovarian cancer, breast cancer, colon cancer, and glioma. They've also had success using it to treat canine patients with melanoma, breast cancer, and sarcoma.

What's also interesting is that cowpea mosaic virus has worked the best at triggering an anti-cancer immune response compared to other plant viruses or virus-like particles the researchers have studied. "We've shown that it works, and now we need to show what makes it so special that it can induce this kind of response," said first author Veronique Beiss, a former postdoctoral researcher in Steinmetz's lab. "That's the knowledge gap we're looking to fill."

To get answers, the researchers compared cowpea mosaic virus with two other plant viruses from the same family that have the same shape and size. One virus, cowpea severe mosaic virus, shares a similar RNA sequence and protein composition. The other, tobacco ring spot virus, is similar only in structure. "We thought these would be great comparisons to see if this potent anti-tumor efficacy runs in this particular family of plant viruses," said Steinmetz. "And we can dig deeper by comparing to relatives with and without sequence homology."

The researchers created plant virus-based nanoparticle immunotherapies and injected them into the melanoma tumors of mice. Each immunotherapy candidate was administered in three doses given 7 days apart. Mice given the cowpea mosaic virus nanoparticles had the highest survival rate and the smallest tumors, with tumor growth essentially stalling four days after the second dose.

The researchers then extracted immune cells from the spleen and lymph nodes from the treated mice and analyzed them. They found that the plant viruses all have a protein shell that activates receptors, called toll-like receptors, that are on the surface of immune cells. But what's unique about cowpea mosaic virus is that it activates an additional toll-like receptor through its RNA. Activating this additional receptor triggers more types of pro-inflammatory proteins called cytokines, which help boost the immune system's anti-cancer response. In other words, triggering a stronger inflammatory response makes the immune system work harder to look for and get rid of tumors, explained Beiss.

The team's analysis also found another unique way that the cowpea mosaic virus boosts the immune response. Four days after the second dose, the researchers measured high levels of cytokines. And these levels stayed high over a long period of time. "We don't see this with the other two plant viruses. The cytokine levels peak quickly, then go down and are gone," said Beiss. "This prolonged immune response is another key difference that sets cowpea mosaic

virus apart."

While this sheds light on cowpea mosaic virus's superior potency and efficacy, Steinmetz acknowledges that there is more work to do. "The answers we've discovered here have opened up more questions," she said. "How does this virus nanoparticle get processed in the cell? What happens to its RNA and proteins? Why is the RNA of cowpea mosaic virus recognized but not the RNA of other plant viruses? Understanding the detailed journey of this particle through the cell and how it compares to other particles will help us nail down what makes cowpea mosaic virus uniquely effective against cancer."

Reference: "Cowpea Mosaic Virus Outperforms Other Members of the Secoviridae as In Situ Vaccine for Cancer Immunotherapy" by Veronique Beiss, Chenkai Mao, Steven N. Fiering and Nicole F. Steinmetz, 25 March 2022, Molecular Pharmaceutics.
DOI: 10.1021/acs.molpharmaceut.2c00058

This work was funded by the National Institutes of Health (grants U01-CA218292, R01-CA224605 and R01 CA253615) and the Department of Defense, Congressionally Directed Medical Research Program (W81XWH2010742).

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Carbon, climate change and ocean anoxia in an ancient icehouse world

A new study describes a period of rapid global climate change in an ice-capped world much like the present—but 304 million years ago.

Within about 300,000 years, atmospheric carbon dioxide levels doubled, oceans became anoxic, and biodiversity dropped on land and at sea.

"It was one of the fastest warming events in Earth's history," said Isabel Montañez, distinguished professor in the Department of Earth and Planetary Sciences at the University of California, Davis.

Although several other 'hyperthermal' or rapid warming events are known in Earth's history, this is the first identified in an icehouse Earth, when the planet had ice caps and glaciers, comparable to the present day. It shows that an icehouse climate may be more sensitive to changes in atmospheric carbon dioxide than warmer conditions, when CO_2levels are already higher. The work is published this week in *Proceedings of the National Academy of Sciences.*

Montañez' lab has studied the period from 300 million to 260 million years ago, when Earth's climate went from a glacial icehouse to a hot, ice-free greenhouse. In 2007, they showed that the climate swung back and forth several times during this period.

More recently, Montañez' team and others have been able to home in on a transition 304 million years ago, the Kasimovian–Gzhelian boundary or KGB. They used multiple proxies, including carbon isotopes and trace elements from rocks and plant fossils, and modeling to estimate atmospheric CO_2 at the time.

The researchers estimate that about 9000 Gigatons of carbon were released into the atmosphere just before the K-G boundary.

"We don't have a rate, but it was one of the fastest in Earth's history," Montañez said. That doubled atmospheric $CO_2$from approximately 350 parts per million, comparable to modern pre-industrial levels, to about 700 ppm.

Deep ocean dead zones

One of the consequences of global warming is marine anoxia, or a drop in dissolved oxygen in the ocean. Melting ice caps release fresh water onto the ocean surface, creating a barrier to deep water circulation and cutting off the supply of oxygen. Without oxygen, marine life dies.

Lack of oxygen leaves its mark in uranium isotopes incorporated into rocks forming at the bottom of the ocean. By measuring uranium isotopes in carbonate rocks in present-day China, the researchers could get a proxy for the amount of oxygen—or lack of it—in the ocean when those rocks were laid down.

About 23 percent of the seafloor worldwide became anoxic dead

zones, they estimate. That lines up with other studies showing big losses in biodiversity on land and at sea at the same time.

The effect of carbon release on ocean anoxia was significantly greater than that seen in other studies of rapid warming during 'greenhouse' conditions. That may be because the baseline level of atmospheric CO_2 was already much higher.

"If you raised CO_2 by the same amount in a greenhouse world, there isn't much affect, but icehouses seem to be much more sensitive to change and marine anoxia," Montañez said.

The massive carbon release may have been triggered by volcanic eruptions that tore through carboniferous coal beds, Montañez said. The eruptions would also have started fires, and warming may have melted permafrost, leading to the release of more organic carbon.

Montañez is co-corresponding author on the paper with Jitao Chen, formerly a postdoctoral scholar at UC Davis and now at the Nanjing Institute of Geology and Palaeontology, China and Xiang-dong Wang, Nanjing University, China.

More information: *Marine anoxia linked to abrupt global warming during Earth's penultimate icehouse, Proceedings of the National Academy of Sciences (2022). DOI: 10.1073/pnas.2115231119*

https://bit.ly/39hz1xo

From Seawater to Drinking Water at the Push of a Button – With No Filters!

Researchers build a portable desalination unit that generates clear, clean drinking water without the need for filters or high-pressure pumps.

By Adam Zewe, Massachusetts Institute of Technology

MIT researchers have developed a portable desalination unit, weighing less than 10 kilograms (22 pounds), that can remove particles and salts to generate fresh drinking water.

The device, which is about the size of a suitcase, needs less power to operate than a cell phone charger. It can also be driven by a small, portable solar panel, which can be purchased online for around $50. It automatically generates drinking water that exceeds World Health Organization (WHO) quality standards. The technology is packaged into a user-friendly device that runs with the push of a single button.

Unlike other portable desalination devices that require water to pass through filters, this unit utilizes electrical power to remove particles from drinking water. Eliminating the need for replacement filters significantly reduces the long-term maintenance requirements.

This could enable the unit to be deployed in remote and severely resource-limited areas, such as communities on small islands or aboard seafaring cargo ships. It could also be used to aid refugees fleeing natural disasters or by soldiers carrying out long-term military operations.

“This is really the culmination of a 10-year journey that I and my group have been on. We worked for years on the physics behind individual desalination processes, but pushing all those advances into a box, building a system, and demonstrating it in the ocean, that was a really meaningful and rewarding experience for me,” says senior author Jongyoon Han, a professor of electrical engineering and computer science and of biological engineering, and a member of the Research Laboratory of Electronics (RLE).

Joining Han on the paper are first author Junghyo Yoon, a research scientist in RLE; Hyukjin J. Kwon, a former postdoc; SungKu Kang, a postdoc at Northeastern University; and Eric Brack of the U.S. Army Combat Capabilities Development Command (DEVCOM). The research has been published online in the journal *Environmental Science and Technology*.

Filter-free technology

Commercially available portable desalination units typically require high-pressure pumps to push water through filters, which are very difficult to miniaturize without compromising the energy-efficiency

of the device, explains Yoon.

Instead, their unit relies on a technique called ion concentration polarization (ICP), which was pioneered by Han's group more than 10 years ago. Rather than filtering water, the ICP process applies an electrical field to membranes placed above and below a channel of water. The membranes repel positively or negatively charged particles — including salt molecules, bacteria, and viruses — as they flow past. The charged particles are funneled into a second stream of water that is eventually discharged.

The process removes both dissolved and suspended solids, allowing clean water to pass through the channel. Since it only requires a low-pressure pump, ICP uses less energy than other techniques.

But ICP does not always remove all the salts floating in the middle of the channel. So the researchers incorporated a second process, known as electrodialysis, to remove remaining salt ions.

Yoon and Kang used machine learning to find the ideal combination of ICP and electrodialysis modules. The optimal setup includes a two-stage ICP process, with water flowing through six modules in the first stage then through three in the second stage, followed by a single electrodialysis process. This minimized energy usage while ensuring the process remains self-cleaning.

"While it is true that some charged particles could be captured on the ion exchange membrane, if they get trapped, we just reverse the polarity of the electric field and the charged particles can be easily removed," Yoon explains.

They shrunk and stacked the ICP and electrodialysis modules to improve their energy efficiency and enable them to fit inside a portable device. The researchers designed the device for nonexperts, with just one button to launch the automatic desalination and purification process. Once the salinity level and the number of particles decrease to specific thresholds, the device notifies the user that the water is drinkable.

The researchers also created a smartphone app that can control the unit wirelessly and report real-time data on power consumption and water salinity.

Beach tests

After running lab experiments using water with different salinity and turbidity (cloudiness) levels, they field-tested the device at Boston's Carson Beach.

Yoon and Kwon set the box near the shore and tossed the feed tube into the water. In about half an hour, the device had filled a plastic drinking cup with clear, drinkable water.

"It was successful even in its first run, which was quite exciting and surprising. But I think the main reason we were successful is the accumulation of all these little advances that we made along the way," Han says.

The resulting water exceeded World Health Organization quality guidelines, and the unit reduced the amount of suspended solids by at least a factor of 10. Their prototype generates drinking water at a rate of 0.3 liters per hour, and requires only 20 watts of power per liter.

"Right now, we are pushing our research to scale up that production rate," Yoon says.

One of the biggest challenges of designing the portable system was engineering an intuitive device that could be used by anyone, Han says.

Yoon hopes to make the device more user-friendly and improve its energy efficiency and production rate through a startup he plans to launch to commercialize the technology.

In the lab, Han wants to apply the lessons he's learned over the past decade to water-quality issues that go beyond desalination, such as rapidly detecting contaminants in drinking water.

"This is definitely an exciting project, and I am proud of the progress we have made so far, but there is still a lot of work to do,"

he says.

For example, while the "development of portable systems using electro-membrane processes is an original and exciting direction in off-grid, small-scale desalination," the effects of fouling, especially if the water has high turbidity, could significantly increase maintenance requirements and energy costs, notes Nidal Hilal, professor of engineering and director of the New York University Abu Dhabi Water research center, who was not involved with this research.

"Another limitation is the use of expensive materials," he adds. "It would be interesting to see similar systems with low-cost materials in place."

Reference: "Portable Seawater Desalination System for Generating Drinkable Water in Remote Locations" by Junghyo Yoon, Hyukjin J. Kwon, SungKu Kang, Eric Brack and Jongyoon Han, 14 April 2022, Environmental Science and Technology.
DOI: 10.1021/acs.est.1c08466

The research was funded, in part, by the DEVCOM Soldier Center, the Abdul Latif Jameel Water and Food Systems Lab (J-WAFS), the Experimental AI Postdoc Fellowship Program of Northeastern University, and the Roux AI Institute.

https://wb.md/3worwwu

Why I Recommend Hepatitis B Vaccination to All My Patients

Over 20,000 people in the United States contract acute hepatitis B, annually with healthcare costs of more than a billion dollars. As many as 40% of them have complications.

Sandra Adamson Fryhofer, MD

This transcript has been edited for clarity.

Hello. I'm Dr Sandra Fryhofer. Welcome to Medicine Matters. The topic: the new hepatitis B vaccination recommendations for 2022. Here's why it matters.

Each year, more than 20,000 people in the United States contract acute hepatitis B, with healthcare costs of more than a billion dollars. As many as 40% of them have complications. Hepatitis B can lead to chronic hepatitis infection and liver cancer, and 15%-25% of those infected will die prematurely of cirrhosis or liver cancer. This is needless suffering and death.

Hepatitis B infection is vaccine preventable. We have several vaccine versions to choose from, and they work. The older, three-dose hepatitis B vaccine preparations are more than 90% protective. Immunity is durable, lasting at least three decades.

Two newer vaccines are now available, but only for those aged 18 or older. One of them, Heplisav, contains a new adjuvant, CpG 1018. Its two-dose series can be completed in just 1 month.

A new triple-target hepatitis B vaccine, PreHevbrio, was FDA-approved in December 2021. It requires three doses in a series and contains three hepatitis B antigens. Other available hepatitis B vaccines contain just one antigen. Like the older hepatitis B vaccines, the adjuvant used in PreHevbrio is aluminum hydroxide. Other hepatitis vaccines are yeast-based. PreHevbrio is grown in mammalian CHO cells. Study data for this triple-antigen version suggest high rates of seroprotection in adults, as well as immune response in key high-risk groups, including people with end-stage renal disease and HIV, and also in low and nonresponders.

The hepatitis B vaccine first became available in 1982. Since then, cases have dropped. Initial decreases in new infections plateaued 10 years ago. Rates are now highest in adults. Rates have also increased among adults aged 40 years or older. Racial and ethnic disparities remain. Current rates among Black American adults are now up to three times those of Asian, Pacific Islander, and Hispanic groups.

This year celebrates the 40th anniversary of hepatitis B vaccine recommendations in the United States. Previous recommendations for adults have been risk-based. Vaccine coverage within the indicated risk group shows that overall, vaccine uptake is lacking. Only two thirds of healthcare personnel have been vaccinated. Only

about one third of those with chronic liver disease are fully vaccinated. Only about one third of adults under age 60 with diabetes have been vaccinated. If you look at who gets infected with hepatitis B, at least two thirds of the time no risk factor was identified or reported. Universal childhood hepatitis B vaccination has been a success. As a result, acute hepatitis B is on the path to complete elimination for those aged 29 years or older, but many older adults still remain unprotected. This led the Advisory Committee on Immunization Practices (ACIP) to consider whether all unvaccinated adults should receive hepatitis B vaccination.

Risk-based recommendations favor individuals with consistent access to preventive health services, as well as those who trust the system enough to disclose potentially stigmatizing risk factors. Risk-based recommendations also depend on awareness of risk for exposure to infected household contacts or infected sex partners. Health literacy also plays a role. We know from experience with other vaccines that universal, age-based recommendations lead to increased vaccine uptake as compared with those based on risk. Universal adult hepatitis B vaccination could decrease infections, prevent transmission, and reduce health disparities.

ACIP's Hepatitis B Workgroup Committee reviewed available data, and their preferred suggestion was for universal vaccination, meaning that all adults previously unvaccinated for hepatitis B should receive hepatitis B vaccination. There was no workgroup support for risk-based–only recommendations. However, the workgroup does not make the final recommendation; ACIP CDC's Independent Advisory Committee does.

ACIP did not accept the workgroup suggestion of universal hepatitis B vaccination on face value. Instead, ACIP voted and approved hepatitis B vaccine universally for those up to age 60. But for those aged 60 or older, the recommendation remains risk-based, with a loophole: Anyone aged 60 or older who wants it can get it. If you look at the risk indications, perhaps some may be uncomfortable or embarrassing to disclose, especially for older patients. The loophole sort of takes care of that, but patients still have to ask for the vaccine.

So if you get right down to it, in essence, in a roundabout way, we do now have a universal hepatitis B recommendation for all adults. Hepatitis B vaccination is clearly recommended universally for all adults up to age 60 — that's in the new recommendation — and adults aged 60 years or older who want it may receive it. I will certainly recommend it for all my patients.

For Medicine Matters. I'm Dr. Sandra Fryhofer.

https://bit.ly/3LbzI8L

Cognitive Impact of Severe COVID Is Equivalent to 20 Years of Aging, Study Finds

We all know that COVID-19 can lead to lingering fatigue and brain fog. But one of the most rigorous examinations to date of the long-term cognitive impacts of severe infection has just yielded some pretty unsettling results.

Fiona Macdonald

In a study comparing 46 severe COVID-19 patients with 460 matched controls, researchers found the mental impacts of severe COVID-19 six months later can be the equivalent to aging 20 years – going from 50 to 70 years old – or losing 10 IQ points.

The specific mental changes were also distinct to those seen in early dementia or general aging.

"Cognitive impairment is common to a wide range of neurological disorders, including dementia, and even routine aging, but the patterns we saw – the cognitive 'fingerprint' of COVID-19 – was distinct from all of these," says neuroscientist David Menon from the University of Cambridge in the UK, who was senior author of the study.

The new paper doesn't set out to alarm the many of us who've

already had COVID, but instead investigate more closely how serious the cognitive changes are following severe cases of the infection, so we can begin to understand how to mitigate them.

"Tens of thousands of people have been through intensive care with COVID-19 in England alone and many more will have been very sick, but not admitted to hospital," says lead researcher and cognitive scientist Adam Hampshire from Imperial College London. "This means there are a large number of people out there still experiencing problems with cognition many months later. We urgently need to look at what can be done to help these people."

The experiment involved 46 people who'd gone to Addenbrooke's Hospital in Cambridge as a result of COVID-19 between March and July 2020. Sixteen of them were put on mechanical ventilation during their stay.

An average of six months after their infection, researchers supervised them using a testing tool called Cognitron to see how they were doing in areas such as memory, attention, reasoning, as well as anxiety, depression, and post-traumatic stress disorder.

The researchers didn't have test results from before these individuals fell ill with COVID to compare to. Instead they did the next best thing, and compared their results against a matched control group of 460 people.

These results were then mapped to see how far they deviated from expected scores for their age and demographic, based on 66,008 members of the general public. The results showed that those who'd survived severe COVID were less accurate and had slower response times than the general public. The magnitude of cognitive loss was similar to the effects of aging between 50 and 70 years of age – and equivalent to losing 10 IQ points.

Accuracy in verbal analogy tasks – where people are asked to find similarities between words – was most impacted. This mirrors anecdotal reports that suggest people post-infection are struggling to find the right word, and feeling like their brain is in slow motion.

Interestingly, even though patients reported varying levels of fatigue and depression, the severity of the initial infection, rather than the survivor's current mental health, could best predict the cognitive outcome, the team found.

"These results indicate that although both fatigue and mental health are prominent chronic [consequences] of COVID-19, their severity is likely to be somewhat independent from the observed cognitive deficits," the researchers write in their paper.

The somewhat good news is that, upon follow up, there were some signs of recovery – but it was gradual at best. "We followed some patients up as late as ten months after their acute infection, so were able to see a very slow improvement," says Menon.

"While this was not statistically significant, it is at least heading in the right direction, but it is very possible that some of these individuals will never fully recover."

This study only looked at the more extreme end of hospitalized patients, but there are plenty of other studies showing that even 'mild' cases can cause similar cognitive impacts. What's still not fully understood is why and how the SARS-CoV-2 virus causes this cognitive decline.

Previous research has shown that during severe COVID, the brain decreases glucose consumption in the frontoparietal network, which is involved in attention, problem solving, and working memory. It's also known that the virus can directly affect the brain.

But the researchers suggest the likely culprit isn't direct infection, but a combination of factors: including reduced oxygen or blood supply to the brain; clotting of vessels; and microscopic bleeds.

There's also mounting evidence that the body's own immune and inflammatory response may be having a significant impact on the brain. "Future work will be focused on mapping these cognitive deficits to underlying neural pathologies and inflammatory

biomarkers, and to longitudinally track recovery into the chronic phase," the researchers write. Until then, take comfort in the fact that if you're still feeling slow and foggy months after recovering from COVID-19, you are most certainly not alone.

The research has been published in *eClinical Medicine*.

https://bit.ly/3szGMWd

Eating one-fifth less beef could halve deforestation

Model suggests that switching to microbial 'meat' can cut carbon emissions.

Giorgia Guglielmi

Replacing just 20% of global beef consumption with a meat substitute within the next 30 years could halve deforestation and the carbon emissions associated with it, finds a modelling study.

The findings, published in *Nature* on 4 May[1], come one month after the United Nations Intergovernmental Panel on Climate Change warned that humanity is nowhere near on track to limit global warming to 1.5 ºC above pre-industrial levels.

Beef farming is a top driver of deforestation worldwide, and cattle raised for beef are a major source of methane, a more potent greenhouse gas than carbon dioxide. Replacing beef with meat alternatives could reduce some of the food production's environmental footprint, but it won't solve the climate crisis, says study lead author Florian Humpenöder, a sustainability scientist at the Potsdam Institute for Climate Impact Research in Germany. "It should not be seen as a silver bullet," he says.

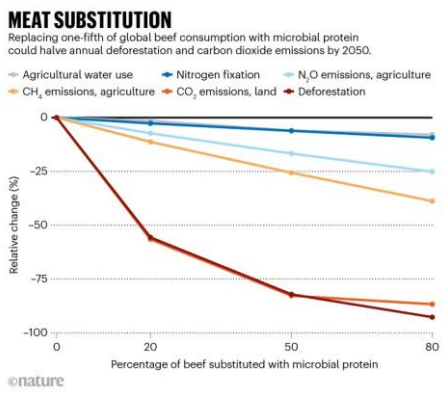
Previous research has shown that replacing beef with a meatless alternative called mycoprotein can have beneficial effects on the environment. Produced in steel tanks by fermenting a soil-dwelling fungus with glucose and other nutrients as a food source, mycoprotein is a meat substitute that made its debut in the United Kingdom in the 1980s under the brand name Quorn and is now readily available in many countries.

Humpenöder and his colleagues are the first to estimate the environmental effects of partially replacing beef with mycoprotein over time, says Franziska Gaupp, who studies food systems at the Potsdam Institute for Climate Impact Research. Previous analyses didn't take into account changes in population growth, food demand and other socio-economic factors.

The team used a mathematical model that considered increases in population growth, income and livestock demand between 2020 and 2050. Under a business-as-usual scenario, the global increase in beef consumption would require the expansion of pasture areas for grazing and of cropland for feed production, which would double the annual rate of deforestation globally. Methane emissions and agricultural water use would also increase.

Replacing 20% of the world's per-capita beef consumption with mycoprotein by 2050 would reduce methane emissions by 11% and halve the annual deforestation and associated emissions, compared with the business-as-usual scenario (see 'Meat substitution'). The mitigating effects on deforestation are so great because, under this scenario, global demand for beef does not increase, so there is no need to expand pasture areas or cropland for feeding cattle, Humpenöder says.

The beneficial effects on deforestation eventually plateau out. Swapping 50% of the beef consumed per person for mycoprotein would result in a more than 80% reduction in deforestation and carbon emissions, and replacing 80% of beef with mycoprotein would eliminate about 90% of forest loss.



Source: Ref. 1

All levels of substitution would result in relatively minor changes in

agricultural water use, the researchers found. That's because the water required to grow crops for feeding cattle would go towards growing other types of crop, including those for human consumption, Humpenöder says.

Global assessments such as the one carried out by Humpenöder's team could help to highlight more-sustainable ways to produce food, says Hanna Tuomisto, who studies sustainable food systems at the University of Helsinki. Tuomisto notes that producing mycoprotein can require more electricity than producing beef, so researchers should consider the environmental impacts of producing extra power. She also points out that replacing beef with mycoprotein means that some by-products of cattle farming, such as leather and milk, might then be made in alternative ways that have environmental impacts.

"This study is a great start," Gaupp says. Future research, she adds, should look at the environmental effects of replacing beef with other types of meat alternative, such as laboratory-grown meat or plant-based alternatives. *doi: https://doi.org/10.1038/d41586-022-01238-5*

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1. Humpenöder, F. et al. Nature https://doi.org/10.1038/s41586-022-04629-w (2022).
Article Google Scholar Download references

https://bit.ly/3NbhRQt

There Are Mountains of Sugar Hidden in The Ocean, And We've Only Just Found Out

Hidden below the waves, the ocean contains vast reserves of sugar that we never were aware of, according to new research.

David Nield

Scientists have discovered that seagrass meadows on the ocean floor can store huge amounts of the sweet stuff underneath their waving fronds – and there are major implications for carbon storage and climate change.

The sugar comes in the form of sucrose (the main ingredient of sugar used in the kitchen), and it's released from the seagrasses into the soil underneath, an area directly affected by the roots, known as the rhizosphere. It means seabed sugar concentrations are some 80 times higher than they would be normally.

Worldwide, seagrasses could be sitting on up to 1.3 million tons of sucrose, the research team says. To put it another way, that's enough for about 32 billion cans of Coca-Cola, so we're talking about a substantial find of hidden sugar.

"Seagrasses produce sugar during photosynthesis," says marine microbiologist Nicole Dubilier from the Max Planck Institute for Marine Microbiology in Germany.

"Under average light conditions, these plants use most of the sugars they produce for their own metabolism and growth. But under high light conditions, for example at midday or during the summer, the plants produce more sugar than they can use or store. Then they release the excess sucrose into their rhizosphere. Think of it as an overflow valve."

What's surprising is that this excess sugar isn't gobbled up by microorganisms in the surrounding environment. To stop this, it seems seagrasses send out phenolic compounds in the same way as many other plants do.

These chemical compounds – found in red wine, coffee, and fruit, as well as many other places in nature – are antimicrobials that inhibit the metabolism of most microorganisms, slowing them down.

The researchers tested out their hypothesis in an actual underwater seagrass field to confirm that this is indeed what was happening, via a mass spectrometry technique.

Studying seagrasses on the seafloor. (HYDRA Marine Sciences GmbH)

"In our experiments we added phenolics isolated from seagrass to the microorganisms in the seagrass rhizosphere," says marine

microbiologist Maggie Sogin from the Max Planck Institute for Marine Microbiology. "And indeed, much less sucrose was consumed compared to when no phenolics were present."

A small set of microbes actually thrived on the sucrose despite the presence of phenolics: the researchers think that these "microbial specialists" are perhaps giving something back to the seagrass in return, like nutrients they need to grow.

Seagrasses are some of the planet's most important sinks for blue carbon (carbon captured by the world's ocean and coastal ecosystems): an area of seagrass can suck up twice as much carbon as a forest of the same size on land, and 35 times as fast too.

When it comes to calculating carbon capture loss from the seagrass meadows – among the most threatened habitats on the planet due to human activity and decreasing water quality – scientists can now factor in the sucrose deposits as well as the seagrass itself.

"We do not know as much about seagrass as we do about land-based habitats," says Sogin.

"Our study contributes to our understanding of one of the most critical coastal habitats on our planet, and highlights how important it is to preserve these blue carbon ecosystems."

The research has been published in *Nature Ecology & Evolution*.

https://bit.ly/3l54xBp

A very specific kind of brain cell dies off in people with Parkinson's

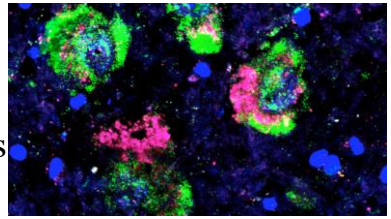
Dopamine-making nerve cells may not be equally culpable in the disease after all

By Laura Sanders

Deep in the human brain, a very specific kind of cell dies during Parkinson's disease.

For the first time, researchers have sorted large numbers of human brain cells in the substantia nigra into 10 distinct types. Just one is especially vulnerable in Parkinson's disease, the team reports May 5 in Nature Neuroscience. The result could lead to a clearer view of how Parkinson's takes hold, and perhaps even ways to stop it.

The new research "goes right to the core of the matter," says neuroscientist Raj Awatramanic of Northwestern University Feinberg School of Medicine in Chicago. Pinpointing the brain cells that seem to be especially susceptible to the devastating disease is "the strength of this paper," says Awatramani, who was not involved in the study.



Certain human brain cells selectively die off in Parkinson's disease. Among cells that produce the chemical messenger dopamine (green), an active AGTR1 gene (labeled in magenta) sets these vulnerable cells apart. **Macosko Lab**

Parkinson's disease steals people's ability to move smoothly, leaving balance problems, tremors and rigidity. In the United States, nearly 1 million people are estimated to have Parkinson's. Scientists have known for decades that these symptoms come with the death of nerve cells in the substantia nigra. Neurons there churn out dopamine, a chemical signal involved in movement, among other jobs (SN: 9/7/17). But those dopamine-making neurons are not all equally vulnerable in Parkinson's, it turns out.

"This seemed like an opportunity to … really clarify which kinds of cells are actually dying in Parkinson's disease," says Evan Macosko, a psychiatrist and neuroscientist at Massachusetts General Hospital in Boston and the Broad Institute of MIT and Harvard.

The tricky part was that dopamine-making neurons in the substantia nigra are rare. In samples of postmortem brains, "we couldn't survey enough of [the cells] to really get an answer," Macosko says. But Abdulraouf Abdulraouf, a researcher in Macosko's laboratory, led experiments that sorted these cells, figuring out a way to selectively pull the cells' nuclei out from the rest of the cells

present in the substantia nigra. That enrichment ultimately led to an abundance of nuclei to analyze.

By studying over 15,000 nuclei from the brains of eight formerly healthy people, the researchers further sorted dopamine-making cells in the substantia nigra into 10 distinct groups. Each of these cell groups was defined by a specific brain location and certain combinations of genes that were active.

When the researchers looked at substantia nigra neurons in the brains of people who died with either Parkinson's disease or the related Lewy body dementia, the team noticed something curious: One of these 10 cell types was drastically diminished.

These missing neurons were identified by their location in the lower part of the substantia nigra and an active AGTR1 gene, lab member Tushar Kamath and colleagues found. That gene was thought to serve simply as a good way to identify these cells, Macosko says; researchers don't know whether the gene has a role in these dopamine-making cells' fate in people.

The new finding points to ways to perhaps counter the debilitating diseases. Scientists have been keen to replace the missing dopamine-making neurons in the brains of people with Parkinson's. The new study shows what those cells would need to look like, Awatramani says. "If a particular subtype is more vulnerable in Parkinson's disease, maybe that's the one we should be trying to replace," he says. In fact, Macosko says that stem cell scientists have already been in contact, eager to make these specific cells. "We hope this is a guidepost," Macosko says.

The new study involved only a small number of human brains. Going forward, Macosko and his colleagues hope to study more brains, and more parts of those brains. "We were able to get some pretty interesting insights with a relatively small number of people," he says. "When we get to larger numbers of people with other kinds of diseases, I think we're going to learn a lot."

https://nyti.ms/3w8ATkO

Signs of an Animal Virus Discovered in Man Who Received a Pig's Heart

The patient showed no sign of rejecting the genetically modified organ, but suffered numerous complications before dying.

By Roni Caryn Rabin

Traces of a virus known to infect pigs were found in a 57-year-old Maryland man who survived for two months with a heart transplanted from a genetically altered pig, according to the surgeon who performed the procedure, the first of its kind.

The disclosure highlights one of the most pressing objections to animal-to-human transplants, which is that widespread use of modified animal organs might facilitate the introduction of new pathogens into the human population.

The presence of the virus's DNA in the patient may have contributed to his sudden deterioration more than a month after the transplant, said the surgeon, Dr. Bartley Griffith of the University of Maryland School of Medicine.

But there was no evidence that the patient developed an active infection with the virus, or that his body had rejected the heart, Dr. Griffith added.

The patient, David Bennett Sr., had been extremely ill before the surgery and suffered numerous other complications after the transplant. He died on March 8.

Dr. Griffith's revelations about the viral traces found in the patient, made last month during an American Society of Transplantation meeting, were first reported by MIT Technology Review.

In an interview with The New York Times on Thursday, Dr. Griffith and his colleague, Dr. Muhammad Mohiuddin, the scientific director of the cardiac xenotransplantation program at University of Maryland School of Medical, said that they were saddened by the loss of Mr. Bennett but that they were not deterred

from their goal of using animal organs to save human lives.

"This doesn't really scare us about the future of the field, unless for some reason this one incident is interpreted as a complete failure," Dr. Griffith said. "It is just a learning point. Knowing it was there, we'll probably be able to avoid it in future."

The pig, which had been genetically modified so that its organs would not trigger rejection by the human immune system, was provided by Revivicor, a regenerative medicine company based in Blacksburg, Va.

Company officials declined to comment on Thursday, and officials with the Food and Drug Administration, which gave the transplant surgeons emergency authorization for the operation on New Year's Eve, said they could not immediately respond to questions.

University officials said that although the pig had been screened several times for the virus, the tests pick up only active infections, not latent ones in which the virus may hide quietly in the pig's body. (The tests were done on nasal swabs, but the virus was later detected in the pig's spleen.)

The latent virus might have "hitched a ride" into the patient on the transplanted heart, Dr. Griffith said.

Mr. Bennett's transplant was initially deemed successful. He did not show signs of rejecting the organ, and the pig's heart continued to function for well over a month, passing a critical milestone for transplant patients.

A test first indicated the presence of porcine cytomegalovirus DNA in Mr. Bennett 20 days after the transplant, but at such a low level that Dr. Griffith said he thought it might have been a lab error.

About 40 days after the surgery, however, Mr. Bennett suddenly became acutely ill, and subsequent tests showed a precipitous rise in viral DNA levels, Dr. Griffith said.

"So we started thinking that the virus that showed up very early at Day 20 as just a twinkle started to grow in time, and it may have been the actor — it could have been the actor — that set this all off," Dr. Griffith told other transplant scientists at the meeting.

At Day 45, Mr. Bennett's health abruptly deteriorated.

Doctors treated Mr. Bennett with antiviral drugs and intravenous immune globulin (IVIG), a product made of antibodies, but the new heart filled with fluid, doubled in size and stopped working, and he was eventually put on a heart-lung machine.

The heart transplant was one of several groundbreaking transplants in recent months that offer hope to the tens of thousands of patients who need new kidneys, hearts and lungs amid a dire shortage of donated human organs.

Surgeons in New York in October successfully attached a kidney grown in a genetically altered pig to a brain-dead patient, and found that the organ worked normally and produced urine.

In January, surgeons at the University of Alabama at Birmingham reported that they had transplanted kidneys from a genetically modified pig into the abdomen of a 57-year-old brain-dead man.

But the prospect of unforeseen consequences — and particularly the potential introduction of animal pathogens into the human population — may dampen enthusiasm for the use of genetically modified organs.

The coronavirus that set off the global Covid pandemic is believed by many scientists to have originated with a virus that was transmitted from an unidentified animal to people in China.

Porcine cytomegalovirus has not been a major concern, since it is a herpesvirus, which tend to be species-specific, said Dr. Jay Fishman, associate director of the transplantation center at Massachusetts General Hospital, who studies infectious diseases.

"They will replicate only in the host with which they are associated," Dr. Fishman said.

Nevertheless, the virus could infect the transplanted animal organ, leading to a cascade of systemic effects that ultimately harm the

patient.

“Did this contribute to the patient’s demise? The answer is obviously, we don’t know, but it might have contributed to his overall not doing well,” Dr. Fishman said.

Dr. Jayme Locke, a transplant surgeon who is director of the Incompatible Kidney Transplant Program at University of Alabama at Birmingham, said genetically modified pigs whose organs are to be used for transplantation must be raised in a pathogen-free facility and weaned from their mothers within 48 hours of birth, in order to prevent transmission of porcine cytomegalovirus during lactation.

The university has such a facility, and Dr. Locke said she was still planning to start a small Phase 1 clinical trial in which she will transplant kidneys from genetically modified pigs into people with end-stage kidney disease.

More sensitive screening of the animals for the virus will be required, she added.

“From my perspective, it’s not slowing down what we need to do, but further emphasizing that data showing our herd is free of that virus will be critical” for regulatory permission to move forward, she said.

https://bit.ly/3sVsTlt

FDA puts the brakes on J&J vaccine after 9th clotting death reported

FDA reports 3 TTS cases per million J&J doses, and 0.48 deaths per million doses.

Beth Mole

The US Food and Drug Administration limited the use of the Johnson & Johnson (Janssen) COVID-19 vaccine late Thursday, citing the risk of a very rare but severe clotting disorder called thrombosis with thrombocytopenia syndrome (TTS).

From now on, the J&J vaccine is only to be used in people ages 18 and up who are unable or unwilling to receive an alternative COVID-19 vaccine. That includes people who have had a life-threatening allergic reaction (anaphylaxis) to an mRNA COVID-19 vaccine, people who have personal concerns about mRNA COVID-19 vaccines and would otherwise not get vaccinated, and people who don't have access to mRNA COVID-19 vaccines.

The limitation comes as the FDA and the Centers for Disease Control and Prevention have been closely monitoring people who received J&J COVID-19 vaccinations for TTS.

To date, the agencies have identified and confirmed 60 cases of TTS linked to the vaccine, including nine deaths. That represents a rate of 3.23 TTS cases per million doses of J&J vaccine administered, and a rate of 0.48 TTS deaths per million doses of vaccine administered, the FDA said Thursday.

Though the risks are small, the FDA determined that they're unnecessary risks for most people to take, given the wide availability of mRNA vaccines (made by Moderna and Pfizer-BioNTech) that are similarly effective and do not carry such risks of severe disease and death.

The FDA's decision follows a downgraded recommendation from the Centers for Disease Control and Prevention last December, which stated that the mRNA COVID-19 vaccines are preferred over the J&J vaccine. The CDC outlined specific instances in which the J&J vaccine could be considered, which match the uses listed by the FDA.

Limits and risks

In a statement Thursday, top vaccine regulator Peter Marks explained the timing of the FDA's move. “We recognize that the Janssen COVID-19 vaccine still has a role in the current pandemic response in the United States and across the global community. Our action reflects our updated analysis of the risk of TTS following administration of this vaccine and limits the use of the vaccine to certain individuals,” he said, and "demonstrates the robustness of

our safety surveillance systems and our commitment to ensuring that science and data guide our decisions. … The agency will continue to monitor the safety of the Janssen COVID-19 Vaccine and all other vaccines, and as has been the case throughout the pandemic, will thoroughly evaluate new safety information."

TTS is a severe condition marked by the unusual combination of blood clots blocking a blood vessel, aka thrombosis, and thrombocytopenia, an overall low count of blood platelets, which help blood clot.

The condition can be particularly dangerous if the blood clot affects the brain, such as in cerebral venous sinus thrombosis (CVST), which is a rare but life-threatening type of stroke that prevents blood from draining out of the brain.

The risk of TTS from the J&J vaccine—which uses an adenovirus-based vaccine design—was first identified in early April 2021, at which point the CDC paused use of the vaccine. The FDA and CDC lifted the pause later that month after determining that the vaccine's benefits in preventing COVID-19 outweighed the small risk of developing TTS.

It still remains unclear how the vaccine may trigger the condition in rare instances, however researchers hypothesized that something about the adenovirus-based vaccine may trigger an immune response that leads to platelet activation and low platelet levels. Another adenovirus-based COVID-19 vaccine, made by AstraZeneca, has also been linked to rare cases of TTS.

Amid the TTS reports, the CDC's pause, and early clinical trial data showing that mRNA vaccines outperformed the J&J vaccine, use of the troubled adenovirus-based vaccine plummeted in the US. Of the 577 million doses administered to date, only 18.7 million were J&J vaccines.

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Scientists "Magically" Mine Metals From Water

Testing a method that employs magnetic nanoparticles to extract important minerals like lithium from various water source

By Steven Ashby, Pacific Northwest National Laboratory

Alchemists sought to transform lead into gold centuries ago. While they were not successful, the notion of extracting precious resources from abundant sources remains alluring.

Scientists at the Department of Energy's Pacific Northwest National Laboratory (PNNL) are collaborating with industry to test a method that employs magnetic nanoparticles to extract important minerals like lithium from various water sources.

Lithium is an essential ingredient in many electronic and energy technologies, including the lightweight lithium-ion batteries that power everything from cell phones to electric vehicles.

The global market for lithium is projected to reach $8.2 billion by 2028, but precious little is produced in the United States.

Not only does PNNL's patent-pending technology potentially give the U.S. an opportunity to produce more of its own lithium and other critical materials, but it also offers a much faster and less expensive way of doing so. PNNL is developing magnetic nanoparticles that are surrounded by an adsorbent shell that latches onto the lithium and other metals found in water associated with various industrial processes.

These sources could include the water in geothermal power plants, known as geothermal brines, or water pulled from the subsurface during oil or gas production. The particles also could be used in effluents from desalination plants, or even directly from seawater. Once the tiny, iron-based particles are added to the water, the lithium is drawn out of the water and binds to them. Then, with the help of a magnet, the nanoparticles can be collected in just minutes with the lithium hitching a ride, no longer suspended in the liquid

and ready for easy extraction. After the lithium is extracted, the recharged nanoparticles can be used again.

This technology offers a promising alternative to conventional extraction methods that pump groundwater into large, costly evaporating ponds. Those processes can take months or even years and impact groundwater management in the arid regions where they are mainly deployed.

While the PNNL process goes to work immediately, today's processes are a bit like waiting for the water to evaporate from a pitcher of lemonade in hopes of reclaiming the powdered mix settling at the bottom. If this technology were deployed at geothermal plants, the value of recovered lithium could potentially increase the cost-effectiveness of this form of renewable energy, which uses water to capture the heat deep below the Earth's surface and then converts it into electricity.

PNNL is further developing this technology in a partnership with Moselle Technologies, which has licensed it and plans to pilot it in several locations.

This effort and the follow-on activities are great examples of how the national laboratories collaborate with commercial entities to transition lab research into real-world solutions.

For instance, researchers at PNNL are conducting long-duration tests of the magnetic separator system for potential use with oil and gas extraction processes, which could create an additional revenue stream to offset production costs.

In addition to Moselle, they are teaming with other commercial partners to evaluate the use of the technology for their lithium resources in Nevada and Canada.

Finally, with an eye on a different set of applications, researchers at PNNL are customizing the shell of the nanoparticle to specifically target other commercially valuable, strategically important elements and minerals used in energy technologies, medical imaging devices, electronics and more.

For example, they are collaborating with Moselle and Geo40 to explore the possibility of extracting cesium and antimony from geothermal brines at a geothermal plant in New Zealand.

Though none of these efforts amount to sorcery, one could forgive the alchemists of yore for mistaking this marvel of chemistry for magic.

PNNL's novel approach is truly remarkable. It offers the promise of extracting critical minerals in a quick, cost-effective manner. And innovation like this just might be worth its weight in gold.

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Genetic Limit on Cell Division Could Explain COVID-19 Deaths Among Elderly

Key hypothesis of a new study is that the body's ability to create cloned immune cells falls off significantly in old age

Your immune system's ability to fight COVID-19, like any infection, largely depends on its ability to replicate the immune cells effective at destroying the SARS-CoV-2 virus that causes the disease. These cloned immune cells cannot be infinitely created, and a key hypothesis of a new University of Washington (UW) study is that the body's ability to create these cloned cells falls off significantly in old age.

According to a new model created by UW research professor James Anderson, this genetically predetermined limit on your immune system may be the key to why COVID-19 has such a devastating effect on the elderly. Anderson is the lead author of a paper published on March 31, 2022, in the journal *The Lancet eBioMedicine* detailing this modeled link between aging, COVID-19, and mortality.

"When DNA split in cell division, the end cap — called a telomere — gets a little shorter with each division," explains Anderson, who is a modeler of biological systems in the School of Aquatic and

Fishery Sciences. “After a series of replications of a cell, it gets too short and stops further division. Not all cells or all animals have this limit, but immune cells in humans have this cell life.”

The average person’s immune system coasts along pretty good despite this limit until about 50 years old. That’s when enough core immune cells, called T cells, have shortened telomeres and cannot quickly clone themselves through cellular division in big enough numbers to attack and clear the COVID-19 virus, which has the trait of sharply reducing immune cell numbers, Anderson said. Importantly, he added, telomere lengths are inherited from your parents. Consequently, there are some differences in these lengths between people at every age as well as how old a person becomes before these lengths are mostly used up.

Anderson said the key difference between this understanding of aging, which has a threshold for when your immune system has run out of collective telomere length, and the idea that we all age consistently over time is the “most exciting” discovery of his research.

“Depending on your parents and very little on how you live, your longevity or, as our paper claims, your response to COVID-19 is a function of who you were when you were born,” he said, “which is kind of a big deal.”

To build this model the researchers used publicly available data on COVID-19 mortality from the Center for Disease Control and US Census Bureau and studies on telomeres, many of which were published by the co-authors over the past two decades.

Assembling telomere length information about a person or specific demographic, he said, could help doctors know who was less susceptible. And then they could allocate resources, such as booster shots, according to which populations and individuals may be more susceptible to COVID-19.

“I’m a modeler and see things through mathematical equations that I am interpreting by working with biologists, but the biologists need to look at the information through the model to guide their research questions,” Anderson said, admitting that “the dream of a modeler is to be able to actually influence the great biologists into thinking like modelers. That’s more difficult.”

One caution Anderson has about this model is that it might explain too much.

“There’s a lot of data supporting every parameter of the model and there is a nice logical train of thought for how you get from the data to the model,” he said of the model’s power. “But it is so simple and so intuitively appealing that we should be suspicious of it too. As a scientist, my hope is that we begin to understand further the immune system and population responses as a part of natural selection.”

Reference: “Telomere-length dependent T-cell clonal expansion: A model linking ageing to COVID-19 T-cell lymphopenia and mortality” by James J. Anderson, Ezra Susser, Konstantin G. Arbeev, Anatoliy I. Yashin, Daniel Levy, Simon Verhulst and Abraham Aviv, 31 March 2022, EBioMedicine. DOI: 10.1016/j.ebiom.2022.103978

Co-authors include Ezra Susser, Mailman School of Public Health, Columbia University; Konstantin Arbeev and Anatoliy Yashin, Social Science Research Institute, Duke University; Daniel Levy, National Heart, Lung, and Blood Institute, National Institutes of Health; Simon Verhulst, University of Groningen, Netherlands; Abraham Aviv, New Jersey Medical School, Rutgers University.