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Flexible work arrangements help women, but only if they are also offered to men

Highlights the need for equal policies for women and men.

by Leah Ruppanner and Jordy Meekes, The Conversation

Flexible workplace policies designed to improve gender gaps in employment and pay might actually make things worse for women.

Flexible work has been on offer to both men and women in many companies for decades. However, it is usually women who are in non-standard employment such as part-time work, often to meet the demands of children, sick parents or partners needing extra care.

Flexible arrangements might support women in maintaining a work-life balance. But policies that make it easier to transition to a part-time job or take leave may actually be weakening their position in the labor market and their lifetime earnings potential, therefore widening gender gaps in pay.

This highlights the need for equal policies for women and men.

COVID-19 and the labor market

The world changed under COVID-19 and the movement towards more flexible work may be one of the silver linings of the pandemic. This International Women's Day (March 8), we are in a unique position to tap into the learnings from the COVID-19 lockdowns, during which many men and women were working from home and sharing housework, home-schooling and childcare responsibilities.

Research shows Australian fathers stepped into more involved roles in the household during the lockdowns and have maintained higher levels of involvement in housework and childcare as things return to normal.

Job flexibility and gender pay gap

New research from the Melbourne Institute suggests flexible work conditions such as part-time hours could be a driving factor in the career decisions of women, but not men, and a key reason why the gender divide in employment is not narrowing.

Gender differences in labor force participation, wages and working hours in Australia are very similar to those in the Netherlands, so a study from there offers valuable insights for policymakers in Australia.

Researchers (including one of us, Jordy Meekes) used data from Statistics Netherlands to analyze how men and women respond to job loss. The study found women remained unemployed for longer than men. When they did find new jobs, women also experienced a larger reduction in working hours than men, which reduced their annual earnings.

It appears women tend to put more emphasis on job flexibility than men, an explanation for why it is hard for women to return to the workforce. Women may even be willing to pass up job opportunities in favor of the flexible work conditions they rely on to balance work and family life.

Women remain largely responsible for the organizational and physical work of making sure kids are completing homework, lunches are prepared and attending numerous after-school activities. Since work and school schedules are seldom aligned, someone has to do the juggle. To keep the family humming, mothers spend more time on housework and care and less time on employment after the birth of the first child.

Part-time mothers

The career penalty for women that comes with having a child in the current system is felt long beyond the period of maternity leave.

It is commonly acceptable for women to return to work in a part-time capacity. And it is often women who are culturally and socially expected to use flexible conditions to leave work and care for a sick child, for example. Less so for men.

The Melbourne Institute study found men who worked part-time in their previous role took longer to secure another job and were more

likely to have to take a pay cut than men who worked full-time.
Men who previously worked part-time earned on average 10% less in the new job. This finding suggests employers attach a penalty to part-time work for men, explained by the fact it is relatively uncommon for men.

Equal policies for women and men

Our beliefs about gender norms are shifting but this is not reflected in workplace and government policies on paper or in practice.
A review of existing policies is an important step in determining how suitable workplace policies are to support all employees.
Having written policies to support diversity and inclusion or flexible work practices is positive but it is not a sign of success. Particularly if, in practice, only a small number of employees can avail of the benefits—and at what cost? The COVID-19 lockdowns, while challenging for many, have given us an insight into what flexibility could truly look like for men and women alike.

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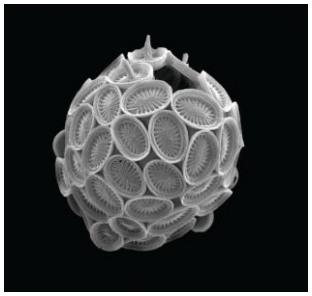
Prehistoric Plankton Became Predators to Survive a Mass Extinction

When the sun disappeared, tiny coccoliths turned to hunting

By Riley Black

An asteroid strike 66 million years ago not only devastated the dinosaurs but almost reset life in the oceans back to a primitive soup of simple microorganisms. What prevented ocean ecosystems from totally collapsing, scientists hypothesize, may have been shell-covered algae that could feed on other organisms but maintained the ability to photosynthesize. This skill would preserve the foundation of the marine realm's complex food webs through a long dark spell.
The predatory plankton belonged to a family of armored, algaelike organisms called coccolithophores, or coccoliths. They have been around for about 200 million years, and many forms still bob along as ocean plankton today. But their survival was especially significant in the wake of the mass extinction at the end of the Cretaceous period, when debris from the asteroid's impact and wildfire ash blotted out the sun for two years. Life experienced a prolonged "impact winter" when photosynthesis all but ceased.



***A modern coccolith has holes that help with locomotion*. Credit: From "Algal Plankton Turn to Hunting to Survive and Recover From End-cretaceous Impact Darkness," by Samantha J. Gibbs et al., in Science Advances, Vol. 6, No. 44; October 30, 2020**

"The food webs in the ocean have photosynthesis as their foundation, just like the land, but in the ocean the photosynthesis is carried out by microscopic bacteria and algae," says University of Southampton paleontologist Samantha Gibbs, lead author of a new study in *Science Advances*. Coccoliths were among these energy converters in the Cretaceous, and about 90 percent of coccolith species went extinct after impact.
Lacking light for their energy needs, Gibbs says, "the handful of survivor species were able to turn to food capture and ingestion." Small holes in coccolith fossils indicate that the survivors possessed whiplike flagella that let them move and stalk other organisms. The researchers tracked hunter algae's prevalence in the fossil record and modeled the organisms' evolution to show how they could have survived and adapted to the sun's disappearance—and then its return, when they proliferated again.
Experts have long wondered how photosynthesis-using organisms such as coccoliths endured without sunlight. "This is a really exciting finding that goes a long way to explaining an apparent paradox in the extinction," says University of Texas at Austin paleontologist Christopher Lowery, who was not involved in the study.
The model may explain changes in other organisms as well. Small

creatures called foraminifera, or forams, also took a hit from the impact but persisted. They were armored, too, and those that survived evolved spines. The spines would have worked together with miniature tentacles to help forams grab larger prey, Lowery says, bolstering the idea that other single-celled organisms also adapted their feeding style.

Eventually coccolith survivors picked up photosynthesis again, revitalizing the ocean's food webs when light returned. Tiny, hungry algae helped to save the seas.

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Paw hygiene no reason to ban assistance dogs from hospitals

Assistance dogs' paws are cleaner than their users' shoe soles, Utrecht University researchers discover

Over 10,000 people in Europe use an assistance dog; think of guide dogs for people with a visual impairment, hearing dogs for people with a hearing impairment, medical response service dogs and psychiatric service dogs.

According to a UN-agreement and the Dutch law, these dogs are welcome in stores, hospitals and other public places. However, in practice, many assistance dog users and their dogs are regularly refused entry. In the Netherlands, four out of five assistance dog users indicate that they regularly experience problems with this.

Often, hygiene reasons are given as the main argument for refusing entry to assistance dogs. Research by Utrecht University now shows that the paws of assistance dogs are cleaner than the shoe soles of their users, and thus, paw hygiene is no reason to ban assistance dogs from hospitals.

To investigate this, Jasmijn Vos, Joris Wijnker and Paul Overgaauw of Utrecht University's Faculty of Veterinary Medicine took samples from the paws of 25 assistance dogs and the shoe soles of their users. For comparison, they also investigated an equally large group of pet dogs and their owners. Vos and her colleagues examined the samples for poop bacteria (Enterobacteriaceae), which are very common outdoors, and for an important diarrhoeal bacteria (Clostridium difficile).

"The dogs' paws turned out to be cleaner than the soles of their shoes," says Jasmijn Vos, Masters student at Utrecht University. "This makes the hygiene argument that is often used to ban assistance dogs from public locations invalid." Moreover, the diarrhoeal bacteria did not occur on the dogs' paws whatsoever, and only once on a shoe sole.

81% of assistance dogs are refused

Dutch assistance dog users were also surveyed about their experiences. 81% are still regularly refused entry to public places with their dog, even though this is prohibited by law. This is mainly down to lack of knowledge on the part of the person refusing entry: lack of knowledge on what an assistance dog is, how it can be recognised, and about the rules of law.

The study also shows that assistance dog users constitute only a small fraction of the total number of patients in Dutch hospitals. Should they decide to bring their assistance dog to the hospital, or elsewhere, this should be made possible; assistance dogs are usually well trained and are no more of a hygiene hazard than people!

Research publication *Vos SJ, Wijnker JJ, Overgaauw PAM. A pilot study on the contamination of assistance dogs' paws and their users' shoe soles in relation to admittance to hospitals and (in)visible disability. Int. J. Environ. Res. Public Health. 2021; 18(2): 513. Full text: https://www.mdpi.com/1660-4601/18/2/513*

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COVID-19: Study from 116 countries suggests surgery should be delayed for at least seven weeks following a COVID-19 diagnosis to reduce mortality risk

More than 15,000 co-authors make this largest ever collaborative surgery study

New international research published in *Anaesthesia* (a journal of the Association of Anaesthetists) concludes that surgery should be delayed for seven weeks after a patient tests positive for SARS-CoV-2, since the data show that surgery that takes place between 0 and 6 weeks after diagnosis is associated with increased mortality.

The study is by the COVIDSurg Collaborative: a global collaboration of over 15,000 surgeons working together to collect a range of data on the COVID-19 pandemic. This study's lead authors are Dr Dmitri Nepogodiev (Public Health) and Dr Aneel Bhangu (Surgeon) of the University of Birmingham, UK.

While it is known that infection with SARS-CoV-2 during surgery increases mortality and international guidelines recommend surgery should be delayed for patients testing positive for COVID-19, there is little evidence regarding the optimal duration of delay.

This international multicentre study included 140,231 patients (1,674 hospitals, 116 countries)* undergoing surgery in October 2020. Participating hospitals included all patients undergoing a surgical procedure.

The number of co-authors (more than 15,000) makes this the largest collaborative surgery study ever undertaken globally.

Patients who became infected with SARS-CoV-2 after their surgery were excluded from the study.

The primary outcome measure was 30-day postoperative death.

Statistical modelling was used to adjust for patient, disease, and operation variables and calculate adjusted 30-day mortality rates for different time periods from SARS-CoV-2 diagnosis to surgery.

The time from SARS-CoV-2 diagnosis to surgery was 0-2 weeks in 1,144 (0.8%) patients, 3-4 weeks in 461 (0.3%), 5-6 weeks in 327 (0.2%), 7 weeks or more in 1,205 (0.9%), and 137,590 (97.8%) patients did not have SARS-CoV-2 infection.

Adjusted 30-day mortality in patients who did not have SARS-CoV-2 infection was 1.5%. This was increased in patients operated at 0-2 weeks (4.0%), 3-4 weeks (4.0%), and at 5-6 weeks (3.6%), but not at 7-8 weeks (1.5%) after SARS-CoV-2 diagnosis.

These findings were consistent across age groups, patient fitness levels, urgency (elective versus emergency) of surgery, and grade (minor versus major) of surgery.

Following a delay of 7 weeks or more, patients with ongoing COVID-19 symptoms (6.0%) had higher mortality than patients whose symptoms had resolved (2.4%) or who had been asymptomatic (1.3%).

Dr Dmitri Nepogodiev says: "We found that patients operated 0-6 weeks after SARS-CoV-2 infection diagnosis are at increased risk of postoperative death, as were patients with ongoing symptoms at the time of surgery.

We recommend that whenever possible surgery should be delayed for at least 7 weeks after a positive SARS-CoV-2 test result, or until symptoms resolve if patients have ongoing symptoms for 7 weeks or more after diagnosis."

Dr Aneel Bhangu adds: "Decisions regarding delaying surgery should be tailored for each patient, since the possible advantages of delaying surgery for at least 7 weeks following SARS-CoV-2 diagnosis must be balanced against the potential risks of delay.

For some urgent surgeries, for example for advanced tumours, surgeons and patients may decide that the risks of delay are not justified."

Dr Mike Nathanson, President of the Association of Anaesthetists, said "This paper provides important information to patients and their carers and will help them determine the right time for surgery after a COVID-19 infection.

Of the millions of patients now waiting for surgery, many will have had COVID-19 and they will want to be informed about the risks.

COVID-19 will be with us for many years and the number of patients with a previous infection will continue to increase."

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Five herbal medicines potent against tick-borne disease babesiosis in lab, says new study

Research supported by Bay Area Lyme Foundation points to need for more effective treatments compared to currently utilized treatments for tick-borne infections

Portola Valley, Ca - Bay Area Lyme Foundation, a leading sponsor of Lyme disease research in the U.S., today announced the publication of new data finding that five herbal medicines had potent activity compared to commonly-used antibiotics in test tubes against Babesia duncani, a malaria-like parasite found on the West Coast of the U.S. that causes the disease babesiosis. Published in the journal *Frontiers in Cellular and Infection Microbiology*, the laboratory study was funded in part by the Bay Area Lyme Foundation. Collaborating researchers were from Johns Hopkins Bloomberg School of Public Health, California Center for Functional Medicine, and FOCUS Health Group, Naturopathic.

"This research is particularly important as babesiosis is a significant emerging health risk. Due to limited therapeutics and a rise in treatment resistance, current treatment options for this disease are inadequate and many patients rely on herbal therapies for which there is only anecdotal evidence of efficacy," said co-author Sunjya K. Schweig, MD, Founder and Director, California Center for Functional Medicine and Scientific Advisory Board Member, Bay Area Lyme Foundation, who has also studied herbal treatments for Lyme disease.

"Increasingly, Americans with chronic diseases are pursuing complementary and alternative medicine to improve general health or quality of life. We hope this data offers inspiration to other researchers to further explore similar options for people living with persistent tick-borne diseases that do not respond to current treatments," added Dr. Schweig.

While current treatment protocols for babesiosis recommend use of antibiotics including atovaquone, azithromycin, clindamycin, quinine, and their combinations, these regimens are often associated with treatment failures and significant side effects, even in immunocompetent patients. In addition, epidemiologic studies have documented that up to 23% of patients with babesiosis experienced concurrent Lyme disease and its associated disabling effects.

According to this laboratory study, the five herbal medicines that demonstrated inhibitory activity against B. duncani are:

- **Cryptolepis sanguinolenta**
- **Artemisia annua (Sweet wormwood)**
- **Scutellaria baicalensis (Chinese skullcap)**
- **Alchornea cordifolia (African Christmas bush)**
- **Polygonum cuspidatum (Japanese knotweed)**

Further, the study discovered that the bioactive compounds derived from *Cryptolepis sanguinolenta*, *Artemisia annua*, and Scutellaria baicalensis, had comparable or even better activity against B. duncani than the commonly used antimicrobial medications quinine and clindamycin.

This is the first study to report the antibabesial activity of Scutellaria baicalensis. However, the antimicrobial and anti-inflammatory activity of *Alchornea cordifolia* and *Polygonum cuspidatum* extracts have been previously documented, and other studies have found benefits of combining agents such as compounds derived from *Cryptolepis sanguinolenta* and an artemisinin-based therapy.

These compounds still need to be tested both in vitro and in animal models as well as in clinical trials. While each of these botanical medicines are already in clinical use, it is important for future studies to evaluate them directly in patients using specific clinical treatment regimens, as each have the potential to produce side effects in patients, and should be taken only under the care of a

clinician knowledgeable of their capabilities and toxicities.

"Herbal medicines have been successfully used by various traditional medicine systems and ancient cultures," said Linda Giampa, executive director, Bay Area Lyme Foundation. "Coinfected tick-borne disease patients frequently experience a greater number of symptoms for a longer duration than those with Lyme disease alone, pointing to the need for novel treatments for babesiosis, one of the most common tick-borne infections after Lyme disease. We hope that findings from this study are an important step towards developing new therapeutic options for doctors and their patients with persistent Lyme disease and other tick-borne infections."

About the Study

The paper titled "Botanical medicines Cryptolepis sanguinolenta, Artemisia annua, Scutellaria baicalensis, Polygonum cuspidatum, and Alchornea cordifolia demonstrate inhibitory activity against Babesia duncani," was authored by Yumin Zhang, Hector Alvarez-Manzo, Jacob Leone, ND, Sunjya Schweig, MD, and Ying Zhang, MD, PhD. It was published in Frontiers in Cellular and Infection Microbiology, the Parasite and Host section.

Researchers tested a panel of 46 herbal medicine extracts against B. duncani compared to the commonly used medications quinine and clindamycin, both of which are used to treat active babesiosis, a common coinfection with Lyme disease.

Plant extracts selected for the study included herbs or agents that are already in clinical use, have been previously used to manage the symptoms of patients who do not respond to standard Lyme antibiotic treatment, and have favorable safety profiles.

The combination of quinine and clindamycin was selected as the control because it is the treatment regimen recommended for all severe babesiosis infections, including B. duncani. However, a clinical trial reported that 72% of patients who received quinine plus clindamycin for babesiosis suffered side effects including tinnitus, vertigo, and gastrointestinal upset, in some cases severe enough to necessitate dosage decrease or treatment suspension.

Most of these natural products in this study were provided as ethanol extracts at 30, 60, and 90% ethanol and the ethanol solvent was also tested as a control in the respective concentrations. The natural products and ethanol controls were added to 96-well plates containing infected red blood cells to obtain final concentrations of 0.01%.

In this study, Scutellaria baicalensis showed good test tube activity against B. duncani, with the IC50 value (a widely used measure of a drug's efficacy) of baicalein practically the same as the antibiotic quinine, and up to three times more favorable than the antibiotic clindamycin. Artemisinin and artemisinin derivatives (artesunate and artemether) alone also had IC50 values that were more favorable than that of quinine and clindamycin.

These data suggest that it may be advantageous to use these herbs to simultaneously target multiple different pathogens in complex Lyme disease with coinfections. The data also might provide a basis for the clinical improvement of patients who take herbal medicines, particularly those whose chronic symptoms may be due to persistent bacteria that are not killed by conventional Lyme antibiotic treatment. However, it is critical to note that additional studies are needed to further evaluate the five active botanical medicines identified in the study. Patients should not attempt to self-treat with these herbal medicines due to potential side effects and lack of clinical trials with these products.

About Lyme Disease

The most common vector-borne infectious disease in the country, Lyme disease is a potentially disabling infection caused by the Borrelia burgdorferi bacteria transmitted through the bite of an infected tick to people and pets. If caught early, most cases of Lyme disease can be effectively treated, but it is commonly misdiagnosed due to lack of awareness and unreliable diagnostic tests. According to the CDC, there are nearly 500,000 new cases of Lyme disease each year. As a result of the difficulty in diagnosing and treating Lyme disease, more than one million Americans may be suffering from the impact of its debilitating long-term symptoms and complications, according to Bay Area Lyme Foundation estimates.

About Babesiosis

Babesiosis is a common tick-borne infection of red blood cells by malaria-like parasites called Babesia. Prevalent strains in North America include Babesia duncani, which was first discovered in Washington state and California in the early 1990's, and Babesia microti, which is endemic to the Northeast and the upper Midwest of the United States. Current diagnostic tests for babesiosis are often inaccurate, and there is no reliable treatment. In addition to transmission by tick bite, Babesia can also be transmitted vertically from mother to a fetus, and through infected blood transfusions, which is why the US. Food and Drug Administration (FDA) recommends testing blood donations for Babesia. Symptoms and pathogenesis may vary based on the strain of Babesia, but symptoms can be similar to those of Lyme disease. Babesiosis frequently presents with a high fever and chills, and progresses to include fatigue, headache, drenching sweats, muscle aches, chest pain, hip pain and shortness of breath, and in severe cases can lead to kidney failure.

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Ancient Earth was a water world

Evidence is mounting that some 3 billion to 4 billion years ago, the planet's oceans held nearly twice as much water

By Paul Voosen

Across the ages, sea levels have risen and fallen with temperatures—but Earth's total surface water was always assumed

to be constant. Now, evidence is mounting that some 3 billion to 4 billion years ago, the planet's oceans held nearly twice as much water—enough to submerge today's continents above the peak of Mount Everest. The flood could have primed the engine of plate tectonics and made it more difficult for life to start on land.

Rocks in today's mantle, the thick layer of rock beneath the crust, are thought to sequester an ocean's worth of water or more in their mineral structures. But early in Earth's history, the mantle, warmed by radioactivity, was four times hotter. Recent work using hydraulic presses has shown that many minerals would be unable to hold as much hydrogen and oxygen at mantle temperatures and pressures. "That suggests the water must have been somewhere else," says Junjie Dong, a graduate student in mineral physics at Harvard University who led a model, based on those lab experiments, that was published today in *AGU Advances*. "And the most likely reservoir is the surface."

The paper makes intuitive sense, says Michael Walter, an experimental petrologist at the Carnegie Institution for Science. "It's a simple idea that could have important implications."

Two minerals found deep in the mantle store much of its water today: y7 and ringwoodite, high-pressure variants of the volcanic mineral olivine. Rocks rich in those minerals make up 7% of the planet's mass, and although only 2% of their weight is water today, "a little bit adds up to a lot," says Steven Jacobsen, an experimental mineralogist at Northwestern University.

Jacobsen and others have created these mantle minerals by squeezing rock powders to tens of thousands of atmospheres and heating them to 1600°C or more. Dong's team stitched together the experiments to show wadsleyite and ringwoodite hold fractionally less water at higher temperatures. Moreover, the team predicts, as the mantle cooled, these minerals themselves would become more abundant, adding to their ability to soak up water as Earth aged.

The experiments aren't alone in suggesting a water-bound planet. "There's pretty clear geological evidence," too, says Benjamin Johnson, a geochemist at Iowa State University. Titanium concentrations in 4-billion-year-old zircon crystals from Western Australia suggest they formed underwater. And some of the oldest known rocks on Earth, 3-billion-year-old formations in Australia and Greenland, are pillow basalts, bulbous rocks that only form as magma cools underwater.

Work by Johnson and Boswell Wing, a geobiologist at the University of Colorado, Boulder, offers more evidence. Samples from a 3.24-billion-year-old chunk of oceanic crust left on Australia's mainland were far richer in a heavy oxygen isotope than the present-day oceans. Because water loses this heavy oxygen when rain reacts with the continental crust to form clays, its abundance in the ancient ocean suggests the continents had barely emerged by that point, Johnson and Wing concluded in a 2020 *Nature Geoscience* study. The finding doesn't necessarily mean the oceans were larger, Johnson notes, but, "It is easier to have submerged continents if the oceans are bigger."

Although the larger ocean would have made it harder for the continents to stick their necks out, it could explain why they appear to have been on the move early in Earth's history, says Rebecca Fischer, an experimental petrologist at Harvard and co-author on the *AGU Advances* study. Larger oceans could have helped kick off plate tectonics as water penetrated fractures and weakened the crust, creating subduction zones where one slab of crust slipped below another. And once a subducting slab began its dive, the dryer, inherently stronger mantle would have helped bend the slab, ensuring its plunge would continue, says Jun Korenaga, a geophysicist at Yale University. "If you cannot bend plates, you cannot have plate tectonics."

The evidence for larger oceans challenges scenarios for how life

began on Earth, says Thomas Carell, a biochemist at Ludwig Maximilian University of Munich. Some researchers believe it began at nutrient-rich hydrothermal vents in the ocean, whereas others favor shallow ponds on dry land, which would have frequently evaporated, creating a concentrated bath of chemicals.

A larger ocean exacerbates the biggest strike against the underwater scenario: that the ocean itself would have diluted any nascent biomolecules to insignificance. But by drowning most land, it also complicates the thin pond scenario. Carell, a pond advocate, says in light of the new paper, he is now considering a different birthplace for life: sheltered, watery pockets within oceanic rocks that broke the surface in volcanic seamounts. “Maybe we had little caves in which it all happened,” he says.

The ancient water world is also a reminder of how conditional Earth’s evolution is. The planet was likely parched until water-rich asteroids bombarded it shortly after its birth. If the asteroids had deposited twice as much water or the present day mantle had less appetite for water, then the continents, so essential for the planet’s life and climate, would never have emerged. “It’s a very delicate system, the Earth,” Dong says. “Too much water, or too little, and it wouldn’t work.”

http://bit.ly/38xKk1q

Outbreak of a rare, polio-like syndrome likely prevented, postponed by social distancing

Social distancing may have prevented the transmission of an outbreak of acute flaccid myelitis

Social distancing not only helped slow the spread of COVID-19 -- it also may have prevented the transmission of an outbreak of a rare polio-like syndrome, according to Princeton University researchers.

Though uncommon, acute flaccid myelitis (AFM) is a critical spinal condition that causes weakness in the limbs, seriously diminishes motor function, and can lead to lifelong disabilities. The syndrome was first reported in the United States in 2012 and has been coming back every two years, hinting it could strike again in 2020.

Using epidemiological surveillance tools, the researchers showed that an AFM outbreak was likely to occur in 2020, but social distancing prevented its spread.

The reason was that social distancing reduced the occurrence of a respiratory illness known as enterovirus 68 (EV-D68), which the researchers found is strongly associated with AFM. EV-D68 is a virus found in infants and children that typically causes respiratory issues such as a runny nose, cough, or sneezing. While the definite cause of AFM remains inconclusive, it has been linked to viral infections and past studies have specifically identified a link to EV-68.

The Princeton-led research team sought to better understand the connection between AFM and EV-D68 and whether another outbreak might occur. Their findings, published in the journal *Science Translational Medicine*, suggest that vaccines targeting EV-D68 could lessen future outbreaks of AFM.

"Though currently uncommon, this syndrome has been increasing in frequency with each successive outbreak since 2014, making it critically important to better understand the patterns and drivers behind it," said first author Sang Woo Park, a Ph.D. student in Princeton's Department of Ecology & Evolutionary Biology.

"Our results underline the importance of epidemic surveillance for projecting future impact of infectious diseases," said Bryan Grenfell, the Kathryn Briger and Sarah Fenton Professor of Ecology and Evolutionary Biology and Public Affairs and an associated faculty member in Princeton's High Meadows Environmental Institute.

Grenfell and Park conducted the study with Kevin Messacar of the Children's Hospital at the University of Colorado; Margarita Pons-Salort of Imperial College London; Lindsay Meyers and Camille Cook, former and current employees, respectively, of bioMérieux

Inc. or its subsidiaries; and Jeremy Farrar of the Wellcome Trust.

EV-D68 outbreaks have been reported every two years, coinciding with the outbreak pattern of AFM, the researchers said. To confirm this connection, they analyzed patterns of EV-D68 outbreaks using unique surveillance data acquired from BioFire® Syndromic Trends (Trend), a cloud-based network of de-identified pathogen results from around the world collected in near-real time.

The results revealed that EV-D68 outbreaks were occurring every two years in many states, though not all. In states such as Ohio, EV-D68 outbreaks revealed more intricate patterns. Still, the association between EV-D68 and AFM syndrome was strong.

Likely thanks to social distancing, AFM cases remained low in 2020. There were only 31 cases in 2020 compared to 153 cases in 2016 and 238 cases in 2018.

"Fortunately, we saw very little EV-D68 circulation in 2020 and few cases of AFM compared to what was expected, but that makes it even more important to be as prepared as possible for what could be coming in 2021 or beyond," said Park.

The paper, "Epidemiological dynamics of enterovirus D68 in the US and implications for acute flaccid myelitis," first appeared online in Science Translational Medicine on March 10. The work was supported by the National Institute of Allergy and Infectious Diseases, the Wellcome Trust, and the Royal Society.

http://bit.ly/3vhLCXH

Jaw-Dropping Fossil Find Contains a Dinosaur Sitting on an Entire Clutch of Eggs

An international team of scientists has announced the discovery of an extraordinary fossilized nest in China, preserving at least eight separate dinosaurs from 70 million years ago.

Carly Cassella

The clutch of ancient eggs belongs to a medium-sized adult oviraptor, and we know that because the parent is actually part of the fossil. The skeleton of this ostrich-like theropod is positioned in a crouch over two dozen eggs, at least seven of which were on the brink of hatching and still contain embryos inside.

The ancient scene is unprecedented, and provides the first hard evidence that dinosaurs were brooding parents, laying their eggs and incubating them for quite a long time.

The 70-million-year-old fossil.
(Shundong Bi/Indiana University of Pennsylvania)

"This kind of discovery - in essence, fossilized behavior - is the rarest of the rare in dinosaurs," says paleontologist Matt Lamanna from the Carnegie Museum of Natural History (CMNH).

"Though a few adult oviraptorids have been found on nests of their eggs before, no embryos have ever been found inside those eggs."

Since the 1980s, paleontologists have unearthed numerous dinosaur nests containing fossilized eggs.

Some rare ones have even been found with the parent's skeleton sitting on top. Other oviraptor eggs suggest they might have been a blue-green color. Inferring behavior from these fossils, however, has proved problematic.

While it seems the oviraptor parents are brooding on their nests, it's also possible these dinosaurs perished while laying or guarding their eggs, not necessarily incubating them.

This is more similar to how crocodiles deal with their nests, not modern birds.

The new specimen was recovered from the Nanxiong Formation of Ganzhou in South China - a region renowned for the world's largest collection of fossilized dinosaur eggs - but it's unlike anything scientists have found before.

The relationship between dinosaur parent and embryo has never been closer than this.

The body of the adult oviraptor is preserved in "extremely close proximity to the eggs", with little to no sediment in between.

In at least seven of the eggs, embryonic material was found exposed, including ossified bones in identifiable shapes.

One of the eggs may actually contain a complete skeleton, with its vertebrae, dorsal ribs, a humerus, both ilia and femora, and a tibia laid out in a curled position.

Analyzing the oxygen isotopes of these embryos, researchers found the estimated incubation temperature was consistent with the body temperature of the parent, sitting somewhere between 30 to 38 degrees Celsius (86 to 100 degrees Fahrenheit).

"In the new specimen, the babies were almost ready to hatch, which tells us beyond a doubt that this oviraptorid had tended its nest for quite a long time," explains Lamanna.

"This dinosaur was a caring parent that ultimately gave its life while nurturing its young."

Interestingly enough, however, not all the embryos were at the same stages of development.

This suggests the clutch may ultimately have hatched at different times - a feature that was thought to show up much later, in only some types of birds.

Artwork of oviraptor dinosaur brooding on a nest of blue-green eggs.
(Zhao Chuang/PNSO)

While oviraptors are often considered an intermediate stage in this evolutionary process, it looks as though they might have independently moved away from simultaneous hatching, and this suggests the evolution of bird reproduction was not a simple linear process.

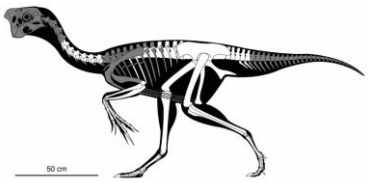
Most modern birds will wait until all their eggs are laid before incubating them - sometimes with the help of both mother and father - and this leads to synchronous hatching.

While oviraptors may also have waited to incubate until all the eggs had been laid, the authors suggest the upper eggs might have been closer to the brooding adult and therefore could have developed more quickly. This, however, is just an idea.

We'll need more data to figure out why some eggs would have hatched earlier than others. In other ways, however, the oviraptor shares similar traits to modern birds.

The sex of the fossilized parent, for instance, may have been male, which suggests the father might have also taken part in brooding, similar to ostrich mothers and fathers, who take turns incubating their young.

The sex of the adult oviraptor is still under debate (it could be a male or a female based on available data), but the idea matches other analyses of theropod nests, which suggest some level of paternal care.



Artwork of the adult oviraptor skeleton; preserved bones shown in white.
(Andrew McAfee/Carnegie Museum of Natural History)

As if all that reproductive information wasn't enough, this remarkable fossil has also given us a glimpse at the oviraptor's potential diet.

For the first time, scientists have found small stones in the stomach of this type of dinosaur, which would have probably been swallowed to aid digestion.

"It's extraordinary to think how much biological information is captured in just this single fossil," says paleontologist Xing Xu from the Institute of Vertebrate Paleontology and Paleoanthropology in Beijing.

"We're going to be learning from this specimen for many years to come."

The study was published in the *Science Bulletin*.

http://bit.ly/38C367v

Placenta is a dumping ground for genetic defects

Placenta resembles a tumour, harbouring many of the same genetic mutations found in childhood cancers

In the first study of the genomic architecture of the human placenta, scientists at the Wellcome Sanger Institute, the University of Cambridge and their collaborators have confirmed that the normal structure of the placenta is different to any other human organ and resembles that of a tumour, harbouring many of the same genetic mutations found in childhood cancers.

The study, published today (10 March 2021) in *Nature*, found evidence to support the theory of the placenta as a 'dumping ground' for genetic defects, whereas the fetus corrects or avoids these errors. The findings provide a clear rationale for studying the association between genetic aberrations and birth outcomes, in order to better understand problems such as premature birth and stillbirth.

In the earliest days of pregnancy, the fertilized egg implants into the wall of the uterus and begins dividing from one cell into many. Cells differentiate into various types of cell and some of them will form the placenta. Around week ten of pregnancy, the placenta begins to access the mother's circulation, obtaining oxygen and nutrients for the fetus, removing waste products and regulating crucial hormones*.

It has long been known that the placenta is different from other human organs. In one to two per cent of pregnancies, some placental cells have a different number of chromosomes to cells in the fetus - a genetic flaw that could be fatal to the fetus, but with which the placenta often functions reasonably normally.

Despite this genetic robustness, problems with the placenta are a major cause of harm to the mother and unborn child, such as growth restriction or even stillbirths.

This new study is the first high-resolution survey of the genomic architecture of the human placenta. Scientists at the Wellcome Sanger Institute and the University of Cambridge conducted whole genome sequencing of 86 biopsies and 106 microdissections from 42 placentas**, with samples taken from different areas of each organ.

The team discovered that each one of these biopsies was a genetically distinct 'clonal expansion' - a cell population descended from a single common ancestor - indicating a clear parallel between the formation of the human placenta and the development of a cancer. Analysis also identified specific patterns of mutation that are commonly found in childhood cancers, such as neuroblastoma and rhabdomyosarcoma, with an even higher number of these mutations in the placenta than in the cancers themselves.

Professor Steve Charnock-Jones, a senior author of the study from the University of Cambridge, said: "Our study confirms for the first time that the placenta is organised differently to every other human organ, and in fact resembles a patchwork of tumours. The rates and patterns of genetic mutations were also incredibly high compared to other healthy human tissues."

The team used phylogenetic analysis to retrace the evolution of cell lineages from the first cell divisions of the fertilised egg and found evidence to support the theory that the placenta tolerates major genetic flaws.

In one biopsy, the researchers observed three copies of chromosome 10 in each cell, two from the mother and one from the father, instead of the usual one copy from each parent. But other biopsies from the same placenta and from the fetus carried two copies of chromosome 10, both from the mother. A chromosomal copy number error such as this in any other tissue would be a major genetic flaw***.

Professor Gordon Smith, a senior author of the study from the University of Cambridge, said: "It was fascinating to observe how

such a serious genetic flaw as a chromosomal copy number error was ironed out by the baby but not by the placenta. This error would have been present in the fertilized egg. Yet derivative cell populations, and most importantly those that went on to form the child, had the correct number of copies of chromosome 10, whereas parts of the placenta failed to make this correction. The placenta also provided a clue that the baby had inherited both copies of the chromosome from one parent, which can itself be associated with problems."

Now that the link between genetic aberrations in the placenta and birth outcomes has been established, further studies using larger sample sizes could help to uncover the causes of complications and diseases that arise during pregnancy.

Dr Sam Behjati, a senior author of the study from the Wellcome Sanger Institute, said: "The placenta is akin to the 'wild west' of the human genome, completely different in its structure from any other healthy human tissue. It helps to protect us from flaws in our genetic code, but equally there remains a high burden of disease associated with the placenta. Our findings provide a rationale for studying the association between genetic aberrations in the placenta and birth outcomes at the high resolution we deployed and at massive scale."

Notes to Editors:

**The Society for Endocrinology has more information on the role of the placenta during pregnancy: https://www.yourhormones.info/glands/placenta/*

*** All samples were sourced from the Pregnancy Outcome Prediction (POP) study: https://www.obgyn.cam.ac.uk/research/pops-2/*

**** Yourgenome.org has more information on chromosomes and how genetic errors can affect health: https://www.yourgenome.org/facts/what-is-a-chromosome-disorder*

Publication:

Tim H. H. Coorens, Thomas R. W. Oliver and Rashesh Sanghvi et al. (2021). Somatic mutations reveal widespread mosaicism and mutagenesis in human placentas. Nature. DOI: https://doi.org/10.1038/s41586-021-03345-1

This research was funded by Wellcome and the National Institute for Health Research (NIHR) Cambridge Biomedical Research Centre.

http://bit.ly/3qU459D

HPV vaccines for adults over age 26 may not be cost-effective

Added health benefit of increasing the vaccination age limit beyond 26 years is minimal

Boston, MA - Vaccinating adults age 26 and older against the human papillomavirus (HPV)--the virus that causes more than 90% of cervical cancers as well as several other cancers--may not be cost-effective, according to a new study led by researchers at the Harvard T.H. School of Public Health.

"Our study found that the added health benefit of increasing the vaccination age limit beyond 26 years is minimal, and that the cost-effectiveness is much lower than in pre-adolescents, the target age group for the HPV vaccine," said Jane Kim, K.T. Li Professor of Health Economics and lead author of the study.

The study will be published March 11, 2021, in *PLOS Medicine.*

HPV vaccines have been shown to be highly effective in preventing HPV infections that are associated with cervical, anal, oropharyngeal, vulvar, vaginal, and penile cancers, as well as genital warts. Current U.S. guidelines recommend HPV vaccination for girls and boys at age 11 or 12, and catch-up vaccination for people through age 26 if they were not vaccinated when younger. For adults beyond age 26, the guidelines don't specifically recommend catch-up vaccination but suggest that, for people aged 27-45, clinicians and patients make decisions about HPV vaccination on an individual basis.

The new study, undertaken to inform these national guidelines, used two mathematical models--from Harvard and Cancer Council New South Wales, Australia--that simulated scenarios of extending HPV vaccination to women and men up to age 45 years. Using U.S. data, the models projected cost and health outcomes of the six HPV-associated cancers and genital warts, taking into account

historical and future vaccination uptake in younger people, cervical cancer screening practices among women, vaccine efficacy, and vaccination costs. The researchers sought to determine whether the benefits of HPV vaccination at older ages would have an incremental cost-effectiveness ratio (ICER) that was in line with a commonly-cited upper threshold of $200,000 per quality-adjusted life year (QALY). QALYs are a measure of life expectancy adjusted to account for quality of life associated with health conditions and events.

The researchers found that HPV vaccination beyond age 26 in the U.S. would provide limited health benefit at the population level, at a substantial cost, given current HPV vaccine prices. Their analysis showed that the ICER for vaccinating people up to age 45 years ranged from $315,700 to $440,600 per QALY gained.

Kim noted that current HPV vaccines are prophylactic and therefore most effective when given prior to HPV exposure, which can happen soon after sexual initiation; once someone is exposed to HPV, the vaccine won't clear those infections. "By the time you vaccinate individuals in their 30s and 40s, many have already been exposed to HPV, so the health benefit really decreases at these older ages," she said. "It's also important to emphasize that cervical cancer screening remains an effective and cost-effective way to protect women from cervical cancer."

The study results, which were previously reported to the Advisory Committee on Immunization Practices, helped inform the committee's June 2019 recommendations to the Centers for Disease Control and Prevention on HPV vaccination. "Other countries that are considering extending the upper age limit of HPV vaccination to include older adults should consider the opportunity costs of doing so," said Kim.

Other Harvard Chan School co-authors of the study included Emily Burger, Stephen Sy, and Catherine Regan.

Funding for the study came from the National Cancer Institute at the National Institutes of Health (grant number U01CA199334).

"Human papillomavirus vaccination for adults aged 30 to 45 years in the United States: A cost-effectiveness analysis," Jane J. Kim, Kate T. Simms, James Killen, Megan A. Smith, Emily A. Burger, Stephen Sy, Catherine Regan, Karen Canfell, PLOS Medicine, online March 11, 2021, doi: 10.1371/journal.pmed.1003534

http://wb.md/2PSZdo6

Janssen's Viral Vector Vaccine: How it Compares

Janssen's viral vector is Ad26, a weakened version of an adenovirus. It's basically a dead virus.

Sandra Adamson Fryhofer, MD

The final week of February 2021 set two contrasting milestones in the COVID-19 pandemic. The week began mourning the more than 500,000 lives lost in this country so far in the pandemic. It ended with hope: a third COVID-19 vaccine, using a new technology platform. Introducing Janssen's new viral vector vaccine, awarded the FDA's emergency use authorization for those age 18 and older. (Janssen is the pharmaceutical arm of Johnson & Johnson.)

Pfizer and Moderna's products are mRNA vaccines. They use messenger RNA to create replicas of coronavirus spike proteins to trigger an immune response. In Janssen's vaccine, the messenger is a viral vector which is genetically engineered to make spike protein "lookalikes" in the body, which then trigger the immune response. Janssen's viral vector is Ad26, a weakened version of an adenovirus. Several of its genes have been removed to make it "replication deficient." It's basically a dead virus. It can't multiply in the body or give someone COVID-19. The genes in the viral vector cannot and do not incorporate into human DNA.

One Dose and Done

Janssen's vaccine has several logistical advantages that make it very user-friendly for both vaccinator and recipient. Transportation and storage are much simpler. No pizza cartons, dry ice, or subzero freezers. Janssen's five-dose unpunctured vials of vaccine can be stored at standard refrigerator temperatures of 2-8 °C (26-46 °F) for

up to 3 months. No dilution is needed, which speeds up the vaccination process. Punctured vials must be discarded after 6 hours if kept refrigerated, or after 2 hours if kept at room temperature.

The Janssen viral vector COVID vaccine requires only one injection. Both the Pfizer and the Moderna vaccines require two doses. With Janssen's single-dose vaccine, you can fully vaccinate your patient in one visit. This makes it a good option for patients who don't want to or can't manage to get back for that second dose, including those who are homebound or from populations that are mobile.

For patients, the "one dose and done" option has several downstream benefits: no need for a second vaccine appointment and only one set of vaccine side effects, which are similar to those for mRNA vaccines. Tell your patients to be prepared for pain at the injection site, headache, fatigue, and muscle pain. Symptoms last at most 1-2 days and are worse in younger as compared with older patients.

How About Efficacy?

Phase 3 studies for all three COVID vaccines are huge: 44,000 for Pfizer; 30,000 for Moderna; and 40,000 for Janssen. All included diverse populations with respect to race/ethnicity and age (both young and old), and all included patients with underlying medical conditions.

Phase 3 study results for all three COVID vaccines far exceed the FDA's bar of at least 50% efficacy. But there is a big difference. The respective trials took place at different calendar times and in different locations. For this reason, you can't directly compare Janssen's efficacy results with those for Pfizer and Moderna, whose studies were done earlier in the pandemic.

When Janssen tested its vaccine, the trial conditions were much more difficult. The background COVID incidence was higher, with more variants circulating, including variants of concern, which can increase transmissibility and disease severity.

Janssen's COVID vaccine was found to be 66.3% effective overall in preventing symptomatic COVID just 14 days after a single dose. It maintained at least 63% effectiveness across age, sex, race, and ethnic categories and also for those with underlying medical conditions. Vaccine efficacy varied geographically and was highest in the United States (74.4%) and lowest in South Africa (52%), where the B.1.351 variant dominated.

Janssen's efficacy results were more impressive in preventing hospitalizations. The Janssen vaccine was 100% effective in preventing hospitalization from COVID-19 by day 28 after vaccination. There were no COVID-associated deaths in those who were vaccinated.

Variants of concern have become a wild card. Moderna is already working on a booster for the South Africa (B.1.351) variant. Pfizer may study an mRNA vaccine using a variant sequence. Janssen already has a study in progress to see if two doses of its single-dose vaccine work better than one.

The Pfizer vaccine was the first-ever mRNA vaccine authorized by the FDA. At the time of authorization, mRNA vaccines were new but not unknown. Researchers had been working with them for years. Janssen's viral vector platform is supported by an even larger body of research, including an Ebola vaccine, already tested in pregnant women and children and approved in Europe in July 2020. More than 193,000 people, including patients of different age groups and conditions, have received various adenovirus-based investigational vaccines.

We now have three safe and effective COVID-19 vaccines. ACIP has expressed no preference for any of the three authorized vaccines. In the vaccine trials of all three vaccines, no one who received a COVID vaccine has died from COVID.

The important thing is to get vaccinated as soon as you can, when it's your turn, with whichever approved COVID-19 vaccine is available. For *Medicine Matters*, I'm Dr Sandra Fryhofer.

http://bit.ly/3bHY9fp

Fukushima: Why we need to look back thousands of years to get better at predicting earthquakes

Much of the data informing our estimates of hazard is from historical records dating back hundreds of years at most.

by Joanna Faure Walker, The Conversation

The aftermath of Fukushima. Credit: Shutterstock/ Fly_and_Dive

Ten years ago, on March 11 2011, a devastating earthquake occurred along part of a fault that scientists believe had not ruptured for more than a thousand years. The quake triggered a tsunami that caused more than 15,000 deaths in Japan, as well as a serious nuclear accident at a power plant in Fukushima.

It's common for earthquakes to occur along faults that haven't ruptured for hundreds or thousands of years. This is because rates of tectonic movement along individual faults vary from less than a millimeter up to several centimeters per year. During damaging earthquakes, a fault can slip a meter or more – more than 20 meters in the 2011 Japan earthquake—within seconds of the event starting. It could take hundreds or thousands of years to store enough stress on a fault before such an event occurs.

These long intervals between damaging earthquakes make assessing fault risks tricky, because much of the data informing our estimates of hazard is from historical records dating back hundreds of years at most.

But Earth holds the secrets to millions of years of earthquakes in its rocks. Studying them—and bringing the data together—we can develop a better idea of where the next big earthquake might happen.

We have only been using modern scientific instruments to measure and monitor earthquakes, and recording the data, for the last hundred years or so. Written records of earthquakes go back several hundred years.

But basing hazard calculations on the events that occurred in a relatively short time period—relative to the long-term average time between earthquakes on individual faults—may cause us to miss data from faults that have not ruptured. For example, in the central Apennines, Italy, the 2016 Amatrice earthquake that killed three hundred people occurred along a known fault that hadn't hosted a historical earthquake.

Historical earthquakes give us clues about what types of earthquake can occur in certain spots. In the same region as the 2011 great east Japan earthquake and tsunami, the Sanriku earthquake occurred, in AD869.

Geological data

There is longer-term evidence, though, that can help. This comes through geologists analyzing the physical structures of faults and looking at changes in the shape of the Earth's surface caused by movements occurring over millions of years. Such data can be used to identify deformation that has occurred through multiple earthquakes over many millennia.

Techniques include tracing the same dated surface, sediment or structure that has been displaced across a fault and using this to measure how much movement has taken place over a time period either measured directly or inferred through relative timing of different geological events.

We can also use sediments to identify past tsunamis. In Japan, researchers have found tsunami deposits buried under beaches and along shorelines showing the extent of where past tsunami have reached, giving us clues about their locations and size.

So why is such data traditionally not fully used in hazard and risk calculations? The problem is that such data can be difficult to

collect and may not have sufficient detail to show which faults or parts of a fault have moved faster than others. Where it's possible to obtain relevant and detailed data, it may not be easy for those who model hazards—trying to predict the likelihood of new events—to use.

Bringing the data together

I'm part of a group that aims to fix that accessibility gap, so that those calculating risk can integrate evidence across tens of thousands of years into their models. We've formed an international team bringing together those with expertise in collecting primary data on the ground and those with the modeling skills to calculate hazard and risk.

Our first endeavor has been to create a database which brings together our mapping of fault and rates of fault slip in an open-access format. We use this data to identify which faults pose the highest risk at particular sites.

For example, looking at the town of L'Aquila which suffered heavy damage in the 2009 earthquake, preliminary findings show that it's not just the faults closest to the city that pose a threat. Significant risk comes from fast-moving faults further away like the fault that crosses the Fucino basin responsible for the 1915 earthquake that killed 33,000 people.

What can we do to help reduce earthquake risk? A first step is having good data about hazard and risk so that governments, civil protection authorities, insurers and residents can identify where to prioritize resources.

We can't currently predict earthquakes—giving exact times and dates of when and where they will occur—and it's not clear if we ever will be able to with precision.

But, we can provide probabilistic modeling identifying where events are more likely and the highest damage is expected. Incorporating long-term evidence can provide a better understanding of the science behind earthquake hazard than using relatively short historical records alone. As in most geological problems, we need to use every possible clue we can to solve the enigma of earthquake occurrence.

http://bit.ly/3eCzyKU

Secrets From Ancient Bones Have Changed What We Know About The Scythians

Some of the people we group in with the Scythians often did settle down, living more agrarian lifestyles with urban centers

Michelle Starr

In both popular culture and the academic record, the Scythians have been described as a force to be reckoned with. For hundreds of years, they ruled the Eurasian steppe, fierce warriors given an even bigger advantage by their highly mobile, nomadic lifestyle.

Scythian stone carving in Adyr-Kahn. **(avtk/iStock/Getty Images Plus)**

Or so we have thought, for millennia. According to a new analysis of Scythian bones, this perception is not quite the full picture; in fact, some of the people we group in with the Scythians often did settle down, living more agrarian lifestyles with urban centers.

"Our study demonstrates overall low levels of human mobility in the vicinity of key urban locales of the Scythian era, in contrast to previous stereotypes of highly nomadic populations," said anthropologist Alicia Ventresca Miller of the University of Michigan.

"While long-distance mobility increased during the Scythian era relative to preceding periods, it was limited to a small percentage of individuals."

Our understanding of the people we classify as Scythians, who rose and thrived between 700 BCE and 200 BCE, is based on a number of different sources. There are historical records, including reports

from the contemporaneous Greek historian Herodotus; and there's the archaeological record, which is rich with the trappings of a warlike nomadic lifestyle, such as weapons, horse tack and burial mounds.

But the steppe is a large place, 500 years is a fairly long time, and humans are complex. Although all the people in that place and time tend to get grouped together under the Scythian label, the research of Ventresca Miller and her colleagues suggests that several, perhaps even many, diverse groups lived on the Pontic steppe during that time.

The team conducted an isotopic analysis of 'Scythian' teeth and bones found throughout what is now Ukraine, and discovered that those people likely had a more stationary lifestyle - growing millet and raising livestock - than the predominant image of the wild 'barbarians' suggests.

The teeth and bones belonged to 56 individuals whose remains were found on three burial sites in central and eastern Ukraine - Belsk, Mamai-Gora and Medvin. From them, the researchers were able to extract enough material to conduct an isotope analysis. They also analysed bones from a pair of sheep and a pig found buried in Bel'sk, providing additional context on livestock and what the ancient people ate.

This technique can reveal when and where a person lived. Combinations of isotopes in the soil can be taken up by plants, to be eaten and absorbed by people and other animals. In the case of strontium, the mix of isotopes replaces a small portion of the calcium in their teeth and bones, preserving the ratio as a record of their diet.

Since each geographic location has a different isotopic signature, and because some isotopes decay at a known rate, these isotopes can be used to place the source of a person's diet not just in geographic space, but also time.

Isotope analysis can even reveal if a person moved around from place to place over the course of their lifetime, so it would be a particularly useful tool for understanding the movement of the Scythians.

The researchers analysed isotopes of strontium, oxygen, nitrogen, and carbon, and compared it to previous studies on human populations in Ukraine from the Neolithic through to the Iron Age. They found strong evidence for the consumption of millet in all three sites, suggesting a reliance on agriculture. Two individuals from Mamai-Gora were found to have been highly mobile; these two ate less millet than the people who didn't move around.

Although these people did move around more than in previous eras, the findings suggest that, by and large, they tended to settle down, farm domesticated grain, and raise livestock, the researchers said.

"The Scythian epoch was clearly a period of contradictions, with strong evidence for complex interactions between agro-pastoralists and pastoralists that contributed to population aggregation in urban locales," Ventresca Miller said. "This study highlights the potential use of using isotopic analysis to directly assess prevailing models of economies and mobilities during the Scythian era."

The team hopes that future work will include larger, multi-generational samples to unveil a more complete picture of how people moved around - or didn't - on the Eurasian steppe during the time of the Scythians. They also hope to study bones from people of different social status, including those buried in rich graves.

This, they believe, could help us move away from cliches and stereotypes towards a richer, more realistic understanding of human history.

"It is clear that if we are to truly uncover the 'Scythians' we need to accept that the Eurasian steppe was home to a myriad of dynamic cultures and subsistence strategies during the Iron Age," the researchers wrote in their paper.

"In fact, it is perhaps variability, rather than a uniformity of nomadic warriors, that truly frames the Scythians as predecessors to incipient globalization in Eurasia."

The research has been published in *PLOS One*.

http://bit.ly/2OtWzEY

Scientists Find a Natural Protein That Stops Allergies And Autoimmune Conditions

For the millions of us plagued by hypersensitive, overactive, or downright abusive immune systems, it can feel like you're constantly fighting your own physical self.

Tessa Koumoundouros

From incessant allergies to life-threatening anaphylaxis and debilitating autoimmune disease, the system that's supposed to be protecting us can be problematic when it goes wrong. Now, we might be closer to fixing these issues in an entirely new way.

Using transgenic mice and cultures of cells taken from human tonsils, researchers have now found evidence of how our bodies might defend against the mistakes that result in conditions such as asthma, food allergies, and lupus. They found a protein called neuritin, produced by immune cells. It acts a bit like an inbuilt, boss-level antihistamine.

"There are over 80 autoimmune diseases, in many of them we find antibodies that bind to our own tissues and attack us instead of targeting pathogens - viruses and bacteria," explained immunologist Paula Gonzalez-Figueroa from the Australian National University (ANU). "We found neuritin suppresses formation of rogue plasma cells which are the cells that produce harmful antibodies."

We have known for some time that the immune system's regulatory T cells suppress self-targeting antibodies and immunoglobulin E (IgE) - the antibodies that instigate release of the notorious histamines in response to allergies - but not how. It took Gonzalez-Figueroa and her team five years to work it out, with the help of genetically engineered mice and lab-grown human cells.

In another of biology's usual games of chain reactions, a special class of cells called follicular regulatory T (or Tfr) pumps out neuritin, which turns down production of IgE (this is its antihistamine action) and suppresses other processes that send plasma cells out on self-targeting missions (hence, quashing our autoimmune responses), the researchers found.

Mice without the ability to produce neuritin had an increased chance of dying from anaphylaxis when injected with albumin from an egg. These mice, genetically bred to lack neuritin-producing Tfr cells, grew a population of faulty plasma cells early on in their life. These are the cells that developed self-antigens.

But when the team treated Tfr-deficient mice by injecting neuritin into their veins, they had some striking results. "Tfr-deficient mice treated with neuritin appeared healthy," Gonzalez-Figueroa and colleagues wrote in their paper, explaining the treatment led to the disappearance of the rogue B cell population too.

The team cautions they're yet to understand the full pathway involved in these immune mechanisms, or the effects of neuritin on other cellular processes. While neuritin has been studied in human nervous systems for quite some time, the exact way it triggers cells hasn't been clear.

To find out, white cells from human blood and tonsils were analysed in the presence of the protein, revealing clues on it acting internally. The results could lead to a better understanding of how we might use neuritin in the future to treat immune conditions.

"This could be more than a new drug - it could be a completely new approach to treat allergies and autoimmune diseases," Vinuesa said.

"If this approach was successful, we would not need to deplete important immune cells nor dampen the entire immune system; instead, we would only need to use the proteins our own body uses to ensure immune tolerance."

If they're right, and neuritin proves safe, it may one day allow the growing number of us facing allergies and autoimmune diseases some peace with our own bodies. Watch this space.

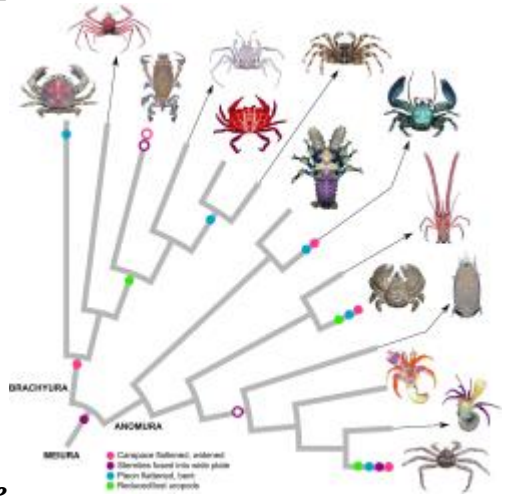
This paper was published in *Cell*.

http://bit.ly/3eHY7Gb

How does a crustacean become a crab?

Crabs are living the meme life on social media lately. The memes joke that everything will eventually look like a crab. But it's actually based in some truth.

The crab shape has evolved so many times the evolutionary biologist L.A. Borradaile coined the term carcinization in 1916 to describe the convergent evolution process in which a crustacean evolves into a crab-like form from a non-crab-like form. Crabs are decapod crustaceans of the infraorder Brachyura and are considered "true crabs", most of which are carcinized. "False crabs" are of the infraorder Anomura. This group evolved crab-like body plans three or more times from an ancestor that was not carcinized.



Phylogenetic evidence from the authors' previous work demonstrates that carcinized body plans have evolved multiple times (indicated by the colored characteristics on branches). Carcinized clades are: sponge crabs, "higher" true crabs, porcelain crabs, hairy stone crabs, and king crabs. Decarcinized clade shown is the frog crabs. **Joanna M. Wolfe.**

In a paper published on March 12 in *BioEssays*, a team of researchers led by Harvard University found that the crab-like body plan evolved at least five times independently in both true crabs (Brachyura) and false crabs (Anomura). They also discovered the crab-like body plan has been lost at least seven times in a process called decarcinization.

The team, led by first author Joanna M. Wolfe, Postdoctoral Researcher, Department of Organismic and Evolutionary Biology (OEB), Harvard University, examined a composite of phylogenetic data for crabs. They synthesized morphological data from key fossil and living crab groups as well as data from behavior, natural history, functional morphology, and development all from previous studies by the authors.

Construction of comprehensive datasets, including fossil and extant species, representing all crab families is crucial to identifying the key characters that define what is a crab," said Wolfe. "This will allow us to resolve the multiple origins and losses of 'crab' body forms through time and identify the timing of origin of key evolutionary novelties and body plans."

Carcinization is characterized by a wide, flat carapace (the hard upper shell) and a folded pleon (the abdomen or tail). The pleon is largely hidden under the crab body, unlike the pleon of the lobster which is visible. In decarcinization the carapace is elongated and narrow. The pleon is not bent and is usually visible or even elongated. Decarcinization is an example of a group re-evolving a morphology that had been lost, which is thought to be a rare event in evolution.

"Biologists want to know how to "predict" if a phenotype, or morphology, would evolve in a group," said senior author Heather D. Bracken-Grissom, Associate Professor, Florida International University. "Examining crab evolution provides a macroevolutionary timescale of 250 million years ago for which, with enough phylogenetic and genomic data, we might be able to predict the morphology that would result."

Wolfe agreed, "Carcinization also allows us to compare convergent evolution in fossil morphology to that in living organisms, which is

not yet commonly done."

The researchers are not completely certain but posit it is likely the common ancestor of Brachyura and Anomura was not carcinized. "This evidence suggests that indeed carcinization evolved independently in those groups," said co-author Javier Luque, Postdoctoral Researcher, OEB, Harvard University and Smithsonian Tropical Research Institute.

Wolfe is currently working with Assistant Professor Javier Ortega-Hernández, OEB, Harvard University, to test the hypothesis that carcinization can be quantitatively characterized by measuring the shapes of extant crab specimens from the Museum of Comparative Zoology, Harvard University, collections.

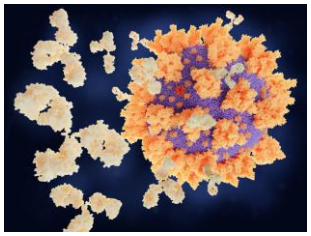
More information: *Joanna M. Wolfe et al, How to become a crab: Phenotypic constraints on a recurring body plan, BioEssays (2021).* *DOI: 10.1002/bies.202100020*

https://go.nature.com/3qRnB6h

COVID antibody treatments show promise for preventing severe disease

But uptake by patients and physicians has been low in the United States, where some therapies have been authorized for months.

Heidi Ledford



Antibodies attacking a coronavirus particle (illustration). **Credit: Juan Gaertner/SPL/Alamy**

Two clinical trials suggest that specific antibody treatments can prevent deaths and hospitalizations among people with mild or moderate COVID-19 — particularly those who are at high risk of developing severe disease.

One study found that an antibody against the coronavirus developed by Vir Biotechnology in San Francisco, California, and GSK, headquartered in London, reduced the chances of hospitalization or death among participants by 85%. In another trial, a cocktail of two antibodies — bamlanivimab and etesevimab, both made by Eli Lilly of Indianapolis, Indiana — cut the risk of hospitalization and death by 87%.

The study results, both announced on 10 March, come from randomized, placebo-controlled, double-blind clinical trials, but have not yet been published. They add to a growing body of evidence that the treatments can help fend off severe disease when administered early, says Derek Angus, an intensive-care physician at the University of Pittsburgh in Pennsylvania.

The antibodies “appear to be incredibly effective”, he says. “I’m very excited about the results of these trials.”

The body’s natural response to viral infection is to generate a variety of antibodies, some of which are able to directly interfere with the virus’s ability to replicate. In the early days of the pandemic, researchers raced to identify the antibodies that are most effective against the coronavirus and to produce them in bulk. The resulting ‘monoclonal antibodies’ have since been tested in a variety of settings as treatments for COVID-19.

Vir and GSK’s antibody, called VIR-7831, was first isolated in 2003 from someone recovering from severe acute respiratory syndrome (SARS), which is caused by a similar coronavirus. The antibody was later found to bind to the SARS-CoV-2 ‘spike’ protein, too.

The companies also announced that in laboratory studies[1], VIR-7831 bound to SARS-CoV-2 variants — including the fast-spreading 501Y.V2 variant (also called B.1.351) first identified in South Africa. They attributed the resilience of the antibody to its target: a particular region of the spike protein that does not tend to accumulate mutations.

Low uptake

VIR-7831 joins a list of monoclonal antibodies that have been tested against COVID-19, some of which — including Lilly’s combination — have already been authorized for use in the United States and elsewhere. But there has been relatively little uptake by

US physicians and their patients, says Angus.

One problem, he says, is that although results have been press released and submitted to the US Food and Drug Administration, companies have yet to publish data from key clinical trials in peer-reviewed journals. The drugs are also expensive and must be administered by infusion in a specialized facility, such as a hospital or outpatient-treatment centre — a difficult task when medical resources have already been stretched by a surge in cases.

Another challenge has been mixed messaging. Earlier in the pandemic, some key clinical trials involving people who had been hospitalized with COVID-19 found no benefit from monoclonal antibodies. Many researchers had anticipated that result: monoclonal-antibody therapy is expected to work best early in disease, and the late-stage symptoms of severe COVID-19 are sometimes driven more by the immune system itself than by the virus.

Even so, those clinical-trial failures created a narrative that competed with positive results in studies of milder infections, says Angus, fuelling scepticism. “People would say, ‘But I thought it didn’t work,’” he says. “It’s totally getting in the way.”

And although studies in mild infections have shown promise, they are too small to allow researchers to draw definitive conclusions, says Saye Khoo, a pharmacologist at the University of Liverpool, UK, who is leading the UK AGILE Coronavirus Drug Testing Initiative. Only a small fraction of people with mild COVID-19 will progress to severe disease, meaning that although the trials have enrolled hundreds of participants, the number of those who were hospitalized or died was low.

But it will be a long wait until everyone is vaccinated, and monoclonal antibodies could provide an important bridge between vaccines and the treatments that have been found for people who are hospitalized, says Jens Lundgren, an infectious-disease physician at the University of Copenhagen and Rigshospitalet. “It is not a replacement for vaccines, but it is a plan B,” he says, adding that the drugs could be particularly important for those who cannot mount an immune response to vaccination.

The speed with which these monoclonal antibodies were developed holds a lesson for future pandemics, says Khoo. “These compounds are without a doubt exciting,” he says. “We shouldn’t forget this, because there will be other pandemics coming to us. This has been a real lesson in how to be prepared.”

doi: https://doi.org/10.1038/d41586-021-00650-7

References

1. Cathcart, A. L. et al. Preprint at bioRxiv https://doi.org/10.1101/2021.03.09.434607 (2021).

http://bit.ly/3bMcw2l

You are not a cat, but a cat could someday help treat your chronic kidney disease

Veterinary regenerative medicine can unlock doors to human disease

Winston-Salem, NC - The Wake Forest Institute for Regenerative Medicine is investigating how cats with chronic kidney disease could someday help inform treatment for humans.

In humans, treatment for chronic kidney disease -- a condition in which the kidneys are damaged and cannot filter blood as well as they should -- focuses on slowing the progression of the organ damage. The condition can progress to end-stage kidney failure, which is fatal without dialysis or a kidney transplant. An estimated 37 million people in the US suffer from chronic kidney disease, according to the Centers for Disease Control.

The American Veterinary Medical Association estimates there are about 58 million cats in the United States. Chronic kidney disease affects 30-50% of cats age 15 years or older. The fibrosis or scarring that occurs as a result of the disease is a common final pathway for kidney disease in both animals and people. For cats,

end-stage kidney disease has no effective cure.

In a new study published online by *Frontiers in Veterinary Science* in the Veterinary Regenerative Medicine platform, the WFIRM research team set out to test the effects of a cell-derived molecular therapy to treat kidney fibrosis in cats. Regenerative therapies using stem cells and vascular fractions have been tested, but the collection of cells or cell fractions is expensive, time consuming, and requires advanced cell processing capabilities not available in most veterinary general practices.

Alternatively, "The use of cell-based molecules to treat kidney fibrosis may be a promising approach," said lead author Julie Bennington, DVM, a WFIRM research fellow and PhD candidate. "Current treatments include pharmaceutical therapies and dietary management to slow disease progression and increase longevity, and alternatives are needed."

In this study, authors used a cell-signaling chemokine -- CXCL12 -- that is produced by cells and stimulates tissue regeneration. Recombinant human CXCL12 is commercially available, inexpensive, and has been shown to reduce fibrosis in rodent models of chronic kidney disease.

The goal of this study was to test the safety, feasibility, and efficacy of ultrasound-guided intra-renal CXCL12 injection in cats with chronic kidney fibrosis, first in a preclinical cat model, and, then in a pilot study in cats that may have early kidney disease.

"Results of these studies together show that intra-renal injection of CXCL12 may be a potential new therapy to treat early kidney disease in cats with a capability for widespread use," said co-author Koudy Williams, DVM, also of WFIRM. "Further clinical evaluations are needed."

Piedmont Animal Health, the company that funded the research, is preparing to set up a clinical pilot study in the US, and Bennington will serve as a consultant.

WFIRM Director Anthony Atala, MD, said this research is a good example of "how a condition like chronic kidney disease, common to both dogs and cats, can be studied and potentially applied to the disease in humans."

Additional co-authors include: Shannon Lankford, Renata Magalhaes, Douglas Shankle, all of WFIRM; Jason Fanning of Wake Forest University; Gopal Badlani, MD, of Wake Forest Baptist Health Urology; and Cucu Kartini, Irma Suparto, Winda Kusumawardhani, M A. Putra, and Silmi Mariya, all of Indonesia.

http://bit.ly/30FCkGY

New Ebola outbreak likely sparked by a person infected 5 years ago

Virus causing the new outbreak barely differs from the strain seen 5 to 6 years ago

By Kai Kupferschmidt

An Ebola outbreak in Guinea that has so far sickened at least 18 people and killed nine has stirred difficult memories of the devastating epidemic that struck the West African country between 2013 and 2016, along with neighboring Liberia and Sierra Leone, leaving more than 11,000 people dead.

But it may not just be the trauma that has persisted. The virus causing the new outbreak barely differs from the strain seen 5 to 6 years ago, genomic analyses by three independent research groups have shown, suggesting the virus lay dormant in a survivor of the epidemic all that time. “This is pretty shocking,” says virologist Angela Rasmussen of Georgetown University. “Ebolaviruses aren’t herpesviruses”—which are known to cause long-lasting infections—“and generally RNA viruses don’t just hang around not replicating at all.”

Scientists knew the Ebola virus can persist for a long time in the human body; a resurgence in Guinea in 2016 originated from a survivor who shed the virus in his semen more than 500 days after

his infection and infected a partner through sexual intercourse. “But to have a new outbreak start from latent infection 5 years after the end of an epidemic is scary and new,” says Eric Delaporte, an infectious disease physician at the University of Montpellier who has studied Ebola survivors and is a member of one of the three teams. Outbreaks ignited by Ebola survivors are still very rare, Delaporte says, but the finding raises tricky questions about how to prevent them without further stigmatizing Ebola survivors.

The current outbreak in Guinea was detected after a 51-year-old nurse who had originally been diagnosed with typhoid and malaria died in late January. Several people who attended her funeral fell ill, including members of her family and a traditional healer who had treated her, and four of them died. Researchers suspected Ebola might have caused all of the deaths, and in early February they discovered the virus in the blood of the nurse’s husband. An Ebola outbreak was officially declared on 13 February, with the nurse the likely index case.

The Guinea Center for Research and Training in Infectious Diseases (CERFIG) and the country’s National Hemorrhagic Fever Laboratory have each read viral genomes from four patients; researchers at the Pasteur Institute in Dakar, Senegal, sequenced two genomes. In three postings today on the website virological.org, the groups agree the outbreak was caused by the Makona strain of a species called *Zaire ebolavirus*, just like the past epidemic. A phylogenetic tree shows the new virus falls between virus samples from the 2013–16 epidemic.

Until recently, scientists assumed Ebola epidemics start when a virus jumps species, from an animal host to humans. Theoretically, that could have happened in Guinea, says virologist Stephan Günther of the Bernhard Nocht Institute for Tropical Medicine, who worked with one of the three teams. But given the similarity between viruses from the epidemic and the new ones, “It must be incredibly unlikely.”

Outside scientists agree but say it hasn’t been proved that Ebola lay dormant in one person for 5 years. “From the tree, you’d conclude that it is a virus that persisted in some way in the area, and sure, most likely in a survivor,” says Dan Bausch, a veteran of several Ebola outbreaks who leads the United Kingdom’s Public Health Rapid Support Team. But it is hard to rule out scenarios such as a small, unrecognized chain of human to human transmission, Bausch adds: “For example, a 2014 survivor infects his wife a few years after recovery, who infects another male, who survives and carries virus for a few years, then infecting another women, who is then seen by a nurse who dies”—the index case in the new outbreak.

The nurse was not known to be a survivor herself, but she could have had contact with a survivor privately or through her job, or she might have been infected herself years ago with few symptoms. “Figuring out what exactly happened is one of the biggest questions now,” Bausch says.

Another ongoing outbreak of Ebola in North Kivu, in the Democratic Republic of the Congo, was also started by transmission from someone infected during a previous outbreak, Delaporte notes. (The survivor had tested negative for Ebola twice after his illness in 2020.) Taken together, that suggests humans are now as likely to be the source of a new outbreak of Ebola as wildlife, he says. “This is clearly a new paradigm for how these outbreaks start.” Outbreaks sparked by survivors may even become more likely, now that increasing mobility and other factors have caused each eruption of Ebola to become bigger, resulting in more survivors, says Fabian Leendertz, a wildlife veterinarian who was involved in the sequencing.

The cases raise important new research questions, Bausch says: “How do we need to change our response to escape from the cycle of outbreak-response-reintroduction-outbreak?” he asks. “Can we

use new therapeutics to clear virus from survivors?"

But the most immediate question is what these results mean for Ebola survivors, who face a lot of hardship already. Many have not only lost friends and family to the virus, but also struggle with long-term aftereffects, such as muscle pains and eye problems. In a study published in February, Delaporte found that about half of more than 800 Ebola survivors in Guinea still reported symptoms 2 years after their illness, and one-quarter after 4 years.

On top of this, survivors have faced intense stigmatization. Many conspiracy theories swirled in the aftermath of the epidemic, including the claim that survivors had sold family members to international organizations to save themselves, says Frederic Le Marcis, a social anthropologist at the École Normale Supérieure of Lyon and the French Research Institute for Development, who is working in Guinea. One man, he says, was the only one to survive out of 11 family members and when he came back, no one wanted to work with him. "He was seen as someone untrustworthy." News that a survivor likely touched off the current outbreak could cause further problems for survivors, Le Marcis says: "Will they be highlighted as a source of danger? Will they be chased out of their own families and communities?"

Alpha Keita, a virologist who led the sequencing work at CERFIG, worries about stigmatization and even violence against survivors have occupied him since he first got the surprising results a week ago. One important message to the public should be that some people infected with Ebola show few symptoms, meaning people may be survivors without knowing it. "So don't stigmatize Ebola survivors—you don't know that you are not a survivor yourself," Keita says.

Bausch calls for an educational campaign explaining that unprotected sex with an Ebola survivor may pose a risk, but casual contacts such as shaking hands and working together do not. And although there needs to be some medical monitoring of survivors, it cannot just be about testing them for Ebola virus, he says. "We need to recognize and assist with all the other challenges, physical, mental, and social, that survivors and their families face." The key, Bausch says, is to "not just treat survivors as some hot potato risk of starting another outbreak." It also presents a challenge to the country's health care system if every patient with fever and diarrhea has to be a considered potential Ebola case, Le Marcis says.

Fortunately, Ebola vaccines and treatments have become available in recent years. Already, several thousand contacts of the new Ebola patients, and contacts of these contacts, have been vaccinated. Health care workers are being immunized as well. Vaccinating survivors might even help clear latent infections, Rasmussen says. And the fact that viral samples were sequenced in Guinea this time around shows the country's scientific capabilities have improved, Delaporte says: "Seven years ago, when the epidemic started, there was no infrastructure in Guinea to be able to do this."

http://bit.ly/30FCCh2

Natural "brake" against malignant neuroblastoma

A factor that turns malignant tumors into benign ones?

That is exactly what scientists at St. Anna Children's Cancer Research Institute have discovered. Together with colleagues from the Medical University of Vienna and the University of Vienna (Faculty of Chemistry), they studied tumors of the peripheral nervous system in children, namely neuroblastomas. The scientists discovered that the uncontrolled growth of benign neuroblastomas is stopped by a signal molecule produced by Schwann cells present within these tumors. This natural "brake" also works on malignant neuroblastoma cultures. The study, published in the journal *Nature Communications*, describes for the first time the function of this signal molecule - not only in tumors, but also in injured nerve fibers. What sounds contradictory at first glance, namely firing a tumor

with a growth factor, makes sense in neuroblastoma. Neuroblastoma is a tumor of the peripheral nervous system and the most common solid cancer in early childhood. In contrast to malignant neuroblastomas, benign neuroblastomas contain, next to tumor cells, many "Schwann cells". These cells normally protect and repair nerve cells. The results of the now published study indicate that Schwann cells in neuroblastoma stimulate tumor cells to mature, thereby halting their unchecked growth.

A cell that stops tumor growth...

To accomplish this, Schwann cells produce, among other factors, a signaling molecule called epidermal growth factor like 8 (EGFL8). The research team demonstrates that EGFL8 stimulates the differentiation, or maturation, of neuroblastoma cells. "Until recently, we only knew that this protein existed, but its function was not known. We now for the first time know where EGFL8 is produced and how it acts," explains study author Sabine Taschner-Mandl, PhD, head of the Tumor Biology Group at St. Anna Children's Cancer Research Institute. Furthermore, the study results show that high levels of EGFL8 was associated with better survival rates in neuroblastoma patients.

"In cell cultures, we have demonstrated that Schwann cells as well as their secreted signaling molecules exert anti-tumor effects, even in aggressive neuroblastoma cells. Thus, we are able to exploit a process that occurs naturally in benign neuroblastomas to stop the malignant ones," Sabine Taschner-Mandl and her colleague Tamara Weiss, PhD, from the Medical University of Vienna, explain. In addition to EGFL8, other, yet uncharacterized Schwann cell molecules could also provide targets for cancer therapies in the future.

However, the effects of Schwann cells are presumably much more extensive: the research team is currently investigating how Schwann cells manipulate immune cells in their environment.

...and promotes the healing of injured nerve fibers

The present study provides another significant finding: Schwann cells in benign neuroblastomas have a similar cellular status to those Schwann cells that support the healing of injured peripheral nerves. Direct comparison revealed that Schwann cells in the tumor express certain repair-associated genes and show specific repair functions. "It is amazing that we have discovered a signaling molecule that plays a role in both tumor development of benign neuroblastomas and regeneration of injured nerves. Since EGFL8 stimulates the formation of nerve cell extensions, it could be of great importance for the treatment of injured nerve fibers", says Tamara Weiss.

Prospective application in aggressive tumors

It is conceivable that EGFL8 and other factors produced by Schwann cells could be applied in the treatment of nerve damage as well as aggressive neuroblastoma. "Using phosphoproteomics, we were able to decipher which signaling pathways are activated by EGFL8 in neuroblastoma cells. There are major differences compared to cells that have not been stimulated with EGFL8," Sabine Taschner-Mandl says. In addition to EGFL8, these downstream signaling pathways also represent potential targets for future treatments. "There is still a long way to go before these findings ultimately reach the patient. But we have now laid the foundation for taking the next steps."

Publication

Schwann cell plasticity regulates neuroblastic tumor cell differentiation via epidermal growth factor like protein 8

Tamara Weiss#, Sabine Taschner-Mandl#, , Lukas Janker, Andrea Bileck, Fikret Rifatbegovic, Florian Kromp, Helena Sorger, Maximilian O. Kauer, Christian Frech, Reinhard Windhager, Christopher Gerner, Peter F. Ambros, Inge M Ambros*

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http://bit.ly/3tjrzGK

Research discovers malaria devastating humans far earlier than expected

Changes discovered in bones have helped provide new answers about malaria.

New bioarchaeological research shows malaria has threatened human communities for more than 7,000 years, earlier than when the onset of farming was thought to have sparked its devastating arrival.

Lead author Dr. Melandri Vlok from the Department of Anatomy, University of Otago, says this ground-breaking research, published today in *Scientific Reports*, changes the entire understanding of the relationship humans have had with malaria, still one of the deadliest diseases in the world.

"Until now we've believed malaria became a global threat to humans when we turned to farming, but our research shows in at least Southeast Asia this disease was a threat to human groups well before that. "This research providing a new cornerstone of malaria's evolution with humans is a great achievement by the entire team," Dr. Vlok says.

Still a serious health issue, as recently as 2019 the World Health Organization reported an estimated 229 million cases of malaria around the world, with 67 percent of malaria deaths in children under the age of five years.

While malaria is invisible in the archaeological record, the disease has changed the evolutionary history of human groups causing consequences visible in prehistoric skeletons. Certain genetic mutations can lead to the inheritance of Thalassemia, a devasting genetic disease that in its milder form provides some protection against malaria.

Deep in humanity's past, the genes for malaria became more common in Southeast Asia and the Pacific where it remains a threat, but up until now the origin of malaria has not been pinpointed. This research has identified thalassemia in an ancient hunter-gatherer archaeological site from Vietnam dated to approximately 7,000 years ago, thousands of years before the transition to farming in the region.

In some parts of the world, slashing and burning in agricultural practice would have created pools of stagnant water attracting mosquitos carrying malaria, but in Southeast Asia these mosquitos are common forest dwellers exposing humans to the disease long before agriculture was adopted.

The study Forager and farmer evolutionary adaptations to malaria evidenced by 7000 years of thalassemia in Southeast Asia is a result of combined efforts from years of investigation by a team of researchers led by Professor Marc Oxenham (currently at the University of Aberdeen) and including researchers from University of Otago, the Australian National University (ANU), James Cook University, Vietnam Institute of Archaeology and Sapporo Medical University.

The research is the first of its kind to use microscopic techniques to investigate changes in bone tissue to identify thalassemia. In 2015, Professor Hallie Buckley from the University of Otago noticed changes in the bone of hunter-gatherers that made her suspicious that thalassemia might be the cause, but the bones were too poorly preserved to be certain. Professor Buckley called in microscopic bone expert Dr. Justyna Miszkiewicz of ANU to investigate. Under the microscope, the ancient samples from Vietnam showed evidence for abnormal porosity mirroring modern-day bone loss complications in thalassemic patients.

At the same time, Dr. Vlok, completing her doctoral research in

Vietnam, found changes in the bones excavated in a 4000-year-old agricultural site in the same region as the 7000-year-old hunter-gatherer site. The combined research suggests a long history of evolutionary changes to malaria in Southeast Asia which continues today.

"A lot of pieces came together, then there was a startling moment of realization that malaria was present and problematic for these people all those years ago, and a lot earlier than we've known about until now," Dr. Vlok adds.

More information: *Melandri Vlok et al. Forager and farmer evolutionary adaptations to malaria evidenced by 7000 years of thalassemia in Southeast Asia, Scientific Reports (2021). DOI: 10.1038/s41598-021-83978-4*

http://bit.ly/3vrGWOY

Volcanic Lands Warm Before Eruptions

Satellite data have revealed that ground radiant temperatures around volcanoes rose in the years leading up to eruptions. The observation may help in forecasting future volcanic activity.

By Ashleigh Papp

Volcanic eruptions big and small can be difficult to see coming. Like meteorologists forecasting weather, volcanologists today combine information from as many methodologies as possible to predict eruptions more accurately. Using thermal, gas emissions, and seismic data, among other resources, scientists study preeruption clues to understand explosive volcanic behavior better.

Társilo Girona, a volcanologist at the Geophysical Institute of the University of Alaska Fairbanks, and his colleagues have, for example, spent the past 3.5 years analyzing ground radiant temperatures around various volcanoes before eruptions. “Of the eruptions we studied, 90% were not forecasted,” said Girona. Now in a study in *Nature Geoscience*, Girona and his team report that ground temperatures around the volcanoes increased notably in the years leading up to eruptions, a finding that could inform efforts to monitor volcanoes and forecast eruptions.

Satellite Data Reveal Increased Ground Temperatures

In 2016, Girona learned of research showing that the temperatures of gas emissions collected at the ground surface near multiple volcanoes were nearly the same as the ambient air temperature, whereas gases contained in deep magma are thought to be several tens of to a thousand times hotter. “That means that during its trip up to the surface, the gas is losing heat,” Girona said. Girona wanted to know where the extra heat was going—hypothesizing that it was absorbed by the surrounding subsurface rock.

To test his idea, Girona’s team investigated five volcanoes that erupted within the past 20 years: Redoubt, Alaska (2009); Calbuco, Chile (2015); Pico do Fogo, Cape Verde (2014); Ontake, Japan (2007 and 2014); and Ruapehu, New Zealand (2006 and 2007).

“Each location experienced a different type of eruptive behavior,” said Girona, who selected the eruptions to represent a broad range of volcanic behavior so that information from this analysis could be applied to many other volcanoes. Some of the eruptions were magmatic (e.g., Redoubt, Calbuco, and Pico do Fogo), whereas others were phreatic (e.g., Ontake and Ruapehu). Also included were events of varying eruptive magnitudes and volcanoes with different formation histories and at different latitudes.

Gathering ground temperature data from active volcanoes is simply too dangerous, “so we went to space. ”Gathering ground temperature data from active volcanoes is simply too dangerous, “so we went to space,” Girona said. He and his colleagues accessed nearly 2 decades’ worth of thermal radiance data collected by the Moderate Resolution Imaging Spectroradiometers on NASA’s Terra and Aqua satellites and created algorithms to convert these data into temperatures for each location and time frame for the eruptions. They then compared differences between ground radiant temperatures at the top and upper flanks of the volcano to temperatures in the area around the volcano, which yielded long-

term radiant temperature anomalies leading up to each eruption.

"We saw a well-defined increase of the median anomaly" in each case, Girona said. He and his colleagues found that the radiant temperature at all five of the volcanoes increased by up to about 1°C with respect to their surroundings between 2 and 7 years before an eruption.

Subtle Changes, Major Impacts

In the case of Calbuco's destructive eruption in 2015, Girona and his team found that the median radiant temperature increased by about 0.3°C in comparison to the surrounding ground nearly 7 years before the event. It's a subtle change in temperature, but in volcanoes, subtleties can have large impacts. A 1°C increase in temperature can cause pressure changes in the shallow ground surrounding a volcano of roughly 1 megapascal, Girona said. "These are critical pressure changes for a volcano."

To understand how the temperature of land surrounding a volcano may be related to eruptive events, we must look underground. Before any eruption, the shallowest magma chamber beneath a volcano, usually about 10 kilometers below the surface, begins to warm up. The molten rock, crystals, and gas in these sorts of reservoirs are typically between 700°C and 1,200°C.

Warming magma releases huge amounts of water vapor, carbon dioxide, and sulfur dioxide gas that gradually rise through the subsurface, transferring heat upward as well, which further vaporizes overlying groundwater. As much of this water vapor then condenses again as it cools near the ground surface, it releases latent heat that raises the temperature of the ground near a volcano. This process, according to Girona and his colleagues, may explain the diffuse heating they've observed before eruptions.

A Tool for Volcanic Monitoring

"Girona's research has shown that satellite data can be used to detect a volcano heating up years before an eruption—we didn't know that before."

"To help get people out of harm's way, we need to have an earlier heads-up of when volcanoes become more active," said Florian Schwandner, deputy chief of the NASA Ames Earth Science Division. Volcanologists have been working for years to uncover clues of preeruptive behavior. "Girona's research has shown that satellite data can be used to detect a volcano heating up years before an eruption—we didn't know that before," Schwandner said.

The current research is limited to volcanoes with infrequent, large eruptions, but Girona plans to apply what his team has learned to more types of volcanoes, including those with shorter and more frequent eruptions.

The most direct application of this research, according to Girona, is in the potential development of a new method to detect volcanic unrest. He's hopeful that monitoring ground temperatures around volcanoes can be added to the current lineup of predictive tools. "To truly understand volcanoes," Girona said, "we have to have as many tools as possible."

Citation: *Papp, A. (2021), Volcanic lands warm before eruptions, Eos, 102, https://doi.org/10.1029/2021EO155726. Published on 12 March 2021.*

http://wb.md/3eEwldS

To Extract More Doses per Vial, Vaccinators Put Squeeze on FDA to Relax Vaccine Handling Advice

Vaccinators are discovering ways to suck the final drops out of each vaccine vial

Arthur Allen

President Joe Biden has promised enough covid vaccine to immunize every willing adult by June 1. But right now, the gap between supply and demand is so dramatic that vaccinators are discovering ways to suck the final drops out of each vaccine vial — if federal regulators will let them.

Pharmacists involved in the covid vaccination drive say it's

common to have half a dose left in a Pfizer vial after five or even six doses have been administered — and to have half a dose left after 10 doses have been drawn out of a Moderna vial. Combining two half-doses could increase vaccinations by thousands at a time when 2 million or so doses are being administered every day in the country.

So, they want to use a single hypodermic needle to withdraw leftover vaccine from two vials from which all full doses already have been removed. The American Society of Health-System Pharmacists asked the Food and Drug Administration consider granting permission to do so in a recent letter. The governors of Colorado and Oregon also have sought permission to allow their pharmacists to pool covid vaccine vials.

Federal health regulators, however, have long opposed the reuse of drug vials because of the risk of introducing a bacterial contaminant. From 1998 to 2014 more than 50 outbreaks of viral or bacterial disease were reported as a result of unsafe injection practices, including injecting multiple patients with a drug from the same vial. The FDA wouldn't comment on the pharmacists' letter but restated to KHN its current policy that "doses not be pooled from different vaccine vials, especially for coronavirus vaccines, which are not formulated with a preservative." On its website, the Centers for Disease Control and Prevention explicitly tells vaccinators to discard vials "when there is not enough vaccine to obtain a complete dose. Do NOT combine residual vaccine from multiple vials to obtain a dose."

"It's a recipe for disaster," said Ann Marie Pettis, president of the Association for Professionals in Infection Control and Epidemiology. There is always a tiny chance that one of the two vials has previously been contaminated, which would contaminate a shot that combined their contents, she said. Spokespeople for both Moderna and Pfizer said excess portions of their vaccines must be discarded and never pooled. Johnson & Johnson had no comment on the issue.

Before the covid vaccination program, public health officials generally frowned on giving multiple patients doses of medicine from a single vial, unless it contained an antibacterial preservative. Most children's vaccines, for example, have been shipped and stored in syringes or single-dose vials since 2001, when drug companies stopped using a preservative containing traces of mercury in some shots.

Rajesh Gupta, a biologics consultant who set up a sterility testing lab while serving at the FDA's Center for Biologics Evaluation and Research from 2006 to 2013, sees little risk in the covid vaccination process, or even in using a single needle to combine vaccine from two vials.

The covid vaccines are being used so quickly after removal from cold storage that there's no danger of contamination, he said. "I can say with some degree of confidence that it's scientifically sound," if vaccinators carefully wipe the rubber stopper atop the vial with disinfectant before each penetration with a syringe, he said.

While their plea for combining vial contents may fall on deaf ears at the FDA, pharmacists already are taking many other steps to maximize the yield of the mRNA vaccines, which have quite finicky shipment, handling and administration requirements.

Documents leaked through a cyberattack on the European drug regulatory agency suggest that Pfizer has had difficulty assuring the quality of the mRNA in its vaccine. The company said in a response that all the vaccine doses it has put on the market had been "double tested to ensure compliance" with regulatory specifications.

Michael Hogue, president of the American Pharmacists Association and dean of the Loma Linda University School of Pharmacy in California, runs a clinic at a university gymnasium that has been administering up to 10,000 vaccines each week since Jan. 28. It's

nowhere near as simple as administering flu shots at a pharmacy, he said. "The planning and procedures for these mRNA vaccines [made by Pfizer-BioNTech and Moderna] require a tremendous amount of focus," said Hogue. "You have to pay close attention to what's going on in the moment."

The Pfizer vaccine, which until recently was always stored in dry ice, is especially challenging. After Pfizer vials are removed from a freezer and thawed, saline solution is squirted into each vial. If the syringe preparer doesn't withdraw air from the vial after adding the saline, vaccine will shoot out. After adding the solution, "you take the vial between thumb and forefinger and make a rainbow sweeping motion 10 times gently to mix the liquids together," Hogue said. Shaking the vaccine could render it ineffective.

Each Pfizer vaccination contains just a bead of liquid — about 1/16th of a teaspoon — and pharmacists must use tiny syringes in which air bubbles tend to form. But they can't tap on the syringe to get the bubble out, because that, too, could damage the vaccine, Hogue said.

To get six doses out of the Pfizer vials requires a type of plunger that pushes the last trace of vaccine out of the syringe. But about 15% of the syringes the federal government has been shipping to Loma Linda have larger needles that leave a bit of vaccine in the syringe, making it impossible to extract all six doses, he said. So, Loma Linda has been purchasing its own syringes to replace the inadequate ones.

U.S. Pharmacopeia, a nonprofit agency that issues standards for use of medical products, issued an 11-page guide on how to store, handle and administer the covid vaccines. Among other things, it urges that vaccine sites set up clean rooms — separate from the areas where vaccines are being administered — to prepare the syringes, said Farah Towfic, director of CEO operations for USP.

"That way we don't have clients breathing on it," not to mention the distraction of greeting old acquaintances who are bubbling over with enthusiasm about getting vaccinated, said Patricia Slattum, a retired Virginia Commonwealth University pharmacy school professor who has been volunteering at a mass vaccination site in Richmond, Virginia. "There's a lot of love to go around in there."

Another technique is to inject each needle into a different spot on the rubber vial stopper. If the syringe goes into the same location over and over, it can create a big hole that causes leakage. This tip is especially important now that Moderna is in talks with FDA to include up to 15 doses of vaccine in each vial, meaning 15 punctures of the stopper, noted Anna Legreid Dopp, director of clinical guidelines and quality improvement at the American Society of Health-System Pharmacists.

"To draw up the vaccine, you stick a needle through the rubber stopper, then turn the vial upside down," said Slattum. "If you stick it in the same place, drops will leak down the needle. So there's an art to not losing vaccine."

Slattum hopes the FDA will consider allowing vaccinators to draw the leftover vaccine from two vials. "We who are doing this work all feel this pressure, that our doing it well is one of the ways we're going to get out of this pandemic," said Slattum. "You just don't want to waste any vaccine!"

http://wb.md/3eQRnGj

First Pill for COVID-19 Could Be Ready by Year's End

New pills to treat patients with COVID-19 are currently in midstage clinical trials and, if successful, could be ready by the end of the year.

Marcia Frellick

Only one treatment — remdesivir (Veklury) — has been fully approved by the US Food and Drug Administration (FDA) for patients in the hospital and it must be administered intravenously.

Hopes for a day when patients with COVID-19 can take a pill to rid

their bodies of the virus got a boost over the weekend when early trial results were presented at a medical conference.

Interim phase 2 results for the oral experimental COVID-19 drug molnupiravir, designed to do for patients with COVID-19 what oseltamivir (Tamiflu) can do for patients with the flu, were presented at the Conference on Retroviruses and Opportunistic Infections (CROI) 2021 Annual Meeting, as reported by *Medscape Medical News*.

In the small study, the pill significantly reduced infectious virus in patients who were symptomatic and had tested positive for COVID-19 during the previous 4 days but were not hospitalized. After 5 days of treatment, no participants who received molnupiravir had detectable virus, whereas 24% who received placebo did.

Two other oral agents are being developed by RedHill Biopharma: one for severe COVID-19 infection for hospitalized patients, and one for patients at home with mild infection.

The first, opaganib (Yeliva), proceeded to a phase 2/3 global trial for hospitalized patients after the company announced topline safety and efficacy data in December. In phase 2, the drug was shown to be safe in patients requiring oxygen and effectively reduced the need for oxygen by the end of the treatment period.

A key feature is that it is both an antiviral and an anti-inflammatory, Gilead Raday, RedHill's chief operating officer, told *Medscape Medical News*. Data are expected midyear on its performance in 464 patients. The drug is being tested on top of remdesivir or in addition to dexamethasone.

The second, upamostat (RHB-107), is currently undergoing a phase 2/3 trial in the United States and is being investigated for use in nonhospitalized COVID-19 patients. "I would expect data to be available in the second half of this year," Raday said.

Upamostat is a novel serine protease inhibitor expected to be effective against emerging variants because it targets human cell factors involved in viral entry, according to the company.

Other drugs are being investigated in trials that are in earlier stages.

Urgent Need for Oral Agents

Infectious disease specialists are watching the move toward a COVID-19 pill enthusiastically. "We badly need an oral treatment option for COVID," said Sarah Doernberg, MD, an infectious disease specialist from the University of California, San Francisco.

"It's a real gap in our armamentarium for COVID in outpatient treatment, which is where most who contract COVID-19 will seek care," she told *Medscape Medical News*.

Although some studies have shown the benefit of monoclonal antibodies for prevention and early treatment, there are major logistical issues because all the current options require IV administration, she explained.

"If we had a pill to treat early COVID, especially in high-risk patients, it would fill a gap," she said, noting that a pill could help people get better faster and prevent hospital stays.

Studies of molnupiravir suggest that it decreases viral shedding in the first few days after COVID infection, Doernberg reported.

There is excitement around the drug, but it will be important to see whether the results translate into fewer people requiring hospital admission and whether people feel better faster.

"I want to see the clinical data," Doernberg said. She will also be watching for the upamostat and opaganib results in the coming weeks. "If these drugs are successful, I think it's possible we could use them — maybe under an emergency use authorization — this year," she said. Once an antiviral pill is a viable option for COVID-19 treatment, questions will arise about their use, she said.

One question is whether patients who are getting remdesivir in the hospital and are ready to leave after 5 days should continue treatment with antiviral pills at home.

Another is whether the pills — if they are shown to be effective —

will be helpful for COVID postexposure. That use would be important for people who do not have COVID-19 but who are in close contact with someone who does, such as a member of their household. "We have that model," Doernberg said. "We know that oseltamivir can be used for postexposure prophylaxis and can help to prevent development of clinical disease."

But she cautioned that a challenge with COVID is that people are contagious very early. A pill would need to come with the ability to test for COVID-19 early and get patients linked to care immediately. "Those are not small challenges," she said.

Vaccines Alone Won't End the COVID Threat

Treatments are part of the "belt-and-suspenders" approach, along with vaccines to combat COVID-19, Doernberg said. "We're not going to eradicate COVID," she said. "We're still going to need treatments for people who either don't respond to the vaccine or haven't gotten the vaccine or developed disease despite the vaccine."

Oral formulations are desperately needed, agreed Kenneth Johnson, PhD, professor of molecular biosciences at the University of Texas at Austin. Right now, remdesivir treatments involve patients being hooked up to an IV for 30 to 120 minutes each day for 5 days. And the cost of a 5-day course of remdesivir ranges from $2340 to $3120 in the United States. "We're hoping we can come up with something that is a little bit easier to administer, and without as many concerns for toxic side effects," he said.

Johnson's team at UT-Austin recently made a key discovery about the way remdesivir stops the replication of viral RNA.

The understanding of where the virus starts to replicate in the infection chain of events and how and where it reacts with remdesivir might lead to the development of better, more concentrated pill forms of antivirals in the future, with fewer toxicities, he said.

The team used a lab dish to recreate the step-by-step process that occurs when a patient who is infected with SARS-CoV-2 receives remdesivir.

The discovery was published online in *Molecular Cell* in January, and will be printed in the April issue of the journal.

The discovery won't lead to an effective COVID-19 pill for our current crisis, but will be important for the next generation of drugs needed to deal with future coronaviruses, Johnson explained.

And there will be other coronaviruses, he said, noting that this one is the third in 20 years to jump from animals to humans. "It's just a matter of time," he said.

http://bbc.in/3bJPGIG

Scientists unlock mysteries of world's oldest 'computer'

A 2,000-year-old device often referred to as the world's oldest "computer" has been recreated by scientists trying to understand how it worked.

The Antikythera Mechanism has baffled experts since it was found on a Roman-era shipwreck in Greece in 1901. The hand-powered Ancient Greek device is thought to have been used to predict eclipses and other astronomical events.

Scientists used computer modelling to recreate the device's complex gear system **Prof Tony Freeth / UCL**

But only a third of the device survived, leaving researchers pondering how it worked and what it looked like. The back of the mechanism was solved by earlier studies, but the nature of its complex gearing system at the front has remained a mystery.

Scientists from University College London (UCL) believe they have finally cracked the puzzle using 3D computer modelling. They

have recreated the entire front panel, and now hope to build a full-scale replica of the Antikythera using modern materials. On Friday, a paper published in Scientific Reports revealed a new display of the gearing system that showed its fine details and complex parts.

"The Sun, Moon and planets are displayed in an impressive tour de force of ancient Greek brilliance," the paper's lead author, Professor Tony Freeth, said. "Ours is the first model that conforms to all the physical evidence and matches the descriptions in the scientific inscriptions engraved on the mechanism itself," he added.

The mechanism has been described as an astronomical calculator as well as the world's first analogue computer. It is made of bronze and includes dozens of gears. The back cover features a description of the cosmos display, which shows the motion of the five planets that were known at the time the device was built.

But only 82 fragments - amounting to around a third of the device - survived, This meant scientists have had to piece together the full picture using X-Ray data and an Ancient Greek mathematical method.

http://bit.ly/3qN1Pki

Is autism the legacy of humans evolving the ability to innovate?

A new book argues that humans evolved innovation, and genes for autism, more than 70,000 years ago

If you find yourself pondering the marvel of aerodynamics when you fly on a plane, or if you concentrate on the structure of music as it plays, rather than simply listening, you may score high on measures of "systemization," according to University of Cambridge neuroscientist Simon Baron-Cohen.

And if so this may reflect abilities that he thinks may have first evolved in humans between 70,000 and 100,000 years ago, when our human ancestors took a cognitive leap forward. This new capacity enabled them to analyze and understand patterns in the world that would, among other things, facilitate the invention of complex tools from bows to musical instruments.

In Baron-Cohen's new book, he argues that humans became "the scientific and technological masters of our planet" because of our brain's "systemizing mechanism." Also, some individuals — particularly those with Autism Spectrum Disorder, are the "hyper-systemizers" of our world. He suggests this should cause us to re-evaluate the capacities and strengths of people with autism.

You joked with your editor that your book could be the shortest book in the universe, just three words long. What are those three words and why are they central to driving human inventiveness?

Yes, the three words are *if*, *and*, and *then*. I think that these three words describe how humans, Homo sapiens, are the only animal that can reason and can reason in order to invent. I mean, we're talking in the time of COVID and we could say *if* the death rate is high *and* we do nothing, *then* the death rate will be even higher.

But *if* the death rate is high *and* we impose lockdown, *then* the death rate will decrease. So lockdown, as an invention happens to be like a public health invention, but it shows the reasoning of how humans, how modern Homo sapiens think in order to invent.

OK, so you're saying *if* I do this, *then* that will happen. But how does this systemizing mind come into that?

What I argue in my book is that between 70,000 and 100,000 years ago, there was a change in the human brain that this systemizing mechanism evolved. And the systemizing mechanism is what allows us to look for systems in the world or invent new systems. And a system is nothing more than these if and then regularities or patterns. So that's why I called the book *The Pattern Seekers*. Other animals don't seem to look for these special patterns, but we do.

Well, what happened back 70,000 years ago that brought about this inventiveness? What changed in the evolution of the human

brain 70,000 years ago?

We see the first bow and arrow to see *if* and *then* logic, if you like, was what allowed us to come up with a complex tool like the bow and arrow. But equally, we can look for other examples in the archaeological record, like the first musical instrument, the oldest or the earliest musical instrument that's been found is a flute made from a bone, a hollow bone from a bird. And it's dated to about 40,000 years ago.

But we can imagine the person who made it was thinking, *if* I blow down this hollow bone *and* I cover one hole, *then* I get a particular note. But *if* I blow down the hollow bone *and* uncover the hole, *then* I get a different note. So what we can see just in these simple examples, although in fact, you know, they are the tools that were being made complex. What we see is that human beings were playing with these if and then patterns.

And it led to what I call generative invention. We didn't just generate ones we could generate in multiple different spheres, whether it's music or mathematics or public health or medicine or cooking. We can invent new systems, new patterns of this kind in any sphere that we choose.

We've been inventing for a while. What's the connection then, between that kind of thinking and autism?

Autistic people love patterns, if we can generalize. And when we give them tests of this kind of reasoning, this *if* and *then* reasoning, they score higher on average than non-autistic people. And, you know, you opened this interview with some questions for the listeners that come from a measure called 'systemizing,' questions that just simply ask questions about how interested are you in a variety of systems.

And autistic people score higher on that measure compared to non-autistic people. But we also worked with the company 23andMe, so we could look at the genes that are associated with how much you like to be systemized, how interested you are in systems.

And what we found was that the genes that are associated with scoring high on systemizing overlap with the genes for autism. So that was telling us that even in our DNA, there's a link between your aptitude at systemizing and autism.

You work with people with autism. What do you think, that the idea that human invention has largely been driven by traits that we associate with autism, what could that mean for our perception of what autism actually is?

Part of the reason I wrote the book was to really change our perception of autism, because for the longest time, autism has been really just characterized as a disability, which it is, but with a focus on all the things that autistic people find difficult, what they struggle with. But we know that autism is more than just a disability, that autistic people think differently. Sometimes they have strengths.

I've suggested strengths in pattern recognition and attention to detail, being able to stay very focused on patterns and even sometimes talent in these areas. The fact that we can now see a link between those strengths in autism and human invention may change the way we look at autistic people. We might want to see them for who they are, people who think differently and have contributed to human progress.