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Potato farmers conquer a devastating worm—with paper made from bananas

Low-tech approach can quintuple yield and slash need for soil pesticide

By Erik Stokstad

Potato cyst nematodes are a clever pest. These microscopic worms wriggle through the soil, homing in the roots of young potato plants and cutting harvests by up to 70%. They are challenging to get rid of, too: The eggs are protected inside the mother's body, which toughens after death into a cyst that can survive in the soil for years. Now, researchers have shown a simple pouch made of paper created from banana tree fibers disrupts the hatching of cyst nematodes and prevents them from finding the potato roots. The new technique has boosted yields fivefold in trials with small-scale farmers in Kenya, where the pest has recently invaded, and could dramatically reduce the need for pesticides. The strategy may benefit other crops as well.

"It's an important piece of work," says Graham Thiele, a research director at the International Potato Center who was not involved with the study. But, "There's still quite a lot of work to take it from a nice finding to a real-life solution for farmers in East Africa," he cautions.

Soil nematodes are a problem for many kinds of crops. For potatoes, the golden cyst nematode (*Globodera rostochiensis*) is a worldwide threat. Plants with infected, damaged roots have yellowish, wilting leaves. Their potatoes are smaller and often covered with lesions, so they can't be sold. In temperate countries, worms can be controlled by alternating potatoes with other crops, spraying the soil with pesticides, and planting varieties bred to resist infection.

These approaches aren't yet feasible in many developing countries, in part because pesticides are expensive and resistant varieties of potatoes aren't available for tropical climates. In addition, small-scale farmers, who can make decent money selling potatoes, are often reluctant to rotate their planting with less valuable crops.

In Kenya, the potato cyst nematode has expanded its range and thrived. "The nematode densities are just so astonishingly high," says Danny Coyne, a nematode expert at the International Institute of Tropical Agriculture. This is leading to an additional problem of biodiversity loss: Potato farmers are cutting down forests to create new fields free of the nematodes.

The idea that banana paper could help farmers rid their soil of nematodes was hatched more than 10 years ago. Researchers at North Carolina State University (NC State) were looking for a way to help farmers in developing countries safely deliver small doses of pesticides. They experimented with various materials. What works best, they found, is paper made from banana plants. Their tubular, porous fibers slowly release pesticides in the soil for several weeks before breaking down. By then, the plant has developed enough so that even if it does get infected, it already has a healthy root system.

In a field trial, researchers added abamectin, a pesticide that kills nematodes, to the paper. They also planted potatoes in banana paper without abamectin as a control. To their surprise, those plants grew nearly as well as the ones with pesticides. Coyne mentioned this puzzling result to a colleague, a chemical ecologist named Baldwyn Torto who studies the interactions between pests and plants at the International Centre of Insect Physiology and Ecology. "This is fascinating indeed," Torto recalls thinking.

Together with Juliet Ochola, now a graduate student at NC State, Torto devised several experiments to figure out what was going on. The duo discovered the banana paper holds onto key compounds released from the roots of young potato plants, some of which attract soil microbes that benefit the plant. Nematodes have also

evolved to notice these compounds. Some, such as alpha-chaconine, are a signal for nematode eggs to hatch. “If a lot of them hatch at the same time, they’re able to bust open the cysts,” Ochola says. After hatching, the young nematodes sense the compounds and use them to seek out the tender potato roots.

Banana fibers absorbed 94% of the compounds, Ochola and colleagues found. When they exposed nematode eggs to the exudates using the paper, the hatching rate decreased by 85% compared with not using the paper, the team reports today in *Nature Sustainability*. Other experiments suggested the nematodes that do hatch are far less likely to be able to find potato roots enclosed in the paper.

In nematode-infested fields in Kenya, Coyne and colleagues showed planting potatoes wrapped in plain banana paper tripled the harvest compared with planting without the paper. A tiny dose of abamectin in the paper—just five-thousandths of what would normally be sprayed on the soil—boosted the harvest by another 50%. Presumably, any nematodes that happened to come across the potatoes were then killed by the abamectin. “We’ve got a win here,” Coyne says.

Now, researchers are figuring out how to bring the wrap-and-plant paper to potato farmers in East Africa. Banana plantations in Kenya and nearby countries could supply the fibers, which are now discarded as a waste product. Paper manufacturers could then make the pouches. The biggest challenge, Coyne suspects, will be convincing farmers to buy the paper for the first time.

Once the farmers try the pouches, they’ll find them easy to use, the researchers say. “It’s just wrap and plant,” Ochola says. Simple, yes, but wrapping a lot of potatoes will still be laborious, notes Isabel Conceição, a nematode expert at the University of Coimbra. If a machine is developed to wrap the potatoes, she says, it’s possible the approach might also be feasible on larger farms that use mechanical planters.

Meanwhile, Coyne and his colleagues say they have encouraging results from trials with other tuber crops, such as yam and sweet potato. He also hopes many kinds of vegetables, planted as seeds or seedlings, could be protected from soil pests and pathogens with small pots or trays made from banana fiber, impregnated with various pesticides or biocontrol agents.

The appeal is natural: Banana paper is a biodegradable product, recycled from waste, and it could help protect both farmers and the environment. “We are reducing the amount of pesticides by so much,” Ochola says. “To me, I feel like that’s amazing.”

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Did Elizabeth Taylor really have violet eyes?

Elizabeth Taylor was known for Cleopatra and Who's Afraid of Virginia Woolf was known for her violet eyes, but were they real?

By Remy Melina , Callum McKelvie

The actress Elizabeth Taylor is primarily remembered for her passionate performances in numerous films, such as 1963's Cleopatra and 1958's Cat on a Hot Tin Roof as well as her marriage to Richard Burton and her love of diamonds. Due to her immense talent as an actress, she was a captivating screen presence and audiences often found themselves hypnotized by her famous violet eyes. But did Elizabeth Taylor really have violet eyes?

Who was Elizabeth Taylor?

Elizabeth Taylor was born on February 27th 1932 and made her film debut in 1942's One Born Every Minute before achieving stardom with 1944's National velvet, according to Biography.com.

One of her most famous roles was as Cleopatra, Queen of the Nile, in the 1963 film of the same name. The film earned Taylor a Guinness World Record for Most Costume Changes in a Film, according to ABC.

However, Cleopatra would also impact Taylor's life in another way

as it brought her close to the actor Richard Burton and the two would begin an obsessive love affair. Burton would present Taylor with some of the world's most famous jewels as tokens of his affections, including the 33.19 Carat Krupp Diamond, according to Vanity Fair. They made several films together, including 1966's Who's Afraid of Virginia Woolf? For which Taylor won one of two academy awards. However the couple had a troubled marriage, they would divorce in 1974 only to remarry and divorce again a year later.

Taylor was also an important activist who used her fame to shine a light on the HIV/AIDS pandemic, curtailing some of the ignorance surrounding the virus, according to the Elizabeth Taylor site.

Taylor remains "one of the world's most iconic women, renowned for her independent spirit, enduring strength and unwavering compassion, she has captured the hearts of millions," the official Elizabeth Taylor site states.

Elizabeth Taylor playing one of her most famous roles, that of Cleopatra in the 1963 film of the same name **(Image credit: Getty/ Hulton Archive/Stringer)**

Did Elizabeth Taylor have violet eyes?

These days, thanks to colored contact lenses, anyone can have violet-colored eyes . Taylor didn't come by her purple peepers that way; the first tinted contact lenses weren't commercially available until 1983. Taylor's eye color was the real deal.

The appearance of the iris, the colored ring that's around the eye's black pupil depends on how much of the natural pigment melanin it contains. The more melanin in your iris, the darker your eyes will look (melanin levels are determined by your genes). For example, the irises of a person with dark brown eyes have more melanin than the eyes of a green-eyed person. Taylor's eyes had a very specific, and rare, amount of melanin, according to The List.

"There are various shades of blues and grays, with many in-between. Violet may have been her typical pigmentation," Norman Saffra, chairman of the ophthalmology department at the Maimonides Medical Center in Brooklyn, N.Y., told Live Science . "It's possible to have that eye color; it all depends on the amount of melanin."

Eye color can also appear to change based on the eye's light absorption, Saffra said. For example, wearing a white shirt will reflect light off of the iris and make its color look slightly lighter.

Makeup can also "bring out" certain colors in the eyes. Taylor was often photographed wearing blue or purple eyeshadow to compliment her eyes' naturally violet hue, or dark brown eyeshadow and black eyeliner to contrast against and play up their unique color.

Additional resources

To read more about Elizabeth Taylor, check out her official site here. To discover more about why eyes are different colors, try this article from Medical News Today. This piece from All About Vision further explains why eye colors develop and change.

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No time to nap in nature

The first study ever to examine sleeping behavior in a wild group of primates has challenged a central tenet of sleep science: that we must make up for lost sleep.

Even after sleeping poorly, wild baboons still spent time on other priorities, such as socializing with group-mates or looking out for predators, rather than catching up on lost sleep. The team of scientists from the Max Planck Institute of Animal Behavior and the University of California, Davis used non-invasive technology to monitor sleep patterns across almost an entire group of individuals at once.

The findings lay bare the competing priorities that suppress sleep homeostasis in wild primate societies—raising the possibility that humans have navigated sleep deprivation throughout our evolutionary history.

Studies of sleep have revealed that animals of every species, from honey bees to humans, put aside a portion of each day to rest. But, with some notable exceptions, all sleep studies share the same thing in common: they were conducted on animals in the laboratory. In laboratory settings, animals perform the phenomenon known as sleep homeostasis—an animal with an accumulated sleep debt will later sleep longer or more deeply than usual. Sleep homeostasis has long been considered a key criterion in the very definition of sleep.

But the new study published in *eLife* demonstrates that animals in the wild face a slew of ecological and social demands that can disrupt sleep homeostasis. Specifically, baboons sacrificed sleep to stay awake in new environments and to remain close to their group-mates, regardless of how much they had slept the prior night or how much they had exerted themselves the preceding day.

The study was led by Ph.D. student Carter Loftus from the University of California, Davis. He says that "the competing priorities that lead humans to accumulate sleep debt might seem unique to a modern, industrialized society like ours. But our findings demonstrate that non-human primates also sacrifice sleep, even when it might be unhealthy to do so, to partake in other activities. The tradeoff between sleep and other pressing demands on our time is, therefore, one that we have likely been navigating throughout our evolution."

"Baboons are highly vulnerable to night-time predation and their fitness depends on maintaining strong social bonds. Trading off sleep to maintain alertness in novel, risky environments and to remain close to group-mates during the night may therefore represent an essential adaptation."

To identify when animals were sleeping and when they were awake, the team collected high resolution movement data from GPS trackers and accelerometers attached to almost all baboons in a troop. As the first study to investigate collective sleeping behavior in wild primates, the findings bring to light the unknown social costs and benefits associated with sleep in animal societies. Baboons experienced shorter, more fragmented sleep when sleeping near more of their group-mates. However, they also synchronized periods of nocturnal awakening with nearby individuals, suggesting that baboons may have actually been interacting with each other and strengthening their social bonds over night.

Meg Crofoot, director of the Department for the Ecology of Animal Societies at the Max Planck Institute of Animal Behavior and Professor at the University of Konstanz, is the senior author of this study and was the first to apply GPS tracking and accelerometry technology to study social behavior in primate societies.

"We discovered that sleep is a collective behavior in baboon groups. Group-mates were highly coordinated in their patterns of awakening during the night, which in turn led to shorter and more fragmented sleep. Our results show that these highly gregarious animals are balancing their physiological need for sleep with the social pressures of group living."

Working at the at the Mpala Research Centre in Kenya, the team fitted 26 wild baboons with GPS and accelerometry collars. In contrast to well-established methods used in sleep studies, which typically involve surgically implanting electrodes to measure brain activity via electroencephalography, the technique used in the present study represents a non-invasive alternative that can identify periods of sleep and wakefulness in wild, free ranging animals. The GPS trackers provided information on where the animals moved. This enabled the researchers to answer questions such as: how far the animals had traveled during the day, in which sleep site they

slept, and with whom they slept. The accelerometers, which are similar to smartwatch and Fitbit technology, gave ultra high-resolution information on body movements. By applying an algorithm adapted from studies of human sleep, the researchers used accelerometry data to determine when the baboons were asleep or when they were awake. They then used thermal video recordings of sleeping baboons to validate their findings.

"This study opens an exciting new frontier of scientific inquiry into the dynamics of sleep," adds Crofoot. "The accelerometry-based method can be easily and cheaply integrated into studies tracking animals in their natural habitats, allowing us to massively expand what we know about sleep across a range of species. In the same way, the technique can be applied to many individuals at the same time, paving the way for understanding how sleeping in groups shapes the structures of animal societies."

More information: *J Carter Loftus et al, Ecological and social pressures interfere with homeostatic sleep regulation in the wild, eL***ife (2022). DOI: 10.7554/eLife.73695**

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The Puzzling Virus That Infects Almost Everyone

For many people, Epstein-Barr virus causes mild initial infection, but it is also linked to cancers and multiple sclerosis. What do we do about it?

By Sarah Zhang

Statistically speaking, the virus known as Epstein-Barr is inside you right now. It is inside 95 percent of us. It spreads through saliva, so perhaps you first caught the virus as a baby from your mother, who caught it as a baby from her mother. Or you picked it up at day care. Or perhaps from a friend with whom you shared a Coke. Or the pretty girl you kissed at the party that cold New Year's Eve.

If you caught the virus in this last scenario—as a teen or young adult—then Epstein-Barr may have triggered mono, or the "kissing disease," in which a massive immune response against the pathogen causes weeks of sore throat, fever, and debilitating fatigue. For reasons poorly understood but not unique among viruses, Epstein-Barr virus, or EBV, hits harder the later you get it in life. If you first caught the virus as a baby or young child, as most people do, the initial infection was likely mild, if not asymptomatic. Unremarkable. And so this virus has managed to fly under the radar, despite infecting almost the entire globe. EBV is sometimes jokingly said to stand for "everybody's virus." Once inside the body, the virus hides inside your cells for the rest of your life, but it seems mostly benign.

Except, except. In the decades since its discovery by the virologists Anthony Epstein and Yvonne Barr in 1964, the virus has been linked not only to mono but also quite definitively to cancers in the head and neck, blood, and stomach. It's also been linked, more controversially, to several autoimmune disorders. Recently, the link to one autoimmune disorder got a lot stronger: Two separate studies published this year make the case—convincingly, experts say—that Epstein-Barr virus is a cause of multiple sclerosis, in which the body mistakenly attacks the nervous system. "When you mentioned the virus and MS 20 years ago, people were like, *Get lost* … It was a very negative attitude," says Alberto Ascherio, an epidemiologist at Harvard and a lead author of one of those studies, which used 20 years of blood samples to show that getting infected with EBV massively increases the risk of developing multiple sclerosis. The connection between virus and disease is hard to dismiss now. But how is it that EBV causes such a huge range of outcomes, from a barely noticeable infection to chronic, life-altering illness?

In the face of a novel coronavirus, my colleague Ed Yong noted that a bigger pandemic is a weirder pandemic: The sheer number of cases means that even one-in-a-million events become not uncommon. EBV is far from novel; it belongs to a family of viruses that were infecting our ancestors before they were really human.

But it does infect nearly all of humanity and in rare occasions causes highly unusual outcomes. Its ubiquity manifests its weirdness. Decades after its discovery and probably millennia after those first ancient infections, we are still trying to understand how weird this old and familiar virus can be. We do little to curb the spread of Epstein-Barr right now. As the full scope of its consequences becomes clearer, will we eventually decide it's worth stopping after all?

From its very discovery, Epstein-Barr confounded our ideas of what a virus can or cannot do. The first person to suspect EBV's existence was Denis Burkitt, a British surgeon in Uganda, who had the unorthodox idea that the unusual jaw tumors he kept seeing in young children were caused by a then-undiscovered pathogen. The tumors grew fast—doubling in size in 24 to 48 hours—and were full of white blood cells or lymphocytes turned cancerous. This disease became known as Burkitt's lymphoma. Burkitt suspected a pathogen because the jaw tumors seemed to spread from area to neighboring area and followed seasonal patterns. In other words, this lymphoma looked like an epidemic.

In 1963, a biopsy of cells from a girl with Burkitt's lymphoma made its way to the lab of Anthony Epstein, in London. One of his students, Yvonne Barr, helped prepare the samples. Under the electron microscope, they saw the distinctive shape of a herpesvirus, a family that also includes the viruses behind genital herpes, cold sores, and chicken pox. And the tumor cells specifically were full of this virus. Case closed? Not yet. At the time, the idea that a virus could cause cancer was "rather remote," says Alan Rickinson, a cancer researcher who worked in Epstein's lab in the 1970s. "There was a great deal of skepticism." What's more, the virus's ubiquity made things confusing. Critics pointed out that sure, children with Burkitt's lymphoma had antibodies to EBV, but so did healthy children in Africa. So did American children for that matter, as well as isolated Icelandic farmers and people belonging to a remote tribe in the Brazilian rainforest. The virus was everywhere scientists looked, yet Burkitt's lymphoma was largely confined to equatorial Africa. What if EBV was just an innocent bystander? Why wasn't the virus causing disease anywhere else?

It was. Scientists just didn't know where to look until a stroke of luck clued them in. In 1967, a technician in a Philadelphia lab studying EBV and cancer fell ill with symptoms of mono. Because she was one of the few people who had tested negative for EBV antibodies, she had regularly donated blood for lab experiments that needed a known negative sample. When she came back after the illness, she started testing positive, highly positive. The timing suggested what we now know: EBV is the most common cause of mono.

Scientists eventually found more links between the virus and other cancers: nasopharyngeal cancer, stomach cancer, Hodgkin's lymphoma, and other forms of lymphoma. In all, it plays a role in 1.5 percent of cancers globally. Those first two are cancers in the cells lining the throat and stomach, which EBV can infect. The others are in white blood cells or lymphocytes, which the virus actually specializes in infecting. In particular, EBV infects a type of lymphocyte called a B cell, each of which is born to recognize a different hypothetical enemy. If a certain B cell never finds its matching enemy, it dies as part of the body's ruthless culling of useless immune cells. If it does find a match, however, the B cell divides and transforms into memory B cells, which will remain to guard against infection for the rest of a person's life.

EBV's genius is that it co-opts this normal process. It manipulates infected B cells into thinking they have been activated, so that they turn into long-lasting memory B cells where the virus can hide for decades. (All herpesviruses in the family have this unusual ability to become latent, though they hide out in different types of cells.

The chicken-pox virus, for example, uses nerve cells, sometimes coming out to cause shingles.) Occasionally, EBV emerges from its hiding place, replicating just enough to get by. If it replicates too little, it won't find another host before getting shut down by the immune system. If it replicates too much, it risks harming its current host. The virus and immune system are in constant balance, each holding the other in check. There's an "elegance with which this virus has established a long-term relationship with the host," says Sumita Bhaduri-McIntosh, an Epstein-Barr virologist and infectious-disease doctor at the University of Florida.

When this balance is interrupted, one possible result is cancer. As part of its manipulation of infected cells, EBV seems to suppress their normal dying process. And if the cell that refuses to die has other aberrant properties, then you can get cancers like Burkitt's lymphoma. "In most cases, when the virus appears in this cancer, and subsequently in other cancers, it is one part of a chain," Rickinson says. "It's obviously not the sole driver of growth." This explains why EBV doesn't cause cancer in everyone it infects, only in those unlucky enough to have also acquired the wrong set of other mutations. In the case of Burkitt's lymphoma, the cancerous cells also have a strange rearrangement of chromosomes, which scientists learned is linked to malaria infection. This accounted for the unique geographic pattern that Burkitt had observed. EBV is everywhere, but Burkitt's lymphoma was common only in places where malaria is also endemic.

Epstein-Barr became known as the first human virus linked to not just an immediate disease but also cancers that can appear years after initial infection. It challenged the traditional paradigm of viruses causing short-term illnesses that resolve and confer immunity. After all, the virus stays inside our bodies and continues to interact with our immune systems for the remainder of our lives.

Over the years, more hints of EBV's unusual abilities started appearing. The virus or the antibodies to it seemed to be disproportionately found in people suffering from autoimmune disorders such as rheumatoid arthritis, lupus, and multiple sclerosis as well as those suffering from chronic fatigue syndrome, also known as myalgic encephalomyelitis. These chronic conditions, whose biological mechanisms are even more elusive than cancer's, are particularly hard to study. While the correlations between EBV and these disorders were suggestive, they were in no way definitive. People who have these conditions might almost all have EBV, but then almost all healthy people have EBV too. "That's not a very good place to start doing epidemiology, when you have 95 percent in the control group," says Paul Farrell, an EBV researcher at Imperial College London.

The recent study from Harvard's Ascherio got around this by looking at a massive archive of serum samples taken from people over 20 years. The collection came from the Department of Defense, which stores serum from routine tests for HIV. Among the 10 million adults with samples in the repository, researchers were able to find enough people who were initially negative for EBV but then contracted it during the 20-year period. And those who did get the virus were 32 times as likely to develop multiple sclerosis as those who did not. A second study from Stanford adds a possible causation to this correlation: Some multiple-sclerosis patients have antibodies that bind both an EBV protein and a protein in the brain, which is erroneously targeted by the immune system in multiple sclerosis. This kind of cross-reaction has long been suspected in MS but only now identified. "It's just like a great volcano of information," says Rickinson about the recent studies. As with EBV-associated cancers, though, only a tiny sliver of people infected with the virus end up developing multiple sclerosis, so some other trigger or triggers must also be in play. We're only at the beginning of understanding this process.

COVID, too, has revived interest in Epstein-Barr's long-term consequences. A recent long-COVID study found EBV infection to be one of four major risk factors, suggesting that some long-COVID symptoms might be caused by reactivation of EBV when the body is weakened from fighting the coronavirus.

This association is perhaps not surprising. The debilitating fatigue associated with long COVID and other post-viral syndromes does look, in some ways, like the fatigue caused by mono. And in the 1980s, doctors noticing the similarity had begun diagnosing chronic Epstein-Barr virus syndrome in patients whose mono-like symptoms of fatigue and sore throat did not go away for months. Eventually, however, experts took Epstein-Barr out of the name and gave it the more general term of chronic fatigue syndrome, because EBV does not seem to be the sole cause of such symptoms. Chronic fatigue syndrome may have several different explanations, but the virus may still play a role in some cases even after mild infections, says Hank Balfour, a pathologist at the University of Minnesota. He has also described cases of "chronic mono," in which a severe initial EBV infection triggers mono symptoms that either linger or recur for months or even years. Mono's acute phase typically lasts for weeks, which is already unusually long for a virus but is well documented. There isn't much research on chronic mono though, and the diagnosis is not widely accepted among doctors. "It needs, I think, more attention," Balfour says. Long COVID remains a baffling consequence of the novel coronavirus, but even the long-term consequences of very common viruses like EBV are poorly understood.

As the long-term picture of EBV comes into focus, how do we think about the danger of a virus that is ubiquitous, that rarely causes serious disease but has devastating consequences when it does? We currently have no way of preventing EBV infection, short of avoiding all human interactions that might share saliva: a mother kissing her baby, a toddler doing almost anything. Vaccines have been in the works for decades; Epstein himself worked on one. The link to multiple sclerosis, many long-time researchers now hope, will revive interest in an EBV vaccine. More than a decade ago, a pharmaceutical company abandoned a vaccine candidate that successfully prevented mono but not EBV infection altogether. The result was "discouraging from a pharmacoeconomic point of view," Balfour says, because there wasn't a clear demand for a vaccine that prevented only mono. Preventing multiple sclerosis, however, might add an extra incentive.

Two new vaccine candidates, from the National Institutes of Health and Moderna, have entered or are about to enter clinical trials. A key question is whether they can do better than the old vaccine. "We would of course like to prevent infection. That's the ultimate goal, but we think even if we don't prevent infection, we can still reduce EBV-associated disease," says Jeffrey Cohen, a virologist at the NIH who works on one of the vaccines. That's because symptomatic EBV infections—such as mono—are associated with a higher likelihood of developing EBV-associated diseases, adds Balfour, who has also worked on a vaccine. However, studying how the vaccine might stop diseases that develop years later, such as cancers or multiple sclerosis, will be very hard in a typical vaccine trial. The incidences are so low, and the diseases take so long to appear, that a vaccine trial in hundreds or thousands of people over a few years is unlikely to offer much definitive evidence. Most likely, Cohen says, if the vaccines work against mono, they can be approved to prevent the disease in people who have not yet been infected by EBV. Once it's on the market and hundreds of thousands of people get it and are followed over years, then the effect on cancer or multiple sclerosis may finally become clear.

All of these recent advances make it a "fascinating time" for EBV

research, says Rickinson, the biologist who once worked with the eponymous Epstein. “Unfortunately,” he says, “I’m unable to pursue it myself.” He recently retired from the University of Birmingham after devoting nearly 50 years to studying this enigmatic virus. It’s up to the next generation now—to figure out EBV’s remaining secrets and perhaps a better way of coexisting with it.

https://bit.ly/3ty3Owk

Common Medications Are Affecting Our Immune Response to Infections Like COVID-19

Some common drugs can help and others hinder immune responses.

The largest clinical review of immune responses to paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), and opioid analgesics, with a focus on infectious diseases, has provided insights into unintended impacts of these commonly used medicines. The findings highlight the potential for some of these medicines to join the fight against old and new infectious diseases.

Although research into these drugs has focused on their effects on pain and fever management, until now, their impact on the treatment of infectious diseases specifically was unclear. The findings highlight the need for more studies in this under-recognized area of research, with wide-reaching implications.

Key findings of the clinical review

- For pain: Morphine suppresses key cells of the immune system and increases the risk of infection, particularly after cancer surgery.

- For fever: Antipyretics – e.g. Paracetamol, Ibuprofen, Aspirin – can reduce the desirable immune response when taken for vaccination.

- Aspirin could be an affordable and accessible therapeutic option for tuberculosis – which mainly afflicts poor countries, with beneficial results shown in animals and humans.

- Anti-inflammatory medicine indomethacin may reduce viral replication in Covid-19 but large-scale human trials are needed.

Researchers led by the University of Sydney’s Faculty of Medicine and Health opted for a ‘clinical’ review in order to have a broader scope to synthesize the available evidence, noting the importance of further research and trials regarding infectious disease responses.

The research was unplanned and the findings unexpected, with lead author Christina Abdel-Shaheed saying they initially were interested in studying possible impacts of paracetamol (acetaminophen) during the pandemic, when people hoarded the drug in the first months of COVID-19.

“We decided to study painkillers and fever medications generally and were amazed by what we found,” she said. “In 14 years of studying pain, this is the most important research I have been involved in.”

The findings are published today in a leading journal, the *British Journal of Clinical Pharmacology*.

Caution urged during the pandemic

Pain researcher Dr. Christina Abdel-Shaheed, from Sydney Musculoskeletal Health, said the relationships uncovered with infectious diseases highlighted the need for rigorous clinical trials.

“Our review shows some of the common pain and fever medications may work with the immune system to fight infection, whereas others work against it and increase the risk of contracting or responding badly to infectious diseases,” Dr. Abdel-Shaheed said.

“Taking paracetamol or ibuprofen before or immediately after vaccination – for example for COVID-19 – to try to prevent mild fever or headache is not recommended, because this could reduce the body’s desirable immune response to the vaccine.

“For chickenpox, use of ibuprofen is not recommended as it might increase the risk of secondary bacterial skin infections.”

Dr. Justin Beardsley, infectious disease specialist at Westmead Hospital and researcher with Sydney Institute for Infectious Diseases, said an important finding of this review during the pandemic was that: "morphine – one of the most commonly used opioid analgesics in post-surgical and critical care – suppresses key innate immunity cells, thereby increasing the risk of infection".

He highlighted: "This is particularly the case with cancer patients, who are already vulnerable to COVID-19.

"Efforts are needed to achieve adequate analgesia whilst avoiding immune-suppression in the immediate postoperative period caused by opioids such as morphine — both for people undergoing cancer surgery as well as for the immunocompromised generally," said Dr. Beardsley, who also works with the Westmead Institute for Medical Research.

Positive impacts on our immunity

Professor Andrew McLachlan said on the positive side, the findings provide new insights for further research to evaluate these commonly used medicines, which could be repurposed to improve outcomes for people undergoing treatment for infectious diseases.

"With the urgent need for new treatments for COVID-19 and the declining efficacy of some antimicrobial agents due to resistance, now more than ever we need medicines which can maintain or enhance the efficacy of anti-infective drug treatments, said Professor McLachlan, the Head of School and Dean of Pharmacy at the University of Sydney.

"The results of this review suggest that commonly used medicines for pain and fever should be further explored as inexpensive and effective adjunctive treatments which influence immune and inflammation pathways for people undergoing treatment for infection."

Under-researched area

Co-author Professor Ric Day from UNSW and St Vincent's Hospital said research was still catching up in this new area of study.

"One of the problems is that widely used medicines –such as paracetamol, nonsteroidal anti-inflammatory drugs like ibuprofen, and corticosteroids such as prednisone – have been around for decades and in the past we didn't tend to consider their impacts on the immune system because it has been an under-recognised area.

"From community use to hospital and acute care, these classes of pain and fever medications are among the most popular drugs worldwide but we need to consider the significant impact these can have on our immune system and our response to infectious diseases, including COVID-19."

Reference: "Immunomodulatory effects of pharmaceutical opioids and antipyretic analgesics: Mechanisms and relevance to infection" by Christina Abdel Shaheed, Justin Beardsley, Richard O. Day and Andrew J. McLachlan, 1 March 2022, British Journal of Clinical Pharmacology.
DOI: 10.1111/bcp.15281

https://wb.md/3IXu2yw

First Possible Case of Deer-to-Human COVID Transmission Identified

A team of Canadian scientists may have discovered the first case of deer spreading the coronavirus to humans, according a new preprint study that hasn't yet been peer-reviewed.

Carolyn Crist

Typically, humans spread the virus to deer, and then deer spread it to other deer. But new evidence suggests that the virus could spill over from deer into humans. The researchers identified a COVID-19 case in someone from Ontario who had recently been in contact with deer.

"This particular case, while raising a red flag, doesn't seem to be hugely alarming," Finlay Maguire, PhD, one of the study authors and an epidemiologist at Dalhousie University, told CBC News.

"While we haven't seen [transmission from deer to humans] happen

directly, we sampled from the human case around the same time we sampled from the deer, and we sampled from around the same location," he said. "There is also a plausible link by which it could have happened, in that the individual involved is known to have had considerable contact with deer."

Maguire and colleagues have been monitoring the spread of the coronavirus among animals. They analyzed nasal swabs and lymph node samples taken from hundreds of deer that were killed by hunters in fall 2021 in southwestern and eastern Ontario. Among 298 sampled deer, 17 tested positive — all from southwestern Ontario.

During the analysis, they found a "highly divergent" coronavirus lineage, which means a cluster of samples with many mutations. Around the same time, they found a genetically similar version in a person from the same region.

The study points to the need for better surveillance of the coronavirus, Maguire told CBC News, including in humans, animals, plants, and the broader environment. Researchers aren't quite sure how deer contract the virus from humans, but it could happen through contaminated water, direct contact, food, farming, or other animals such as mink.

The coronavirus lineage identified in the study is different from what's circulating among humans now, and it's not related to the Delta or Omicron variants. The closest genetic relative came from samples taken from humans and mink in Michigan in 2020, which means the divergent lineage mutated and evolved over time.

"It's reassuring that we found no evidence of further transmission, during a time when we were doing a lot of sampling and a lot of sequencing," Samira Mubareka, MD, one of the study authors and a virologist at Sunnybrook Health Sciences Centre, told CBC News.

"If we continue to do this surveillance, we'll get a much better sense of what the actual risk is," she said.

So far, the coronavirus has been found in wild white-tailed deer in the northeastern U.S. and central Canadian provinces.

Other known cases of transmission from animals to humans have been identified in farmed mink and potentially hamsters, the news outlet reported. But for the most part, humans transmit the virus to animals and are most likely to catch the virus from other people.

At the same time, the Public Health Agency of Canada has issued guidance for hunters, trappers, and those who handle wild deer. People should wear gloves, goggles, and a mask when they could be exposed to respiratory tissues and fluids, especially indoors.

Coronaviruses are killed by normal cooking temperatures, the agency said, and there has been no evidence that cooked venison can spread the virus.

Sources

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CBC News: "Canadian researchers discover 1st possible case of deer spreading COVID-19 virus to a human."

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https://wb.md/3KiMClb

Malpractice Case: Would Focus on History Have Saved Patient?

This claim illustrates the importance of differential diagnoses and the unfortunate turn a case can take when a differential diagnosis is not considered.

Jacqueline Ross, PhD, RN; David L. Feldman, MD, MBA

Disclosures

A 47-year-old patient presented to his primary care physician with complaints of back pain that had started the prior week. The patient had a history of Mallory-Weiss tear (a tear of tissue in the lower esophagus) and type 1 thoracic ascending and descending aortic dissection (a tear in the inner layer of the aorta), which had occurred 5 years earlier.

The ascending dissection was repaired; however, the residual descending aortic dissection was left unrepaired due to potential surgical complications that could include paralysis of the legs and lower body. The patient was seeing a cardiologist, who monitored his blood pressure and conducted annual echocardiograms.

During the primary care visit, the patient reported no trauma or nausea. He also reported that the back pain had resolved at one point but then returned below his shoulder blade. Later the pain wrapped around his abdomen and up into his neck and throat. It lasted for an hour. Pain medication helped reduce the pain.

During the examination, the patient's back was not tender upon palpation. He experienced no pain when bending or twisting at the waist. His lungs were clear. He appeared anxious.

The primary care provider thought that the patient's pain could be a sign of shingles. However, the physician ordered a chest x-ray that was performed later that day.

At home the next day, the patient retrieved an ice pack from the refrigerator to relieve his increased back pain. A short time later, he cried out and collapsed. He was transported to the hospital emergency room, where he was pronounced dead. The previous day's x-ray, read after the patient died, showed a massive enlargement of descending thoracic aorta. The patient died of a ruptured dissecting aortic aneurysm.

A claim was filed against the primary care provider, cardiologist, and cardiac surgeon.

What Did the Experts Say?

Considering the patient's history, medical experts testified that the primary care provider should have included dissecting aortic aneurysm on the differential and sent the patient to the emergency department immediately. The experts stated that the patient's symptoms were classic for dissecting aortic aneurysm.

The cardiologist and cardiac surgeon were also criticized by experts in the case, who said the cardiac surgeon should have communicated a plan for regular follow-up to the cardiologist and primary care provider.

In addition, the cardiologist should have consulted with the cardiac surgeon on periodic monitoring. The annual echocardiograms performed by the cardiologist were not the appropriate tests for tracking the patient's condition, they said. He should have ordered annual CT scans to monitor the aorta.

Experts agreed that had there been a good plan for monitoring and early diagnosis of the new dissection, the patient would have had a reasonable chance of survival. All parties agreed to settle the case.

Tips for Malpractice Risk Reduction: Dr Feldman's 3 P's

1. Prevent adverse events by considering differential diagnoses, especially in patients with significant health history and a preexisting condition like this one. Ruling out life-threatening conditions first is critical and would have necessitated sending this patient, who had a residual aneurysm, to an emergency department immediately. Open communication and collaboration might have allowed the primary care physician to contact the cardiac surgeon when the patient was first seen, resulting in immediate referral and an opportunity to prevent this death.

2. Preclude malpractice claims by assuring that the patient is aware of the signs and symptoms of their preexisting condition, such as this patient's dissecting aneurysm, and what to do in the event that these symptoms occur and/or worsen. Had the patient gone to an emergency room when he experienced the back pain, the imaging would have shown the expanding aneurysm.

3. Prevail in lawsuits by documenting your rationale for diagnosis and plan of care. This patient was at high risk for descending aortic dissection and rupture. Documenting how the follow-up plan would adequately address these risks would have been critical in service of the defense. In a case like this, where the care was substandard, it

would have been difficult to defend regardless, but when care teams meet the standard of care, documentation can make all the difference.

This case comes from "Cardiology Closed Claims Study," published by The Doctors Company.

https://bit.ly/3hJd7UI

This is your gut on sushi

The next time you get a craving for sushi rolls, you may feel a renewed appreciation for the ocean.

It's to thank not only for your fish and seaweed wrapper, but, as a new Michigan Medicine study suggests, for the bacteria in your gut that digest seaweed.

The ocean is one of the largest reservoirs of carbon on the planet, much of it locked inside seaweed. Marine bacteria play a critical role in the carbon cycle by breaking down seaweed. A little over a decade ago, researchers found the genes that enable ocean bacteria to degrade the complex carbohydrate known as porphyran, found in cold-water seaweed, in a microbiome sample from a Japanese adult.

A new study, led by Nicolas Pudlo, Ph.D., Gabriel Vasconcelos Pereira, Ph.D., and Eric Martens, Ph.D., of the U-M Medical School, has found that these genes of oceanic origin are more common than previously recognized, entering the human gut microbiome through a process known as lateral gene-transfer.

During digestion, gut bacteria in humans break down dietary fiber, or polysaccharides, found in fruits, vegetables, and grains. However, the polysaccharides found in seaweed have different chemical structures than land-sourced foods. Somehow, genes from the ocean-dwelling Bacteroidetes—a genus of bacteria that is a key player in the microbiome—found their way into the human gut.

"Whether they came directly from an oceanic bacterium someone just happened to consume or through a more complex path into the human gut is still a mystery," said Martens, a professor in the Department of Microbiology and Immunology.

To examine just how extensive the seaweed gene clusters are in gut Bacteroidetes, the team turned to an unusual source: stool samples from U-M undergraduate students.

"We received the samples in small glass tubes and did all of our culturing within the lab's anaerobic chamber," commented Ahmed Ali, one of the student researchers on the study. "I remember working in the chamber was hot and somewhat difficult, but this was definitely offset by the fact that we did not have to 'smell the scientific process' at work," he quipped.

They then analyzed the bacteria's ability to degrade several seaweed-derived polysaccharides, including porphyran, laminarin, alginate and carrageenan.

The team found that genes for processing laminarin were broadly represented in the samples, possibly linked to the related ability to process beta-glucans, sugars also found in oats and whole grains. Yet, the other seaweed polysaccharides were used by fewer bacterial species and present in fewer samples.

"The genes to process agarose and porphyran, two of the more commonly consumed seaweeds in Southeast Asia, tended to be enriched in the people living there," said Martens. Taking a closer look at the geographic distribution of the gene clusters, the team referenced genomic surveys from samples taken from more than 2000 people in Asia, Africa, North and South America, and Europe. The genes for degrading porphyran were indeed enriched in samples from China and Japan. Genes for processing carrageenan, consumed since 400 B.C in China, and now widely used as a food additive in everything from oat milk to infant formula in the United States, were also enriched in samples from China, Japan and North America.

Adding further intrigue to the evolution of seaweed digestion, the team fortuitously discovered that the bacteria Firmicutes, which are

even more prevalent in the human gut than Bacteroidetes, also have picked up the genetic ability to grow on seaweed polysaccharides.

"Firmicutes are known to live in fish intestines and the closest ancestors of the genes that appear to have jumped into human gut Firmicutes were ones found in fish," said Martens.

The study, notes the team, opens new questions about the complex interplay between diet and the adaptation of the human gut microbiome in populations around the world.

Additional authors on the paper include Jaagni Parnami, Melissa Cid, Stephanie Markert, Jeffrey P. Tingley, Frank Unfried, Austin Campbell, Karthik Urs, Yao Xiao, Ryan Adams, Duña Martin, David N. Bolam, Dörte Becher, Thomas M. Schmidt, Wade Abbott, Thomas Schweder and Jan Hendrik Hehemann.

More information: *Nicholas A. Pudlo et al, Diverse events have transferred genes for edible seaweed digestion from marine to human gut bacteria, Cell Host & Microbe (2022). DOI: 10.1016/j.chom.2022.02.001*

https://bit.ly/3pFwmTk

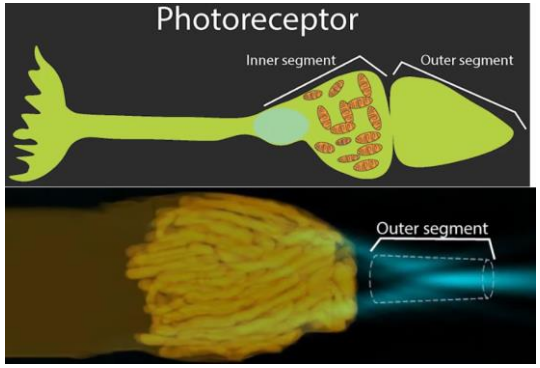
Vision Scientists Discover New Angle on Path of Light Through Eye's Photoreceptors

NIH study in ground squirrels suggests dual function for mitochondria in photoreceptor cells.

Researchers at the National Eye Institute (NEI) have discovered that power-producing organelles in the eye's photoreceptor cells, called mitochondria, function as microlenses that help channel light to these cells' outer segments where it's converted into nerve signals. The discovery in ground squirrels provides a more precise picture of the retina's optical properties and could help detect eye disease earlier. The findings, published today in *Science Advances*, also shed light on the evolution of vision. NEI is part of the National Institutes of Health.

"We were surprised by this fascinating phenomenon that mitochondria appear to have a dual purpose: their well-established metabolic role producing energy, as well as this optical effect," said the study's lead investigator, Wei Li, Ph.D./B.M., who leads the NEI Retinal Neurophysiology Section.

The findings also address a long-standing mystery about the mammalian retina. Despite evolutionary pressure for light to be translated into signals and pass instantly from the retina to the brain, the trip is hardly direct. Once light reaches the retina, it must pass through multiple neural layers before reaching the outer segment of photoreceptors, where phototransduction (the conversion of light's physical energy into cellular signals) occurs.



(Top) Mitochondria in cone photoreceptors have a dual purpose: They generate energy for the cell and in a new study they also act as microlenses. This optical role helps concentrate light as it moves from the cell's inner to outer segment. (Bottom) The outer segment is where the light's physical energy is translated into cellular signals. **Credit: National Eye Institute**

Photoreceptors are long, tube-like structures divided into inner and outer segments. The last obstacle a photon must traverse before moving from the inner to the outer segment is an unusually dense bundle of mitochondria.

Those bundles of mitochondria would seem to work against the process of vision either by scattering light or absorbing it. So, Li's team set out to investigate their purpose by studying cone photoreceptors from the 13-lined ground squirrel.

Unlike other animal models used for vision research, the 13-lined ground squirrel's retina comprises mostly cones, which see color, as opposed to rods that enable night vision. Li's team studies the 13-lined ground squirrel to better understand the causes of human eye diseases that primarily affect cone photoreceptors.

The researchers used a modified confocal microscope to observe

the optical properties of living cone mitochondria exposed to light. Far from scattering light, the tightly packed mitochondria concentrated light along a thin, pencil-like trajectory onto the outer segment. Computational modeling using high-resolution mitochondrial reconstructions corroborated the live-imaging findings.

"The lens-like function of mitochondria also may explain the phenomenon known as the Stiles Crawford effect," said first author of the paper, John Ball, Ph.D., a staff scientist in the Retinal Neurophysiology Section.

Scientists measuring retinal responses to light have long observed that when light enters the eye near the center of the pupil, it appears brighter compared to light of equal intensity entering the eye near the edge of the pupil.

In this study, Li found that the lens-like effect of mitochondria followed a similar directional light intensity profile. That is, depending on light source location, the mitochondria focused light into the outer segment of the cell along trajectories that mirrored those observed from the Stiles-Crawford effect.

Linking mitochondria's lens-like function to the Stiles-Crawford effect has potential clinical implications. The long-observed effect may now be used as the basis for non-invasively detecting retinal diseases, many of which are thought to involve mitochondrial dysfunction at their origin. For example, patients with retinitis pigmentosa have been reported to have abnormal Stiles-Crawford effect even when they have good visual acuity. More research is needed to explore the structural and functional changes in cone mitochondria and their manifestations in detectable optic features.

Finally, the findings provide new insights into how our eyes may have evolved.

Like the mitochondria in Li's study, within the photoreceptors of birds and reptiles, tiny oil droplets are located in the portion of the inner segment closest to the outer segment, and they are thought to serve an optical role. Furthermore, the mitochondrial "microlens" in mammalian cone photoreceptors confers a functionality reminiscent of that achieved by the compound eye of arthropods like flies and bumblebees.

"This insight conceptually bridges compound eyes in arthropods with the camera eyes of vertebrates, two independently evolved image-forming systems, demonstrating the power of convergent evolution," Li said.

Reference: "Mitochondria in cone photoreceptors act as microlenses to enhance photon delivery and confer directional sensitivity to light" by John M. Ball, Shan Chen and Wei Li, 2 March 2022, Science Advances. DOI: 10.1126/sciadv.abn2070

The study was funded by the NEI Intramural Research Program.

https://bit.ly/3IOJxci

Africa battles out-of-control polio outbreaks

Cases tumble in Pakistan and Afghanistan, but African outbreaks have become a grave threat to eradication

By Leslie Roberts

On 17 February, Malawi's Ministry of Health announced a nasty surprise: A 3-year-old girl who was paralyzed in November 2021 was infected with the wild poliovirus, which Africa officially vanquished in 2020. The sequence of the virus showed it had somehow made the leap from Pakistan, one of the last two holdouts of the wild virus. A week later came bad news from Afghanistan: Gunmen killed eight polio workers in the country's northeast.

The incidents are the latest setbacks on the long, bumpy road to global polio eradication. Yet Pakistan has "exported" wild poliovirus before, sparking outbreaks that were quickly snuffed out, and the situation in Afghanistan and Pakistan improved dramatically last year, with polio cases tumbling to a historic low.

Instead, perhaps the biggest threat to the effort now is an explosion of vaccine-derived polio outbreaks in Africa that affected almost two dozen countries last year and paralyzed more than 500 children

in 2020 and again in 2021. Vaccine-derived strains emerge where children are un- or underimmunized, allowing the live, weakened virus in the oral polio vaccine (OPV) to circulate and accumulate enough mutations to revert to its neurovirulent form and paralyze kids. These outbreaks—which almost always emerge from type 2 poliovirus, one of the three virus strains—are "very worrying" and "front burner" at the Global Polio Eradication Initiative (GPEI), says John Vertefeuille of the U.S. Centers for Disease Control and Prevention (CDC), a partner in the initiative.

A big part of the problem is that countries don't view vaccine-derived strains as an emergency, says Simona Zipursky, an adviser to the World Health Organization's (WHO's) polio program, even though they behave just like the wild virus. "It is not like there is a milder variant as there is with COVID-19," Zipursky says.

Nigeria's widely lauded victory over the wild virus—it was the last African country to achieve that feat—fed a sense that "the job was done," says WHO's Aidan O'Leary, who directs GPEI. The quality of Nigeria's polio program, once among the best in the world, slipped, and today the country is "the most important generator" of vaccine-derived polioviruses, says Jay Wenger of the Bill & Melinda Gates Foundation, another partner in GPEI. Nigeria accounted for more than half of all vaccine-derived polio cases globally last year and exported the virus to 18 countries.

Other factors have contributed, too. Lately, many African countries have been slow to respond to new outbreaks as they wait for a new vaccine that they think will solve the problems, which has allowed the virus to spread. Many are frustrated with the existing vaccine, monovalent OPV2 (mOPV2); they would use it to quash an outbreak but then, because the vaccine virus occasionally reverts, the response would seed more outbreaks.

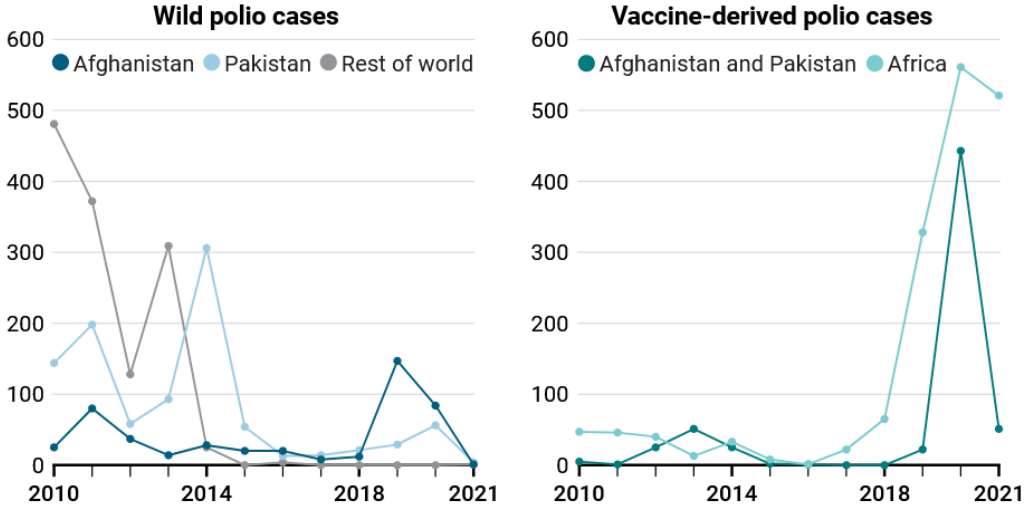
Known as novel OPV2 (nOPV2), the new vaccine was engineered to be as effective as mOPV2 but more genetically stable, greatly lessening the chance it will revert. The vaccine, funded by the Gates foundation, was rolled out in a few countries in March 2021 under an emergency use authorization.

Pending its arrival, Senegal waited for almost 1 year before responding to a virus detected in late 2020, instead of using readily available supplies of mOPV2. "If the virus gets a head start for such a long time it is harder to stop," says Mark Pallansch, who recently retired from CDC but remains involved in GPEI.

Although early data suggest nOPV2 is indeed less likely to trigger outbreaks, Pallansch thinks its promise has been oversold. "Governments thought, if I can just get it, things will be fine," he says. But countries ran nOPV2 campaigns of poor quality, reaching just a fraction of the target population. Nigeria has burned through about 184 million nOPV2 doses, out of 255 million used so far, and still hasn't stopped many of its outbreaks. The new vaccine "is not a magic bullet," Zipursky says.

A new threat

Pakistan and Afghanistan are the last two countries where the wild poliovirus is endemic. Cases in both dropped sharply last year (left). Vaccine-derived outbreaks are now a big threat to polio eradication—especially in Africa (right).



(GRAPHIC) K. FRANKLIN/*SCIENCE*; (DATA) GLOBAL POLIO ERADICATION INITIATIVE

GPEI and other international bodies are hammering home that countries should respond to any outbreak immediately with whatever type 2 vaccine is available. The mantra is "faster, better, bigger," O'Leary says: Be quicker to detect and respond to outbreaks, improve the vaccination campaigns, and broaden them. "We need to conduct them not where you think the virus is, but, based on migration patterns, where you think it will be," he says.

The Africa campaign is also suffering from a "self-inflicted wound," Pallansch says. GPEI has long planned to put itself out of business once polio is gone. As part of a transition plan, many of GPEI's substantial assets and staff would be integrated into existing WHO programs, for instance, to deal with other infectious diseases—GPEI has already helped with Ebola and COVID-19—and to boost routine immunization. WHO planned to complete this transition in nonendemic countries—including all of Africa—by January 2022.

Accordingly, in February 2021, WHO's Africa office sent pink slips to all GPEI staff. Unfortunately, the office was slow to say who would be kept on, and some people got nervous and quit, officials say.

GPEI soon realized the Africa situation was "too hot right now" to proceed with the plan, Wenger says, and decided to continue to fund the 10 highest risk countries in Africa for another 2 years. But the damage had been done. "Things didn't have to happen this way," Pallansch says. "They could have done it in a different sequence and not have viruses all over the continent."

The new worries come as Pakistan and Afghanistan, the last two endemic countries, are doing surprisingly well, with just five reported cases of wild poliovirus last year, down from 140 in 2020. Pakistan has just gone an entire year without a case. (Vaccine-derived cases in both countries are way down as well.) "It looks better than it ever has," Wenger says. The low numbers are "absolutely not" an artifact, says Hamid Jafari, who heads the eradication program in the region; surveillance remains "really, really good." Some of the gains stem from very favorable epidemiology. Polio resurged in both countries in 2019 and 2020, and "after a peak we always see a trough," Jafari says, in part because of increased population immunity. Reduced travel during the COVID-19 pandemic helped.

In Pakistan, vaccination drives already cover most of the target population, and they are improving, Jafari says. Imran Khan, Pakistan's prime minister, is actively involved. Bill Gates just visited the country to bolster enthusiasm. In Afghanistan, too, "we've made more progress than we could have anticipated," O'Leary says.

After resuming power in August 2021, the Taliban rescinded its ban on house-to-house polio vaccination in its strongholds, which had left 3.5 million children out of reach. (In some areas GPEI is still restricted to vaccinating in mosques.) Vaccination campaigns in November, December, and January reached 8.5 million out of 9.9 million children, Jafari says, including 2.6 million who were inaccessible for 3.5 years.

But future campaigns could be hobbled if last week's killings are a harbinger of further violence. And Jafari suspects the virus may survive in small populations that move back and forth across the border between the two countries. A couple of positive environmental samples detected in December in southern Khyber Pakhtunkhwa in Pakistan show the virus is still lurking there. Jafari worries it could resurge when the weather warms and people begin to travel for Ramadan and Eid al-Fitr.

The recent spread to Malawi underscores the risk of further delays, he says: "We want to kill the virus now."

https://bit.ly/3MuT5v5

Genetic Screening Shows a Causal Link Between Blood Group and Severe COVID-19

A new study has analyzed over 3000 proteins to identify which are causally linked to the development of severe COVID-19.

This is the first study to assess such a large number of proteins for their connection to COVID-19. The findings provide insight into potential new targets for approaches to treat and prevent severe COVID-19. Published in *PLOS Genetics* and part-funded by the National Institute for Health Research (NIHR) Maudsley Biomedical Research Centre, the study used a genetic tool to screen over 3000 proteins. Researchers identified six proteins that could underlie an increased risk of severe COVID-19 and eight that could contribute to protection from severe COVID-19.

One of the proteins (ABO) that was identified as having a causal connection to the risk of developing severe COVID-19 determines blood groups, suggesting that blood groups play an instrumental role in whether people develop severe forms of the disease.

Co-first author Dr. Alish Palmos from Institute of Psychiatry, Psychology & Neuroscience (IoPPN) King's College London said: "We have used a purely genetic approach to investigate a large number of blood proteins and established that a handful have causal links to the development of severe COVID-19. Honing in on this group of proteins is a vital first step in discovering potentially valuable targets for development of new treatments."

Assessing how blood proteins are linked to disease can help understand the underlying mechanisms and identify potential new targets for developing or repurposing drugs. Protein levels can be measured directly from blood samples but conducting this type of research for large numbers of proteins is costly and cannot establish causal direction.

This is where genetics can play a role. Mendelian randomization, a method of comparing causal relations between risk factors and health outcomes, using large genetic datasets can assess the relationship between genetic variants connected with an exposure (in this case high levels of individual blood proteins) and genetic variants connected with disease outcome (in this case severe COVID-19).

Co-first author Dr. Vincent Millischer from the Medical University of Vienna explained: "Causality between exposure and disease can be established because genetic variants inherited from parent to offspring are randomly assigned at conception similar to how a randomized controlled trial assigns people to groups. In our study the groups are defined by their genetic propensity to different blood protein levels, allowing an assessment of causal direction from high blood protein levels to COVID-19 severity whilst avoiding influence of environmental effects."

The study considered two incremental levels of severity of COVID-19: hospitalization and respiratory support or death. Using data from a number of genome-wide association studies the researchers found six proteins that were causally linked to an increased risk of hospitalization or respiratory support/death due to COVID-19 and eight causally linked to protection against hospitalization or respiratory support/death.

Analysis showed some distinction in types of proteins linked to hospitalization and those linked to respiratory support/death, indicating different mechanisms may be at work in these two stages of disease.

The analysis identified that an enzyme (ABO) that determines blood group was causally associated with both an increased risk of hospitalization and a requirement for respiratory support. This supports previous findings around the association of blood group with higher likelihood of death. Taken together with previous research showing that the proportion of group A is higher in

COVID-19 positive individuals, this suggests blood group A is candidate for follow-up studies.

Co-last author Dr. Christopher Hübel from the IoPPN, King's College London said: "The enzyme helps determine the blood group of an individual and our study has linked it with both risk of hospitalization and the need of respiratory support or death. Our study does not link precise blood group with risk of severe COVID-19 but since previous research has found that proportion of people who are group A is higher in COVID-19 positive individuals, this suggests that blood group A is more likely candidate for follow-up studies."

Researchers also identified three adhesion molecules as being causally linked to a decreased risk of hospitalization and requirement of respiratory support. As these adhesion molecules mediate interaction between immune cells and blood vessels this chimes with previous research suggesting that late stage COVID-19 is also a disease involving the linings of blood vessels.

By identifying this suite of proteins, the research has highlighted a number possible targets for drugs that could be used to help treat severe COVID-19. These will need further clinical investigation which can be undertaken as part of the wider COVID-Clinical Neuroscience Study (COVID-CNS) which is investigating the causes behind different aspects of COVID-19.

Gerome Breen, Professor of Genetics at the IoPPN, and co-last author on the paper said: "What we have done in our study is provide a shortlist for the next stage of research. Out of 1000s of blood proteins we have whittled it down to about 14 that have some form of causal connection to the risk of severe COVID-19 and present a potentially important avenue for further research to better understand the mechanisms behind COVID-19 with an ultimate aim of developing new treatments but potentially also preventative therapies."

Reference: "Proteome-wide Mendelian randomization identifies causal links between blood proteins and severe COVID-19" by Alish B. Palmos,Vincent Millischer, David K. Menon, Timothy R. Nicholson, Leonie S. Taams, Benedict Michael, Geraint Sunderland, Michael J. Griffiths, COVID Clinical Neuroscience Study Consortium, Christopher Hübel and Gerome Breen, 3 March 2022, PLOS Genetics. DOI: 10.1371/journal.pgen.1010042

The research was supported by NIHR Maudsley Biomedical Research Centre, Medical Research Council, UK Research and Innovation, Wellcome Trust and the Lundbeck Foundation.

https://bit.ly/3pFZOZm

Tiny New Species of Stegosaur Unearthed in China

A newly discovered fossilized stegosaur found in China is the most ancient ever found in Asia, and could be the oldest in the world.

Michelle Starr

Treading the Earth some 170 million years ago, during the Middle Jurassic Bajocian age, the beastie was also small for a stegosaur, measuring just 2.8 meters (just over 9 feet) from its nose to the tip of its spiny tail; larger stegos could grow up to 9 meters long.

Artist's impression of Bashanosaurus primitivus. (Banana Art Studio)

It's unclear whether the specimen is an adult or baby, but its discovery could tell us more about how the stegosaurus genus evolved – a process about which we know woefully little.

The remains consisted of bones from the shoulder, back, thigh, feet, spine, and ribs, as well as several armor plates. These enabled a team of paleontologists led by Dai Hui from Chongqing Bureau of Geological and Mineral Resource Exploration and Development to make comparisons with other stegosaur species.

They found that, while the newly found stego, named *Bashanosaurus primitivus*, has features in common with other stegosaurs, some features seem to be unique. Its shoulder is smaller

and less developed, its thighbone is slightly different, and its armor plates are narrower across, but thicker at the base.

Interestingly, it also has some characteristics in common with the first armored dinosaurs, which lived some 20 million years earlier. This suggests that *Bashanosaurus* could be a "missing link" between these older dinosaurs and the later stegosaurs.

"*Bashanosaurus* can be distinguished from other Middle Jurassic stegosaurs, and clearly represents a new species," Hui said.

"What's more, our analysis of the family tree indicates that it is one of the earliest-diverging stegosaurs along with the Chongqing Lizard (*Chungkingosaurus*) and *Huayangosaurus*. These were all unearthed from the Middle to Late Jurassic Shaximiao Formation in China, suggesting that stegosaurs might have originated in Asia."

Stegosaurs are among the most beloved of the Jurassic dinosaurs. The herbivorous beast was protected by plates of armor down the length of its spine and wicked spikes protruding from the end of its tail, to be wielded like a club.

Other characteristics include quadrupedal locomotion, and a tiny little head, surprisingly dainty on such a tank-like body.

These physical traits are characteristic of the genus, and *Bashanosaurus* appears to have had them too. But it also bears some similarities with early thyreophorans, the armored dinosaurs from which stegosaurs emerged, as well as early stegosaurs such as *Gigantspinosaurus* and *Huayangosaurus*, both also from China.

These similarities can be seen in the tail vertebrae, which are more elongated; a narrower, but flaring shoulder blade; and a lack of deep depressions in the spinal vertebrae. These similarities and differences suggest that *Bashanosaurus* is placed quite early on the stegosaurus family tree, which means that it represents quite an important discovery for understanding the genus.

"The discovery of this stegosaur from the Middle Jurassic of China adds to an increasing body of evidence that the group evolved in the early Middle Jurassic, or perhaps even in the Early Jurassic, and as such represent some of the earliest known bird-hipped dinosaurs," said paleontologist Susannah Maidment of the London Natural History Museum in the UK.

"China seems to have been a hotspot for stegosaur diversity, with numerous species now known from the Middle Jurassic right the way through until the end of the Early Cretaceous period."

The research has been published in the *Journal of Vertebrate Paleontology*.

https://bit.ly/3HQdOGe

Scientists Identify The Optimal Number of Daily Steps For Longevity, And It's Not 10,000

Conventional wisdom would have us believe the journey to a long and healthy life begins with 10,000 steps. Each and every day.

Mike McRae

For those living a more sedentary lifestyle, it's a goal that can take some effort to maintain. We've also known for some time it's also almost certainly wrong.

By analyzing data on tens of thousands of people across four continents compiled between 15 existing studies, a team of researchers has now landed on a more comfortable figure: the optimal number is probably closer to 6,000 steps per day, depending on your age. Anything more is unlikely to further reduce your chances of stumbling into an early grave.

"So, what we saw was this incremental reduction in risk as steps increase, until it levels off," says University of Massachusetts Amherst epidemiologist Amanda Paluch. "And the leveling occurred at different step values for older versus younger adults."

Humans are essentially built to ambulate. Evolution has honed our physiology to walk long distances, shedding heat easily as we tick-tock back and forth like inverted pendulums across the landscape in search of food and water.

This means our metabolisms, cardiovascular fitness, impact on our bones and muscles, and even our mental health are all tuned to appreciate a good hike. Squeezing just about any kind of stroll into our busy schedule will serve us well by helping us live longer, healthier, happier lives.

This is easier said than done for those pressed for time or lacking motivation, which is why tech companies invented small devices that help us keep track of the number of steps we take each day.

Half a century ago, the Yamasa Clock and Instrument Company in Japan sought to cash in on the buzz left by the 1964 Tokyo Olympics by producing a pedometer they called 'Manpo-kei' – a word that translates into 10,000 steps.

Why 10,000? Good old fashioned marketing. It's a nice, round number that sounds taxing enough to be a goal, but achievable enough to be worth striving for. What it doesn't have going for it is any scientific backing.

Having a single figure to promote to a general population is certainly useful. "It's such a clear communication tool for public health messaging," says Paluch. But getting that number right could make the difference between encouraging everybody to get enough exercise and putting people off trying altogether.

Last year, Paluch and her team published research based on a cohort of more than 2,000 middle-aged individuals living across the US. They found taking at least 7,000 steps a day reduced chances of premature death by 50 to 70 percent.

Those words 'at least' are doing some heavy lifting. With questions remaining over whether more is better, and whether squeezing all those steps into a more rapid pace is in any way useful, the research team widened their net to include previously published research.

Their latest meta-analysis included information collected on the health and step-counts of 47,471 adults from Asia, Australia, Europe, and North America. They found the 25 percent of adults who stepped the most each day had 40 to 53 percent lower chance of dying, compared with those in the bottom 25 percent of step-counts.

For adults aged 60 and older, this reduced risk topped out at around 6,000 to 8,000 steps a day. Pushing further might have other benefits, but a reduced chance of death isn't one.

The study found that those who are younger could do well to walk a little more, but there wasn't evidence that they'd necessarily live longer by walking more than 8,000 to 10,000 steps a day.

As for the rate of steps, the team found volume is what really matters. "The major takeaway is there's a lot of evidence suggesting that moving even a little more is beneficial, particularly for those who are doing very little activity," says Paluch.

None of this is to say we wouldn't benefit from working our bodies harder in other ways. Half an hour of intense activity each day could be a big boost for those of us who sit around a lot. Throwing in some strength training in old age could help our brains stay sharp and our hearts and bones stay health and strong.

But if nothing else, setting our sights on at least 6,000 to 8,000 paces before bedtime could be a far easier step towards a longer life.

This research was published in *The Lancet: Public Health*.

https://bit.ly/3pIG4o1

Dog walking creates social bonds within communities, research finds

Research shows that simply walking down the street with a dog can lead to significantly more social interactions than walking without a dog.

by Megan Mueller, The Conversation

Companion animals are a core part of family life in the United States, with 90 million American households having at least one pet. Many of us view pets as beloved family members who provide nonjudgmental emotional support and companionship during times

of stress.

That's not all. Research shows our pets can also strengthen our relationships and trust with other people. In addition, pets contribute positively to trust in our broader social communities.

Companion animals as social facilitators

As many of us know, animals provide an avenue for approaching another person socially, serving as a conversational starting point for connection. Pet ownership alone could be a source of shared interest and knowledge, even among people who may not have similar interests otherwise.

Simply walking down the street with a dog can lead to significantly more social interactions than walking without a dog. Assistance dogs can also facilitate these interactions. One study found that individuals using a wheelchair were more likely to be approached when their assistance animal was present.

The presence of an animal can also enhance perceptions of trustworthiness and responsibility, which in turn fosters positive social interactions. Researchers found that people were more likely to help a stranger with a dog than one without a dog, suggesting that the presence of an animal conferred perceptions of trust.

For children, interacting with a pet can also provide an additional opportunity to practice positive social interactions and develop empathy and compassion. Recent research indicates that living with dogs is associated with better social and emotional skills for children. In our own research at the Tufts Pets and Well-Being Lab, we also found that teenagers with high levels of attachment to their pets were likely to have higher levels of social skills and empathy toward others than those without such attachments.

Pets and social capital

Pets have also been shown to foster social capital in communities. Social capital is a concept that encompasses the broader community and neighborhood networks of social relationships, and the degree to which the community has a culture of helping others. The trust inherent in these connections can lead to better health and well-being.

Interestingly, pet owners have consistently reported higher levels of social capital in their communities than people without pets, both in the United States and internationally.

In addition to social facilitation, pets can contribute to social capital by strengthening social trust within communities. Neighbors may rely on one another to assist with animal care, which builds reciprocal trust. Pet owners' use of shared spaces, such as dog parks or green spaces, can lead to better social relationships.

In spite of it, during the COVID-19 pandemic dog owners were more likely than those without dogs to go for regular walks outdoors, providing an opportunity for community engagement during a period of extreme social isolation. The presence of an animal has even been found to increase positive social interactions in the workplace.

While evidence continues to support the idea that pets foster positive interactions between people, animals are not a universal solution for creating trust. There is still a lot we need to learn about the interrelated relationships between pets and people.

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Some *E. coli* set off viral grenades inside nearby bacteria

A toxin called colibactin awakens dormant viruses embedded in bacterial DNA

By Tina Hesman Saey

Some bacteria can trigger unexploded viral grenades in neighboring bacteria’s DNA.

Certain *Escherichia coli* bacteria, including some that live in human intestines, make a chemical called colibactin. That chemical awakens dormant viruses inside nearby bacteria, sometimes leading

to their destruction, researchers report February 23 in *Nature*.

This type of biological warfare among bacteria hasn't been described before. "It's an interesting strategy, and it's also a dangerous strategy," says Heather Hendrickson, an evolutionary microbiologist at the University of Canterbury in Christchurch, New Zealand, who was not involved in the work.

Colibactin producers must creep up on their bacterial enemies and trigger the unexploded ordinance hiding in the enemies' DNA. Those grenades are prophages — bacteria-infecting viruses that have inserted themselves into their hosts' DNA, where they hide out harmless and dormant until something triggers their awakening. That something, in this case, is DNA damage caused by colibactin.

When colibactin dings DNA, a bacterial repair system called the SOS response kicks in, chemical biologist Emily Balskus and colleagues found. "What many phages have done is to tap into that response," says Balskus, a Howard Hughes Medical Institute investigator at Harvard University.

"It's a signal for them to move out of this dormant lifestyle and awaken to kill their host and move on to find a new host," she says. Once phages wake up, they replicate and burst out of the host cell, destroying it.

But once these viral grenades go off, they can infect other bacteria, potentially exposing the attacking bacteria and other close-by microbes to biological shrapnel.

Humans might also get caught in the cross fire. Researchers already knew that colibactin can cause damage to human DNA that may lead to colon cancer. But why the bacteria would use the chemical against people wasn't known.

The new research suggests that *E. coli* may not be producing colibactin to assault its human hosts, but as a countermeasure against other microbes, Hendrickson says (*SN: 12/14/21*). "It's easy to forget that there's this continual conversation and warfare going on between bacteria, and we might not be the focus of their activities."

Among bacteria, colibactin isn't usually a lethal weapon. In most bacteria that Balskus and her colleagues examined, colibactin caused DNA damage, but the bacteria were able to repair the wounds. That may be because colibactin is an unstable chemical that quickly degrades before it can break enough DNA to do irreparable harm, Balskus says. Some bacteria also make other chemicals that defuse colibactin before it can damage DNA, her team found. Only bacteria that have unexploded prophages in their DNA and no other defenses were vulnerable to colibactin-producing bacteria in laboratory dishes.

Because colibactin decays quickly, "it suggests this is a very short-range communication," says Michael Dougherty, a microbiome researcher at the University of Florida in Gainesville who was not involved in the study. "Maybe it could have an effect when bacteria are forming biofilms where you have trillions of bacteria stacked on top of each other."

Colibactin may not be the only factor involved in exploding neighboring bacteria, says Dougherty's University of Florida colleague Christian Jobin. Balskus' team did not demonstrate that colibactin alone could detonate prophages. Perhaps something else about the colibactin-producing bacterium's presence is required to kick off the fireworks, he suggests.

The researchers don't yet know whether colibactin can trigger prophages when bacteria are in their natural habitats, such as human and other animal intestines. And perhaps awakening the viruses is an accident, Balskus speculates.

"Maybe [colibactin] didn't really evolve to kill. Maybe its primary ecological function involves doing something else," she says. What that might be is a mystery that Balskus and her colleagues are working to solve.

Citations *J.E. Silpe, et al. The bacterial toxin colibactin triggers prophage induction. Nature. Published online February 23, 2022. doi: 10.1038/s41586-022-04444-3.*

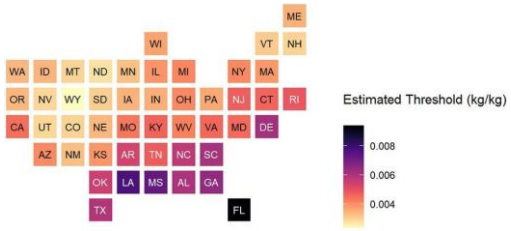
https://bit.ly/3tB6OrA

NASA finds each state has its own climatic threshold for flu outbreaks

A new study of the flu in the 48 contiguous U.S. states, using data from the Atmospheric Infrared Sounder on NASA's Aqua satellite

by Carol Rasmussen, Jet Propulsion Laboratory

What triggers an outbreak of the influenza virus? A new study of the flu in the 48 contiguous U.S. states, using data from the Atmospheric Infrared Sounder (AIRS) on NASA's Aqua satellite, has found that the answer is closely tied to local weather—specifically, to low humidity—and varies from state to state.



This chart shows low-humidity thresholds that signal flu outbreaks in 48 U.S. states. The color range from lighter to darker indicates lower to higher humidity thresholds, with the driest state, Wyoming, having the lowest threshold and Florida the highest. Units are kilograms of water per kilogram of air. **Credit: NASA/JPL-Caltech**

Average humidity varies widely across the United States, but even in the most humid states, it begins to drop as winter approaches. Researchers at NASA's Jet Propulsion Laboratory in Southern California and the University of Southern California correlated AIRS measurements of water vapor in the lower atmosphere with flu case estimates for each week from 2003 to 2015. The researchers found that in each state, there is a specific level of low humidity that may signal a flu outbreak is imminent. When this threshold is crossed each year, a large increase in flu cases follows within two or three weeks, on average.

These threshold levels of low humidity closely parallel each state's average climate. Although all 48 states have different thresholds, states with humid climates, such as those in the Southeast, have higher threshold values than arid states, including those in the West and Southwest.

The study wasn't designed to answer why lower humidity leads to flu outbreaks.

More information: E. Serman et al, Spatial Variation in Humidity and the Onset of Seasonal Influenza Across the Contiguous United States, GeoHealth (2021). DOI: 10.1029/2021GH000469

https://bit.ly/3J18DVa

In Mice, a Potential New Treatment Eradicates Ovarian And Colorectal Cancer in Days

An experimental new type of cancer treatment has yielded some impressive results in mice: the eradication of advanced-stage ovarian and colorectal cancer in the animals as little as six days.

David Nield

The new therapy has only been tested in mice so far, so let's not get too excited just yet. However, the early signs are promising, and human clinical trials could be underway by the end of the year.

The treatment involves tiny 'drug factory' beads that are implanted into the body and deliver a continuous, high dose of interleukin-2 (IL2) – a natural compound that enlists white blood cells in the fight against cancer.

"We just administer once, but the drug factories keep making the dose every day, where it's needed until the cancer is eliminated," says bioengineer Omid Veiseh from Rice University in Texas.

"Once we determined the correct dose – how many factories we needed – we were able to eradicate tumors in 100 percent of animals with ovarian cancer and in seven of eight animals with colorectal cancer."

Interleukin-2 is one of a group of immune system-triggering proteins called cytokines. Although cytokines are already used in cancer treatment for melanoma and renal carcinoma, but the

problem scientists have is getting cytokines to fight tumors effectively while avoiding dangerously high levels of inflammation elsewhere in the body, causing dramatic side effects.

In this study, the beads were placed in the peritoneum, a sac-like lining around the intestines, ovaries, and other abdominal organs. That enables the drugs to specifically target the cancer without burdening the body in terms of volume or weight.

The dose of interleukin-2 given by these drug factories would be too toxic if delivered through an IV drip, but here it works because the high concentrations are focussed on the tumor. The concentration of the protein elsewhere in the body seems to be around 30 times lower than near the tumor, according to tests.

Each bead has an outer cell made of hydrogel which shields the cytokine-producing cells, protecting them from attack. These beads are recognized as foreign objects by the surrounding immune system, but not as immediate threats, which enables them to do their work. They can then be programmed to turn off automatically.

"We found foreign body reactions safely and robustly turned off the flow of cytokine from the capsules within 30 days," says Veiseh. "We also showed we could safely administer a second course of treatment should it become necessary in the clinic."

The drug factory beads can potentially be adopted for cancers elsewhere in the body, as long as there's a lining where they could house them, and they could be tweaked to deliver different types of drugs, the researchers say. It's a flexible system as well as an innovative one.

What's more, the drugs that are being used here have already been approved as safe for use in clinical trials, which should speed up the process. The final treatment should be minimally-invasive and relatively straightforward to administer.

"In this study, we demonstrated that the 'drug factories' allow regulatable local administration of interleukin-2 and eradication of tumors in several mouse models, which is very exciting," says Amir Jazaeri, a professor of gynecologic oncology and reproductive medicine at the University of Texas. "This provides a strong rationale for clinical testing."

The research has been published in *Science Advances*.

https://bit.ly/3KkfjhB

Expanded alphabet, precise sequencing make DNA the next data storage solution

Adding seven new letters to DNA's molecular alphabet and developing a precise readout method enabled Illinois researchers to transform the double helix into a robust, sustainable data storage platform fit for the Information Age.

By Jenna Kurtzweil

Imagine Bach's "Cello Suite No. 1" played on a strand of DNA.

This scenario is not as impossible as it seems. Too small to withstand a rhythmic strum or sliding bowstring, DNA is a powerhouse for storing audio files and all kinds of other media.

"DNA is nature's original data storage system. We can use it to store any kind of data: images, video, music — anything," said Kasra Tabatabaei, a researcher at the Beckman Institute for Advanced Science and Technology and a coauthor on this study.

Expanding DNA's molecular makeup and developing a precise new sequencing method enabled a multi-institutional team to transform the double helix into a robust, sustainable data storage platform.

The team's paper appeared in Nano Letters in February 2022.

In the age of digital information, anyone brave enough to navigate the daily news feels the global archive growing heavier by the day. Increasingly, paper files are being digitized to save space and protect information from natural disasters.

From scientists to social media influencers, anyone with information to store stands to benefit from a secure, sustainable data lock box — and the double helix fits the bill.

“DNA is one of the best options, if not the best option, to store archival data especially,” said Chao Pan, a graduate student at the University of Illinois Urbana-Champaign and a coauthor on this study.

Its longevity rivaled only by durability, DNA is designed to weather Earth’s harshest conditions — sometimes for tens of thousands of years — and remain a viable data source. Scientists can sequence fossilized strands to uncover genetic histories and breathe life into long-lost landscapes.

Despite its diminutive stature, DNA is a bit like Dr. Who’s infamous police box: bigger on the inside than it appears.

“Every day, several petabytes of data are generated on the internet. Only one gram of DNA would be sufficient to store that data. That’s how dense DNA is as a storage medium,” said Tabatabaei, who is also a fifth-year Ph.D. student.

Another important aspect of DNA is its natural abundance and near-infinite renewability, a trait not shared by the most advanced data storage system on the market today: silicon microchips, which often circulate for just decades before an unceremonious burial in a heap of landfilled e-waste.

“At a time when we are facing unprecedented climate challenges, the importance of sustainable storage technologies cannot be overestimated. New, green technologies for DNA recording are emerging that will make molecular storage even more important in the future,” said Olgica Milenkovic, the Franklin W. Woeltge Professor of Electrical and Computer Engineering and a co-PI on the study.

Envisioning the future of data storage, the interdisciplinary team examined DNA’s millennia-old MO. Then, the researchers added their own 21st-century twist.

In nature, every strand of DNA contains four chemicals — adenine, guanine, cytosine, and thymine — often referred to by the initials A, G, C, and T. They arrange and rearrange themselves along the double helix into combinations that scientists can decode, or sequence, to make meaning.

The researchers expanded DNA’s already broad capacity for information storage by adding seven synthetic nucleobases to the existing four-letter lineup.

“Imagine the English alphabet. If you only had four letters to use, you could only create so many words. If you had the full alphabet, you could produce limitless word combinations. That’s the same with DNA. Instead of converting zeroes and ones to A, G, C, and T, we can convert zeroes and ones to A, G, C, T, and the seven new letters in the storage alphabet,” Tabatabaei said.

Because this team is the first to use chemically modified nucleotides for information storage in DNA, members innovated around a unique challenge: not all current technology is capable of interpreting chemically modified DNA strands. To solve this problem, they combined machine learning and artificial intelligence to develop a first-of-its-kind DNA sequence readout processing method.

Their solution can discern modified chemicals from natural ones, and differentiate each of the seven new molecules from one another.

“We tried 77 different combinations of the 11 nucleotides, and our method was able to differentiate each of them perfectly,” Pan said. “The deep learning framework as part of our method to identify different nucleotides is universal, which enables the generalizability of our approach to many other applications.”

This letter-perfect translation comes courtesy of nanopores: proteins with an opening in the middle through which a DNA strand can easily pass. Remarkably, the team found that nanopores can detect and distinguish each individual monomer unit along the DNA strand — whether the units have natural or chemical origins.

“This work provides an exciting proof-of-principle demonstration

of extending macromolecular data storage to non-natural chemistries, which hold the potential to drastically increase storage density in non-traditional storage media," said Charles Schroeder, the James Economy Professor of Materials Science and Engineering and a co-PI on this study.

DNA literally made history by storing genetic information. By the looks of this study, the future of data storage is just as double-helical.

Editor's note: The paper associated with this work can be accessed at https://pubs.acs.org/doi/10.1021/acs.nanolett.1c04203.

Additional UIUC collaborators include Aleksei Aksimentiev, the Center for Biophysics and Quantitative Biology; and Alvaro Hernandez, the Roy J. Carver Biotechnology Center. Partner institutions include the University of Massachusetts at Amherst and Stanford University. For a full list of collaborators and their affiliations, please consult the published work.