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World's first test to accurately predict depression and bipolar disorder

University of South Australia scientists have developed the world's first test to accurately predict mood disorders in people, based on the levels of a specific protein found in the brain.

Links between low levels of mature brain-derived neurotrophic factor (mBDNF) and depression are well known but, until now, it hasn't been possible to distinguish between the three forms of the BDNF protein in blood samples.

The mature form promotes the growth of neurons and protects the brain, but the other two BDNF forms - its precursor and the prodomain of BDNF - bind to different receptors, causing nerve degeneration and inflammation.

An assay kit developed by researchers from UniSA can now precisely distinguish between these proteins, unlike other commercial kits in the market. The finding, in collaboration with the University of Adelaide and Kunming Medical University in China, has been published in a new paper in the *Journal of Psychiatric Research* led by UniSA PhD student Liying Lin.

UniSA Professor Xin-Fu Zhou, one of the researchers, says there is strong evidence to suggest that psychological stress decreases mBDNF and a lack of mBDNF causes depression.

In a study of 215 people in China, including 90 patients with clinical depression and 15 with bipolar disorder, researchers found clear links with low levels of mBDNF in their blood. The more severe the depression, the lower the mBDNF level.

Mature BDNF levels in patients not on antidepressants was also lower than patients treated with antidepressants.

Surprisingly, there was no difference in mBDNF levels between 14 people with a history of suicide attempts and the control group of 96 people.

No significant gender differences were found.

"As mature BDNF and proBDNF have different biological activities, working in opposition to each other, it is essential that we can distinguish between these two proteins and detect changes in their levels," Prof Zhou says.

"The existing commercial BDNF ELISA (enzyme-linked immunosorbent assay) kits are not specific and can cross react with each other. The kit we have developed has an accuracy rate of 80-83 per cent."

The researchers say serum mBDNF levels less than 12.4 ng/ml could be used as a cut off point to diagnose depression and bipolar disorder. "This could be an objective biomarker in addition to a clinical assessment by a doctor," Prof Zhou says.

"Growing evidence indicates that inflammation in brain cells is linked with depressive behaviours and proBDNF seems to activate the immune system. Therefore, we must separate it from mature BDNF to get an accurate reading.

"Interestingly, our recent studies in animals showed that proBDNF injected in both the brain and muscle can directly trigger depressive behaviours," Prof Zhou says.

The next step is to examine whether imbalances between proBDNF and mature BDNF can be restored in electric convulsion therapy. This project will be led by UniSA Associate Professor Larisa Bobrovskaya in collaboration with University of Adelaide psychiatrists Associate Professor Dennis Liu and Dr Oliver Schubert.

"Mood disorders affect millions of people worldwide. However, about one third of people with depression and bipolar disorder are resistant to antidepressants or alternative therapies. The reasons are not understood but it could have something to do with the imbalances between the different forms of BDNF, which we hope to investigate next," Prof Zhou says.

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Fatty acid may help combat multiple sclerosis

Triggered by the lack of a specific fatty acid in fat tissue

The abnormal immune system response that causes multiple sclerosis (MS) by attacking and damaging the central nervous system can be triggered by the lack of a specific fatty acid in fat tissue, according to a new Yale study. The finding suggests that dietary change might help treat some people with the autoimmune disease. The study was published Jan. 19 in *The Journal of Clinical Investigation*.

Fat tissue in patients diagnosed with MS lack normal levels of oleic acid, a monounsaturated fatty acid found at high levels in, for instance, cooking oils, meats (beef, chicken, and pork), cheese, nuts, sunflower seeds, eggs, pasta, milk, olives, and avocados, according to the study.

This lack of oleic acids leads to a loss of the metabolic sensors that activate T cells, that mediate the immune system's response to infectious disease, the Yale team found. Without the suppressing effects of these regulatory T cells, the immune system can attack healthy central nervous system cells and cause the vision loss, pain, lack of coordination and other debilitating symptoms of MS.

When researchers introduced oleic acids into the fatty tissue of MS patients in laboratory experiments, levels of regulatory T cells increased, they found.

"We've known for a while that both genetics and the environment play a role in the development of MS," said senior author David Hafler, William S. and Lois Stiles Edgerly Professor of Neurology and professor of immunobiology and chair of the Department of Neurology. "This paper suggests that one of environmental factors involved is diet."

Hafler noted that obesity triggers unhealthy levels of inflammation and is a known risk factor for MS, an observation that led him to study the role of diet in MS. He stressed, however, that more study is necessary to determine whether eating a diet high in oleic acid can help some MS patients.

Saige L. Pompura of the Yale School of Medicine is lead author of the study.

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Research establishes antibiotic potential for cannabis molecule

The main nonpsychoactive component of cannabis has been shown to kill Gram-negative bacteria for the first time

Synthetic cannabidiol, better known as CBD, has been shown for the first time to kill the bacteria responsible for gonorrhoea, meningitis and legionnaires disease.

The research collaboration between The University of Queensland and Botanix Pharmaceuticals Limited could lead to the first new class of antibiotics for resistant bacteria in 60 years.

The UQ Institute for Molecular Bioscience's Associate Professor Mark Blaskovich said CBD - the main nonpsychoactive component of cannabis - can penetrate and kill a wide range of bacteria including Neisseria gonorrhoeae, which causes gonorrhoea.

"This is the first time CBD has been shown to kill some types of Gram-negative bacteria. These bacteria have an extra outer membrane, an additional line of defence that makes it harder for antibiotics to penetrate," Dr Blaskovich said.

In Australia, gonorrhoea is the second most common sexually-transmitted infection and there is no longer a single reliable antibiotic to treat it because the bacteria is particularly good at developing resistance.

The study also showed that CBD was widely effective against a much larger number of Gram-positive bacteria than previously known, including antibiotic-resistant pathogens such as MRSA (methicillin-resistant Staphylococcus aureus) or 'golden staph'.

Dr Blaskovich said cannabidiol was particularly good at breaking

down biofilms--the slimy build-up of bacteria, such as dental plaque on the surface of teeth--which help bacteria such as MRSA survive antibiotic treatments.

Dr Blaskovich's team at the Centre for Superbug Solutions mimicked a two-week patient treatment in laboratory models to see how fast the bacteria mutated to try to outwit CBD's killing power.

"Cannabidiol showed a low tendency to cause resistance in bacteria even when we sped up potential development by increasing concentrations of the antibiotic during 'treatment'."

"We think that cannabidiol kills bacteria by bursting their outer cell membranes, but we don't know yet exactly how it does that, and need to do further research.

The research team also discovered that chemical analogs - created by slightly changing CBD's molecular structure--were also active against the bacteria.

"This is particularly exciting because there have been no new molecular classes of antibiotics for Gram-negative infections discovered and approved since the 1960s, and we can now consider designing new analogs of CBD within improved properties."

Vince Ippolito, the President and Executive Chairman of Botanix, said the research showed vast potential for the development of effective treatments to fight the growing global threat of antibiotic resistance.

"Congratulations to Dr Blaskovich and his team for producing this significant body of research--the published data clearly establishes the potential of synthetic cannabinoids as antimicrobials," Mr Ippolito said.

"Our Company is now primed to commercialise viable antimicrobial treatments which we hope will reach more patients in the near future. This is a major breakthrough that the world needs now."

Dr Blaskovich said collaborating with Botanix has sped up the research, with Botanix contributing formulation expertise that has led to the discovery that how cannabidiol is delivered makes a huge difference in its effectiveness at killing bacteria.

The collaboration has enabled Botanix to progress a topical CBD formulation into clinical trials for decolonisation of MRSA before surgery.

"Those Phase 2a clinical results are expected early this year and we hope that this will pave the way forward for treatments for gonorrhoea, meningitis and legionnaires disease.

"Now we have established that cannabidiol is effective against these Gram-negative bacteria, we are looking at its mode of action, improving its activity and finding other similar molecules to open up the way for a new class of antibiotics."

This research has been published in Communications Biology.

Explainer video - https://youtu.be/QoXF2kfIOFM

http://bit.ly/2KDPuQl

Researchers create new form of cultivated meat

McMaster researchers have developed a new form of cultivated meat using a method that promises more natural flavor and texture than other alternatives to traditional meat from animals.

Researchers Ravi Selvaganapathy and Alireza Shahin-Shamsabadi, both of the university's School of Biomedical Engineering, have devised a way to make meat by stacking thin sheets of cultivated muscle and fat cells grown together in a lab setting.

The technique is adapted from a method used to grow tissue for human transplants.

The sheets of living cells, each about the thickness of a sheet of printer paper, are first grown in culture and then concentrated on growth plates before being peeled off and stacked or folded together. The sheets naturally bond to one another before the cells die.

The layers can be stacked into a solid piece of any thickness,

Selvaganapathy says, and "tuned" to replicate the fat content and marbling of any cut of meat—an advantage over other alternatives.

"We are creating slabs of meat," he says. "Consumers will be able to buy meat with whatever percentage of fat they like—just like they do with milk."

As they describe in the journal *Cells Tissues Organs*, the researchers proved the concept by making meat from available lines of mouse cells. Though they did not eat the mouse meat described in the research paper, they later made and cooked a sample of meat they created from rabbit cells.

"It felt and tasted just like meat," says Selvaganapathy.

There is no reason to think the same technology would not work for growing beef, pork or chicken, and the model would lend itself well to large-scale production, Selvaganapathy says.

The researchers were inspired by the meat-supply crisis in which worldwide demand is growing while current meat consumption is straining land and water resources and generating troubling levels of greenhouse gases.

"Meat production right now is not sustainable," Selvaganapathy says. "There has to be an alternative way of creating meat."

Producing viable meat without raising and harvesting animals would be far more sustainable, more sanitary and far less wasteful, the researchers point out.

While other forms of cultured meat have previously been developed, the McMaster researchers believe theirs has the best potential for creating products consumers will accept, enjoy and afford.

The researchers have formed a start-up company to begin commercializing the technology.

More information: *Alireza Shahin-Shamsabadi et al. Engineering Murine Adipocytes and Skeletal Muscle Cells in Meat-like Constructs Using Self-Assembled Layer-by-Layer Biofabrication: A Platform for Development of Cultivated Meat, Cells Tissues Organs (2021).* DOI: 10.1159/000511764

http://bit.ly/367Ghat

Astronomers estimate Titan's largest sea is 1,000-feet deep

Far below the gaseous atmospheric shroud on Saturn's largest moon, Titan, lies Kraken Mare, a sea of liquid methane.

Ithaca, N.Y. - Cornell University astronomers have estimated that sea to be at least 1,000-feet deep near its center - enough room for a potential robotic submarine to explore.

After sifting through data from one of the final Titan flybys of the Cassini mission, the researchers detailed their findings in "The Bathymetry of Moray Sinus at Titan's Kraken Mare," which published in the *Journal of Geophysical Research*.

"The depth and composition of each of Titan's seas had already been measured, except for Titan's largest sea, Kraken Mare - which not only has a great name, but also contains about 80% of the moon's surface liquids," said lead author Valerio Poggiali, research associate at the Cornell Center for Astrophysics and Planetary Science (CCAPS).

A billion miles from Earth, frigid Titan is cloaked in a golden haze of gaseous nitrogen. But peeking through the clouds, the moonscape has an Earthlike appearance, with liquid methane rivers, lakes and seas, according to NASA.

The data for this discovery was gathered on Cassini's T104 flyby of Titan on Aug. 21, 2014. The spacecraft's radar surveyed Ligeia Mare - a smaller sea in the moon's northern polar region - to look for the mysteriously disappearing and reappearing "Magic Island."

While Cassini cruised at 13,000 mph nearly 600 miles above Titan's surface, the spacecraft used its radar altimeter to measure the liquid depth at Kraken Mare and Moray Sinus, an estuary located at the sea's northern end.

The Cornell scientists, along with engineers from NASA's Jet Propulsion Laboratory, had figured out how to discern lake and sea

bathymetry (depth) by noting the radar's return time differences on the liquid surface and sea bottom, as well as the sea's composition by acknowledging the amount of radar energy absorbed during transit through the liquid.

It turns out that Moray Sinus is about 280 feet deep, shallower than the depths of central Kraken Mare, which was too deep for the radar to measure. Surprisingly the liquid's composition, primarily a mixture of ethane and methane, was methane-dominated and similar to the composition of nearby Ligeia Mare, Titan's second-largest sea.

Earlier scientists had speculated that Kraken may be more ethane rich, both because of its size and extension to the moon's lower latitudes. The observation that the liquid composition is not markedly different from the other northern seas is an important finding that will help in assessing models of Titan's Earth-like hydrologic system.

Beyond deep, Kraken Mare also is immense - nearly the size of all five Great Lakes combined.

Titan represents a model environment of a possible atmosphere of early Earth, Poggiali said.

One puzzle is the origin of the liquid methane. Titan's solar light - about 100 times less intense than on Earth - constantly converts methane in the atmosphere into ethane; over roughly 10 million-year periods, this process would completely deplete Titan's surface stores, according to Poggiali.

In the distant future, a submarine - likely without a mechanical engine - will visit and cruise Kraken Mare, Poggiali said.

"Thanks to our measurements," he said, "scientists can now infer the density of the liquid with higher precision, and consequently better calibrate the sonar aboard the vessel and understand the sea's directional flows."

NASA provided funding for this research.

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Bonobos, chimpanzees, and oxytocin

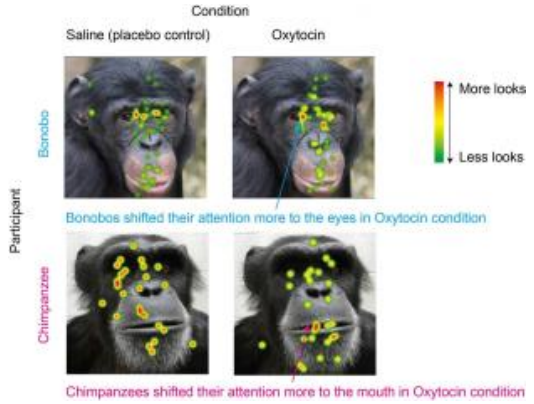
A key hormone may underlie social differences among great apes

Japan -- Despite being our two closest relatives -- separated by just two million years of evolution from one another and six million from us -- chimpanzees, bonobos, and humans have numerous important differences, such as in lethal aggression demonstrated by chimpanzee males and the high social status of bonobo females.

Now a research study suggests that the hormone *oxytocin* may have played a central role in this evolutionary divergence.

"Oxytocin is a hormone neuropeptide found in mammals," explains author James Brooks, "but despite its ancient origins, its role can vary even among closely-related species." Among these roles are a wide array of social behaviors, some of which have recently been associated with certain species-typical behaviors in great apes.

Based on these behavioral findings, a team from Kyoto University and Azabu University in Japan examined oxytocin's effect on eye contact, a key social behavior that is known to both differ widely between bonobos and chimpanzees and is tightly tied to the oxytocin system in humans, monkeys, and dogs. The researchers predicted that if oxytocin is key to the divergence of social traits, it would act differently in the two species and promote species-specific behaviors.



Tracking eyesight differences in chimpanzees and bonobos based on varying levels of the hormone oxytocin **Credit: Kyoto University/Kano Lab**

Using a non-invasive technique similar to that employed in tests with humans, oxytocin was *nebulized* -- made into an aerosol -- into

a box where the apes had access to juice should they choose to participate. While drinking the juice, the apes passively inhaled the nebulized mist and were then shown still and video images prepared for each species, while their gaze was recorded with an eye-tracking device.

The team found that for bonobos -- as with humans -- oxytocin shifted attention more to the eyes in the images, while chimpanzees instead shifted their gaze more to mouths. Significantly, these changes enhanced known species differences.

"Due to the importance of eye contact in many social behaviors, such discrepancies could lead to broader behavioral differences through feedback loops, with greater eye contact leading to species-typical behavior leading to further oxytocin release," says co-author Fumihiro Kano.

"These are the first results to demonstrate an effect of administered oxytocin on great ape behavior, pointing to the significant role this hormone plays in the critical differences among the species."

The paper "Divergent effects of oxytocin on eye contact in bonobos and chimpanzees" appeared 21 December 2020 in the journal Psychoneuroendocrinology, with doi: 10.1016/j.psyneuen.2020.105119

http://bit.ly/3sY6hz9

The Massive Genome of The Lungfish May Explain How We Made The Leap to Land

Struck enough genetic jackpots to allow them to climb out of the water and access the whole new world of land

Tessa Koumoundouros

If you are a lucky species, you will stumble into random gene mutations that just happen to help you survive better - allowing you and your descendants to keep and build on the helpful traits they encode. As with anything involving luck, the more chances you take, the more chances you have of hitting the jackpot.

That's what seems to have happened with our long-ago ancestors - the ones we share with still living lungfish. They struck enough genetic jackpots to allow them to climb out of the water and access the whole new world of land, around 420 million years ago.

In doing so, they became the ancestors of all land animals with backbones (tetrapods). Having a massive genome, like that found in modern lungfish, may have helped with this.

Researchers just sequenced the entire genome of the endangered Australian lungfish (*Neoceratodus forsteri*), which has the largest known animal genome. It is 14 times the size of ours.

Australian Lungfish (Neoceratodus forsteri). **(Haus des Meeres aquazoo)**

This required new DNA sequencing techniques and masses of computing power, only now technically possible - to piece together a whopping 43 billion nucleotides ('letters' in the genetic code).

"When you look at it from a genomic perspective, [lungfish are] genomically halfway between a fish and a land-based vertebrate," biologist Siegfried Schloissnig from the Research Institute of Molecular Pathology (IMP) in Austria told *New Scientist*.

Of six still living species of lungfish, four are African, one South American, and one Australian. They first appeared in the fossil record 400 million years ago.

The Australian species has retained the most ancestral features, and was mistakenly classed as an amphibian when first discovered, due to its bizarre mix of fish and newt features, including its weird, leg-like lobed fins. These strange in-between 'living fossils' can live up to 100 years.

Australian lungfish still appear to closely resemble the fossils of their 100-million-year-old (and now extinct) ancestral species that hauled themselves out of the water, eventually spawning mammals, birds, reptiles, and amphibians. Its genome confirms that this air-

gulping swimmer is our closest living fish relative, beating the other contender, coelacanths - another group of lobed finned fish.

So within the Australian lungfish's giant haystack of genes are clues to how animals made the transition from aquatic to terrestrial.

"This... required a number of evolutionary innovations including airbreathing, limbs, posture, prevention of desiccation, nitrogen excretion, reproduction, and olfaction," the researchers write in their paper.

They identified the same genes responsible for our embryonic lung development already present in the lungfish, as are our familiar ulna and radius arm bones, and the genes that encode them. Tetrapod limb patterning genes like hox-c13 and sal1 had never been seen before in fish.

"Such novelties might have predisposed the [lobe-finned fish] to conquer land demonstrating how the lungfish genome can contribute to better understanding of this major transition during vertebrate evolution," the team write.

The researchers also found huge additions to the lungfish's genes associated with smell - what would have been a new suite of sensors suitable to their ancestors' new environment. These genes code for receptors of airborne odours, while groups of receptors for waterborne scents shrunk.

Many of the excess genes that bulk out their hefty genome arose through copied sections of their DNA. Some of the lungfish's individual chromosomes contain as many nucleotides as our entire human genome. This form of genome expansion, through copies, is known to be an important driving force of evolution, with evidence that it helps provide organisms with the ability to rapidly adapt to a changing environment.

The Australian lungfish is an incredible living record of our evolution, and after preserving this genetic history for so long, it's now under threat by human activities altering the freshwater habitats it calls home.

The animal hunts for frogs, worms and snails, as well as munching on plants in the water. It usually relies on gills to breathe, but its single lung allows the lungfish to surface for fresh air when dry conditions reduce their watery environment, making it murky and stagnant.

"There is no doubt that the newly sequenced genome will unveil more of the secrets of this bizarre vertebrate in the future," said IMP cellular geneticist Elly Tanaka. "Not only can it teach us things about adaptations to life on land, but it may also explain how certain genomes evolve to be so big." This research was published in *Nature*.

http://wb.md/3c4KTlJ

COVID-19 in Pregnancy: Finally, Some Hard Data

Women who are pregnant or are thinking of becoming pregnant will need to make decisions about getting a vaccine

F. Perry Wilson, MD, MSCE

This transcript has been edited for clarity.

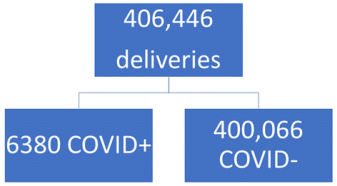
Welcome to *Impact Factor*, your weekly dose of commentary on a new medical study. I'm Dr F. Perry Wilson of the Yale School of Medicine.

In the coronavirus era, pregnant women represent a unique cohort in the hospital. They can have florid COVID-19 symptoms, and deaths have been reported. Of course, they may also be in the hospital just to deliver a baby and have COVID detected incidentally.

Early on in the pandemic, a friend of mine — an anesthesiologist in New York City — told me how overwhelmed he was with COVID cases. Not in the ICU; he was working in the maternity ward. Ordinary pregnancies became complicated, C-sections spiked, and outcomes worsened. But until I saw this paper appearing in *JAMA Internal Medicine*, his experience was just another anecdote in a sea of COVID war stories.

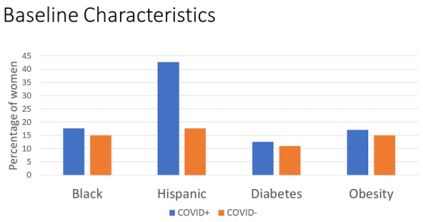
Finally, we have some hard data on the risks of COVID-19 in pregnancy. And we need it now more than ever, as women who are pregnant or are thinking of becoming pregnant will need to make decisions about getting a vaccine — a vaccine that was evaluated in studies specifically excluding pregnant women.

Women who become pregnant tend to be younger and healthier than the general US adult. As such, in the absence of pregnancy, they would often be considered low risk and not a vaccine priority group. But this paper shows that COVID-19 has some pretty significant effects in pregnancy, and we need to take those risks into account when we consider whether to advise vaccination.



Medscape

The study leveraged an absolutely huge database that combines records from multiple payers to capture 20% of all deliveries in the US between April 1 and November 23, 2020 — 406,446 women total, of whom 6380 (1.6%) had COVID at the time of delivery. The authors compared baseline characteristics and outcomes across these two groups.



Medscape

Women delivering a baby while infected with COVID tended to be younger than those without COVID. Mirroring the national prevalence, they were more likely to be Black or Hispanic, more likely to have diabetes, and more likely to have obesity.

Relative Risk ≠ Absolute Risk

Condition	Risk in COVID+	Risk in COVID-	RELATIVE risk
Mechanical ventilation	1.3%	0.05%	26 times higher!

Medscape

The authors adjusted for those and other factors to determine what the independent effect of COVID-19 was on pregnancy outcomes. Now, bad things happening during pregnancy is pretty rare in this country, so I want to be clear that I am presenting *relative* increases in risk, not absolute risk. For example, COVID was associated with a 25-fold increase in the risk for mechanical ventilation — but just 1.3% of women with COVID were intubated overall.

Women with COVID had a relative 7% increased risk of having a cesarean delivery, a 19% increased risk for preterm labor, and a 23% increased risk for stillbirth. They had a sixfold increased risk of going to the intensive care unit and a 3.5-fold increased risk for venous thromboembolism. Nine women died in the COVID group and only 20 in the 60-fold bigger COVID-negative group.

Increased Risks With COVID in Pregnancy

Condition	Adjusted relative risk (95% CI)
Cesarean delivery	1.07 (1.02 – 1.13)
Preterm labor	1.19 (1.06 – 1.33)
Stillbirth	1.23 (0.87 – 1.75)
Needed ICU	6.47 (5.55 – 7.55)
Venous thromboembolism	3.43 (2.01 – 5.82)
Death	26.1 (11.3 – 60.4)

Medscape

Again, most women had none of these things, but the presence of COVID *clearly* increases the risk.

Against that backdrop, what do we know about the risks and benefits of vaccination in pregnant women? Not much. They were excluded from the major clinical trials that led to the current vaccine approvals in the US. Some women did get pregnant *during* their participation in the Pfizer and Moderna trials — I break down their outcomes here — but the vast majority of outcomes are unknown, presumably because these women are still pregnant.

There are no red flags, but obviously not a lot of data to go on. There's not much reason to think, biologically, that the mRNA vaccines would lead to adverse pregnancy outcomes, but that may not be reassuring to many women. For many women, the vaccine will best balance their assessment of risk and benefit. For others, enhanced vigilance to hand hygiene, mask-wearing, and avoiding crowds may be the best choice to mitigate risk.

One thing is clear: If you can avoid getting COVID while you're pregnant, you probably should.

Pregnancies in Pfizer / Moderna Phase 3 Trials

V = vax; P = placebo

Trial	Pregnancies	Live births	Loss / Adverse event	Unknown
Pfizer	12V, 11P	????	0V, 2P	12V, 9P
Moderna	6V, 7P	????	0V, 2P	6V, 5P

Medscape

F. Perry Wilson, MD, MSCE, is an associate professor of medicine and director of Yale's Clinical and Translational Research Accelerator. His science communication work can be found in the Huffington Post, on NPR, and here on Medscape. He tweets @fperrywilson and hosts a repository of his communication work at www.methodsman.com.

http://bit.ly/3a16cSe

Early humans used chopping tools to break animal bones and consume the bone marrow

The toolkit of prehistoric humans

Researchers from the Sonia and Marco Nadler Institute of Archaeology at Tel Aviv University unraveled the function of flint tools known as 'chopping tools', found at the prehistoric site of Revadim, east of Ashdod. Applying advanced research methods, they examined use-wear traces on 53 chopping tools, as well as organic residues found on some of the tools. They also made and used replicas of the tools, with methods of experimental archaeology. The researchers concluded that tools of this type, found at numerous sites in Africa, Europe and Asia, were used by prehistoric humans at Revadim to neatly break open bones of medium-size animals such as fallow deer, gazelles and possibly also cattle, in order to extract the nutritious high-calory bone marrow.

The study was conducted by Dr. Flavia Venditti of the University of Tübingen and Prof. Ran Barkai and Dr. Aviad Agam of the Sonia and Marco Nadler Institute of Archaeology at Tel Aviv University, in collaboration with the Laboratory of Technological and Functional Analyses of Prehistoric Artefacts (Sapienza, University of Rome) and researchers from Sapienza, University of Rome. The paper was published in January 2021 in the *PLOS One* Journal.

A chopping tool from late Acheulian Revadim. **Prof. Ran Barkai.**

Prof. Ran Barkai: "For years we have been studying stone tools from prehistoric sites in Israel, in order to understand their functions. One important source of tools is Revadim, an open-air site (as opposed to a cave) dating back to 500,000-300,000 years before our time, and rich with remarkably well-preserved findings. Over the years we have discovered that Revadim was a highly favored site, reinhabited over and over again by humans, most probably of the late Homo Erectus species. Bones of many types of game, including elephants, cattle, deer, gazelles and others, were found at the site."

The researchers add that the prehistoric inhabitants of Revadim developed an effective multipurpose toolkit - not unlike the toolkits of today's tradesmen. After discovering the functions of some stone tools found at the site, the researchers now focused on chopping tools - flint pebbles with one flaked, sharp and massive edge. Prof. Barkai: "The chopping tool was invented in Africa about 2.6 million years ago, and then migrated with humans wherever they went over the next two million years. Large quantities of these tools have been found at almost every prehistoric site throughout the Old World - in Africa, Europe, the Middle East and even China - evidence for their great importance. However, until now, they had

never been subjected to methodical lab testing to find out what they were actually used for."

The researchers analyzed a sample of 53 chopping tools from Revadim, looking for use-wear traces and organic residues. Many specimens were found to exhibit substantial edge damage as a result of chopping hard materials, and some also showed residues of animal bones, preserved for almost half a million years! Following these findings, experimental archaeology was also applied: The researchers collected flint pebbles from the vicinity of Revadim, manufactured replicas of prehistoric chopping tools and used them to break open bones of dead medium-size animals. Comparisons between the use-wear traces and organic residues on the replicated tools and those on the prehistoric originals significantly substantiated the study's conclusions.

Prof. Barkai: "Early humans broke animal bones in two to extract bone marrow. This requires great skill and precision, because shattering the bone would damage the bone marrow. The chopping tool, which we examined in this study, was evidently outstandingly popular, because it was easy to make, and highly effective for this purpose. This is apparently the reason for its enormous distribution over such a long period of time. The present study has expanded our knowledge of the toolkit of early humans - one more step toward understanding their way of life, tracking their migrations, and unraveling the secrets of human evolution."

http://nyti.ms/3690qgi

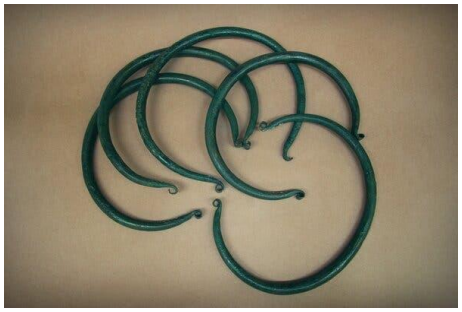
An Ancient Form of European Money: Bronze Rings, Ribs and Blades

Because the objects had a standardized weight, scientists suggest they were a form of currency used some 3,500 years ago.

By Becky Ferreira

The modern world runs on a constant flow of money that has its roots in simpler proto-currencies pioneered on regional levels by ancient peoples.

A pair of archaeologists believe they have identified a very early example of commodity money in Europe, used some 3,500 years ago during the Bronze Age, with denominations that took the form of bronze rings, ribs and ax blades.



People at this time frequently buried collections of these ubiquitous items, leaving a wealth of scattered "hoards" across the European continent.

***The Bronze Age rings found in the Czech Republic were so similar in mass that they would have been indistinguishable if weighed by hand....*Helena Motyckova**

In a study published on Wednesday in PLOS ONE, Maikel Kuijpers, an assistant professor in European prehistory at Leiden University in the Netherlands, and Catalin N. Popa, who was a postdoctoral researcher there, compared the weights of more than 5,000 Bronze Age rings, ribs and blades, sourced from over 100 hoards that contained five or more items.

The results revealed that 70 percent of the rings were so close in mass — averaging about 7 ounces — that they would have been indistinguishable if weighed by hand.

While the ribs and ax blades are not quite as uniform, the study concludes that the artifacts are similar enough to collectively demonstrate "the earliest development of commodity money in prehistoric Central Europe."

"It is a very clear standardization," Dr. Kuijpers said.

While other researchers questioned some of their conclusions, they agreed that the study added to our knowledge of the economic activities of ancient peoples.

As bronze smithing spread through Europe, these rings, ribs and ax

blades were cast for functional purposes — such as jewelry and tools — that might have been unrelated to money. Some of the items in the data set probably maintained strictly utilitarian or ornamental roles because their weights were well beyond the calculated average.

But the comparable weights of a large portion of the artifacts leaves "no doubt that at least the rings and ribs conform to the definition of commodity money," the authors wrote.

The bronze items mirror forms of currency based on tools, known as utensil money, discovered elsewhere, such as knife and spade money found in China and Aztec hoe and ax money found in Mesoamerica.

"We do have examples in other areas of the world where you seem to have this sort of similar development" in which "a practical tool turns into this utensil money, and then into this commodity money," Dr. Kuijpers said.

***Bronze Age ribs. A central innovation of bronze is the ability to make duplicates by casting the metal in molds, and the study speculates these copies gave rise, over time, to an abstract concept of weight...*Helena Motyckova**

A central innovation of bronze is the ability to make duplicates by casting the metal in molds. The study speculates that these near-identical copies gave rise, over time, to an abstract concept of weight, which laid the mental groundwork for the invention of weighing tools and technologies that emerged in Europe centuries later in the Bronze and Iron Ages.

Nicola Ialongo, a prehistoric archaeologist at Georg August University of Göttingen in Germany, said that the study offered "an important contribution to understanding how early monies work," but that there was a less complicated explanation for how these standardized objects emerged.

"As the authors acknowledge, the regularity of their samples might simply be explained by imagining that the objects in their data sets were cast with a limited number of molds, or that the molds themselves had a standardized shape," Dr. Ialongo said.

Furthermore, he added, ancient peoples might have counted this currency the way we count coins today, rather than focusing on weight.

"Simply put, you don't need a weight system to be able to use metals — or any other commodity — as money," he said, adding that many other less durable things may have been used as money before these bronze items.

The authors counter that "weight mattered" because "there are indications that for some types of objects a deliberate effort was made to achieve a specific weight interval."

Barry Molloy, an associate professor of archaeology at University College Dublin who was not involved in the study, noted that there "has long been a suspicion that systems of weights and measures were in use in Bronze Age Europe."

"The quest was for a precise metric, as found in Southwest Asia and the Mediterranean," Dr. Molloy said. "While this paper does not demonstrate that there was such a coherent system, it provides important insights into how ancient people in Europe themselves may have approached these issues pragmatically before formal weight systems were developed in the Iron Age."

While Dr. Ialongo disagreed with some of the researchers' methods, he also praised the study as "a remarkable attempt to break one of the oldest and most persistent taboos in prehistoric archaeology, that 'primitive' societies do not have a proper commercial economy."

http://bit.ly/3qK9RL6

A Tweak to Immune Cells Reverses Aging in Mice

Knocking out the receptor for a lipid that causes inflammation rejuvenates macrophage metabolism and restores cognitive function in an Alzheimer's disease model.

Abby Olena

Excess inflammation is a problem in aging, contributing to issues such as atherosclerosis, cancer, and cognitive decline. But the mechanisms behind age-related inflammation are not well understood. In a study published today (January 20) in *Nature*, researchers show that older immune cells have a defect in metabolism that when corrected in a mouse model of Alzheimer's disease can decrease inflammation and restore cognitive function.

After a decade of progress in understanding metabolism and nutrient usage in immune cells and how that affects their function, this study is a "beautiful example" of now knowing enough to intervene, push buttons, and influence outcomes, says Eyal Amiel, who studies immune cell metabolism at the University of Vermont and was not involved in the new work. "To have a specific metabolic signature associated with a pathology is one thing. To be able to manipulate it is another thing. To be able to manipulate it and reverse the pathology is an incredible sequence of events."

As a postdoc in the late 1990s, Katrin Andreasson, now a neurologist and researcher at Stanford University School of Medicine, was intrigued by epidemiological studies showing that people who took nonsteroidal anti-inflammatory drugs—such as ibuprofen and naproxen—occasionally for aches and pains had a decreased risk of Alzheimer's disease. During her postdoc in Paul Worley's lab at Johns Hopkins School of Medicine, she and her colleagues showed that overexpression of *cyclooxygenase-2* (*COX-2*)—a major mediator of inflammation—in the brain led to Alzheimer's disease-like symptoms in mice: age-dependent inflammation and cognitive loss.

COX-2 activation is the first step in the production of a lipid called prostaglandin E_2 (PGE_2), which can bind to one of its receptors, EP2, on immune cells and promote inflammation. To plug up the pathway, Andreasson's group has shown that deleting the EP2 receptor in mouse macrophages and brain-specific microglia—the cells normally responsible for detecting and destroying immune invaders and cellular debris—reduces inflammation and increases neuronal survival in response to both a bacterial toxin and a neurotoxin.

In the current study, the researchers wanted to understand how eliminating PGE_2 signaling in macrophages could have these effects. They started by comparing macrophages from human blood donors either younger than 35 or older than 65. The cells from older donors made much more PGE_2 and had higher abundance of the EP2 receptor than did macrophages from younger donors. When the researchers exposed human macrophages to PGE_2, the cells altered their metabolism. Rather than using glucose to make energy, the cells converted it to glycogen and stored it, locking it up where the mitochondria couldn't access it for ATP production.

"The result of that is that the cells are basically energy-depleted. They're just fatigued, and they don't work well," explains Andreasson. "They don't phagocytose. They don't clear debris." This debris includes misfolded proteins associated with neurodegeneration, the authors write in the paper.

When the scientists treated human macrophages from donors with an average age of about 48 with one of two EP2 receptor inhibitors, glycogen storage decreased, energy production increased, and cells shifted to express anti-inflammatory markers. As in human cells, aged mice also have higher levels of PGE_2 in the blood and brain and EP2 receptor levels in macrophages, compared to younger mice. When the researchers knocked down the receptor in macrophages

throughout the body in a mouse model of Alzheimer's disease or treated animals with either of two drugs to suppress EP2 function, cells had improved metabolism. The mice's age-associated inflammation also reversed and, with it, age-associated cognitive decline. Treating animals with an EP2 antagonist that couldn't get in the brain and thus only targeted the receptor in peripheral macrophages also led to cognitive improvement in older mice.

"The most interesting thing that they were able to show is that the macrophages are causal in driving age-associated cognitive decline, and, in particular, that it's sufficient to reprogram the macrophages outside of the brain," says Jonas Neher, a neuroimmunologist at the German Center for Neurodegenerative Diseases and the University of Tübingen in Germany who authored an accompanying commentary. The next steps are "to figure out what the signal is that comes from the periphery and changes the microglia in the brain. If you can identify this particular signal, then you have another handle on how to reprogram microglia."

"The hypothetical clinical promise of these findings is obviously outstanding because as you can imagine, it wouldn't require brain surgery or any kind of gross-level, high-risk intervention," says Amiel. "Rather, you can manipulate cells systemically and see these outcomes."

Investigating how those systemic effects work is just one of the questions that Andreasson's group is currently pursuing. They're also interested in how and why metabolism declines during aging, as well as other mechanisms that might prevent it. In terms of translating the work to the clinic, one of the only ways to target the EP2 receptor is to go far upstream with COX-2 inhibitors, such as Vioxx, a drug that was withdrawn from the market after some people who took it experienced strokes or heart attacks. There aren't any drugs that specifically block the EP2 receptor yet, Andreasson tells *The Scientist*. "There have been attempts made by pharmaceutical companies, but my understanding is it's been very, very difficult to do."

P.S. Minhas et al., "Restoring metabolism of myeloid cells reverses cognitive decline in ageing," Nature, doi:10.1038/s41586-020-03160-0, 2021.

http://bit.ly/3c63kWV

Male Mantises Evolved a Vital Trick to Avoid Being Decapitated After Sex

A male Springbok praying mantis looking for a hook-up doesn't have to worry about a female stealing his heart away.

Marlowe Hood & Eleonore Hughes, AFP

There is, however, a very good change she'll bite his head off, and he knows it. Indeed, 60 percent of sexual encounters between Springboks – one of nearly 2,000 mantis species across the globe – end in males being eaten as a snack.

"Males play Russian roulette whenever they encounter cannibalistic females," explained Nathan Burke, an entomologist at the University of Auckland and an expert on mantis mating rituals.

All male mantises show extreme caution when approaching a prospective partner. Hard to blame them.

But whereas most will sneak up from behind or distract the female with a tasty morsel, the Springbok has an entirely different – and previously unreported – strategy for staying alive, according to findings published Wednesday in *Biology Letters*.

"Under threat of cannibalistic attack, males try to subdue females by pinning them down in violent struggles," said Burke, co-author with colleague Gregory Holwell of the study.

Males who win the lovers' tussle are far more likely to succeed in consumating the relationship, "which suggests that wrestling is both a mating tactic and a survival tactic," he added.

The key to victory, according to gladiatorial experiments with 52 pairs of mantises, was striking first.

If the male was quicker to the draw and grabbed the female with its

serrated raptorial forelegs, he stood a 78 percent chance of escaping unscathed. And when, in addition, the male inflicted a serious but non-fatal wound to the abdomen, he kept his head every time.

"I was very surprised to discover that males injure females while trying to subdue them for mating," said Burke. "Nothing like that has ever been observed in mantises before." If the female grasped first, however, males were always killed and devoured.

Asexual reproduction

Overall, males came out top more than half the time in these jousts, which lasted 13 seconds on average.

Winning the match did not automatically lead to mating – coupling followed only two-thirds of the time, and even then the male wound up in the female's stomach half the time.

The bright green Springbok mantis, aka *Miomantis caffra*, is native to southern Africa, but has spread to New Zealand, southern Europe and California, probably through the pet trade.

The nutrients gained when a female praying mantis eats her suitor benefit her offspring as they grow. Sexual cannibalism – when the female of a species consumes the male during or after mating – is also known among spiders, such as the black widow, and scorpions. Typically smaller males do what they can to avoid getting gobbled up, including playing dead.

But female Springbok mantises have another trick up their spiky sleeve: the ability to reproduce asexually, or without any help from males. "They can produce clones of themselves if they don't mate," said Burke.

Having this Plan B fallback raises an interesting question: if females are so good at cannibalising males and can reproduce without sex, how do males continue to exist?

"That's what motivated me to look so closely at male mating tactics," Burke said.

Sexual conflict theory, he explained, tells us that males in this situation should evolve counter-measures to help them mate and stay relevant. And sure enough, that is what the researchers found.

"It's a fascinating example of how sexual conflict can lead to the evolution of mating tactics that help one sex but hinder the other."

http://bit.ly/3om3eqF

Important cause of preeclampsia discovered

Cholesterol crystals are the missing piece of the puzzle

Despite being the subject of increasing interest for a whole century, how preeclampsia develops has been unclear - until now.

Researchers believe that they have now found a primary cause of preeclampsia. "We've found a missing piece to the puzzle. Cholesterol crystals are the key and we're the first to bring this to light," says researcher Gabriela Silva.

Silva works at the Norwegian University of Science and Technology's (NTNU) Centre of Molecular Inflammation Research (CEMIR), a Centre of Excellence, where she is part of a research group for inflammation in pregnancy led by Professor Ann-Charlotte Iversen.

The findings are good news for the approximately three per cent of pregnant women in Norway who get this disease. Worldwide, preeclampsia is a leading cause of illness and death in both mother and foetus.

In a preeclamptic pregnancy, the placenta does not develop properly, and the baby sometimes also receives too little nutrition.

The symptoms of preeclampsia are often mild, but in some cases the condition becomes so severe that the baby needs to be delivered prematurely. Preeclampsia does not disappear until the baby is born. Since no one has understood why the condition occurs, the current treatment is to monitor and alleviate the symptoms.

Silva believes that future treatment will now become more effective. "A pregnancy is actually a kind of natural inflammatory condition, and in the case of preeclampsia, the inflammation has become too

strong and leads to disease," Silva says.

Women who have had preeclampsia have an increased risk of developing cardiovascular disease later in life.

It was precisely this connection that led the researchers to choose to examine cholesterol in pregnant women with preeclampsia. Cholesterol is a major cause of cardiovascular disease.

Cholesterol crystals are found in plaque that clogs blood vessels. The crystals are formed when bad cholesterol accumulates in the blood vessel walls. Studies have shown that cholesterol crystals are a particularly powerful initiator of inflammation in the body and can cause the blood to clot.

Cholesterol crystals are identified as harmful substances in the body that need to be cleared out. But the defence cells that come in to do the job aren't able to break them down. They call for reinforcements, and more immune cells come in, to no avail. The immune response runs wild, and the inflammatory process escalates.

Silva found that the inflammation was at its highest in the region called the maternal-foetal interface, where the mother's cells come into direct contact with foetal cells. This happens in the placenta and uterine wall.

"This direct contact means that the inflammation directly affects the communication between mother and foetus and contributes to even greater inflammation in the mother," says Silva.

Cholesterol levels are high in all pregnant women, because both the foetus and the placenta need cholesterol. But levels were even higher in women with preeclampsia. They also had much more of the bad cholesterol, which is the type of cholesterol found in people who are at high risk for cardiovascular disease.

Silva went to great lengths to solve the riddle. She used tissue samples from a biobank that the research group at CEMIR has built up, and included placenta samples from 90 women with preeclampsia obtained immediately after birth. The researchers therefore had tissue samples from both the uterine wall and the placenta. The samples were examined using advanced microscopes. It has taken years of research to arrive at the result.

Future treatment for preeclampsia may simply include cholesterol-lowering medications, such as statins, but further research is needed to clarify their effects.

"Some women have an increased risk of preeclampsia right from the start. They should be followed up with a cholesterol check. This isn't done regularly today, but it should be done regularly in the future. The use of statins during pregnancy is not recommended now, but several clinical studies are looking more closely at this and are showing that pravastatin, for example, can be safe to use during pregnancy," says Silva.

http://bit.ly/2Y7ERZ4

Massive new dinosaur might be the largest creature to ever roam Earth

The unnamed titanosaur could have weighed more than 69 tons.

By Harry Baker - Staff Writer

The 98 million-year-old remains of what might be the largest animal to walk Earth — a long-necked titanosaur dinosaur — were recently unearthed in Argentina.

An artist's impression of Argentinosaurus huinculensis, believed to be one of the closest related species to the newly discovered titanosaur. **(Image: © Elena Duvernay/Stocktrek Images via Getty Images)**

The remains of the unnamed dinosaur were first discovered in 2012 in Neuquén Province of northwest Patagonia, but have still not been fully excavated. However, the bones that have been unearthed so far suggest the ancient behemoth was likely a titanosaur, possibly the largest one on record. Titanosaurs were amongst the largest

sauropods — long-necked, plant-eating giant dinos — and lived from the late Jurassic period (163.5 million to 145 million years ago) to the end of the Cretaceous period (145 million to 66 million years ago).

"Given the measurements of the new skeleton, it looks likely that this is a contender for one of the largest, if not the largest, sauropods that have ever been found," Paul Barrett, a paleobiologist at the Natural History Museum in London who was not involved in the study, told Live Science.

Not enough of the remains have been uncovered for the researchers to declare this dinosaur as a new species or assign it to an already known one. However, the researchers are confident that once the excavation is complete, they'll be able to classify it as a completely new species.

"The place of the finding is very hard to access, so the logistics is pretty complicated," lead study author Alejandro Otero, a paleontologist at La Plata Museum in Argentina, told Live Science. "But we expect to return there after the pandemic situation."

The remains themselves date to about 98 million years ago, meaning the creature lived during the Cretaceous period.

A giant among giants

In 1993, another titanosaur called *Argentinosaurus huinculensis* claimed the title of largest land-based dino, but was later superceded by the even larger titanosaur *Patagotitan mayorum* in 2014. However, it's challenging to determine which species was the heaviest dinosaur — *Argentinosaurus* is known from just 13 fossilized bones, and *Patagotitan's* weight was based on a composite of six individuals, Live Science previously reported.

Right now, the researchers can't say how large the new titanosaur was, given that the long limb bones used to make such estimates, such as the humerus and femur, have not yet been excavated. However, analyses of the bones that have been found — including 24 vertebrae of the tail and parts of the pelvic and pectoral girdle — show that it was most likely the largest of the titanosaurs.

"The specimen is considered one of the largest sauropods ever found, probably exceeding *Patagotitan* in size," the researchers wrote. *Patagotitan* was roughly 50 feet (15 meters) tall and weighed 69 tons (62 metric tons), which is equivalent to the weight of nearly a dozen Asian elephants.

"It is a huge dinosaur, but we expect to find much more of the skeleton in future field trips, so we'll have the possibility to address with confidence how big it really was," Otero said.

The newly discovered titanosaur is just one of many sauropod fossils uncovered in South America, including *Dreadnoughtus* and *Sarmientosaurus*.

These have helped to fill in multiple knowledge gaps surrounding these giants and also raise questions about how they grew so big.

"This new skeleton provides yet another example of sauropods pushing at the extremes of what's possible with respect to maximum animal size on land," Barrett said. The study was published online Jan. 12 in the journal Cretaceous Research.

http://bit.ly/3iKrA2q

Does aspirin lower colorectal cancer risk in older adults? It depends on when they start

Study finds that daily aspirin use does not reduce risk of colorectal cancer among adults who begin taking it after age 70

BOSTON - Regular aspirin use has clear benefits in reducing colorectal cancer incidence among middle-aged adults, but also comes with some risk, such as gastrointestinal bleeding. And when should adults start taking regular aspirin and for how long?

There is substantial evidence that a daily aspirin can reduce risk of colorectal cancer in adults up to age 70. But until now there was little evidence about whether older adults should start taking aspirin. A team of scientists set out to study this question. They were led by

Andrew T. Chan MD, MPH, a gastroenterologist and chief of the Clinical and Translational Epidemiology Unit at Massachusetts General Hospital (MGH). Their report appears in *JAMA Oncology*.

The researchers carried out a pooled analysis of two large U.S. cohort studies: The Nurses' Health Study (January 1980 - June 2014) and the Health Professionals Follow-up Study (January 1986 - January 2014). These two studies contributed data on more than 94,500 participants' use of aspirin over about 35 years, offering a unique opportunity to understand the effect of aspirin use across the lifespan on cancer risk.

The researchers found that regular aspirin use was linked to lower colorectal cancer risk among people aged 70 or older. However, this advantage was only significant among people who started taking aspirin before the age of 70. People who started regular aspirin use at the age of 70 or older did not seem to reap any benefit.

"There is considerable evidence that aspirin can prevent colorectal cancer in adults between 50 and 70 years old," says Chan. "But it has not been clear whether the effect is similar in older adults."

Aspirin is considered the most well-established agent that protects against colorectal cancer (CRC). It is currently recommended by the U.S. Preventive Services Task Force for people aged 50-59 years with specific cardiovascular risk profiles because of its protective effect against heart disease.

However, the recent Aspirin in Reducing Events in the Elderly (ASPREE) trial reported that participants who took a daily low dose of aspirin (100 mg) after age 70 for about five years actually had an unexpected 30% higher risk of death from cancer. The vast majority of the ASPREE participants (89%) had never taken aspirin regularly before joining the study. Chan's team also recently reported that ASPREE participants on aspirin did not experience an increase or decrease in risk of developing a cancer despite having an increase in risk of death from cancer.

That led to the question: Does regular aspirin benefit or harm people older than 70 and does it matter when aspirin was started?

The current study confirms that initiating aspirin at an older age was not associated with a lower risk of colorectal cancer. However, importantly, there is a potential benefit of continuing aspirin if is started at an earlier age. These results, the researchers say, "strongly suggest that there is a potential biological difference in the effect of aspirin at older ages which requires further research."

Adds Chan: "As people get older, if they are not already taking aspirin, a discussion is warranted about whether to start aspirin after weighing the benefits against the risks."

http://bit.ly/3obtdY0

Cancer vaccine helped keep melanoma under control for years in small study

A personalized "cancer vaccine" may help keep a deadly form of skin cancer from growing for years, a small new study in humans suggests.

By Nicoletta Lanese - Staff Writer

Unlike vaccines that prevent infections, such as measles and influenza, cancer vaccines are a form of immunotherapy that take down cancer cells that already exist. The vaccines train immune cells, called T cells, to better recognize cancer and target it for destruction, while sparing healthy cells in the body.

For example, the new experimental vaccine works by training T cells to spot specific proteins on melanoma cells, a type of skin cancer. In the study, scientists found that the T cells continue to "remember" these proteins for at least four years after the vaccination — and they even learn to recognize more melanoma-related proteins over time.

"The only way that could have happened is if there was actually killing of the tumor cells. And presumably it was the T cells induced by the vaccine that did that killing," said study author Dr.

Catherine Wu, a physician-scientist with the Dana-Farber Cancer Institute and Harvard Medical School in Boston and the Broad Institute in Cambridge, Massachusetts. That's because, once killed, tumor cells fall apart and spill their contents; T cells then swoop in to examine these remains and log that information away for future attacks, Wu said.

While the results are promising, the new study only included eight patients, and more trials need to be conducted to pin down exactly how effective the vaccine is, she added. But as of now, the limited data hint that the vaccine triggers a persistent immune response and can help keep cancer under control, especially when combined with other immunotherapies, the authors noted.

Personalized vaccines

The new study, published Jan. 21 in the journal Nature Medicine, included patients with advanced melanoma who had recently undergone surgery for the cancer. The researchers took samples of the patients' removed tumors and used them to craft personalized vaccines for each of the eight participants.

"It's not just taking something off the shelf, but actually taking information directly from the patient's own tumor in order to direct the composition of the vaccine," Wu said. By examining RNA, a genetic blueprint for proteins inside the cells, the team predicted which unique proteins would be built in different cancer cells; these proteins, called neoantigens, act like a red flag to the immune system.

The final vaccines contained segments of these neoantigens, so the patients' immune cells could learn what they looked like and track the cancer down.

The eight participants each received their personalized vaccine around 4 months after surgery, and the team collected safety data for several years after that. The patients only experienced mild side effects, such as fatigue and flu-like symptoms, the authors noted. The team also collected blood samples at several points during the trial, up to a median of four years after vaccination, to examine patients' T cell responses.

"What's really striking is the durability of the responses," said study author Dr. Patrick Ott, a medical oncologist with the Dana-Farber Cancer Institute, Harvard Medical School and Broad Institute. "You see persistent responses in all treated patients several years out," he said. In addition to being long-lived, the responses diversified over time, meaning T cells learned to recognize neoantigens that weren't present in the original vaccines.

By the end of the 4-year follow-up period, all eight patients were alive and six out of eight showed no signs of active disease. That said, some had experienced cancer recurrence earlier in the study period and received additional treatments.

"From the beginning, we conceived vaccines as a very important adjunct therapy that can be used in combination with other potent agents," Wu said. In other words, no one expected the vaccines, alone to completely eliminate the patients' cancer. And because several patients received treatment during the trial, the team could see whether the vaccine amplified or undermined these therapies.

Two of the patients who received additional treatment stood out, in this respect. In both their cases, the cancer had spread to their lungs and they received drugs called "checkpoint blockades," which essentially rip the brakes off of T cells and help amplify their activity. With both the vaccine and checkpoint blockade drugs in their systems, both patients' detectable cancer was quickly eliminated.

"It's fairly unusual to see a complete response just after the initial treatment period … which was the case in both patients," Ott said. This is an early signal that the vaccine is working together with those checkpoint drugs, basically boosting the effect of the drugs, he said.

Next steps

In general, only a fraction of melanoma patients benefit from checkpoint blockade drugs, said Dr. Pawel Kalinski, director of Cancer Vaccine and Dendritic Cell Therapies at the Roswell Park Comprehensive Cancer Center in Buffalo, New York, who was not involved in the study. Other studies have also hinted that cancer vaccines can boost the efficacy of such drugs, so the new clinical trial adds to that evidence, he said in an email.

That said, "in this small number of patients, [it's] hard to draw significant conclusions on the effect of checkpoint inhibitors," Dr. Joshua Brody, director of the Lymphoma Immunotherapy Program at the Icahn School of Medicine at Mount Sinai, who was not involved in the study, said in an email. However, logically, "we imagine" that the vaccines do boost the effects of these drugs and that such findings should hold up in larger clinical trials, Brody said.

Theoretically, vaccines could be given to patients to prime their immune systems and drive T cells toward the site of the cancer; then, checkpoint blockade drugs would come in for the kill, Ott said. While it's not known why some patients don't respond to checkpoint blockades, alone, evidence hints that the drugs work best when T cells are already at the tumor site, Nature News reported; so vaccines may help set up the drugs for success. Vaccines and checkpoint blockades could also be paired with various adjuvants — substances that provoke a strong immune response — and substances that support T cell survival, Kalinski said. But of course, many more trials will need to be conducted before that future becomes a reality.

"The data presented in the current paper is certainly very provocative, but addresses relatively few patients whose tumors were completely resected" via surgery, Kalinski said. Future trials will need a control group — to see how patients who have surgery plus the vaccine fare compared with those who have surgery, alone, he said. In addition, scientists will need to figure out which T cell responses are associated with long-term positive outcomes, he added.

In addition, to be practical in medical care, the vaccines need to be produced more quickly than they were in this study, Wu noted. During the trial, vaccine production took between 12 and 20 weeks; in the future, this process could be streamlined to take only four to five weeks, she said.

http://bit.ly/2MhMWrB

Ancient Dogs Had Complex Genetic Histories

Some dog population genetics show similarities to ours, such as in the ability to digest grains, but other lineages differ.

By Eliene Augenbraun

Dogs were the first animals to be domesticated. And they stuck with us as we changed lifestyles from hunting/gathering to farming to city living.

“The dog is a species that is intimately linked to human history.” Anders Bergström, a postdoc at the Francis Crick Institute in London. He and his colleagues studied the genomes of 27 ancient dog bones dug up around the world. They found that by 11,000 years ago:

Bergström: “We see that the dog started to diversify genetically. So we find evidence of at least five major lineages of dogs already at this time.” Dog remains have been found in Europe, Asia and the Americas in a pattern similar to how humans moved and mixed.

Bergström: “To a large degree the history of dogs seems to have been shaped by human history, so likely reflecting how when humans moved they would have brought their dogs with them.”

Ancient humans clearly found dogs to be very useful.

Bergström: “In the Arctic there's evidence that sled dogs actually emerged very early and people used them for the particular purpose

of sledding, perhaps as early as 10,000 years ago."

A few modern breeds—like the African Basenji, New Guinea Singing Dog or Australian Dingo—are similar to one of the five ancient lineages. Most other modern breeds derive at least in part from European dogs, which came to dominate dog genomes.

Bergström: "If you go back four or five thousand years ago there's a great diversity of dogs in Europe, but at some point there was probably a single population that expanded and basically replaced other populations in Europe. This was something that we did not predict, and you couldn't really see just from studying archaeology. But when we look at the DNA we see that there's all this diversity in the past that is not represented in present day dogs."

The study is in the journal *Science*, where you'll find maps of dog migrations over time. [Anders Bergström et al, Origins and genetic legacy of prehistoric dogs] One odd finding: about 11,000 years ago it looks like dogs spread more widely than humans did.

Bergström: "That's actually a process we don't really understand. So how could the dog spread so quickly and widely? We're not aware of any human migrations at this time that could have facilitated the spread of the dog but somehow it spreads very quickly to human groups all across the world, perhaps because it was a very useful thing for these early human hunter-gatherer groups."

Humans were also useful to dogs. Prehistoric Petcos didn't exist, so dogs probably ate what humans did. And as humans started to farm, both species quickly adapted to digest more grains. The number of copies of a starch-digesting gene in both humans and dogs increased in the generations following the invention of agriculture.

Bergström: "Yeah, so that's a very striking example of convergent evolution between humans and dogs…in a way it's kind of interesting to think of the dog as a kind of an evolutionary experiment that runs alongside human history and undergoes the same lifestyle changes that we do."

http://bit.ly/36pBxqP

Iodine thruster could slow space junk accumulation

For the first time ever, a telecommunications satellite has used an iodine propellant to change its orbit around Earth.

The small but potentially disruptive innovation could help to clear the skies of space junk, by enabling tiny satellites to self-destruct cheaply and easily at the end of their missions, by steering themselves into the atmosphere where they would burn up.

The technology could also be used to boost the mission lifetime of small CubeSats that monitor agricultural crops on Earth or entire mega-constellations of nanosats that provide global internet access, by raising their orbits when they begin to drift towards the planet.

The technology was developed by ThrustMe, a spin-off company from the École Polytechnique and the French National Centre for Scientific Research (CNRS), and supported by ESA through its program of Advanced Research in Telecommunications Systems (ARTES).

It uses a novel propellant—iodine—in an electric thruster that controls the satellite's height above Earth. Iodine is less expensive and uses simpler technologies than traditional propellants.

Unlike many traditional propellants, iodine is non-toxic and it is solid at room temperature and pressure. This makes it easier and cheaper to handle on Earth.

When heated, it turns to gas without going through a liquid phase, which makes it ideal for a simple propulsion system. It is also denser than traditional propellants, so it occupies smaller volumes onboard the satellite.

ThrustMe launched its iodine thruster on a commercial research nanosat called SpaceTy Beihangkongshi-1 that went into space in November 2020. It was test fired earlier this month before being used to change the orbit of the satellite.

http://bit.ly/2MnS65e

Single atoms as a catalyst: Surprising effects ensue

Everything is suddenly different when you arrive at the smallest possible size: a single atom

For years, the metal nanoparticles used in catalysts have been getting smaller and smaller. Now, a research team at TU Wien in Vienna, Austria have shown that everything is suddenly different when you arrive at the smallest possible size: a single atom.

Metals such as gold or platinum are often used as catalysts. In the catalytic converters of vehicles, for example, platinum nanoparticles convert poisonous carbon monoxide into non-toxic CO2. Because platinum and other catalytically active metals are expensive and rare, the nanoparticles involved have been made smaller and smaller over time.

"Single-atom" catalysts are the logical end point of this downsizing: The metal is no longer present as particles, but as individual atoms that are anchored on the surface of a cheaper support material. Individual atoms can no longer be described using the rules developed from larger pieces of metal, so the rules used to predict which metals will be good catalysts must be revamped - this has now been achieved at TU Wien. As it turns out, single atom catalysts based on much cheaper materials might be even more effective. These results have now been published in the journal *Science*.

Smaller is sometimes better

Only the outer atoms of the piece of metal can play a role in chemical processes - after all, the atoms inside never come into contact with the environment. In order to save material, it is therefore best to use tiny metal particles instead of large lumps, so that a greater proportion of the atoms reside at the surface. If we go to the ultimate limit and use individual atoms, every single atom is chemically active. Over the last decade the field of "single atom" catalysis has grown dramatically, achieving great success.

Wrong model, right solution

"The reasons why some precious metals are good catalysts was already researched in the 1970s," says Prof. Gareth Parkinson from the Institute for Applied Physics at TU Wien. "For example, Gerhard Ertl was awarded the Chemistry Nobel Prize in 2007 for providing atomic-scale insights into catalysis."

In a piece of metal, an electron can no longer be assigned to a specific atom; the electronic states result from the interaction of many atoms. "For individual atoms, the old models are no longer applicable" says Gareth Parkinson. "Individual atoms do not share electrons like a metal, so the electron bands, whose energy was key to explaining catalysis, simply do not exist in this case."

Gareth Parkinson and his team have therefore been intensively investigating the atomic mechanisms behind this single-atom catalysis in recent years. "In many cases the metals that we think of as good catalysts remain good catalysts in the form of individual atoms" says Gareth Parkinson. "In both cases it is the same electrons, the so-called d electrons, that are responsible for this."

Customized properties through tailored surfaces

Entirely new possibilities arise in single-atom catalysis that are not available when using ordinary metal particles: "Depending on the surface on which we place the metal atoms and which atomic bonds they form, we can change the reactivity of the atoms", explains Parkinson.

In some cases, particularly expensive metals like platinum are no longer necessarily the best choice. "Individual nickel atoms show great promise for carbon monoxide oxidation. If we understand the atomic mechanisms of single atom catalysis, we have a lot more leeway to influence the chemical processes," says Parkinson.

Eight different metals were precisely analyzed in this way at TU Wien - the results fit perfectly with the theoretical models that have

now been developed in a collaboration with Prof. Cesare Franchini at the University of Vienna.

"Catalysts are very important in many areas, especially when it comes to chemical reactions that play a major role in attempts to develop a renewable energy economy," emphasizes Gareth Parkinson. "Our new approach shows that it doesn't always have to be platinum." The decisive factor is the local environment of the atoms - and if you choose it correctly, you can develop better catalysts and at the same time save resources and costs.

http://bit.ly/2MhFblF

New perspectives challenge the idea that saturated fats cause heart disease

In science, sometimes a new perspective can turn our interpretation of the data upside-down, and necessitate a paradigm shift.

There has been, and continues to be, fierce disagreements in nutrition science as to what constitutes a healthy diet. A key controversy is the role of saturated fats in health and disease. Saturated fats are known to increase blood cholesterol levels, and increased blood cholesterol is often observed in people who develop cardiovascular disease.

It has been thought for more than half a century that saturated fats in the diet promote heart disease by increasing blood cholesterol. However, a new model explains why this so-called "diet-heart hypothesis", which has had a major influence on dietary guidelines, may have an alternative explanation.

In a new article published today in the *American Journal of Clinical Nutrition*, three scientists have raised a question that challenges the diet-heart-hypothesis: Why do saturated fats increase blood cholesterol, and why should this be dangerous? After all, saturated fats occur naturally in a wide variety of foods, including breast milk.

"Cholesterol is a critically important molecule for all cells in the body," explains associate professor Marit Zinöcker, the lead author at Bjørknes University College, Oslo, Norway. "A cell is surrounded by a fluid membrane that controls cell function, and the cells depend on the ability to incorporate a certain amount of cholesterol molecules, so that their membranes don't become too stiff or too fluid."

"The basis of the model is that when saturated fats replace polyunsaturated fats in the diet, less cholesterol is needed in the cell membranes," she explains. The opposite is true when eating more polyunsaturated fatty acids, which include omega-3 and omega-6 fatty acids. "This is because polyunsaturated fats from the diet enter our cell membranes and make them more fluid. The cells adjust the fluidity of their membranes by incorporating cholesterol recruited from the bloodstream. According to the model presented by the researchers, this can explain why blood cholesterol levels decrease when we eat more polyunsaturated fats.

The authors have named the model the "Homeoviscous Adaptation to Dietary Lipids" (HADL) model.

"Cells need to adjust their membrane fluidity according to changes in their environment, such as the access to different types of fat", says co-author Simon N. Dankel, researcher at the Department of Clinical Science, University of Bergen, Norway.

"This phenomenon is called homeoviscous adaptation, and has been described in both microorganisms, vertebrates and in human skin cells. We argue that this is a critical principle in human physiology. Our cells are normally capable of adjusting their cholesterol content according to changes in dietary fats."

"Nutrition research often focuses on what changes in the body, but the question of why something, such as the blood cholesterol, changes, is of equal importance", says co-author Karianne Svendsen, postdoctoral fellow at the Department of Nutrition,

University of Oslo, Norway.

This is where the new HADL model comes into play, providing an explanation based on adaptive human physiology. "From the perspective of the HADL model, we find logical explanations for why cells need to change their cholesterol content, and thereby the blood cholesterol, when fats in the diet change," says Zinöcker.

In the paper, other reasons for elevated LDL-cholesterol in people with cardiovascular disease are discussed, such as low-grade inflammation and insulin resistance. This indicates that elevated blood cholesterol caused by metabolic disruptions must be uncoupled from elevated blood cholesterol caused by a major change in intake of dietary saturated fatty acids. It also questions the benefit of lowering blood cholesterol by adding polyunsaturated fatty acids to the diet, and not addressing the root cause.

"There is at best weak evidence that a high intake of saturated fat causes heart disease," says Dankel. "The overall data are inconsistent and unconvincing, not to mention the lack of a logical biological and evolutionary explanation."

"Also, people with metabolic disorders often do not show the expected changes in blood cholesterol when changing their fat intake, suggesting loss of the normal response."

"The research and reasoning that the HADL model is based on indicates that the effect of dietary fats on blood cholesterol is not a pathogenic response, but rather a completely normal and even healthy adaptation to changes in diet." Zinöcker concludes.

The authors state that although the model is based on existing knowledge of cellular mechanisms, the model still needs to be verified. The authors therefore urge researchers to discuss the HADL model using #HADLmodel and to test the model.

The paper was published online on January 20 and can be found here: https://academic.oup.com/ajcn/advance-article-abstract/doi/10.1093/ajcn/nqaa322/6104795

http://wb.md/3iQdE72

Consensus on Diagnosis, Management of Acute Flaccid Myelitis

A large group of researchers has reviewed the literature related to acute flaccid myelitis (AFM) and has summarized current knowledge of this illness in a new consensus document.

Erik Greb

In it, researchers describe the epidemiology and potential causes of AFM, the disease's clinical presentation, the methods required to diagnose it, effective strategies for acute management, and considerations for long-term rehabilitation.

The authors intended "to achieve a consensus for diagnosis and management of AFM to facilitate better and more effective care of patients affected by this disorder," Carlos A. Pardo, MD, professor of neurology and pathology at Johns Hopkins University School of Medicine, Baltimore, Maryland, told *Medscape Medical News*. "The final goal is that any healthcare provider around the world be aware about AFM, the diagnostic criteria, and acute management and care of the long-term consequences of AFM."

The incidence of AFM has increased since 2012, and the disease should be regarded as a major global public health concern, the authors write. The possibility of future AFM outbreaks makes it necessary to increase awareness of the disease and educate clinicians about diagnosis and treatment, they note.

Questions that remain unanswered include how common exposures such as enterovirus infections cause severe neurologic disease, what the optimal therapeutic approach is, and whether prevention is necessary.

The review was published online January 23 in *The Lancet.*

Pleocytosis Common

AFM is a disabling disease that resembles polio and mainly affects children. It has been diagnosed around the world and often occurs

in geographical clusters. Researchers suspect that the D68 enterovirus causes the seasonal, biennial outbreaks that have been observed.

Other enteroviruses, such as A71 and coxsackievirus strains, also may cause AFM. Defining the disease by its associated organism may not be appropriate for clinical practice, however, inasmuch as D68 may be detectable only at an early stage of the disease, the authors write.

The median age of patients with AFM is 6.3 years. Most experience a prodrome marked by fever and respiratory symptoms, such as cough, rhinorrhea, or pharyngitis, they note. Neurologic symptoms generally begin 1 to 10 days after the onset of the prodrome.

Patients develop flaccid weakness and hyporeflexia or areflexia in one or more limbs. Onset typically is asymmetric and favors the upper limbs and proximal muscles. Patients also may have weakness of the neck, trunk, diaphragm, or other respiratory muscles. Most patients require hospitalization, and some need intubation.

The most useful diagnostic test, the researchers suggest, is MRI of the spinal cord. The characteristic finding in AFM is T2 hyperintensity of the spinal cord gray matter. Spinal cord gray matter lesions tend to be longitudinally extensive. The cervical cord is the most commonly affected.

For almost all patients, lumbar puncture reveals cerebrospinal fluid (CSF) pleocytosis, the authors note. The white blood cell count is mildly to moderately elevated; levels resolve over several weeks. In the acute phase, CSF analysis helps distinguish AFM from other causes of flaccid paralysis that are less likely to cause pleocytosis.

Identifying the causes of AFM or its mimics requires investigation outside the central nervous system or CSF, they note. Respiratory samples may indicate enterovirus D68, and stool samples may indicate enterovirus A71. Electromyography or nerve conduction studies often are not required for diagnosis.

Early management of AFM centers on supportive treatment. This includes securing the airway, treating autonomic dysfunction, managing pain, preventing the complications of acute immobility, and beginning early rehabilitation. The pathophysiology of AFM is incompletely understood, and no medical therapies have been studied in prospective, controlled trials. Intravenous immunoglobulin often is administered because the primary cause of AFM is believed to be viral infection.

Residual Impairment

After remission, many patients with AFM develop residual impairment. Data suggest that fewer than 10% of patients achieve full recovery. Electromyography, nerve conduction studies, and MRI could help predict patients' outcomes.

Recovery in the limbs appears to progress from distal to proximal areas. The worst-affected muscle groups are the least likely to recover. Deaths from AFM are rare. Although rehabilitation can lead to continuing functional recovery, patients may have neurologic, musculoskeletal, or psychological sequelae.

"Prognosis and outcome biomarkers of AFM are not very well established," said Pardo. "However, the magnitude of MRI abnormalities within the spinal cord during the acute stage and the need for critical care management and mechanical ventilation are perhaps the most recognized factors that identify poor outcomes."

The most urgent focus of research is the mechanism of AFM pathogenesis, said Pardo. Investigators also are searching for reliable tools for the rapid laboratory diagnosis of AFM. These tools may identify viruses or diagnostic biomarkers. Another priority of research is the identification and development of treatment approaches for limiting the rapid progression of neurologic damage after symptom onset, said Pardo.

Comprehensive Review

"This is the most comprehensive review [of AFM] published to date," Marc C. Patterson, MD, professor of neurology, pediatrics, and medical genetics at Mayo Clinic Children's Center, Rochester, Minnesota, told *Medscape Medical News*. "The review emphasizes the importance of considering this diagnosis in any child with weakness, particularly asymmetric weakness, and provides useful guidance in differentiating alternative diagnoses."

Recognition of AFM has improved significantly in recent years, although it remains a challenge, Patterson added. "Access to the appropriate diagnostic tests represents a continued unmet need, particularly in resource-poor areas," he said.

A majority of patients who are exposed to the virus may be mildly affected, and the biggest unanswered question may be which host factors predispose a patient to develop severe disease.

"These are not new questions; in the age of polio pandemics, only a minority of susceptible individuals developed severe neurologic disease," said Patterson. "If we understood the host factors (presumably related to genetically determined variations in individual immune systems), it might be possible to recognize highly susceptible individuals and to tailor specific therapies for them."

The review was supported by the Siegel Rare Neuroimmune Association and the Bart McLean Fund for Neuroimmunology Research. Pardo is an unpaid advisor to the AFM Task Force of the Centers for Disease Control and Prevention. He receives support from the National Institutes of Health and the Bart McLean Fund for Neuroimmunology Research. Patterson has disclosed no relevant financial relationships.

Lancet. Published online January 23, 2021. Abstract

http://wb.md/3qLRMfK

Lifestyle Fallout From Hip Fracture Declines by Year 2

Most people recover from the depression associated with a hip fracture in about a year as they return to normal activities, researchers find.

Laird Harrison

Physicians can help by encouraging these patients to stay in contact with friends and family, said senior author Timothy Bhattacharyya, MD, head of the Clinical and Investigative Orthopedics Surgery Unit at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) in Bethesda, Maryland.

"The patients that had larger social networks recovered faster," he told *Medscape Medical News.* The finding can help guide the expectations of patients and their family about recovery, he said.

The findings were published January 1 in the *Journal of the American Academy of Orthopaedic Surgeons.*

Previous studies have found that hip fractures can restrict mobility and increase the risk of depression, and that depressed patients recover more slowly. But these studies have not compared large populations of people with fractures to matched cohorts without fractures.

To fill that gap, Jay Swayambunathan, also with the Clinical and Investigative Orthopedics Surgery Unit at NIAMS, and colleagues drew data from a nationally representative sample of subjects aged 65 and older from the National Health and Aging Trends Study (NHATS).

Overall, hip fracture incidence was 1.3% per year. Swayambunathan and colleagues analyzed a cohort of 82 people who had a single hip fracture between 2011 and 2016, and who were able to drive before the fracture. They compared those individuals with the 4495 other people in the database.

The demographics of the two groups were similar, except that the hip fracture patients were slightly older and more likely to have dementia.

In the first year after a fracture, 20.2% of men and 17.3% of women died. By comparison, the overall yearly mortality rate in the NHATS sample was 7.9%. Among those with hip fractures, 76% reported driving in the first year, vs 95% of control subjects.

Eighty-six percent of those with fractured hips reported leaving the house regularly vs 99% of control subjects.

In the first year, 44% of those with fractured hips reported they couldn't pursue their favorite activity, compared with 18% of control subjects. And only 17% of those with hip fractures reported working or volunteering in the past month compared with 44% of control subjects. Also in that first year, 20% of surviving hip fracture patients reported feeling down, depressed, or hopeless on most days compared with 10% of control subjects.

The differences between the two groups diminished each year, most of them becoming statistically insignificant by the second year. That's useful information to share with patients, said Bhattacharyya. "You can reassure them that people do continue to experience improvement for up to 2 years after their fracture."

The size of the social network of people with fractured hips did not seem to affect driving, leaving the house, or depression for the first year.

But among hip fracture subjects, 68% of those with small social networks (two people or fewer) reported being kept from their favorite activities by their health in the first year, compared with 40% of those with large social networks (at least three people). And 30% of those with large social networks reported working or volunteering in the past month compared with 12% of those with small social networks.

Bhattacharyya said he encourages his patients not to isolate themselves after a hip fracture. "It's a natural tendency, when you're feeling under the weather, or you're feeling depressed or sad. You don't want to spread that to everyone else. But people really want to hear from you."

That advice is even more important under the restrictions imposed to prevent the spread of COVID-19, he said.

J Am Acad Orthop Surg. 2021;29:e22-e30. Abstract

http://nyti.ms/3sQRB4x

Six Stars, Six Eclipses: 'The Fact That It Exists Blows My Mind'

A handful of other six-star systems have been discovered, but this one is unique.

By Robin George Andrews

From star-destroying black holes to exploding comets, NASA's Transiting Exoplanet Survey Satellite, or TESS, has spotted its share of surprises since it began searching the galaxy for exoplanets in 2018. But the source of starlight that was mysteriously brightening and dimming some 1,900 light-years away may top all those discoveries for its science fiction-like grandeur.

The source, named TIC 168789840, is a system of six stars. That alone makes it a rarity, but what makes this sextuplet even more remarkable is that they consist of three pairs of binary stars: three different stellar couplets revolving around three different centers of mass, but with the trio remaining gravitationally bound to one another and circling the galactic center as a single star system. Although a handful of other six-star systems have been discovered, this one is unique: It is the first in which the stars within each of those three pairings pass in front of and behind each other, eclipsing the other member of its stellar dance troupe, at least from our space telescope's line of sight.

In other words, scientists have found a sextuply eclipsing sextuple star system. The discovery, posted online this month, has been accepted for publication in The Astronomical Journal.

Exoplanets within the star cluster have not yet been confirmed, but if you lived on a world within, the night sky would be something special, said Tamás Borkovits, an astronomer at the Baja Astronomical Observatory in Hungary and co-author. Any inhabitants of these worlds, "could see two suns, just like Luke Skywalker on Tatooine," Dr. Borkovits said, as well as four other

very bright stars dancing around the sky.

But only one of the pairs could have any planets. Two of the system's binaries orbit extremely close to one another, forming their own quadruple subsystem. Any planets there would likely be ejected or engulfed by one of the four stars. The third binary is farther out, orbiting the other two once every 2,000 years or so, making it a possible exoplanetary haven.

Watching: Recommendations on the best TV shows and films to stream and watch.

Exotic stellar collections like this don't just look cool. They refine and challenge our understanding of how multiple star systems form, said Patricia Cruz, an astrophysicist at the Center of Astrobiology in Madrid who was not involved with the work.

The depth and duration of TIC 168789840's eclipses let astronomers determine the dimensions, masses and relative temperatures of its stars — vital information that can be plugged into models of star formation. But even with those clues, the origin of this whirling six-star system will remain a puzzle until we find others like it.

"The system exists against the odds," said Brian Powell, a data scientist at NASA's High Energy Astrophysics Science Archive Research Center in Greenbelt, Md. and the study's lead author.

NASA's TESS satellite looks for exoplanets by searching for temporary dips in a star's light, caused by a planet orbiting in front of it from our perspective. But, Dr. Cruz said, scientists originally used the same light-blocking principle with other telescopes to spy stars obscuring other stars.

Using this concept, Mr. Powell, working with Veselin Kostov, an astrophysicist at the SETI Institute, designed a neural network that could identify eclipsing binary stars using TESS data.

The neural network studied an archive of nearly 80 million records of light-intensity changes, way more than humans alone could handle. "What machine learning can do is take this intractable data set and turn it into something a human can work with," Mr. Powell said. It found a surfeit of multiple star systems, including the superlative TIC 168789840 last March.

Late last year the data was turned over to "hawk-eyed and very enthusiastic" professional and amateur stargazers all over the world, Dr. Borkovits said. Their efforts confirmed that TIC 168789840 was a sextuple system and helped clarify its stars' characteristics, orbital dimensions and paths.

Andrei Tokovinin, an astronomer at the Cerro Tololo Inter-American Observatory in La Serena, Chile, and a co-author of the study, suggests one explanation for how the system came to be: Three stars formed within an expansive gas cloud, all orbiting each other in a triple-star system. Later, they encountered a dense clump of gas from the same cloud. That encounter led to disks forming around the original trio of stars, eventually giving each of them smaller companions.

Trying to unravel its origins is a worthwhile endeavor. But for Mr. Powell, "working with literally the most interesting data in the universe" to simply find this strange sextuplet is reward enough.

"Just the fact that it exists blows my mind," he said. "I'd love to just be in a spaceship, park next to this thing and see it in person."

http://wb.md/3sNK8mZ

ColCORONA: Colchicine Reduces Complications in Outpatient COVID-19

The oral, anti-inflammatory drug colchicine can prevent complications and hospitalizations in nonhospitalized patients newly diagnosed with COVID-19, according to a press release from the ColCORONA trial investigators.

Patrice Wendling

After 1 month of therapy, there was a 21% risk reduction in the primary composite endpoint of death or hospitalizations that missed

statistical significance, compared with placebo among 4488 outpatients enrolled in the global, phase 3 trial.

After excluding 329 patients without a confirmatory PCR test, however, the use of colchicine was reported to significantly reduce hospitalizations by 25%, the need for mechanical ventilation by 50%, and deaths by 44%.

"We believe that this is a medical breakthrough. There's no approved therapy to prevent complications of COVID-19 in outpatients, to prevent them from reaching the hospital," lead investigator Jean-Claude Tardif, MD, from the Montreal Heart Institute in Quebec, Canada, told *theheart.org | Medscape Cardiology*. "I know that several countries will be reviewing the data very rapidly and that Greece approved it today," he said. "So this is providing hope for patients."

Having been burned by hydroxychloroquine and other treatments brought forth without peer review, the response to the announcement was tempered by a desire for more details.

Asked for comment, Steven E. Nissen, MD, Cleveland Clinic Foundation, Cleveland, Ohio, was cautious. "The press release about the trial is vague and lacks details such as hazard ratios, confidence intervals, and *P* values," he told *theheart.org | Medscape Cardiology*.

"It is impossible to evaluate the results of this trial without these details. It is also uncertain how rigorously data were collected," he added. "We'll need to see the manuscript to adequately interpret the results."

The evidence in the press release is hard to interpret, but early intervention with anti-inflammatory therapy has considerable biologic appeal in COVID, said Paul Ridker, MD, MPH, who led the pivotal CANTOS trial of the anti-inflammatory drug canakinumab in the post-MI setting, and is also chair of the ACTIV-4B trial currently investigating anticoagulants and antithrombotics in outpatient COVID.

"Colchicine is both inexpensive and generally well tolerated, and the apparent benefits so far reported are substantial," Ridker, from Brigham and Women's Hospital in Boston, Massachusetts, told *theheart.org | Medscape Cardiology*. "We are eager to see the full data as rapidly as possible."

The commonly used gout and rheumatic disease agent costs about 26 cents in Canada and between $4 and $6 in the United States. As previously reported, it reduced the time to clinical deterioration and hospital stay but not mortality in the 105-patient Greek Study in the Effects of Colchicine in COVID-19 Complications Prevention (GRECCO-19) study.

Tardif said he's looking forward to having the data in the public domain and that they acted swiftly because the evidence was "clinically persuasive" and "the health system is congested now."

"We received the results Friday, January 22 at 5 p.m., an hour later we were in meetings with our data safety monitoring board [DSMB], 2 hours later we issued a press release, and a day later we're submitting a full manuscript to a major scientific journal, so I don't know if anyone has done this at this speed," he said. "So we are actually very proud of what we did."

ColCORONA was designed to enroll 6000 outpatients, at least 40 years of age, who were diagnosed with COVID-19 infection within the previous 24 hours, and had a least one high-risk criterion, including age at least 70 years, body mass index $\geq$ 30 kg/m^2, diabetes mellitus, uncontrolled hypertension, known respiratory disease, heart failure or coronary disease, fever of $\geq$ 38.4°C within the last 48 hours, dyspnea at presentation, bicytopenia, pancytopenia, or the combination of high neutrophil count and low lymphocyte count.

Participants were randomly assigned to receive either placebo or colchicine 0.5 mg twice daily for 3 days and then once daily for

another 27 days. The number needed to prevent one COVID-19 complication is about 60 patients, Tardif said.

Colchicine was well-tolerated and resulted in fewer serious adverse events than with placebo, he said. Diarrhea occurred more often with colchicine, but there was no increase in pneumonia. Caution should be used, however, in treating patients with severe renal disease.

Tardif said he would not prescribe colchicine to an 18-year-old COVID outpatient who doesn't have any concomitant diseases, but would for those meeting the study protocol.

"As long as a patient appears to me to be at risk of a complication, I would prescribe it, without a doubt," he said. "I can tell you that when we held the meeting with the DSMB Friday evening, I actually put each member on the spot and asked them, 'If it were you — not even treating a patient, but if you had COVID today, would you take it based on the data you've seen?' and all of the DSMB members said they would.

"So we'll have that debate in the public domain when the paper is out, but I believe most physicians will use it to treat their patients."

The trial was coordinated by the Montreal Heart Institute and funded by the Government of Quebec; the National Heart, Lung, and Blood Institute of the US National Institutes of Health; Montreal philanthropist Sophie Desmarais; and the COVID-19 Therapeutics Accelerator launched by the Bill & Melinda Gates Foundation, Wellcome, and Mastercard. CGI, Dacima, and Pharmascience of Montreal were also collaborators.

http://bit.ly/39aXe5P

No Trees Harmed: MIT Aims to One Day Grow Your Kitchen Table in a Lab

The big vision is to grow instead of build some products made of biomaterials

By Jason Dorrier

You've likely heard the buzz around lab-grown (or cultured) meat. We can now take a few cells from a live animal and grow those cells into a piece of meat. The process is kinder to animals, consumes fewer resources, and has less environmental impact.

MIT researchers will soon publish a paper describing a proof-of-concept for lab-grown plant tissues, like wood and fiber, using a similar approach. The research is early, but it's a big vision. The idea is to *grow* instead of build some products made of biomaterials.

Consider your average wooden table. Over the years, a tree (or trees) converted sunlight, minerals, and water into leaves, wood, bark, and seeds. When it reached a certain size, the tree was logged and transported to a sawmill to be made into lumber. The lumber was then transported to a factory or wood shop where it was cut, shaped, and fastened together.

Now, imagine the whole process happening at the same time in the same location. That's the futuristic idea at play here. Wood grown from only the cells you're interested in (no seeds, leaves, bark, or roots) could be manipulated to produce desirable properties and grown directly into shapes (like a kitchen table). Fewer 18-wheelers and power tools.

No fuss, no muss.

And of course, once refined, the technique wouldn't be confined to growing tables. Other products could be made from a variety of biomaterials. In theory, and at scale, the process would be more efficient, less wasteful, and save a few forests too.

That's the vision. But first, researchers need to figure out if it's even viable.

Coaxing Wood From Cells

Lead author and MIT PhD student in mechanical engineering, Ashley Beckwith, said she was inspired by time spent on a farm. Viewed through the exacting lens of an engineer, Beckwith was struck by agriculture's inefficiencies. The weather and seasons are beyond our control. We use land and resources to grow whole plants but only use bits and pieces of them for food or materials.

"That got me thinking: Can we be more strategic about what we're

getting out of our process? Can we get more yield for our inputs?" Beckwith said in an MIT release about the research. "I wanted to find a more efficient way to use land and resources so that we could let more arable areas remain wild, or to remain lower production but allow for greater biodiversity."

To test the idea, the team took cells from the leaves of a zinnia plant and fed them in a liquid growth medium. After the cells grew and divided, the researchers placed them in a gel scaffold and bathed the cells in hormones. You may be wondering what cells from zinnias—which are a small flowering plant—have to do with wood. Turns out, their properties can be "tuned" like stem cells to express desired attributes. The hormones, auxin and cytokinin, induced the zinnia cells to produce lignin, a polymer that makes wood firm.

By adjusting their hormonal knobs, the team was able to dial in lignin production. Further, the gel scaffold, which is itself firm, coaxed the cells to grow into a particular shape.

"The idea is not only to tailor the properties of the material, but also to tailor the shape from conception," said Luis Fernando Velásquez-García, a principal scientist in MIT's Microsystems Technology Laboratories, coauthor on the paper, and Beckwith's coadvisor.

Velásquez-García's lab works with 3D printing technology, and he sees the new technique as a kind of additive manufacturing, where each cell is a printer and the gel scaffold directs their production. While it's still early, the team believes their work proves plant cells can be manipulated to produce a biomaterial with properties suitable for a specified use. But of course, much more work is required to take the idea beyond proof-of-concept.

Growing Things

The researchers say they need to figure out if what they've learned can be adapted to other cell types. The hormonal knobs and dials may differ species to species. Also, scaling up requires solving problems like maintaining healthy gas-exchange between cells. Pending more research, whether the idea makes a strong case compared to traditional methods outside of the lab is, of course, also an open question. But this isn't unusual.

Early research answers the basic question: Is this idea worth pursuing further? It often, necessarily, leaves key questions unanswered, such as cost and scalability. Early experiments in lab-grown meat, for example, were incredibly costly and lacked key properties. The first lab-grown burger famously cost a few hundred thousand dollars but lacked the fatty (tasty) bits of a traditional ground-beef burger.

It wasn't ready for prime time in terms of cost or quality, but in the years since, investment and interest have grown and costs declined. Now it's not so laughable to imagine lab-grown meat in your local grocery or restaurant. Just last year, Singapore became the first country to approve lab-grown meat for commercial consumption.

Whether or not this particular vision gathers steam, seeing cells as miniature factories isn't new. Increasingly, the worlds of bioengineering and manufacturing are colliding. Engineered cells are already being put to work in industrial settings, and last fall, a Japanese clothing brand offered a limited edition (and extremely pricey) sweater made of 30% fiber produced by gene-hacked bacteria grown in a bioreactor.

Down the road, it's possible we'll not only build furniture—but grow it too.