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

Giant, free index to world's research papers released online

Catalogue of billions of phrases from 107 million papers could ease computerized searching of the literature.

Holly Else

In a project that could unlock the world's research papers for easier computerized analysis, an American technologist has released online a gigantic index of the words and short phrases contained in more than 100 million journal articles — including many paywalled papers.

The catalogue, which was released on 7 October and is free to use, holds tables of more than 355 billion words and sentence fragments listed next to the articles in which they appear. It is an effort to help scientists use software to glean insights from published work even if they have no legal access to the underlying papers, says its creator, Carl Malamud. He released the files under the auspices of Public Resource, a non-profit corporation in Sebastopol, California, that he founded.

Malamud says that because his index doesn't contain the full text of articles, but only sentence snippets up to five words long, releasing it does not breach publishers' copyright restrictions on the reuse of paywalled articles. However, one legal expert says that publishers might question the legality of how Malamud created the index in the first place.

Some researchers who have had early access to the index say it's a major development in helping them to search the literature with software — a procedure known as text mining. Gitanjali Yadav, a computational biologist at the University of Cambridge, UK, who studies volatile organic compounds emitted by plants, says she aims to comb through Malamud's index to produce analyses of the plant chemicals described in the world's research papers. "There is no way for me — or anyone else — to experimentally analyse or measure the chemical fingerprint of each and every plant species on Earth. Much of the information we seek already exists, in published literature," she says. But researchers are restricted by lack of access to many papers, Yadav adds.

Malamud's General Index, as he calls it, aims to address the problems faced by researchers such as Yadav. Computer scientists already text mine papers to build databases of genes, drugs and chemicals found in the literature, and to explore papers' content faster than a human could read. But they often note that publishers ultimately control the speed and scope of their work, and that scientists are restricted to mining only open-access papers, or those articles they (or their institutions) have subscriptions to. Some publishers have said that researchers looking to mine the text of paywalled papers need their authorization.

And although free search engines such as Google Scholar have — with publishers' agreement — indexed the text of paywalled literature, they only allow users to search with certain types of text queries, and restrict automated searching. That doesn't allow large-scale computerized analysis using more specialized searches, Malamud says.

Terabytes of data

Malamud's project is his latest venture in a career spent releasing locked-up information for free access online — often in the face of legal challenges. He originally focused on publishing government-produced legal and financial information. But more recently he has turned his attention to opening up the scientific literature.

He began with a project to allow scientists to text mine — but not read — a giant store of research papers he's holding on a server in India; an idea he says he's still working on. The General Index now allows anyone to mine scientific works, but it doesn't have its own web-search portal, so if scientists want to search it, they will have

to download its files and develop their own programs. Malamud is hoping that users will make any search engines they create available to others.

In its compressed format, the catalogue totals almost 5 terabytes, and then expands to 38 terabytes. As well as sentence fragments, the files also include tables of nearly 20 billion keywords in the literature, and tables of a paper's title, authors and DOI (article identifier), so that users can track down a full paper if they have access to read it.

Michael Carroll, a legal researcher at the American University Washington College of Law in Washington DC, says that distributing the index should be legal worldwide because the files do not copy enough of an underlying article to infringe the publisher's copyright — although laws vary by country. "Copyright does not protect facts and ideas, and these results would be treated as communication of facts derived from the analysis of the copyrighted articles," he says.

The only legal question, Carroll adds, is whether Malamud's obtaining and copying of the underlying papers was done without breaching publishers' terms. Malamud says that he did have to get copies of the 107 million articles referenced in the index to create it; he declined to say how, but emphasizes that researchers will not have access to the full texts of the papers, which are stored in a secured, undisclosed location in the United States.

"I am very confident that what I'm doing is legal. We are not doing this to provoke a lawsuit, we are doing it to advance science," he says.

Nature contacted six publishers about the General Index for this article: all but one declined to comment. In a statement, Springer Nature said that the company supports open-research initiatives that use technology and algorithms to meet the needs of researchers. "We have seen some initiatives run into trouble, however, when the necessary rights have not been secured to enable their sustainability," the statement added. (Springer Nature publishes this journal; *Nature*'s news team is editorially independent of its publisher.)

Another legal researcher, Arul George Scaria at Delhi's National Law University, says that any publishers that tried to use copyright laws to prevent researchers from using the General Index "would eventually be disappointed". The release of the index, Scaria says, is a "major development for the wealth of information it has unlocked from those 107 million journal articles".

doi: https://doi.org/10.1038/d41586-021-02895-8

https://bit.ly/3GD7pic

What You Eat Affects Tumors: Diet May Slow Cancer Growth

A new study finds cutting off cells' supplies of lipids can slow the growth of tumors in mice.

By Anne Trafton, Massachusetts Institute of Technology

In recent years, there has been some evidence that dietary interventions can help to slow the growth of tumors. A new study from MIT, which analyzed two different diets in mice, reveals how those diets affect cancer cells, and offers an explanation for why restricting calories may slow tumor growth.

The study examined the effects of a calorically restricted diet and a ketogenic diet in mice with pancreatic tumors. While both of these diets reduce the amount of sugar available to tumors, the researchers found that only the calorically restricted diet reduced the availability of fatty acids, and this was linked to a slowdown in tumor growth.

The findings do not suggest that cancer patients should try to follow either of these diets, the researchers say. Instead, they believe the findings warrant further study to determine how dietary interventions might be combined with existing or emerging drugs to

help patients with cancer.

"There's a lot of evidence that diet can affect how fast your cancer progresses, but this is not a cure," says Matthew Vander Heiden, director of MIT's Koch Institute for Integrative Cancer Research and the senior author of the study. "While the findings are provocative, further study is needed, and individual patients should talk to their doctor about the right dietary interventions for their cancer."

MIT postdoc Evan Lien is the lead author of the paper, which was published on October 20, 2021, in *Nature*.

Metabolic mechanism

Vander Heiden, who is also a medical oncologist at Dana-Farber Cancer Institute, says his patients often ask him about the potential benefits of various diets, but there is not enough scientific evidence available to offer any definitive advice. Many of the dietary questions that patients have focus on either a calorie-restricted diet, which reduces calorie consumption by 25 to 50 percent, or a ketogenic diet, which is low in carbohydrates and high in fat and protein.

Previous studies have suggested that a calorically restricted diet might slow tumor growth in some contexts, and such a diet has been shown to extend lifespan in mice and many other animal species. A smaller number of studies exploring the effects of a ketogenic diet on cancer have produced inconclusive results.

"A lot of the advice or cultural fads that are out there aren't necessarily always based on very good science," Lien says. "It seemed like there was an opportunity, especially with our understanding of cancer metabolism having evolved so much over the past 10 years or so, that we could take some of the biochemical principles that we've learned and apply those concepts to understanding this complex question."

Cancer cells consume a great deal of glucose, so some scientists had hypothesized that either the ketogenic diet or calorie restriction might slow tumor growth by reducing the amount of glucose available. However, the MIT team's initial experiments in mice with pancreatic tumors showed that calorie restriction has a much greater effect on tumor growth than the ketogenic diet, so the researchers suspected that glucose levels were not playing a major role in the slowdown.

To dig deeper into the mechanism, the researchers analyzed tumor growth and nutrient concentration in mice with pancreatic tumors, which were fed either a normal, ketogenic, or calorie-restricted diet. In both the ketogenic and calorie-restricted mice, glucose levels went down. In the calorie-restricted mice, lipid levels also went down, but in mice on the ketogenic diet, they went up.

Lipid shortages impair tumor growth because cancer cells need lipids to construct their cell membranes. Normally, when lipids aren't available in a tissue, cells can make their own. As part of this process, they need to maintain the right balance of saturated and unsaturated fatty acids, which requires an enzyme called stearoyl-CoA desaturase (SCD). This enzyme is responsible for converting saturated fatty acids into unsaturated fatty acids.

Both calorie-restricted and ketogenic diets reduce SCD activity, but mice on the ketogenic diet had lipids available to them from their diet, so they didn't need to use SCD. Mice on the calorie-restricted diet, however, couldn't get fatty acids from their diet or produce their own. In these mice, tumor growth slowed significantly, compared to mice on the ketogenic diet.

"Not only does caloric restriction starve tumors of lipids, it also impairs the process that allows them to adapt to it. That combination is really contributing to the inhibition of tumor growth," Lien says.

Dietary effects

In addition to their mouse research, the researchers also looked at

some human data. Working with Brian Wolpin, an oncologist at Dana-Farber Cancer Institute and an author of the paper, the team obtained data from a large cohort study that allowed them to analyze the relationship between dietary patterns and survival times in pancreatic cancer patients. From that study, the researchers found that the type of fat consumed appears to influence how patients on a low-sugar diet fare after a pancreatic cancer diagnosis, although the data are not complete enough to draw any conclusions about the effect of diet, the researchers say.

Although this study showed that calorie restriction has beneficial effects in mice, the researchers say they do not recommend that cancer patients follow a calorie-restricted diet, which is difficult to maintain and can have harmful side effects. However, they believe that cancer cells' dependence on the availability of unsaturated fatty acids could be exploited to develop drugs that might help slow tumor growth.

One possible therapeutic strategy could be inhibition of the SCD enzyme, which would cut off tumor cells' ability to produce unsaturated fatty acids.

"The purpose of these studies isn't necessarily to recommend a diet, but it's to really understand the underlying biology," Lien says. "They provide some sense of the mechanisms of how these diets work, and that can lead to rational ideas on how we might mimic those situations for cancer therapy."

The researchers now plan to study how diets with a variety of fat sources — including plant or animal-based fats with defined differences in saturated, monounsaturated, and polyunsaturated fatty acid content — alter tumor fatty acid metabolism and the ratio of unsaturated to saturated fatty acids.

Reference: "Low glycaemic diets alter lipid metabolism to influence tumour growth" by Evan C. Lien, Anna M. Westermark, Yin Zhang, Chen Yuan, Zhaoqi Li, Allison N. Lau, Kiera M. Sapp, Brian M. Wolpin and Matthew G. Vander Heiden, 20 October 2021, Nature. DOI: 10.1038/s41586-021-04049-2

The research was funded by the Damon Runyon Cancer Research Foundation, the National Institutes of Health, the Lustgarten Foundation, the Dana-Farber Cancer Institute Hale Family Center for Pancreatic Cancer Research, Stand Up to Cancer, the Pancreatic Cancer Action Network, the Noble Effort Fund, the Wexler Family Fund, Promises for Purple, the Bob Parsons Fund, the Emerald Foundation, the Howard Hughes Medical Institute, the MIT Center for Precision Cancer Medicine, and the Ludwig Center at MIT.

https://bit.ly/3Brw71q

Wildfires burned Antarctica 75 million years ago, charcoal remnants reveal

Volcanic activity may have sparked ancient wildfires.

By Laura Geggel

Raging wildfires tore through Antarctica 75 million years ago, back when dinosaurs still roamed the Earth, a new study finds.

During the late Cretaceous period (100 million to 66 million years ago), one of the warmest periods on Earth, Antarctica's James Ross Island was home to a temperate forest of conifers, ferns and flowering plants known as angiosperms, as well as to a slew of dinosaurs. But it wasn't a total paradise; ancient paleo-fires burned parts of those forests to a crisp, leaving behind charcoal remnants that scientists have now scooped up and studied.

Dinosaurs attempt to flee a wildfire on Antarctica during the late Cretaceous.
(Image credit: Illustration by Maurilio Oliveira; De Lima, F.J. et al. Polar Research (2021); CC BY 4.0)

"This discovery expands the knowledge about the occurrence of vegetation fires during the Cretaceous, showing that such episodes were more common than previously imagined," study lead researcher Flaviana Jorge de Lima, a paleobiologist at Federal University of Pernambuco in Recife, Brazil, said in a statement.

The finding marks the first evidence on record of a paleo-fire on

James Ross Island, a part of the Antarctic Peninsula that now sits below South America. The discovery adds evidence that spontaneous fires were common in Antarctica during the Campanian age (about 84 million to 72 million years ago); in 2015, in a separate study, researchers documented the first known evidence of dinosaur-age wildfires in West Antarctica, according to a study in the journal Palaeogeography, Palaeoclimatology, Palaeoecology.

A fossilized piece of charcoal next to a coin. **(Image credit: De Lima, F.J. et al. Polar Research (2021); CC BY 4.0)**

For the new work, an international team of scientists analyzed fossils collected during a 2015-2016 expedition to the northeastern part of James Ross Island. These fossils contained fragments of plants that looked like charcoal residue, which had weathered away over the past tens of millions of years.

The charcoal fragments were small — the largest paper-thin pieces were just 0.7 by 1.5 inches (19 by 38 millimeters). But scanning electron microscope images revealed their identity: These fossils are likely burned gymnosperms, likely from a botanical family of coniferous trees called Araucariaceae, the researchers found.

Intense forest fires were frequent and widespread during the late Cretaceous, although most of the evidence for these blazes lies in the Northern Hemisphere, with a few documented cases in the Southern Hemisphere in what is now Tasmania, New Zealand and Argentina, the researchers said.

During the late Cretaceous, the supercontinent of Gondwana was breaking up, leaving places like Antarctica more isolated than before. This ice-free region had plenty of ignition sources, including lightning strikes, fireballs from falling meteors and volcanic activity, as well as flammable vegetation and high oxygen levels, which help fires burn, the researchers noted.

"Antarctica had intense volcanic activity caused by tectonics during the Cretaceous, as suggested by the presence of fossil remains in strata related to ash falls," the researchers wrote in the study. "It is plausible that volcanic activity ignited the palaeo-wildfire that created the charcoal reported here."

Now, the researchers are looking for new records of paleo-fires in other locations in Antarctica. The study was published online Oct. 20 in the journal Polar Research.

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COVID Vaccine Dosing "Mistake" Leads to Surprising Discovery

Study warrants a re-evaluation of current vaccine trial protocols for SARS-CoV-2, other diseases.

A dosing error made during an AstraZeneca-University of Oxford COVID-19 vaccine trial has led to a new dosage finding in mice, reports a new Northwestern Medicine study.

During the AstraZeneca-Oxford trial, some human participants erroneously received a half dose of their first shot, followed by a full dose for their second shot. Paradoxically, the trial showed that volunteers who got a lower dose of the first shot were better protected against COVID-19 than those who received two full doses.

However, it was not clear if the improvement of the low-dose vaccine was due to the dose itself or the fact that people who received the lower dose had also had a longer time between the first and the second shot, known as an extended prime-boost interval.

Scientists from Northwestern University Feinberg School of Medicine tested the effect of a SARS-CoV-2 vaccine prime dose in mice and found that a lower-dose first shot, followed by a full-dose booster shot, significantly improved the potency of a SARS-CoV-2 vaccine. The booster shot produced more antibodies and T-cells in the mice, allowing them to develop much more robust immune

responses against SARS-CoV-2, the study found. The findings were recently published in the journal *Science Immunology*.

Study questions idea of 'dose escalation' in vaccine trials

Vaccine clinical trials use a method known as dose escalation, in which one person receives a lower dose and is boosted with that same lower dose; a second person receives a higher dose and is boosted with that same higher dose, and so on.

"The idea is to make sure the vaccine is safe, so scientists use dose escalation to determine the 'goldilocks zone': what is the minimum dose of vaccine that you can give to someone while still getting a good immune response?" said lead author Pablo Penaloza-MacMaster, assistant professor of microbiology-immunology at Feinberg.

The Northwestern study did not use the AstraZeneca-Oxford vaccine but instead used one that was similar: an adenovirus serotype 5 vaccine that is akin to the Chinese-developed CanSino and Russian-developed Sputnik V vaccines. Penaloza-MacMaster said their ongoing studies are now examining this dosing regimen in mRNA vaccines.

Why did the lower dose/standard dose work better?

In the AstraZeneca trial, participants who received the full first dose were boosted around three to four weeks after the first shot whereas those who received the lower dose had a much more extended prime-boost interval. The Northwestern study replicated this extended prime-boost interval in mice, and also reported that increasing the prime-boost interval improves the immune response.

Extending the time between the first and second shot also improved the SARS-CoV-2 vaccine.

"An extended prime-boost interval allows the immune system to rest and mature in a way that the immune response can then expand more robustly upon a booster vaccination," Penaloza-MacMaster said. "The longer you wait before boosting, the better that secondary immune response will be."

This can be a tricky game, though, he said, because waiting longer to boost might increase one's susceptibility of getting the virus.

"With a pandemic, it's ethically challenging to extend that prime-boost interval because you need people to get fully protected as soon as possible," Penaloza-MacMaster said. "But this approach may have its benefits in terms of improving the durability and magnitude of immune responses in the long run, which may be useful not just for SARS-CoV-2 vaccines, but also for other vaccines."

The team also observed similar positive effects of lowering vaccine doses with an experimental HIV vaccine based on an adenovirus vector, suggesting that these findings may be generalizable to other vaccines.

Reference: "Fractionating a COVID-19 Ad5-vectored vaccine improves virus-specific immunity" by Sarah Sanchez, Nicole Palacio, Tanushree Dangi, Thomas Ciucci and Pablo Penaloza-MacMaster, 14 October 2021, Science Immunology.
DOI: 10.1126/sciimmunol.abi8635
Other authors of this study include Sarah Sanchez, Nicole Palacio and Tanushree Dangi, members of the Penaloza-MacMaster laboratory at Northwestern University.
Funding for the study was provided by the National Institutes of Health (grant DP2 DA051912-01).

https://bit.ly/3nLbus0

You only live once: Epidemiologists analyze health risks in all the James Bond films

Biggest risk might be to Bond's sexual partners: 27.1% of them died shortly after sex.

Jennifer Ouellette

A graduate student in epidemiology working in the field leads a perilous life, as Wouter Graumans discovered when he came down with a serious case of food poisoning while visiting Burkina Faso to study infectious diseases. He may have also had a touch of delirium, as his experience prompted him to wonder how James Bond, Britain's most famous secret agent, managed to travel all around the

world without picking up so much as a case of the sniffles.

Graumans, who is working on his PhD at Radboud University Medical Center in the Netherlands, decided to undertake an epidemiological analysis of all 25 Bond films between 1962 and 2021.

He found willing accomplices in Teun Bousema, an epidemiologist, and Will Stone, who studies malaria, both affiliated with the London School of Hygiene and Tropical Medicine in England.

Enlarge / Epidemiologists analyzed all 25 James Bond films to assess 007's health risks while traveling around the world. **Aurich Lawson | Getty Images**

The result is a highly entertaining, tongue-in-cheek short paper in the journal Travel Medicine and Infectious Disease. The paper details 007's exposure risk to infectious agents during his global travels, covering everything from foodborne pathogens to ticks and mites, hangovers and dehydration from all those martinis, parasites, and unsafe sex. (The authors' emails requesting funding from EON Productions sadly went unanswered.)

Conducting the study meant rewatching all 25 James Bond films, representing a time investment of about 3,113 minutes per author—hours "that were not spent on more pressing societal issues or forms of relaxation that are more acceptable in academic circles," the researchers wrote. In all, they counted 86 international journeys to 46 different countries and based their analysis on the Centers for Disease Control's travel recommendations for each of those countries. They excluded Bond's trip to space to attack Hugo Drax's space station in *Moonraker* on the grounds that "travel advice for this region is currently unavailable."

Foodborne pathogens are an obvious risk factor for global travelers (as Graumans can attest). For instance, in *Live and Let Die*, Bond faces a horde of hungry crocodiles on an island but manages to distract them by tossing pieces of raw chicken at them. But did 007 wash his hands afterward? He most certainly did not, being preoccupied with blowing up a drug lab and engaging in a daring speedboat pursuit. The authors note that raw chicken is known to sometimes carry bacteria like *Campylobacter*, *Salmonella*, and *Clostridium*, all of which can cause severe diarrhea.

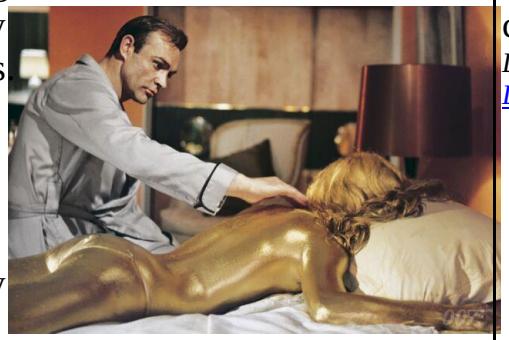
What about 007's famous penchant for martinis that are shaken, not stirred? We hardly ever see Bond drink anything non-alcoholic, according to the authors, yet he never seems to experience a hangover. He drinks orange juice in *From Russia With Love*, (poisoned) coffee in *Dr. No*, and saltwater in *Casino Royale*—the latter solely to induce vomiting after his drink (a Vesper) is poisoned mid-poker tournament. Apart from the constant risk of poisoning, Bond also risks dehydration, heatstroke, or sunstroke, since he engages in very strenuous physical activity, often in very hot environments, while eschewing sunscreen. He increases his dehydration risk even further in *The Spy Who Loved Me* by doing all of this in a black three-piece suit—hardly health-appropriate attire under the circumstances.

Then there's the matter of sex. James Bond has always been quite the ladies' man—Graumans *et al*. counted 59 "amorous activities" across 25 films for an average of 2.4 per film—and he's not particularly diligent about safe-sex practices. He beds a woman in *Thunderball* within 20 minutes of meeting her, which leaves little time to exchange information on past sexual histories or preferences for contraception.

That said, it's the women who appear to be at greatest risk in these encounters. A "shockingly high percentage" (27.1 percent) of Bond's sexual partners die shortly after sleeping with him—and not because of any STDs Bond might be spreading. The women tend to die violent deaths—like poor Jill Masterson (Shirley Eaton) in

Goldfinger, whose bikini-clad body Bond discovers lying face-down on the bed they recently shared, covered in gold paint, which caused her to expire from "skin suffocation."

Bond also faces potential health risks from the many dangerous bugs that inhabit some of the exotic locations he visits. For instance, in *You Only Live Twice*, Bond must hike for hours through swaying tall grass in Japanese mountains. The authors approve of 007's choice to wear long pants (unlike his bikini-clad female companion). Grasslands like this are often infested with ticks—which can transmit deadly pathogens like the virus that causes meningitis—and mites, which carry bacteria that can cause scrub typhus. "Bond is likely to have benefitted from his partner's relative lack of clothing," the authors note. "Given a choice between hosts, a bathing suit provides far greater opportunity for successful blood feeding."



***Enlarge** / In Goldfinger, one of Bond's romantic conquests, Jill Masterson (Shirley Eaton), ends up dead from "skin suffocation" caused by being covered in gold paint.* **EON Productions**

The biggest stretch in Graumans *et al.*'s analysis is that of feline-borne Toxoplasmosis, a parasite carried by cats. Those who contract the parasite tend to exhibit reckless behavior, such as mice losing their fear of cats. Bond engages in all manner of reckless behavior, and the authors suggest he may have contracted the parasite from Ernst Stavro Blofeld's fluffy white Persian cat (featured in both *From Russia With Love* and *Spectre*). The possibility is admittedly far-fetched, but isn't that the essence of a good Bond film?

Don't even get the authors started on Bond's cavalier attitude toward safety measures when he goes diving with no thought to the risk of decompression sickness. "Overall, we found Bond poorly prepared for travel-associated health risks and particularly naive to the threat of infectious disease," the authors concluded, calling out MI6 for negligence in this regard. "Given the central role that agents with the double-0 status have in international counter-terrorism activities, we sincerely hope that MI6 will take its responsibility seriously. We only live once."

I hereby nominate this paper as a contender for an Ig Nobel Prize. And of course, I eagerly await the *Austin Powers*-like Bond parody film involving 007 combating all of the above as he tries to complete his missions.

DOI: Travel Medicine and Infectious Disease, 2021. 10.1016/j.tmaid.2021.102175 (About DOIs).

https://bit.ly/3w2ZqyH

The Pupil in Your Eye Can Perceive Numerical Information, Not Just Light

The pupil shifts in size depending on how many objects we're observing

David Nield

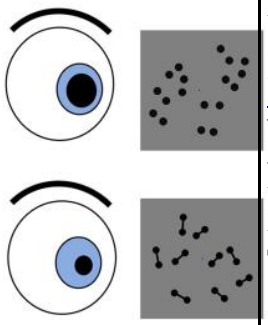
You might know that the size of the pupils in our eyes changes depending on how well lit our environment is, but there's more to the story: Scientists have now discovered that the pupil also shifts in size depending on how many objects we're observing.

The more objects in a scene, the bigger the pupil grows, as if to better accommodate everything that it has to look at. This "perceived numerosity" is a simple and automatic reflex, the new research shows.

In a new study, researchers observed the pupil sizes of 16 participants while they looked at pictures of dots. In some of the pictures, the dots were linked together in dumbbell shapes – creating the illusion that there were fewer objects – and pupil size then shrank.

"This result shows that numerical information is intrinsically related to perception," says psychologist and neuroscientist Elisa Castaldi from the University of Florence in Italy.

"This could have important, practical implications. For example, this ability is compromised in dyscalculia which is a dysfunction in mathematical learning, so our experiment may be useful in early identification of this condition in very young children."



How the pupil reacts to different objects and patterns. **(Castaldi et al., Nature Communications, 2021)**

Even though the numbers of black or white dots in the pictures being viewed didn't change, the perceived number of objects did, because of the joining lines. The participants were asked to look at these images passively, without paying special attention to the overall number of items and without a specific task to complete.

As for where this reaction comes from, it's likely to be linked to the need for survival – most species are thought to have a dedicated 'number sense' that enables them to spot enemies in the wild, find food, get back home, and more besides.

When it comes to humans, being able to weigh up numbers is something that seems to appear as soon as a few hours after birth – even if you're terrible at math, you have a built-in aptitude for judging numerosity, and it appears the dilation of our pupils is part of a response to that.

"When we look around, we spontaneously perceive the form, size, movement and color of a scene," says psychologist David Burr from the University of Sydney in Australia, and also affiliated with the University of Florence.

"Equally spontaneously, we perceive the number of items before us. This ability, shared with most other animals, is an evolutionary fundamental: it reveals immediately important quantities, such as how many apples there are on the tree, or how many enemies are attacking."

Previous research had indicated that pupil size wasn't just affected by light: visual illusions involving brightness, size, and context have an effect too, backing up the idea that this dilation in our eyes is at least partly controlled by signals higher up in the brain.

The researchers are keen to dig further into why this is happening, and what else could be having an impact on pupil size – such as the movement required by the eye to take in everything that appears in a scene.

And there's lots more to explore here as well. Our eyes seem to be more sensitive to the number of items we're looking at rather than how they're spaced or arranged, which is another reaction that can be analyzed in future studies.

"Recent research from our laboratory shows that pupil size is also regulated by cognitive and perceptual factors," says physiologist Paola Binda from the University of Pisa in Italy.

The research has been published in *Nature Communications*.

https://bit.ly/2ZASTXP

Gigantic Movie Monster Discovered Lurking in Space... If You Look Closely

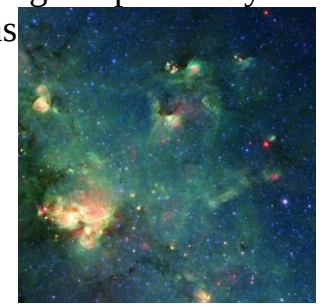
Think about monsters... specifically monsters originating from Japanese films of the 1950s

David Nield

We've seen plenty of awe-inspiring images of space captured by telescopes and spacecraft in the past: whether it's a supernova blast wave, the textures of a planet, or pillars of interstellar gas and dust, there's a virtually endless stream of fascinating pictures available for us to pore over.

Sometimes though there's something more hidden in the patterns of stars and light. Take a look at the image below, for example, and

see if it suggests anything to you. It's an image captured by the NASA Spitzer Space Telescope, which was operational from 2003 to 2020.



Getting anything yet? We'll give you a clue: Think about monsters... specifically monsters originating from Japanese films of the 1950s. You might have to squint a little and use your imagination before we tell you any more.

The nebula, hiding a certain someone. **(NASA/JPL-Caltech)**

In terms of specifics, the picture shows a nebula nursery of stars located in the Sagittarius constellation, along the plane of the Milky Way. The bright region in the lower left (which looks like it might be being held by a massive creature?) is a star-forming region known as W33, and is around 7,800 light-years away from Earth.

The picture was captured as part of Spitzer's GLIMPSE Survey, which stands for Galactic Legacy Infrared Mid-Plane Survey Extraordinaire. Although Spitzer is now retired, the images it collected are still being analyzed.

One of those doing the analyzing is astronomer Robert Hurt, from the California Institute of Technology (Caltech), and he's managed to spot something in the image. As you might have guessed by now, Hurt thinks there's a definite hint of Godzilla in there.

"I wasn't looking for monsters," says Hurt. "I just happened to glance at a region of sky that I've browsed many times before, but I'd never zoomed in on. Sometimes if you just crop an area differently, it brings out something that you didn't see before. It was the eyes and mouth that roared 'Godzilla' to me."

Pareidolia is the tendency to see something meaningful in a meaningless image, and it happens quite often – including in pictures of the cosmos: Take a look at the Spitzer images that resemble a jack-o'-lantern, a black widow spider, or the Starship Enterprise, for example.

The color processing helps: here blue, cyan, green, and red are used to represent different wavelengths of infrared light, with yellow and white combinations of those wavelengths. Blue and cyan show light emitted by stars, green shows dust and organic molecules called hydrocarbons, and red shows warm dust heated by stars or supernovae.

The monster revealed. **(NASA/JPL-Caltech)**

Work continues to catalog and examine the data collected by Spitzer, and to raise awareness of its findings – and sometimes that means using an iconic sea monster to help tell a story.

"It's one of the ways that we want people to connect with the incredible work that Spitzer did," says Hurt.

"I look for compelling areas that can really tell a story. Sometimes it's a story about how stars and planets form, and sometimes it's about a giant monster rampaging through Tokyo."

https://nyti.ms/3Gq43z8

Merck Will Share Formula for Its Covid Pill With Poor Countries

The company announced a licensing deal that will allow the drug, molnupiravir, to be made and sold cheaply in 105 developing nations.

By Stephanie Nolen

Merck has granted a royalty-free license for its promising Covid-19 pill to a United Nations-backed nonprofit in a deal that would allow the drug to be manufactured and sold cheaply in the poorest nations, where vaccines for the coronavirus are in devastatingly short supply.

The agreement with the Medicines Patent Pool, an organization that works to make medical treatment and technologies globally

accessible, will allow companies in 105 countries, mostly in Africa and Asia, to sublicense the formulation for the antiviral pill, called molnupiravir, and begin making it.

Merck reported this month that the drug halved the rate of hospitalizations and deaths in high-risk Covid patients who took it soon after infection in a large clinical trial. Affluent nations, including the United States, have rushed to negotiate deals to buy the drug, tying up large portions of the supply even before it has been approved by regulators and raising concerns that poor countries could be shut out of access to the medicine, much as they have been for vaccines.

Generic drug makers in developing countries are expected to market the drug for as little as $20 per treatment (a 5-day course), compared to the $712 per course that the U.S. government has agreed to pay for its initial purchase.

Treatment-access advocates welcomed the new deal, which was announced Wednesday morning, calling it an unusual step for a major Western pharmaceutical company.

“The Merck license is a very good and meaningful protection for people living in countries where more than half of the world’s population lives,” said James Love, who leads Knowledge Ecology International, a nonprofit research organization.

“The license isn’t perfect,” he added, “they never are, but it’s going to be very helpful if the drugs work as well as the hype and are safe enough. It will make a difference.”

Merck had already taken the step of licensing eight large Indian drug makers to produce generic versions of molnupiravir, pending authorization. But the company feared that production in just one region would not be enough to ensure rapid access to the drug across the developing world, said Jenelle Krishnamoorthy, Merck’s vice president for global policy.

So Merck also engaged in talks with the patent pool, which has deep experience in working with a network of global drug makers that can meet high-quality standards, including those required for W.H.O. prequalification, she said.

“We knew we had to work faster, we had to do things we hadn’t done before, we had be more efficient,” Ms. Krishnamoorthy said.

Merck has promised assistance with technology transfer to any generic licensee that requires help to make the drug. That offer, and the company’s quick moves to make its product available in the developing world, stand in contrast to the ongoing refusal of Pfizer and Moderna to do technology transfer to potential mRNA vaccine producers in Africa, Asia or Latin America. The company is the rare pharmaceutical brand to be receiving largely positive media coverage these days.

During the long fight for affordably priced drugs to treat H.I.V. in the early 2000s, Merck was a frequent target of activist ire, and the legacy of that battle clearly informs the company’s decision-making about access today. The processes that Merck is using for molnupiravir — including voluntary licenses to Indian generic makers, and a handing-off of the market where governments or consumers won’t be able to pay much for the drug — are also standard practices in the drug industry today, and date from the struggle for accessible medications for H.I.V.

Charles Gore, director of the Medicines Patent Pool, said the new agreement with Merck is the first transparent public health license for a Covid medicine. “Really importantly, it is for something that could be used outside of hospitals, and which is potentially going to be very cheap,” he said. “This is hopefully going to make things a lot easier in terms of keeping people out of hospital and stopping people dying in low- and middle-income countries.”

Mr. Gore said that more than 50 companies, from all regions of the developing world, have already approached the organization about obtaining a sublicense.

The agreement with Merck, Mr. Gore said, is also critically important as a precedent. “I hope this will start a landslide of people coming to the Medicines Patent Pool, wanting to do licensing, because there’s no question that access has been the problem,” he said. “From a scientific point of view, industry have done a really brilliant job — firstly, providing the vaccines, and now providing treatments. But the access side of it has let the whole thing down.”

Pfizer also has a Covid antiviral pill in late-stage trials, and Mr. Gore said the company is in talks with the patent pool.

Molnupiravir was developed by Merck and Ridgeback Biotherapeutics of Miami, based on a molecule first studied at Emory University in Atlanta. All three organizations are party to this deal, which will not require a fee from any sublicensing company.

Merck has submitted its clinical trial data to the Food and Drug Administration seeking emergency-use authorization; a decision could come in early December. Regulatory agencies in other nations that produce a version of molnupiravir will need to evaluate it. Some drug manufacturers will likely seek World Health Organization prequalification for their versions, so that they can bypass the country-by-country regulatory steps.

Stephen Saad, chief executive of Aspen Pharmacare in South Africa, said his company expects to apply for a license to make molnupiravir and distribute it across Africa. He said that he believed that Aspen could make the drug for about $20 per course.

Mr. Gore said that he has been told by some in the field that a generic version of molnupiravir could be profitably produced for as little as $8 per course.

Under the new licensing deal, Merck would continue to produce and sell molnupiravir in wealthy nations and many middle-income ones at significantly higher prices.

In South Africa, treatment access activists called the patent pool license a positive step. “We have lost so many lives to the blocking of licensing,” said Sibongile Tshabalala, chairwoman of the Treatment Action Campaign, the South African organization that lobbied global drug companies for affordable H.I.V. drugs and has been campaigning in recent months for Covid vaccine access.

Broadening the range of countries where molnupiravir is made will ensure the lowest possible price for the drug, and make it more feasible for public health systems in Africa to purchase it for widespread use, Ms. Tshabalala said.

The licenses that Merck issued to the Indian generic makers restrict sales to developing countries and excludes most middle-income countries, including China and Russia — the site of a current raging Covid outbreak — raising the possibility that citizens in these nations, which often have weak health systems, will not get access to the drug.

The patent pool agreement for molnupiravir also excludes middle-income countries and most nations in Latin America, Mr. Love said. “What are you going to do for countries like Chile or Colombia, Thailand or Mexico?” he asked. “They’re not in the license.”

Lynsey Chutel contributed reporting from Johannesburg.

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Red paint on 1,000-year-old gold mask from Peru contains human blood proteins

A red paint sample taken from a 1,000-year-old mask contains human blood and bird egg proteins, in addition to a red pigment.

Thirty years ago, archeologists excavated the tomb of an elite 40-50-year-old man from the Sicán culture of Peru, a society that predated the Incas. The man's seated, upside-down skeleton was painted bright red, as was the gold mask covering his detached skull. Now, researchers reporting in ACS' *Journal of Proteome Research* have analyzed the paint, finding that, in addition to a red pigment, it

contains human blood and bird egg proteins.

The Sicán was a prominent culture that existed from the ninth to 14th centuries along the northern coast of modern Peru. During the Middle Sicán Period (about 900–1,100 A.D.), metallurgists produced a dazzling array of gold objects, many of which were buried in tombs of the elite class.

A red paint sample taken from a 1,000-year-old mask excavated from a Sicán tomb in Peru contains human blood and bird egg proteins, in addition to a red pigment. **Credit: Journal of Proteome Research**

In the early 1990s, a team of archaeologists and conservators led by Izumi Shimada excavated a tomb where an elite man's seated skeleton was painted red and placed upside down at the center of the chamber. The skeletons of two young women were arranged nearby in birthing and midwifing poses, and two crouching children's skeletons were placed at a higher level. Among the many gold artifacts found in the tomb was a red-painted gold mask, which covered the face of the man's detached skull. At the time, scientists identified the red pigment in the paint as cinnabar, but Luciana de Costa Carvalho, James McCullagh and colleagues wondered what the Sicán people had used in the paint mix as a binding material, which had kept the paint layer attached to the metal surface of the mask for 1,000 years.

To find out, the researchers analyzed a small sample of the mask's red paint. Fourier transform-infrared spectroscopy revealed that the sample contained proteins, so the team conducted a proteomic analysis using tandem mass spectrometry. They identified six proteins from human blood in the red paint, including serum albumin and immunoglobulin G (a type of human serum antibody). Other proteins, such as ovalbumin, came from egg whites. Because the proteins were highly degraded, the researchers couldn't identify the exact species of bird's egg used to make the paint, but a likely candidate is the Muscovy duck. The identification of human blood proteins supports the hypothesis that the arrangement of the skeletons was related to a desired "rebirth" of the deceased Sicán leader, with the blood-containing paint that coated the man's skeleton and face mask potentially symbolizing his "life force," the researchers say.

More information: *Elisabete Pires et al, Human Blood and Bird Egg Proteins Identified in Red Paint Covering a 1000-Year-Old Gold Mask from Peru, Journal of Proteome Research (2021). DOI: 10.1021/acs.jproteome.1c00472*

https://bit.ly/3bocOvn

Why do placebos work? Scientists identify key brain pathway

Study finds opposite impacts on brainstem of placebo and "nocebo" effects

By Daryl Austin

The placebo effect can bring powerful relief—but what does that look like in your brain? A new study finds fake therapies and fake side effects have a real impact on your brainstem, a hub of pain processing, affecting it in opposite ways. The work could help scientists develop better treatments for chronic pain.

It's "a major rigorous contribution to the field," says Ted Kaptchuk, a biomedical scientist at Harvard Medical School who was not involved with the study. Still, he cautions that more work is needed to see whether this laboratory-based study translates to the real world.

Scientists have known about the placebo effect for more than 400 years. In 1572, a French philosopher wrote that "there are men on whom the mere sight of medicine is operative." Yet researchers have struggled to understand why patients given a nonactive therapy such as a sugar pill still feel relief. They've also been

confounded by the opposite phenomenon: When patients are told a placebo has harmful side effects, they often feel bad afterward—the so-called "nocebo" effect.

To find the signature of these two effects in brain, researchers brought 27 participants—13 men and 14 women with an average age of 23—into their laboratory at the University of Melbourne. The scientists strapped a device called a thermode to their arm, which heated up to a moderately painful temperature. Afterward, the researchers told the participants they were applying one of three creams to the affected area: a pain reliever, a pain inducer (which would make the heat feel worse), and a control cream with no effect. In reality, all three substances were petroleum jelly.

All the while, the team scanned the volunteers with a high-resolution functional magnetic resonance imaging (fMRI) machine to detect which parts of their brain were most active. Most participants in the study experienced either the placebo or nocebo effect. About one-third reported lower levels of pain when the "pain reliever" was applied, whereas slightly more than half reported more pain when the "pain inducer" was applied.

The fMRI results reflected these responses. Both the placebo and nocebo effects influenced activity in the brainstem, the researchers report this week in *The Journal of Neuroscience*. The placebo effect increased activity in an area called the rostral ventromedial medulla, which relays pain information, and decreased activity in the periaqueductal gray, which helps the body suppress pain. The nocebo effect induced the opposite change. (The findings may seem counterintuitive, but multiple areas of the brainstem act in complex ways when it comes to creating the sensation of pain, the authors say.)

The approach is excellent, says Tor Wager, a neuroscientist who studies the placebo effect at Dartmouth College. "It was done at ultra–high resolution, which makes it much better for identifying [parts of] the brainstem that play key roles in pain control." Though other studies have shown brain activity in response to both the placebo and nocebo effects, he and other experts say the new work offers the most detailed view yet of how the brain responds to these phenomena.

The results may offer a route for future treatments of chronic pain, says Lewis Crawford, a neuroscientist at the University of Sydney School of Medical Sciences and the study's lead author.

Doctors have applied electrical impulses to the brainstem—an approach known as deep brain stimulation—to treat burning "neuropathic" pain, which can be caused by nerve damage, as well as carpal tunnel syndrome, and cancer-related pain (such as that resulting from nervous system tumor invasion or radiation-induced nerve damage) with only mixed success for decades, he notes.

Part of the problem was an inability to identify exactly which parts of the brainstem are responsible for controlling the modulation of pain, Crawford says. By localizing placebo- and nocebo-induced sensations to more precise brain areas, the new study could help narrow down targets for stimulation, he says.

Placebo or not, that's a valuable dose of good news.

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https://bit.ly/3mtt1FI

Forget Me Not: Target Identified for Preventing and Reversing Alzheimer's and Related Dementias

A novel tau protein conformation, cis P-tau, is a toxic early driver of Alzheimer's disease and related dementias. Silencing of this protein through immunotherapy ameliorates dementia symptoms in preclinical models.

Researchers remain perplexed as to what causes dementia and how to treat and reverse the cognitive decline seen in patients.

In a first-of-its-kind study, researchers at the Medical University of South Carolina (MUSC) and Beth Israel Deaconess Medical Center

(BIDMC), Harvard Medical School discovered that cis P-tau, a toxic, non-degradable version of a healthy brain protein, is an early marker of vascular dementia (VaD) and Alzheimer's disease (AD).

Their results, published recently in *Science Translational Medicine*, define the molecular mechanism that causes an accumulation of this toxic protein.

Furthermore, they showed that a monoclonal antibody (mAb) that targets this toxic protein was able to prevent disease pathology and memory loss in AD- and VaD-like preclinical models.

Additionally, this treatment was even capable of reversing cognitive impairment in an AD-like preclinical model.

"We believe our findings have not only discovered cis P-tau as a previously unrecognized major early driver of VaD and AD but also identified a highly effective and specific immunotherapy to target this common disease driver for treating and preventing AD and VaD at early stages," said Onder Albayram, Ph.D., co-lead author and assistant professor in the Division of Cardiology in the Department of Medicine at MUSC.

Aging is a normal part of life – we experience weakening of our bones and muscles, stiffening of our blood vessels and some memory lapses.

But for around 50 million people worldwide, these memory lapses become progressively more severe, ultimately leading to a diagnosis of dementia.

Dementia is an umbrella term that covers AD, which accounts for 60% to 80% of cases; VaD, the second most common cause; and other less common pathologies.

Currently, there are no effective treatments for AD.

Interestingly, most AD cases have a vascular component, suggesting a broader relationship between cognitive function and healthy brain vasculature.

A better understanding of that relationship could provide a platform to discover novel therapeutic targets.

"Our work provides evidence that cis P-tau may be a pathogenic factor that explains VaD, which is not generally linked to other dementias," added Chenxi Qiu, Ph.D., co-lead author and a postdoctoral research fellow at BIDMC, Harvard Medical School.

In a preclinical model of VaD, young mice showed signs of brain inflammation and memory loss within one month.

However, treating these mice with the cis P-tau mAb prevented neural degradation and cognitive decline out to six months.

In a separate preclinical model of AD, old mice showed severe cognitive impairment.

Excitingly, this severe impairment was significantly reversed when mice were given the cis P-tau mAb.

"These data show that cis P-tau could be an early upstream pathogenic factor common to both diseases," said Albayram.

Translating information gained from preclinical models to humans is often difficult, but this study offers reasons to be optimistic.

Accumulation of cis P-tau caused dramatic changes in the genetic architecture of affected cells in a VaD model; these changes were consistent with those seen in human AD patients.

The researchers went on to show that treatment with the cis P-tau mAb reversed 85% to 90% of those changes suggesting the power of this potential therapy.

"The genomic landscape really adapts after the silencing of this toxic protein," said Albayram.

"That was a big discovery."

Not only are Albayram and Qiu excited about these findings, but colleagues at MUSC are already quite enthusiastic about this work.

"I can go on and on about this paper," said Adviye Ergul, M.D., Ph.D., professor in the College of Medicine, Department of Pathology and Laboratory Medicine at MUSC.

"They provide robust evidence that there is accumulation of a specific form of the tau protein – cis P-tau – that highlights a different tau protein pathology in VaD research."

This groundbreaking research has opened the door for new potential immunotherapies and highlighted several new areas of research that need to be explored.

While the researchers delineated a pathway that leads to the accumulation of cis P-tau, the underlying linkage between vascular abnormalities and activation of the pathway needs to be identified.

A better understanding of how toxic cis P-tau interacts with the healthy trans P-tau could provide further insights into the progression of AD disease.

AD and VaD might not be the only diseases affected by high levels of cis P-tau. Other brain disorders with a vascular component might also arise from this toxic protein, but further study will be required to establish such a link.

"Cis P-tau may be a common, early and pathogenic factor underlying traumatic brain injury, VaD and AD," said Qiu.

As we get older and our memory begins to lapse – misplacing our car keys or forgetting the name of a new acquaintance – we fear the possibility that these are the first signs of dementia.

And while there is currently no approved treatment to reverse the physiological effects of dementia, this new research may provide hope that new therapies are around the corner.

Reference: "Cis P-tau underlies vascular contribution to cognitive impairment and dementia and can be effectively targeted by immunotherapy in mice" by Chenxi Qiu, Onder Albayram, Asami Kondo, Bin Wang, Nami Kim, Ken Arai, Cheng-Yu Tsai, Mahmoud A. Bassal, Megan K. Herbert, Kazuo Washida, Peter Angeli, Shingo Kozono, Joseph E. Stucky, Sean Baxley, Yu-Min Lin, Yan Sun, Alexander Rotenberg, Barbara J. Caldarone, Eileen H. Bigio, Xiaochun Chen, Daniel G. Tenen, Mark Zeidel, Eng H. Lo, Xiao Zhen Zhou and Kun Ping Lu, 2 June 2021, Science Translational Medicine.
DOI: 10.1126/scitranslmed.aaz7615

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https://bit.ly/3ErwsCU

Cheap Antidepressant Shows Promise Treating Early COVID

A cheap antidepressant reduced the need for hospitalization among high-risk adults with COVID-19 in a study that was looking for existing drugs that could be repurposed to treat coronavirus.

Researchers tested the pill used for depression and obsessive-compulsive disorder because it was known to reduce inflammation and looked promising in smaller studies.

They've shared the results with the U.S. National Institutes of Health, which publishes treatment guidelines, and they hope for a World Health Organization recommendation.

"If WHO recommends this, you will see it widely taken up," said study co-author Dr. Edward Mills of McMaster University in Hamilton, Ontario, adding that many poor nations have the drug readily available. "We hope it will lead to a lot of lives saved."

The pill, called fluvoxamine, would cost $4 for a course of COVID-19 treatment. By comparison, antibody IV treatments cost about $2,000 and Merck's experimental antiviral pill for COVID-19 is about $700 per course. Some experts predict various treatments eventually will be used in combination to fight the coronavirus.

Researchers tested the antidepressant in nearly 1,500 Brazilians recently infected with coronavirus who were at risk of severe illness because of other health problems, such as diabetes. About half took the antidepressant at home for 10 days, the rest got dummy pills. They were tracked for four weeks to see who landed in the hospital or spent extended time in an emergency room when hospitals were full.

In the group that took the drug, 11% needed hospitalization or an extended ER stay, compared to 16% of those on dummy pills.

The results, published Wednesday in the journal *Lancet Global*

Health, were so strong that independent experts monitoring the study recommended stopping it early because the results were clear. Questions remain about the best dosing, whether lower risk patients might also benefit and whether the pill should be combined with other treatments.

The larger project looked at eight existing drugs to see if they could work against the pandemic virus. The project is still testing a hepatitis drug, but all the others — including metformin, hydroxychloroquine and ivermectin — haven't panned out.

The cheap generic and Merck's COVID-19 pill work in different ways and "may be complementary," said Dr. Paul Sax of Brigham and Women's Hospital and Harvard Medical School, who was not involved in the study. Earlier this month, Merck asked regulators in the U.S. and Europe to authorize its antiviral pill.

https://bit.ly/3w1fatu

First-of-Its-Kind Breast Cancer Vaccine Set to Begin Clinical Trials in The US

A vaccine against the most aggressive and deadly form of breast cancer is one step closer to reality.

Anna Medaris Miller

The Cleveland Clinic announced Tuesday it's launching a first-of-its kind human trial testing a shot designed to prevent triple-negative breast cancer, which currently doesn't respond to hormone or targeted drug therapies and can only be prevented with mastectomy.

Until now, developments in triple-negative breast cancer vaccines have been limited to lab work and animal research. The human trial can begin now that the US Food and Drug Administration approved an investigational new drug application for the shot.

While the trial will only include early-stage triple-negative breast cancer survivors who are at high risk for recurrence, the researchers hope to next take the vaccine to healthy people at high risk for the disease, like those with BRCA1 gene mutations.

"Long term, we are hoping that this can be a true preventive vaccine that would be administered to healthy women to prevent them from developing triple-negative breast cancer, the form of breast cancer for which we have the least effective treatments," Dr. G. Thomas Budd, of Cleveland Clinic's Taussig Cancer Institute and principal investigator of the study, said in a press release.

Participants will receive three shots

Triple-negative breast cancer accounts for about 12 percent to 15 percent of all breast cancers and kills nearly a quarter of patients within five years of diagnosis. It's more common among African-American women and those with BRCA1 mutations.

The presence of a certain protein, α-lactalbumin, usually accompanies the disease, even though it's only supposed to appear when a person is lactating.

The vaccine, then, will target that protein, prompting the immune system to stave off emerging breast tumors that express it. The shot will also include a drug that alerts the immune system to a-lactabalbumin so that it can halt emerging tumor growth.

The trial will include 18 to 24 patients who are tumor-free after being treated for early-stage triple-negative breast cancer within the past three years. They'll receive three shots, each two weeks apart. Researchers will start with low doses in just a few patients and monitor them closely before upping the dose and including more participants.

"Once we've figured out how much of the vaccine we can give, we'll look at its effects on the immune system," Budd told the Cleveland Clinic. "That will help us know whether the vaccine is doing what we want it to do, and then we'll expand each dose level."

The study is estimated to be completed in September 2022. It's funded by the US Department of Defense.

"This vaccine strategy has the potential to be applied to other tumor types," added Tuohy.

"Our translational research program focuses on developing vaccines that prevent diseases we confront with age, like breast, ovarian and endometrial cancers. If successful, these vaccines have the potential to transform the way we control adult-onset cancers and enhance life expectancy in a manner similar to the impact that the childhood vaccination program has had."

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Why do dogs tilt their heads? New study offers clues -

"Gifted" dogs often make the gesture before correctly identifying a toy

By Rachel Fritts

Of all the cute things dogs do, cocking their head to one side while they look at you may be the most endearing. Yet surprisingly little research has looked into why they do it. Now, a new study of "gifted" canines—those capable of quickly memorizing multiple toy names—shows they often tilt their heads before correctly retrieving a specific toy. That suggests the behavior might be a sign of concentration and recall in our canine pals, the team suggests.

The researchers stumbled upon their find by chance while conducting a study of "gifted word learner" dogs. Most dogs can't memorize the names of even two toys, but these talented pups—all border collies—could recall and retrieve at least 10 toys they had been taught the names of. One overachiever named Whisky correctly retrieved 54 out of 59 toys he had learned to identify.

Over the course of several months, the researchers tested the dogs' abilities to learn and recall labels for toys, comparing their skills with those of 33 "typical" dogs. Owners placed toys in another room and asked for them by name. Only the seven gifted dogs were able to rapidly learn and remember names. But these dogs shared something else in common: the head tilt.

The pattern was too consistent to be pure coincidence, says Andrea Sommese, an animal behavior researcher at Eötvös Loránd University who led the study. "So we decided to dig into it."

A quick internet search turned up plenty of speculative results positing that dogs tilt their heads to hear better, to listen for specific words or tones, or to see past their snouts. Sommese found one poster hypothesizing that shelter dogs do it more often because they know on some level that humans find it irresistible.

The scientific literature was much more sparse. A search for previous studies on head tilting yielded surprisingly few results. There were some veterinary papers about the practice as a symptom of certain health problems, Sommese says, but nothing about the quizzical behavior familiar to dog owners. That led researchers back to their own data to look for clues.

The scientists found that—when asked to retrieve a toy—gifted dogs cocked their heads 43% of them time over dozens of trials, compared with just 2% of the time in typical dogs, they report this week in *Animal Cognition*. (Although gifted dogs tilted their heads much more often, they were just as likely to retrieve the correct toy regardless of whether they made the motion.) The animals even had a favored side, just like humans favor their left or right hand. This was consistent over months of recordings, regardless of where the owner was standing in relation to the dog. "If a dog was a left tilter, it would stay a left tilter," Sommese says.

All of the border collies in the study were familiar with the words being spoken, he notes, but only the gifted dogs who had correctly attached a meaning to each word consistently exhibited the tilting behavior. That means head tilting isn't just a sign of familiarity with particular sounds, Sommese argues. If it were, all 40 dogs would be equally likely to do it. The team thinks it could be linked to mental processing—a sign of high attentiveness or concentration in the gifted dogs. The dogs might be cross-referencing the

command with their visual memories of the toys, for instance.

Monique Udell, a human-animal interaction researcher at Oregon State University, Corvallis, has never seen head tilting featured in a study like this before. She cautions that these observations are preliminary, but says she thinks they could provide an exciting new direction for research on canine cognition. “The next step is asking more questions to get at what the head tilt really means,” Udell says. “Can we use head tilting to predict word-learning aptitude, or attention, or memory?”

Sommese hopes to follow up on this study by figuring out what sorts of sounds might be similarly meaningful to the nongifted dogs, to elicit the same behavior. Until then, dog owners will have to be content knowing that when a pooch tilts its head, it’s probably just trying its best to understand what you’re doing.

https://wb.md/3brDoUb

5 Tips for Approaching the 'Internet Expert' Patient

"Can you diagnose me with this? I saw it on TikTok and I'm sure I have it."

Mena Mirhom, MD

The first time I heard this from a patient, I had to Google what TikTok even was. I came to find out that the usual internet search of random symptoms has now evolved into searching social media for diagnostic criteria.

How are we to react to this new trend?

1. Resist the urge to be dismissive.

"Don't confuse your Google search for my medical degree" is the old quote that you may have heard or even said. It now may be closer to "do not confuse your TikTok views for my thousands of hours of training."

It is natural to be somewhat defensive when a patient approaches a trained healthcare professional with information that they gathered from a potentially less reliable source such as social media. However, we must first recognize that if we respond with hostility or defensiveness, we do not help the alliance that we want to build with the patient. As frustrating as it may be at times, we must learn to coexist with the reality that our patients will be getting information from social media and not our favorite medical journal.

2. Join the patient first.

If a patient is searching the dark corners of the internet for information, tips, and community, there is a reason! We can first take the opportunity to meet the patient where they are and acknowledge that they are struggling with something here. We can even commend them on their attempt to be a well-informed patient. This will open a door of conversation with the patient who can see that we are actually concerned about their pain and are validating their effort rather than just fact-checking their sources.

3. Take a "mis-information" history.

We may have our own impressions or experiences with social media. Our newsfeeds can be radically different as each algorithm attempts to personalize its approach to maximize our time logged on. So another critical step before we assume the patient's experience is to gather data. Who are they following? What are those people's credentials? What makes them feel connected to this person and the information they share? There is a growing trend whereby board-certified physicians and other healthcare workers are getting on social media and providing free, reliable, and evidence-based information in 15 seconds.

4. Guide the patient on how to choose reliable information.

During healthcare training, one of the skills that is learned and acquired is how to evaluate data critically. Developing a critical lens for social media content is probably just as valuable in the age we currently live in. We can help patients with one or two things to look for in particular when evaluating information, such as an individual's credentials, experience, agenda, and/or sponsorship. Is

the video or tweet part of paid programming? Content creators are required to indicate that their content is part of an "#ad" or "paid partnership," but this can be subtle and missed by a viewer who is not looking for it. The patient may not become an expert in spotting misinformation, but this is a good start.

5. Develop a social media referral network.

Rather than telling a patient that the internet is simply unreliable (which it certainly can be) or that social media is full of misinformation (which it certainly is), it may be more productive to "refer" a patient to trusted sources. Finding these sources within your specialty may take some work.

If you are not satisfied with what you find and feel that there is a void in that space, consider becoming that resource! It can be tremendously rewarding to help guide patients with brief, reliable information in the palm of their hands.

https://bit.ly/3GzIOuK

Newly named human species may be the direct ancestor of modern humans

Homo bodoensis lived more than half a million years ago.

By Charles Q. Choi 3 days ago

Scientists have named a new species that may have been the direct ancestor of modern humans. The newly proposed species, *Homo bodoensis* — which lived more than half a million years ago in Africa — may help to untangle how human lineages moved and interacted across the globe.

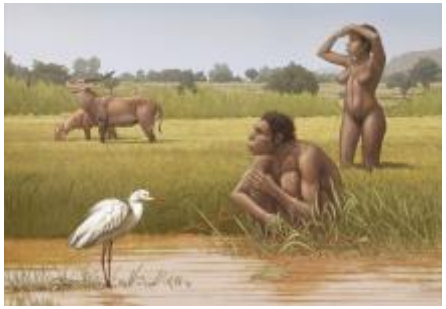
Homo bodoensis may help to untangle how human lineages moved and interacted across the globe. **(Image credit: Ettore Mazza)**

Although modern humans, *Homo sapiens*, are the only surviving human lineage, other human species once roamed Earth. For example, scientists recently discovered that the Indonesian island Flores was once home to the extinct species *Homo floresiensis*, often known as "the hobbit" for its miniature body.

Deciding whether a set of ancient human fossils belongs to one species or another is often a challenging problem open to heated debate. For instance, some researchers suggest that skeletal differences between modern humans and Neanderthals mean they were different species. However, other scientists argue that because there is recent abundant genetic evidence that modern humans and Neanderthals once interbred and had fertile, viable offspring, Neanderthals should not be considered a single species.

In the new study, researchers analyzed human fossils dating from about 774,000 to 129,000 years ago (once known as the Middle Pleistocene and now renamed the Chibanian). Previous work suggested modern humans arose during this time in Africa, while Neanderthals emerged in Eurasia. However, much about this key chapter in human evolution remains poorly understood — a problem paleoanthropologists call "the muddle in the middle."

Chibanian-era human fossils from Africa and Eurasia are often assigned to one of two species: *Homo heidelbergensis* or *Homo rhodesiensis*. However, both species often carried multiple, and often contradictory, definitions of the skeletal characteristics and other traits that described them.



Recent DNA evidence has revealed that some fossils in Europe dubbed *H. heidelbergensis* were actually from early Neanderthals. As such, *H. heidelbergensis* was a redundant name in those cases, the scientists noted.

The newly named species Homo bodoensis, a human ancestor, lived in Africa during the middle Pleistocene. **(Image credit: Ettore Mazza)**

Similarly, recent analyses of many fossils in East Asia now suggest

they should no longer be called *H. heidelbergensis*, the researchers added. For instance, many facial and other features seen in Chibanian East Asian human fossils differ from those seen in European and African fossils of the same age.

In addition, Chibanian fossils from Africa are sometimes called both *H. heidelbergensis* and *H. rhodesiensis*. The scientists also noted that *H. rhodesiensis* was a poorly defined label that was never widely accepted in science, due in part to its association with controversial English imperialist Cecil Rhodes.

To help deal with all this confusion, the researchers now propose the existence of a new species, *H. bodoensis*, named after a 600,000-year-old skull found in Bodo D'ar, Ethiopia, in 1976. This new name would encompass many fossils previously identified as either *H. heidelbergensis* or *H. rhodesiensis*. The researchers suggest that *H. bodoensis* was the direct ancestor of *H. sapiens*, together forming a different branch of the human family tree than the one that gave rise to the Neanderthals and the mysterious Denisovans, which Siberian and Tibetan fossils suggested they lived about the same time as their Neanderthal cousins.

"Giving a new name to a species is always controversial," study co-lead author Mirjana Roksandic, a paleoanthropologist at the University of Winnipeg in Canada, told Live Science. "However, if people start using it, it will survive and live."

In this new classification, *H. bodoensis* will describe most Chibanian human fossils from Africa and the Eastern Mediterranean. Many Chibanian human fossils from Europe would get reclassified as Neanderthals. The names *H. heidelbergensis* and *H. rhodesiensis* would then disappear. Chibanian human fossils from East Asia may get their own names with more research.

"We are not claiming to rewrite human evolution," Roksandic said. Instead, the researchers seek to organize the variation seen in ancient humans "in a way that makes it possible to discuss where it comes from and what it represents," she explained. "Those differences can help us understand movement and interaction."

In the future, the researchers want to see if they can find any *H. bodoensis* specimens in Europe from the Chibanian, Roksandic said.

The scientists detailed their findings online Thursday (Oct. 28) in the journal Evolutionary Anthropology: Issues News, and Reviews.

https://wb.md/3w58SJw

The Most Haunted Hospitals in America: Why Spirits Never Left

Hospitals are fertile ground for all sorts of otherworldly tales

Jay Lankau

For those of us who want to believe, hospitals are fertile ground for all sorts of otherworldly tales: Perhaps a patient witnesses a nurse strolling the halls in an anachronistic white dress and cap, or a loved one hears their family member say goodbye to them in a dream.

Of course, as Hollywood can attest, sometimes hospitals are home to darker lore. The trope of a labyrinth-like hellscape complete with disembodied voices, inexplicable power outages, and things that go *bump* in the night takes its cue from the past, as many of the most frightful things do.

Why Hospitals?

The term "insane asylum," which is now outdated, is emblematic of an era when mental illness was horribly misunderstood. These asylums began with good intentions: Local governments could avoid the costs of caring for people in public hospitals by determining that they were mentally unwell. And while the number of patients in these hospitals skyrocketed across the United States, the hospitals' infrastructure began to buckle under the weight.

Unfortunately, in many cases, these people were "unwanted" or otherwise unable to be cared for by family members or the state. A

high number of sanatorium patients were disabled and afraid, only to be mislabeled as violent and then neglected — or even punished.

In his book *Shrinks: The Untold History of Psychiatry*, Jeffrey A. Lieberman writes: "The purpose of the earliest mental institutions was neither treatment nor cure, but rather the enforced segregation of inmates from society. The mentally ill were considered social deviants or moral misfits suffering divine punishment for some inexcusable transgression."

One can imagine how much pain and terror resided in these buildings. According to veteran paranormal investigator Zak Bagans, principal host of Travel Channel's *Ghost Adventures*, this kind of traumatic energy can create both residual and traditional hauntings. Bagans explains here that locations of tragedy or violence are ideal for residual hauntings — when an event (or multiple events) "imprints itself on the atmosphere." Then, like a loop of film, the location plays back the traumatic events.

Traditional, or intelligent, hauntings, on the other hand, are when the spirits present are intelligent and can interact with their surroundings in real time. These types of hauntings, according to Bagans, are similarly created when a person is unable to "pass on" because of an emotional connection to the site, trauma, or unfinished business.

"The spirits may also linger because of emotions that tie them to the Earth, from anger to love," Bagans says. "In other cases, there is the chance that the spirit didn't even realize they had died. This may occur when a death is sudden or unexpected, like with an accident or a murder."

This explains why many historical asylums are rife with reports of the paranormal. Many abandoned hospitals across the United States allege hauntings — but which ones are the *most* haunted?

Waverly Hills Sanatorium

Located in southwestern Louisville/Jefferson County, Kentucky, the Waverly Hills Sanatorium is one of the most notable haunted hospitals in the world. It opened in 1910 as a two-story building meant to accommodate tuberculosis patients but soon grew to a vast five-story facility with its own zip code. Those who worked or were treated there (treatment typically included removing ribs or parts of the lung) were quarantined away from society and instead forced to become residents of the self-contained Waverly Hills community. Over 400 tuberculosis patients would live (and die) within its walls until its closure in 1961.

The *Ghost Adventures* team captured electronic voice phenomenon evidence in their episode and reported sightings of "shadow figures." Those at the hospital, both those going on the paranormal tours and the tour guides and volunteers themselves, report steady streams of activity. This often includes apparitions in photographs and sightings of doctor- and nurse-spirits walking in and out of the many rooms.

Tour guides nicknamed one of the spirits Timmy, who they believe is the presence of a young boy who often rolls items like balls down the hallway to groups of visitors. Another distinct spirit is a nurse who, in the 1930s, reportedly hung herself in one of the fifth-floor rooms. A lengthy history of experiences and evidence that continues to this day make Waverly Hills one of the most haunted hospitals and locations in the United States.

Rolling Hills Asylum

The Rolling Hills Asylum in East Bethany, New York, was originally the Genesee County Poor Farm, a poorhouse and self-sufficient farm established in 1826 for orphans, families in poverty, "the handicapped," the mentally unstable, and others who were disadvantaged. However, many of these residents had no family to claim them once they died and were buried on the property. Rolling Hills Asylum has over a thousand documented deaths but little, if any, marked graves, leading historians to believe that the building

itself is surrounded by unmarked and unclaimed dead.

Featured on a slew of shows like Buzzfeed's *Unsolved* and SyFy's *Ghost Hunters*, *Destination Fear*, *Ghost Adventures*, and *Haunted USA*, Rolling Hills Asylum has become synonymous with paranormal investigation due to the wide array of documented evidence and encounters. Photos collected at Rolling Hills include moving apparitions, shadowy figures, orbs, unexplained streaks of light, and more. The building is currently still open for tours and other events.

Pennhurst Asylum

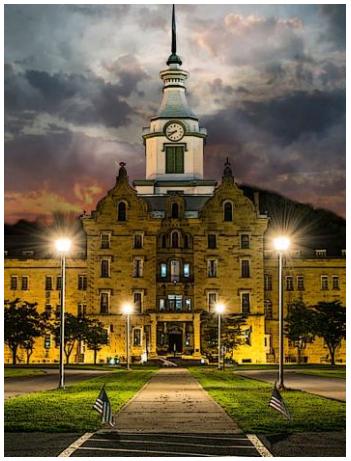
Perhaps one of the most controversial locations on this list, the Pennhurst State School and Hospital (known today as Pennhurst Asylum) opened in 1908 in Spring City, Pennsylvania, as an institution for the mentally and physically disabled. At that time in the area, it was believed that those with disabilities were unfit for society and required custodial care. Most of Pennhurst's patients were children who suffered there in cramped, dirty living spaces until media investigations and court cases forced the hospital to close in 1981.

It is believed that the pain of those who suffered and died at Pennhurst still lingers. There are many reports of paranormal activity in the hospital, including disembodied voices and figures. The hospital was even the subject of the A&E special *World's Biggest Ghost Hunt: Pennhurst Asylum*, which involved a team of paranormal investigators locking themselves inside the hospital for 2 weeks.

Pennhurst's history of controversy continues today; the building is home to a haunted house attraction featuring actors and sets, which has been condemned for insensitivity by the Pennhurst Memorial & Preservation Alliance.

Trans-Allegheny Lunatic Asylum

Notable for its architecture and construction, the Trans-Allegheny Lunatic Asylum is also known as the Weston State Hospital, located in Weston, West Virginia. Opened in 1864, the hospital — constructed of huge, staggered wings — was meant to house up to 250 mentally disabled patients. But in the 1950s, up to 2400 patients were recorded to be living there in crowded, poor conditions. The facility's deterioration and changes in the way mental health was approached forced its closure in 1994.



***The Trans-Allegheny Lunatic Asylum was in operation for 130 years and finally closed due to an inability to appropriately care for its patients.* : Ben Sanford**

The Trans-Allegheny Lunatic Asylum has too many paranormal claims to keep track of and has also been featured on investigation shows like the other hospitals on this list. Psychics who have visited the grounds claim to feel numerous presences from various time periods, and tour guides have countless experiences coming face-to-face with solid-looking apparitions. One spirit who has been seen repeatedly is believed to be the presence of a young girl named Lily.

Taunton State Hospital

A psychiatric hospital established in 1894 in Taunton, Massachusetts, Taunton State Hospital was known as the State Lunatic Hospital at Taunton. Similar to the Trans-Allegheny Lunatic Asylum's winged construction, the Taunton State Hospital followed what is called the Kirkbride Plan, which was a favored design system for mental hospitals. As the Taunton hospital grew, it expanded multiple times to eventually include over 40 different structures. At Taunton, those who were deemed mentally unstable or "disobedient" (this could range from PTSD and Alzheimer's to anxiety and postpartum depression) were essentially forgotten by

society. "Cures" at Taunton included treatments like electric shock therapy and sound therapy. The notorious lobotomy was also used there during this era.

Taunton is shrouded in rumors of Satanic cults and the paranormal. It's not hard to understand why when you look at some of its inhabitants. Notable patients at Taunton included Anthony Santo, a man that had confessed to murdering his two cousins and an unrelated girl, and Jane Toppan, an American serial killer who was given the nickname "Jolly Jane." Toppan confessed to 31 murders, of which only 12 were confirmed. The main building of Taunton State Hospital was demolished in 2009, but some of its newer structures still remain.

Have you ever had a paranormal encounter at your job? Comment about your experience below.

https://bit.ly/2Y1Kqfh

Time for the Flu Shot? The Surprising Connection Between Influenza and Fatal Heart Attacks

Did you know that coming down with the flu can substantially increase the risk of a serious or even fatal cardiac event?

If you have heart disease or risk factors for heart disease, you already know about the increased risk of heart attack and stroke. But did you know that coming down with the flu can substantially increase the risk of a serious or even fatal cardiac event? Or that getting the influenza vaccine can substantially reduce that risk, even if you do wind up contracting the seasonal virus?

Probably not, if annual influenza vaccination rates are any indication, especially if you're under the age of 65. According to a Houston Methodist review published in the *Journal of the American Heart Association*, Americans with heart disease continue to have low vaccination rates every year despite higher rates of death and complications from influenza.

The flu vaccination rate for American adults who are less than 65 years of age and have heart disease is less than 50%, compared to 80% in older adults with heart disease.

"It seems that younger Americans with high-risk conditions have not gotten the same memo that their older counterparts have received about the importance of getting the influenza vaccine," says Dr. Priyanka Bhugra, internal medicine specialist at Houston Methodist and lead author of the JAHA article. "That's dangerous, considering people with heart conditions are particularly vulnerable to influenza-related heart complications, whether they've reached retirement age or not."

It's well-known that the flu can lead to significant respiratory symptoms such as pneumonia, bronchitis and bacterial infection of the lungs. The virus' effects on the heart have historically been harder to parse out, in part because many patients already have a known predisposition to cardiac events and in part because the cardiac event often occurs weeks after the onset of the flu.

But here's what recent research has shown:

- ***Cardiovascular deaths and influenza epidemics spike around the same time.***
- ***Patients are six times more likely to experience a heart attack the week after influenza infection than they are at any point during the year prior or the year after the infection.***
- ***In one study looking at 336,000 hospital admissions for flu, 11.5% experienced a serious cardiac event.***
- ***Another study looking at 90,000 lab-confirmed influenza infections showed a strikingly similar rate of 11.7% experiencing an acute cardiovascular event.***
- ***One in eight patients, or 12.5%, admitted to the hospital with influenza experienced a cardiovascular event, with 31% of those requiring intensive care and 7% dying as a result of the event, another study found.***

The reason influenza stresses the heart and vascular system so much has to do with the body's inflammatory response to the

infection.

Inflammation occurs when your body's "first responders" — white blood cells and what they produce in order to protect you — convene in an area and get to work fighting an infection, bacteria or virus. When you're sick, you can typically feel the effects of these "combat zones" in the swelling, tenderness, pain, weakness and sometimes redness and increased temperature of your joints, muscles and lymph nodes.

The increased activity can also cause a traffic jam of sorts, leading to blood clots, elevated blood pressure and even swelling or scarring within the heart. The added stressors make plaque within your arteries more vulnerable to rupture, causing a blockage that cuts off oxygen to the heart or brain and results in heart attacks or strokes, respectively.

Additionally, non-cardiac complications from the viral illness, including pneumonia and respiratory failure, can make heart failure symptoms or heart arrhythmia much worse.

In short, the added stress on the cardiovascular system could be overwhelming to an already weakened heart muscle.

Because influenza viruses are constantly mutating, scientists alter the vaccine each year to match the likely prevalent strands. On average, it's effective at preventing infection 40% of the time. While that might not sound great — especially in comparison to the highly effective mRNA COVID-19 vaccines — it's enough to significantly lower the risk of severe illness in most people.

Lately, studies have been able to show that not only is the vaccine effective at protecting the general population and the most vulnerable age groups (over 65 and under 2) from severe cases of the flu, but it's also protective against cardiovascular mortality as well, especially among the high-risk population.

Some of the recent findings:

- ***Adults who received the vaccine were 37% less likely to be hospitalized for the flu and 82% less likely to be admitted to the ICU because of it. Among people admitted to the hospital with the flu, those vaccinated were 59% less likely to be admitted to the ICU. Vaccinated patients admitted to the ICU spent four fewer days in the ICU than unvaccinated patients.***
- ***Vaccination was associated with a lower risk of cardiovascular events (2.9% vs 4.7%) if the patient got the flu. Among the highest-risk patients with more active coronary disease, vaccination was associated with considerably better outcomes.***
- ***Patients admitted to the hospital with acute coronary syndrome were randomly assigned to either receive a flu vaccine or not before discharge. Major cardiovascular events occurred less frequently in the vaccine group than the control group (9.5% vs. 19%).***

As a result of the demonstrated benefits conferred by influenza vaccination and the risks posed by flu infection among those with cardiovascular disease, the CDC and numerous other international societies strongly recommend annual influenza vaccination in patients with cardiovascular disease.

Clinicians should ensure high rates of influenza vaccination, especially in those with underlying chronic conditions, to protect against acute cardiovascular events associated with influenza.

Unfortunately, many heart patients visit their cardiologist more frequently than their primary care providers, and cardiology practices typically do not provide flu vaccinations, though proposed recommendations may change in the future. Until then, it is incumbent upon both the cardiology provider and the primary care provider to communicate the increased risk to their patients and the importance of getting vaccinated.

For patients with heart conditions, there are two important steps you can take to reduce your risk:

- ***Make sure you do obtain your influenza vaccine from your local pharmacy or primary care provider. The earlier you get it, the better it is at protecting you, as you never know when the virus may begin to spread.***
- ***Make sure you are taking your medications and following your recommended diet, exercise and stress reduction plans. If your heart condition is stable and you end up with the flu, chances are you'll experience fewer, less severe complications than if your heart condition is poorly managed.***

Reference: "Determinants of Influenza Vaccine Uptake in Patients With Cardiovascular Disease and Strategies for Improvement" by Priyanka Bhugra, Gowtham R. Grandhi, Reed Mszar, Priyanka Satish, Rahul Singh, Michael Blaha, Ron Blankstein, Salim S. Virani, Miguel Cainzos-Achirica and Khurram Nasir, 28 July 2021, Journal of the American Heart Association. DOI: 10.1161/JAHA.120.019671

https://bit.ly/3BCxzOh

Analysis of Mummy May Completely Rewrite The History of Ancient Egyptian Mummification

Advanced mummification techniques were used 1,000 years earlier than previously believed

Alia Shoaib, Business Insider

A new analysis of an ancient Egyptian mummy suggests that advanced mummification techniques were used 1,000 years earlier than previously believed, rewriting the understood history of ancient Egyptian funerary practices.

The discovery centers around a mummy, known as Khuwy, believed to have been a high-ranking nobleman. He was excavated at the necropolis, a vast ancient burial ground of Egyptian pharaohs and royals near Cairo, in 2019.

Scientists now believe that Khuwy is much older than previously thought, dating back to Egypt's Old Kingdom, which would make him one of the oldest Egyptian mummies ever to be discovered, *The Observer* reported. The Old Kingdom spanned 2,700 to 2,200 BCE and was known as the "Age of the Pyramid Builders."

Khuwy was embalmed using advanced techniques thought to have been developed much later. His skin was preserved using expensive resins made from tree sap, and his body was impregnated with resins and bound with high-quality linen dressings.

The interior of Khuwy's tomb, located at the Saqqara necropolis. **(Mohamed El-Shahed/AFP via Getty Images)**

The new analysis suggests that ancient Egyptians living around 4,000 years ago were carrying out sophisticated burials.

"This would completely turn our understanding of the evolution of mummification on its head," Professor Salima Ikram, head of Egyptology at the American University in Cairo, told *The Observer*. "If this is indeed an Old Kingdom mummy, all books about mummification and the history of the Old Kingdom will need to be revised."

"Until now, we had thought that Old Kingdom mummification was relatively simple, with basic desiccation – not always successful – no removal of the brain, and only occasional removal of the internal organs," Ikram told *The Observer*.

Ikram was surprised by the amount of resin used to preserve the mummy, which is not often recorded in mummies from the Old Kingdom. She added that typically more attention was paid to the exterior appearance of the deceased than the interior.

"This mummy is awash with resins and textiles and gives a completely different impression of mummification. In fact, it is more like mummies found 1,000 years later," she said.

Ikram told *The National* that the resin used would have been imported from the Near East, most likely Lebanon, demonstrating that trade with neighboring empires around that time was more extensive than previously thought.

The discovery has been documented in National Geographic's new series, *Lost Treasures of Egypt*, which starts airing on 7 November.

Tom Cook, who produced the series for Windfall Films, told *The Observer* that Ikram initially could not believe that Khuwy dated back to the Old Kingdom because of the advanced mummification techniques.

"They knew the pottery in the tomb was Old Kingdom but [Ikram] didn't think that the mummy was from [that period] because it was preserved too well," Cook told the outlet. "But over the course of the investigation she started to come round [to the idea]."

Khuwy's ornate tomb featured hieroglyphics that suggested the burial took place during the Fifth Dynasty period, spanning the early 25th to mid-24th century BCE, *Smithsonian Magazine said*.

Archeologists also found pottery and jars used to store body parts during the mummification process that dated back to that time.

Ikram's team will conduct more tests to confirm that the remains do belong to Khuwy. She told *The National* that one possibility was that another person could have been mummified and buried centuries later in a re-purposing of the tomb.

"I remain hesitant until we can conduct carbon-14 dating," Ikram told the outlet, adding that it would likely take six to eight months.

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New COVID-19 Danger Revealed: SARS-CoV-2 Virus Can Infect the Inner Ear

A new study from MIT and Massachusetts Eye and Ear provides evidence that the SARS-CoV-2 virus can infect cells of the inner ear.

By Anne Trafton, Massachusetts Institute of Technology

The prevalence of auditory symptoms in Covid-19 patients is unknown, but infection of the inner ears may be responsible for hearing and balance problems.

Many Covid-19 patients have reported symptoms affecting the ears, including hearing loss and tinnitus. Dizziness and balance problems can also occur, suggesting that the SARS-CoV-2 virus may be able to infect the inner ear.

A new study from MIT and Massachusetts Eye and Ear provides evidence that the virus can indeed infect cells of the inner ear, including hair cells, which are critical for both hearing and balance. The researchers also found that the pattern of infection seen in human inner ear tissue is consistent with the symptoms seen in a study of 10 Covid-19 patients who reported a variety of ear-related symptoms.

The researchers used novel cellular models of the human inner ear that they developed, as well as hard-to-obtain adult human inner ear tissue, for their studies. The limited availability of such tissue has hindered previous studies of Covid-19 and other viruses that can cause hearing loss.

“Having the models is the first step, and this work opens a path now for working with not only SARS-CoV-2 but also other viruses that affect hearing,” says Lee Gehrke, the Hermann L.F. von Helmholtz Professor in MIT’s Institute for Medical Engineering and Science, who co-led the study.

Konstantina Stankovic, a former associate professor at Harvard Medical School and former chief of otology and neurotology at Massachusetts Eye and Ear, who is now the Bertarelli Foundation Professor and chair of the Department of Otolaryngology – Head and Neck Surgery at Stanford University School of Medicine, co-led the study. Minjin Jeong, a former postdoc in Stankovic’s laboratory at Harvard Medical School, who is now at Stanford Medical School, is the lead author of the paper, which was published on October 29, 2021, in *Communications Medicine*.

Models of ear infection

Before the Covid-19 pandemic began, Gehrke and Stankovic began working together on a project to develop cellular models to study

infections of the human inner ear. Viruses such as cytomegalovirus, mumps virus, and hepatitis viruses can all cause deafness, but exactly how they do so is not well-understood.

In early 2020, after the SARS-CoV-2 virus emerged, the researchers altered their plans. At Massachusetts Eye and Ear, Stankovic started to see patients who were experiencing hearing loss, tinnitus, and dizziness, who had tested positive for Covid-19. "It was very unclear at the time whether this was causally related or coincidental, because hearing loss and tinnitus are so common," she recalls.

She and Gehrke decided to use the model system they were working on to study infection of SARS-CoV-2. They created their cellular models by taking human skin cells and transforming them into induced pluripotent stem cells. Then, they were able to stimulate those cells to differentiate into several types of cells found in the inner ear: hair cells, supporting cells, nerve fibers, and Schwann cells, which insulate neurons.

These cells could be grown in a flat, two-dimensional layer or organized into three-dimensional organoids. In addition, the researchers were able to obtain samples of hard-to-obtain inner ear tissue from patients who were undergoing surgery for a disorder that causes severe attacks of vertigo or for a tumor that causes hearing loss and dizziness.

In both the human inner ear samples and the stem-cell-derived cellular models, the researchers found that certain types of cells — hair cells and Schwann cells — express the proteins that are needed for the SARS-CoV-2 virus to enter the cells. These proteins include the ACE2 receptor, which is found on cell surfaces, and two enzymes called furin and transmembrane protease serine 2, which help the virus to fuse with the host cell.

The researchers then showed that the virus can actually infect the inner ear, specifically the hair cells and, to a lesser degree, Schwann cells. They found that the other cell types in their models were not susceptible to SARS-CoV-2 infection.

The human hair cells that the researchers studied were vestibular hair cells, which are involved in sensing head motion and maintaining balance. Cochlear hair cells, which are involved in hearing, are much harder to obtain or generate in a cellular model. However, the researchers showed that cochlear hair cells from mice also have proteins that allow SARS-CoV-2 entry.

Viral connection

The pattern of infection that the researchers found in their tissue samples appears to correspond to the symptoms observed in a group of 10 Covid-19 patients who reported ear-related symptoms following their infection. Nine of these patients suffered from tinnitus, six experienced vertigo, and all experienced mild to profound hearing loss.

Damage to cochlear hair cells, which can cause hearing loss, is usually evaluated by measuring otoacoustic emissions — sounds given off by sensory hair cells as they respond to auditory stimulation. Among the six Covid-19 patients in the study who underwent this testing, all had reduced or absent otoacoustic emissions.

While this study strongly suggests that Covid-19 can cause auditory and balance problems, the overall percentage of Covid-19 patients who have experienced ear-related issues is not known.

"Initially this was because routine testing was not readily available for patients who were diagnosed with Covid, and also, when patients were having more life-threatening complications, they weren't paying much attention to whether their hearing was reduced or whether they had tinnitus," Stankovic says. "We still don't know what the incidence is, but our findings really call for increased attention to audiovestibular symptoms in people with Covid exposure."

Possible routes for the virus to enter the ears include the Eustachian tube, which connects the nose to the middle ear. The virus may also be able to escape from the nose through small openings surrounding the olfactory nerves, Stankovic says. That would allow it to enter the brain space and infect cranial nerves, including the one that connects to the inner ear.

“This article provides very compelling evidence that Sars-CoV-2 infects the inner ear, and may be causally related to the hearing and balance symptoms in a number of patients with Covid-19 infection,” says Yuri Agrawal, a professor of otolaryngology-head and neck surgery at Johns Hopkins School of Medicine, who was not involved in the study. “Another exciting advance for our field is the use of 2D and 3D in vitro organoids to observe Sars-CoV-2 infection of the inner ear. This provides a powerful platform to study the impact of a number of other exposures, including other infections, toxins, and cancers, on the inner ear.”

The researchers now hope to use their human cellular models to test possible treatments for the inner ear infections caused by SARS-CoV-2 and other viruses.

Reference: “Direct SARS-CoV-2 infection of the human inner ear may underlie COVID-19-associated audiovestibular dysfunction” by Minjin Jeong, Karen E. Ocwieja, Dongjun Han, P. Ashley Wackym, Yichen Zhang, Alyssa Brown, Cynthia Moncada, Andrea Vambutas, Theodore Kanne, Rachel Crain, Noah Siegel, Valerie Leger, Felipe Santos, D. Bradley Welling, Lee Gehrke and Konstantina M. Stankovic, 29 October 2021, Communications Medicine.

DOI: 10.1038/s43856-021-00044-w

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https://bit.ly/3BEt3za

Human Birth Canals Are Seriously Twisted. Researchers Think They've Figured Out Why

Study using biomechanical modelling on gait and posture has provided some insights into this long-standing mystery

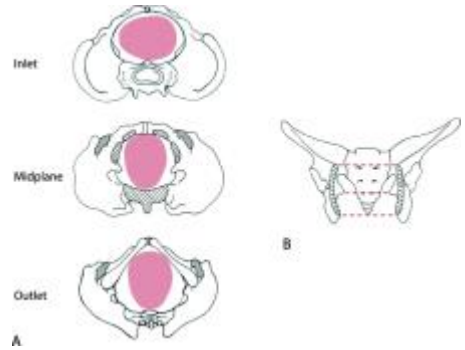
Carly Cassella

There's an odd twist to human physiology not seen in any other primate, that makes giving birth more complicated for our species. Now, a study using biomechanical modelling on gait and posture has provided some insights into this long-standing mystery.

The narrow shape of the human birth canal is kinked at the inlet, so that contractions of the mother must rotate the baby's big brain and wide shoulders nearly 90 degrees to fit into the pelvis.

Imagine sliding a foot into a tight boot with a twisted entrance and you've got a rough idea of how challenging this can be. If the baby gets stuck, it can endanger both the life of the mother and child. In fact, this is thought to occur in as many as 6 percent of all births worldwide.

So what's the advantage?



Above: The rotational birth of humans. A) shows the head turning about 90° to fit into the largest dimension of the pelvic plane; B) shows the layers of the birth canal. **(Stansfield et al., BMC Biology, 2021)**

Surprisingly, for such a key element in the reproduction of our very species, we're still trying to figure that out.

Today, some of the most fundamental parts of human pregnancy are a complete mystery. We don't know, for instance, why our species undergoes such long and dangerous labors compared to other mammals.

Traditionally, it is thought the human pelvis is shaped the way it is to make walking easier. Evolutionarily speaking, the advantages of bipedal movement on a daily basis were clearly worth the extra risks that came with having narrow hips and big-brained babies.

In the new study, extensive biomechanical models of the pelvic floor suggest the shape of the birth canal doesn't help us walk so much as it helps us stand up.

"We argue that the transverse elongation of the pelvic inlet has evolved because of the limits on the front-to-back diameter in humans imposed by balancing upright posture, rather than by the efficiency of the bipedal locomotion", says Philipp Mitteroecker, who was also involved in this study."

If the inlet from the womb to the birth canal was a deeper oval, a baby could slide right through without very many fussy movements at all, as they do in other primates.

But in a human, this would require the pelvis to tilt at an even greater degree than it already does, which would add a deeper curve to the lower back.

Ultimately, the new models suggest that extra curve would compromise the stability and health of our spines, which is possibly why the inlet to the birth canal evolved a new shape instead.

In comparison, other primates, like chimpanzees, can afford to have a deeper inlet to the pelvis because they are mostly on all fours and aren't putting a lot of weight on their hips. To get through to the birth canal, chimpanzee young only have to twist their heads a little. The human baby, by comparison, has to move their body nearly 90 degrees to face the mother's spine to fit through the tight ellipsoid.

Even after this tricky maneuver, it's not a straight slide into the world. The outlet of the human birth canal is also shaped slightly different to primates. It requires the baby to once again turn to get its shoulders out, which are widest on a different axis to the head.

The models run by researchers suggest the outlet of the birth canal is shaped this way to better support the pelvic floor.

If the lower birth canal had an outlet that was wider still, the results indicate it would help pelvic floor stability even more; however, it would ultimately make childbirth too risky. The final twist would be too hard for the head and shoulders to shimmy through.

"Our results provide a novel evolutionary explanation for the twisted shape of the human birth canal," the authors conclude.

It's an intriguing idea from a well-thought out model, but real-world research will be needed to determine if this is really why humans are born with a twist and a shout.

Evolutionary studies, for instance, have shown female Neanderthals had birth canals more similar to chimpanzees, which suggests twisting is a uniquely human and relatively recent evolutionary development.

Given that Neanderthals also stood and walked on two feet, it would be interesting to compare the biomechanics of ancient humans to figure out why the modern human pelvis stands out.

The study was published in *BMC Biology*.

https://bit.ly/3BsfyCo

Nearly 90% of Human Genes Are Mentioned in Cancer Studies, And That's a Problem

Research into almost any human gene and its relationship to cancer can be justified based on previous studies

David Nield

A detailed analysis of scientific research has revealed that nearly 9 in 10 human genes have been mentioned in at least one cancer-related study – and those that haven't probably will be in the years to come.

That makes looking for therapeutic targets very difficult for experts: Research into almost any human gene and its relationship to cancer can be justified based on previous studies, which can slow down the search for genuine genetic causes of the disease, as well as genetic causes involved in other health issues.

The findings are based on results returned by the PubMed search engine, which covers tens of millions of articles on life sciences and biomedical topics, some of them stretching all the way back to the 1950s.

"Cancer is the most widely studied topic in biological and biomedical sciences," writes microbiologist João Pedro de

Magalhães, from the University of Liverpool in the UK, who carried out the research.

"However, the huge amount of data gathered concerning cancer means that there is much more information concerning genes associated with cancer than for any other disease or process."

Right now, around 4 million of the more than 30 million publications in the PubMed database mention cancer. Compare that to around 350,000 that mention strokes, and you get an idea of the sheer volume of research on the topic.

While having this huge body of cancer research is of course helpful in working towards treatments, cures, and a better understanding of the disease, it can make large-scale, systematic analysis more difficult when it comes to genetic links.

In other words, a clear picture of which genes cause cancer can get lost within the sea of genes that are merely linked to the disease in other ways.

These papers don't necessarily point to a causal association between particular genes and cancer, but they do mean that the majority of human genes have been studied in a cancer context. That can lead to biases when researchers decide what to study next.

"The study of nearly any human gene can be justified based on existing literature by its potential relevance to cancer," writes de Magalhães.

"Understanding the reasons for biases in large-scale analyses and correcting for them is of growing importance to increase the value of insights and predictions."

With cancer now thought to affect roughly one in two of us during our lives, there's no sign of research into the disease slowing down – and indeed previous studies have noted how growth in the volume of cancer research is outpacing everything else at the moment.

After all, cancer is relatively 'easy' to study, given the number of data and laboratory resources like established cell lines that are available. It is also a topic that attracts a lot of funding, although this funding is by no means distributed equally amongst all types of cancer.

According to de Magalhães, if a human gene hasn't yet been linked with cancer, it's probably because it hasn't been studied enough – it's only a matter of time before it joins the list.

There's no doubt that studies linking genes and cancer are vital in tackling the disease, but this latest report warns that researchers should be aware of potential biases in terms of connecting every part of our genetic make-up with cancer.

"In a scientific world where everything and every gene can be associated with cancer, the challenge is determining which are the key drivers of cancer and more promising therapeutic targets," concludes de Magalhães.

The research has been published in *Trends in Genetics*.