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Alzheimer's drugs targeting amyloid plaque may be doomed to fail

In a study of the cause of Alzheimer's, cognitive decline tracked something other than high levels of amyloid plaques

Rose Egelhoff

In June, the Food and Drug Administration approved the first drug designed to slow the progression of Alzheimer's disease. The drug, called aducanumab, clears amyloid plaques — clumps of brain proteins that are characteristic of Alzheimer's disease. Proponents of the drug say that amyloid plaques are toxic, and that they lead to brain inflammation and the loss of brain cells, causing cognitive impairment.

But critics say there is scant evidence that the drug actually helps people with Alzheimer's, and not all scientists agree that amyloid plaques cause the disease, though there is a correlation. In fact, some people with amyloid plaques do not show cognitive decline.

In new study, University of Cincinnati researchers sought to understand this apparent paradox. Their idea is maybe the cause of Alzheimer's is not an accumulation of these protein clumps, but rather a decrease in their precursor: soluble un-clumped amyloid proteins in the brain. Soluble amyloid proteins have a number of important jobs in brain function, including brain development and protecting brain cells from premature death.

To test this idea, the researchers looked at soluble amyloid protein levels in people with varying stages of cognitive decline. They found that healthy individuals with amyloid plaques in their brains still had high levels of the soluble amyloid protein. Dementia was much more related to low soluble protein levels than it was to high levels of amyloid plaques. These results add to the evidence that plaques may not be the direct cause of Alzheimer's, and they calls into question the FDA's decision to approve aducanumab.

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Lumpy tumor shown on facial reconstruction of Neanderthal who lived on 'drowned land'

The Neanderthal lived up to 70,000 years ago.

By Laura Geggel

You can now gaze into the crinkly eyes of "Krijn," a young Neanderthal man who had a tumor growing on his skull when he died up to 70,000 years ago.

In 2001, an amateur paleontologist found a piece of Krijn's skull while sifting through sediments collected from the bottom of the North Sea, off the coast of the Netherlands. Now, paleo-anthropological artists have used that hunk of skull to create a lifelike bust of Krijn, including the bulge above his right eyebrow where the tumor sat.

A 3D facial reconstruction of the Neanderthal, dubbed Krijn, who had a tumor above his right eyebrow. **(Image credit: RMO)**

"Luckily, it's a very distinctive piece," Adrue Kennis, a paleo-anthropological artist with Kennis & Kennis Reconstructions, said of the skull specimen in a translated video created by the National Museum of Antiquities (RMO) in the Netherlands, which is showing Krijn's bust in a new exhibit.

When Krijn was alive, between 70,000 and 50,000 years ago, he lived in Doggerland, a vast swath of land between the United Kingdom and continental Europe, which is now submerged beneath the North Sea. A 2009 study in the Journal of Human Evolution revealed a few details about Krijn: The young man was highly carnivorous, but his body didn't show any evidence of seafood in his diet, according to an analysis of the isotopes, or element variants, of carbon and nitrogen found in his skull. Moreover, a

lesion above Krijn's eyebrow indicated that he had a tumor known as an intradiploic epidermoid cyst.

These cysts are uncommon, slow-growing lesions that are usually benign, especially when they're small, as Krijn's is, the 2009 study found. The conduction is associated with a slew of symptoms. It's possible that Krijn experienced pain and swelling, headaches, dizziness, convulsions, visual problems or seizures, or maybe he was lucky and didn't have any symptoms, the authors of the 2009 study wrote. That was the first time such a tumor had been documented in Neanderthal remains, they noted.

Despite Krijn's diagnosis, his new bust depicts him with an infectiously happy smile. The Kennis brothers recreated the Neanderthal's features by relying not only on the skull specimen but also other Neanderthal skulls, as well as previous data on Neanderthal eye, hair and skin color. The new bust is the latest from their studio, which includes other early human recreations, including one of Ötzi the Iceman mummy, who lived about 5,300 years ago in the Alps.

Krijn may be smiling for another reason; he's the first fossil hominin dating to the Pleistocene epoch (2.6 million to 11,700 years ago) found under seawater and the first recorded Neanderthal in the Netherlands, according to the 2009 study.

A menagerie of animals, including mammoths, lions, woolly rhinoceroses, reindeer and horses used to live on the Doggerland steppe, but it was very cold, meaning that Krijn likely had a challenging life, according to an RMO statement. In addition to Krijn's remains, scientists sifting through the North Sea sediments found several middle Paleolithic artifacts, including small hand axes and pointed stones known as Levallois flakes.

The RMO exhibit "Doggerland: Lost World in the North Sea," which includes Krijn's bust, is open to the public through Oct. 31.

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Bioscientists Have an Ambitious New Plan to Resurrect The Extinct Woolly Mammoth

It is the elephant in the genomics room: can extinct species be resurrected?

One bioscience firm insists they can, announcing Monday its intent to use emerging technology to restore the woolly mammoth to the Arctic tundra. New company Colossal, capitalizing on a partnership with a Harvard geneticist, said its species "de-extinction" effort has the potential to anchor a working model for restoring damaged or lost ecosystems and thereby help slow or even halt the effects of climate change.

"Never before has humanity been able to harness the power of this technology to rebuild ecosystems, heal our Earth and preserve its future through the repopulation of extinct animals," Colossal chief executive and co-founder Ben Lamm, an emerging technology entrepreneur, said in a statement.

"In addition to bringing back ancient extinct species like the woolly mammoth, we will be able to leverage our technologies to help preserve critically endangered species that are on the verge of extinction and restore animals where humankind had a hand in their demise."

> ***Climate change can be tied back to human activity, so it is our duty to restore Earth to a healthier state. It begins with a new wave of disruptive conservationism and restorative biology. #ItIsColossal pic.twitter.com/fQdfNgUKQI***
>
> **— Colossal (@ItIsColossal) September 13, 2021**

Woolly mammoths roamed much of the Arctic, and co-existed with early humans who hunted the cold-resistant herbivores for food and used its tusks and bones as tools.

The animals died out about 4,000 years ago. For decades, scientists have been recovering bits and pieces of mammoth tusks, bones,

teeth, and hair to extract and try to sequence the mammoth's DNA.
Colossal says it aims to insert DNA sequences of woolly mammoths, collected from well-preserved remains in the permafrost and frozen steppes, into the genome of Asian elephants, to create an "elephant-mammoth hybrid".
Asian elephants and woolly mammoths share a 99.6 percent similar DNA makeup, Colossal says on its website.
Company co-founder George Church is a renowned geneticist and professor of genetics at Harvard Medical School, who is using pioneering techniques, including CRISPR technology, to advance species de-extinction. "Technologies discovered in pursuit of this grand vision – a living, walking proxy of a woolly mammoth – could create very significant opportunities in conservation and beyond," Church said in the statement.
The woolly mammoth's vast migration patterns were seen as critical to preserving the Arctic region's environmental health.
Colossal says restoring the beasts has the potential to revitalize the Arctic grasslands, a vast region with major climate change-combatting properties, such as carbon sequestering and methane suppression. Colossal is funded in part through a US$15 million seed round from investors and says its advisors include leaders in bioethics and genomics.

https://bit.ly/3lyt8OR

Your saliva affects the way you spread pathogens

Our saliva can vary depending on our physiological state, making us more or less likely to pass on bugs to others

Marnie Willman*

We've all been in a crowded place and seen someone sneezing or coughing nearby. You do your best to get away from them, but somehow they always end up right there beside you. The COVID-19 pandemic has increased our collective use of masks and other protective measures that have reduced the transmission of many viruses beyond coronaviruses, including influenza.
Researchers are now finding that there are specific qualities of saliva that might change how easy it is to catch certain pathogens. You may think that everyone's saliva is the same, but our physiological state changes our saliva! If you're stressed or dehydrated, for example, your saliva makeup is different than it would be if you weren't. Saliva thickness also differs between genders: women tend to have thinner saliva, and less of it than men.
University of Florida researchers have found that what compounds are in your saliva, your salivary flow rate (how much saliva you produce), thickness, and other features make the saliva able to travel further when you cough or sneeze. This comes into play when we talk about respiratory viruses like the one that causes COVID-19, which are transmitted by respiratory droplets.
With these suggestions, it may be possible to alter your saliva to decrease your ability to pass potentially deadly bugs to others. Could simply keeping yourself hydrated and being less stressed reduce virus and bacterial transmission? University of Florida researchers say very possibly!

**University of Manitoba Bannatyne and National Microbiology Laboratory*

https://bit.ly/3hC0jzL

Lab-grown cochlear organoids enable screening for hair cell–inducing drugs

Organoid culture-based models for cochlear hair cell formation can be used to identify drugs that promote hair cell regeneration

New research published in *Stem Cell Reports* found that organoid culture-based models for cochlear hair cell formation can be used to identify drugs that promote hair cell regeneration in a high throughput drug library screen. Hair cells in the ear mediate the perception of sound.
Consequently, when hair cells are destroyed or lost through exposure to loud sounds, certain chemicals, disease, or aging,

partial or complete hearing loss is the consequence. According to WHO estimates, one in every 10 people worldwide will have disabling hearing loss by 2050.

Lost hair cells in mammals cannot be repaired or replaced, but intriguingly hair cells in other species like fish and birds have the potential to regenerate.

The reasons for those differences are not fully understood, but it means that hair cell regeneration in humans may be possible under the right conditions.

To identify those conditions, Guoqiang Wan and colleagues from Nanjing University, China, generated cultures of inner ear-like structures, so-called cochlear organoids, from immature cochlear tissue of neonatal mice. Over time, these cochlear organoids multiplied and grew hair cells in the lab.

The study, recently published in *Stem Cell Reports*, used these cochlear organoids to screen a collection of over one thousand FDA-approved drugs for substances stimulating hair cell formation.

One of the most potent substances, an anti-cancer drug called Regorafenib, promoted hair cell formation in the lab-grown cochlear organoids. Notably, this compound also promoted hair cell formation in mouse cochlear tissues.

Remarkably, hair cells were even regenerated in mouse cochlear tissues after having been destroyed by chemical exposure.

This work sets the stage for high throughput screening approaches to identity stimulators of hair cell regeneration in mammals as a potential treatment for hearing loss.

Before this can be applied in patients, additional research is needed to address safety and to determine if the identified drugs can induce hair cells in the human cochleas.

More information: *High throughput screening on cochlear organoids identifies VEGFR-MEK-TGFB1 signaling promoting hair cell reprogramming, Stem Cell Reports (2021). DOI: 10.1016/j.stemcr.2021.08.010 , www.cell.com/stem-cell-reports ... 2213-6711(21)00428-8*

https://bit.ly/2XizQQq

Protein Made in the Liver May Cause Alzheimer's Disease in the Brain

Peripherally produced amyloid causes neurodegeneration.

Amyloid protein made in the liver can cause neurodegeneration in the brain, according to a new study in the open-access journal *PLOS Biology*, by John Mamo of Curtin University in Bentley, Australia, and colleagues.

Since the protein is thought to be a key contributor to development of Alzheimer's disease (AD), the results suggest that the liver may play an important role in the onset or progression of the disease.

Deposits of amyloid-beta (A-beta) in the brain are one of the pathological hallmarks of AD and are implicated in neurodegeneration in both human patients and animal models of the disease.

But A-beta is also present in peripheral organs, and blood levels of A-beta correlate with cerebral amyloid burden and cognitive decline, raising the possibility that peripherally produced a-beta may contribute to the disease.

Testing that hypothesis has been difficult, since the brain also produces A-beta, and distinguishing protein from the two sources is challenging.

In the current study, the authors surmounted that challenge by developing a mouse that produces human a-beta only in liver cells.

They showed that the protein was carried in the blood by triglyceride-rich lipoproteins, just as it is in humans, and passed from the periphery into the brain.

They found that mice developed neurodegeneration and brain atrophy, which was accompanied by neurovascular inflammation and dysfunction of cerebral capillaries, both commonly observed with Alzheimer's disease.

Affected mice performed poorly on a learning test that depends on

function of the hippocampus, the brain structure that is essential for the formation of new memories.

The findings from this study indicate that peripherally derived A-beta has the ability to cause neurodegeneration and suggest that A-beta made in the liver is a potential contributor to human disease.

If that contribution is significant, the findings may have major implications for understanding Alzheimer's disease.

To date, most models of the disease have focused on brain overproduction of A-beta, which mimics the rare genetic cases of human Alzheimer's.

But for the vast majority of AD cases, overproduction of A-beta in the brain is not thought to be central to the disease etiology.

Instead, lifestyle factors may play a more important role, including a high-fat diet, which might accelerate liver production of A-beta.

The effects of peripheral A-beta on brain capillaries may be critical in the disease process, Mamo adds.

"While further studies are now needed, this finding shows the abundance of these toxic protein deposits in the blood could potentially be addressed through a person's diet and some drugs that could specifically target lipoprotein amyloid, therefore reducing their risk or slowing the progression of Alzheimer's disease."

Reference: "Synthesis of human amyloid restricted to liver results in an Alzheimer disease–like neurodegenerative phenotype" by Virginie Lam, Ryusuke Takechi, Mark J. Hackett, Roslyn Francis, Michael Bynevelt, Liesl M. Celliers, Michael Nesbit, Somayra Mamsa, Frank Arfuso, Sukanya Das, Frank Koentgen, Maree Hagan, Lincoln Codd, Kirsty Richardson, Brenton O'Mara, Rainer K. Scharli, Laurence Morandeau, Jonathan Gauntlett, Christopher Leatherday, Jan Boucek, John C. L. Mamo, 14 September 2021, PLOS Biology. DOI: 10.1371/journal.pbio.3001358

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https://bit.ly/3tHApiU

Groundbreaking Research Identifies Likely Cause of Alzheimer's Disease – Potential for New Treatment

A likely cause of Alzheimer's disease offers a significant finding that offers potential new prevention and treatment opportunities for Australia's second-leading cause of death.

Ground-breaking new Curtin University-led research has discovered a likely cause of Alzheimer's disease, in a significant finding that offers potential new prevention and treatment opportunities for Australia's second-leading cause of death.

The study, published in the prestigious *PLOS Biology* journal and tested on mouse models, identified that a probable cause of Alzheimer's disease was the leakage from blood into the brain of fat-carrying particles transporting toxic proteins.

Lead investigator Curtin Health Innovation Research Institute (CHIRI) Director Professor John Mamo said his collaborative group of Australian scientists had identified the probable 'blood-to-brain pathway' that can lead to Alzheimer's disease, the most prevalent form of dementia globally.

"While we previously knew that the hallmark feature of people living with Alzheimer's disease was the progressive accumulation of toxic protein deposits within the brain called beta-amyloid, researchers did not know where the amyloid originated from, or why it deposited in the brain," Professor Mamo said.

"Our research shows that these toxic protein deposits that form in the brains of people living with Alzheimer's disease most likely leak into the brain from fat carrying particles in blood, called lipoproteins. "This 'blood-to-brain pathway' is significant because if we can manage the levels in blood of lipoprotein-amyloid and prevent their leakage into the brain, this opens up potential new treatments to prevent Alzheimer's disease and slow memory loss."

Building on previous award-winning research that showed beta-

amyloid is made outside the brain with lipoproteins, Professor Mamo's team tested the ground-breaking 'blood-to-brain pathway' by genetically engineering mouse models to produce human amyloid-only liver that make lipoproteins. "As we predicted, the study found that mouse models producing lipoprotein-amyloid in the liver suffered inflammation in the brain, accelerated brain cell death, and memory loss," Professor Mamo said.

"While further studies are now needed, this finding shows the abundance of these toxic protein deposits in the blood could potentially be addressed through a person's diet and some drugs that could specifically target lipoprotein amyloid, therefore reducing their risk or slowing the progression of Alzheimer's disease."

Alzheimer's WA Chairman Adjunct Professor Warren Harding said the findings may have a significant global impact for the millions of people living with Alzheimer's disease. "Having universities like Curtin working with the pharmaceutical industry is important if we are to tackle this devastating disease," Mr. Harding said.

"In Australia, approximately 250 people are diagnosed with dementia daily, adding to the staggering half a million Australians who are already living with dementia. Without significant medical advances like the breakthrough Professor Mamo's team has made, it is estimated that the number of Australians living with dementia will exceed one million by 2058. This has a significant impact on families, carers and communities."

Professor Mamo and his research team's previous research in this area was awarded the NHMRC-Marshall and Warren Award for the most innovative and potentially transformative research.

Currently, the team is conducting a clinical trial, the Probucol in Alzheimer's-clinical trial, which is based on previous findings that a historic cardiovascular agent lowers lipoprotein-amyloid production and supports cognitive performance in mice.

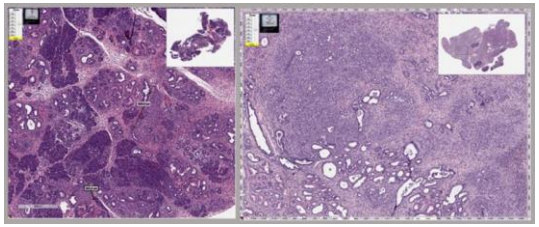
Reference: "Synthesis of human amyloid restricted to liver results in an Alzheimer disease–like neurodegenerative phenotype" by Virginie Lam, Ryusuke Takechi, Mark J. Hackett, Roslyn Francis, Michael Bynevelt, Liesl M. Celliers, Michael Nesbit, Somayra Mamsa, Frank Arfuso, Sukanya Das, Frank Koentgen, Maree Hagan, Lincoln Codd, Kirsty Richardson, Brenton O'Mara, Rainer K. Scharli, Laurence Morandeau, Jonathan Gauntlett, Christopher Leatherday, Jan Boucek, John C. L. Mamo, 14 September 2021, PLOS Biology. DOI: 10.1371/journal.pbio.3001358

https://bit.ly/3tKnLj6

Johns Hopkins: Anti-Parasitic Drug Slows Pancreatic Cancer in Mice

Anti-parasitic drug prevents pancreatic cancer's initiation, progression, and metastasis

As the third-most lethal cancer in the United States, with only a 1% five-year survival rate for people with its most aggressive form, pancreatic cancer has long been a target of researchers who search for ways to slow or stop its growth and spread. Now, a team of Johns Hopkins Medicine researchers have found that an anti-parasitic drug prevents pancreatic cancer's initiation, progression, and metastasis in genetically engineered mice.



The image on the left (Control) is a magnified view of an example mouse pancreas that has developed pancreatic cancer due to mutations in cancer susceptibility genes and an inflammatory agent. On the right (MBZ) is the same mouse strain treated with the same inflammatory agent, but mebendazole was added to the same mouse feed, and it has little or no microscopic evidence of cancer or pathology. **Credit: Tara Williamson**

In a study published in the journal *Oncotarget*, Gregory Riggins, M.D., Ph.D., professor of neurosurgery and oncology at the Johns Hopkins University School of Medicine, and his team used two different mouse models to determine that the anti-parasitic drug mebendazole could slow or stop the growth and spread of both early and late-stage pancreatic cancer.

"We think that mebendazole could have a role in all stages," Riggins says. "It was particularly effective for pancreatic cancer that was detected early."

Riggins and his team administered mebendazole to mice that were genetically engineered to develop pancreatic cancer. The team measured the inflammation and the change in tissue, as well as the stage, grade and metastatic status in each tumor.

Originally used to fight roundworm, hookworm and other parasitic infections by cutting off the parasites' supply of nutrition, mebendazole inhibits the formation of tubulin. Tubulin, Riggins explains, is both a micro-skeleton of the inner cell and a highway for transport. The drug gets into the parasite's gut and collapses the tubulin, starving the parasite to death. The study shows that mebendazole may act similarly in pancreatic cancer by collapsing cancer cells' structure, along with other mechanisms such as reducing inflammation. Riggins says he hopes to continue his team's research through human clinical trials.

"We are advocating for use of mebendazole as a therapy for those diagnosed before metastasis to see if we can slow or prevent pancreatic cancer," Riggins says. "For those with more advanced cancers, it could be an alternative to certain surgeries. Mebendazole may have utility as a therapy after initial treatment to prevent tumor recurrence in the 15% to 20% of pancreatic adenocarcinoma patients who undergo surgery. It may also increase the durability of response to standard chemotherapy in the remaining 80% to 85% of patients with advanced disease."

Reference: "Mebendazole disrupts stromal desmoplasia and tumorigenesis in two models of pancreatic cancer" by Tara Williamson, Michelle Carvalho de Abreu, Dimitri G. Trembath, Cory Brayton, Byunghak Kang, Thais Biude Mendes, Paulo Pimentel de Assumpção, Janete M. Cerutti and Gregory J. Riggins, 6 July 2021, Oncotarget.
DOI: 10.18632/oncotarget.28014

The Virginia and D.K. Ludwig Fund for Cancer Research provided funding for the research.

Other scientists who conducted the research include Tara Williamson, Michelle Carvalho de Abreu, Dimitri G. Trembath, Cory Brayton, Byunghak Kang, Thais Biude Mendes, Paulo Pimentel de Assumpção and Janete M. Cerutti.

Riggins and Williamson are inventors on intellectual property related to mebendazole owned and managed by Johns Hopkins University conflict of interest policies. Riggins has a financial interest in Benizole Therapeutics, PBC.

https://bit.ly/3hFaRy9

Earth's oxygen is projected to run out in a billion years

As the Sun ages, Earth's processes will change

Briley Lewis

Our Sun is middle-aged, with about five billion years left in its lifespan. However, it's expected to go through some changes as it gets older, as we all do — and these changes will affect our planet. New research published in *Nature Geoscience* shows that Earth's oxygen will only stick around for another billion years.

One of the Sun's age-related changes is getting brighter as it gets older. When a star runs out of hydrogen fuel in its core, the core has to get hotter in order to fuse the next element, helium. As the core gets hotter, the outer layers expand, and the star gets brighter. This extra energy hitting Earth will eventually cause our planet to warm up and slowly lose its oceans and its oxygen.

The exact timing of *when* we lose our oxygen depends on more complicated factors — particularly our planet's carbonate-silicate cycle, which releases carbon dioxide into the atmosphere from volcanoes. As the mantle cools and this cycle slows, less carbon dioxide will be available for the plants that produce oxygen, leading to a rapid loss of oxygen in the atmosphere. The researchers' model took into account all these factors — our biosphere, the Sun's changes, our planet's changes, and more — to come up with their estimate of about a billion years.

Interestingly, this means that planets like Earth only have oxygen for a fraction of their lifetimes. When we try to find habitable worlds, this will be important to keep in mind.

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Recent Ebola outbreak emerged from someone infected 5 years earlier

We knew the virus could go dormant but not that it could do so for five years.

John Timmer

A large international research group released a paper today suggesting that Ebola viruses can emerge from five years of dormancy to trigger a new outbreak of infections. While this isn't the first instance in which Ebola re-emerged from a previously infected individual, the new results extend the timeframe of risk substantially.

At present, we have little idea how and where the virus persists in the human body. But there are now tens of thousands of people who have survived previous infections, so it's an area where more research is urgently needed.

A re-outbreak

The African nation of Guinea experienced a small Ebola outbreak that started in January of 2021 when a nurse fell ill. Due to a misdiagnosis, she was not immediately isolated, allowing the virus to spread.

Fortunately, a major outbreak that occurred in the same region from 2013 to 2016 resulted in the local health authorities obtaining sophisticated diagnostic equipment, including the real-time RT-PCR machines that are used for COVID-19 testing. This ultimately allowed the authorities to determine that Ebola was the cause of her illness, identify 15 additional cases, and take measures that brought the outbreak to a halt. In all, 12 of the 16 infected died.

In order to better understand the source and spread of the outbreak, samples from these patients were used to obtain the genome of the virus behind the outbreak. This process allows the comparison of the genome's sequence to that of prior outbreaks and samples taken from bats, which can also carry the virus. An evolutionary analysis can then suggest how the earliest patient became infected.

But in this case, the analysis produced a strange result. All the cases clustered in a tight group that fell within the group of viral variants that had caused the 2013-2016 outbreak in the same region. These cases included some mutations that had only occurred during the earlier outbreak and haven't been found in any bat populations.

On its own, this result isn't entirely shocking. It's possible that the virus could circulate at low levels in isolated populations without drawing the attention of health authorities. If it were to do so, however, it would continue to pick up mutations. But the strain behind the 2021 outbreak didn't look much different from the one that had been circulating in 2016. It's like it spent much of the period in between frozen in time.

Suspended animation

For the 2021 strain to have picked up so few mutations in the time since the 2013–2016 outbreak, its normal mutation rate would have needed to drop by a factor of five. The alternative is that, as in the case mentioned earlier, the virus remained dormant in someone who recovered from an infection in the earlier outbreak. The virus has been found in seminal fluid up to 500 days after infections were cleared, and there has been at least one instance of transmission after that amount of time. But the new outbreak would require a dormancy of over three times as long.

Past studies suggest that this sort of persistence would be uncommon. But there are currently over 17,000 survivors from the earlier outbreak, so there's certainly an opportunity for a rare event to occur.

At the moment, however, we have no idea what tissue Ebola might be hiding out in, much less the mechanism that allows it to go dormant. The only RNA viruses that are known to cause long-lasting infections (called retroviruses) do so by integrating a DNA

copy of themselves into their host's genome. But Ebola doesn't appear to have any of the genes needed to do this.

The obvious solution is to work with Ebola survivors to check for persistent infections—something that might be integrated into a more general monitoring program given the apparent risk of long-term dormancy. But that poses its own challenges. Ebola survival bears a stigma in many of the communities hit hard by the virus, with those who outlived their infections often losing their jobs and housing. So it won't necessarily be easy to recruit people to work with the research community on this project.

The situation may be changing, however, as two vaccines against Ebola have recently been approved for use, and others are in testing; they have been deployed to help contain outbreaks over the last few years.

Along with changing the public health situation in Africa, these vaccines may begin to shift the social perception of those infected, as well.

Nature, 2021. DOI: 10.1038/s41586-021-03901-9 (About DOIs).

https://bit.ly/2XqEEDc

Milk fueled Bronze Age expansion of 'eastern cowboys' into Europe

Ancient proteins show the Yamnaya dairy revolution took just 300 years

By Andrew Curry

More than 5000 years ago, nomads known today as the Yamnaya rumbled out of the grasslands of modern-day Russia and Ukraine in heavy, ox-drawn wagons. Within just a few centuries they had expanded across Eurasia, leaving a genetic signature in populations from Mongolia to Hungary. Now, fossilized plaque from the teeth of more than 50 Bronze Age skeletons suggests an unlikely weapon powered their expansion: milk.

"It's great to see this type of evidence finally there," says Wolfgang Haak, an archaeogeneticist at the Max Planck Institute for Evolutionary Anthropology who was not involved in the research. "It's a convincing argument as far as dairy is concerned."

Researchers have long speculated that a combination of wagons, dairying, and horseback riding might have made it possible for the Yamnaya—whom Haak refers to as "eastern cowboys"—to develop a new, more mobile way of life, unleashing their unprecedented expansion. But there was little direct evidence to back that up that idea, aside from a few wagon burials and pottery sherds.

To see what might have fueled the Yamnaya's success, researchers from the United States, Europe, and Russia looked for milk proteins trapped and preserved in the dental calculus, or plaque, of people living on the steppes of modern-day Russia between 4600 and 1700 B.C.E.

They examined 56 skeletons from more than two dozen sites north of the Caspian Sea. The team separated the preserved proteins from the mineral matrix of the plaque and then used mass spectrometry to identify individual proteins.

Prior to 3300 B.C.E., calculus from the teeth of people living in settlements along the Volga and Don rivers contained virtually no milk proteins. Instead, these pre-Yamnaya groups likely consumed lots of freshwater fish, wild game, and the occasional meal of domesticated cow, sheep, or goat meat, as suggested by previous analysis of isotopes in their skeletons and animal bones at the sites.

Then, around 3300 B.C.E., something changed.

Samples scraped from the teeth of people living after that date were full of cow, sheep, and goat milk proteins—direct evidence they were eating dairy products.

A few even had trace amounts of preserved horse milk. "There's a cultural switch," says lead author Shevan Wilkin, a biomolecular archaeologist at the University of Zurich Institute of Evolutionary Medicine. "It's a huge change of perspective from 'we eat these

animals sometimes' to 'we milk them all the time.'"

The proteins suggest the adoption of dairying and herding was key to the rapid transformation of hunter-gatherers into nomadic herders—and their expansion across Eurasia in the space of just 300 years, the researchers write today in *Nature*

"Horses, cattle, sheep, and goats turned grass into food, clothing, and shelter," says Hartwick College archaeologist and co-author David Anthony. "The Yamnaya invented a new economy."

Hard, mineralized dental calculus can preserve evidence of diet and disease for thousands of years. **Egor Kitov/Samara Valley Project**

But dairy didn't do it alone: The introduction of wagons around the same time made carrying water and following grazing animals to distant pastures possible.

Meanwhile, early domesticated horses might have enabled the newly nomadic Yamnaya to manage bigger herds. Together, the innovations opened up a vast new landscape. "Milk is a contributing factor, but not the only factor," says University of Helsinki archaeologist Volker Heyd, who was not involved in the research. "It's a new economy and a new way of life, and the origins are the invention of the wheel, horse riding, and dairying."

One mystery remains. Previous analyses of ancient DNA have shown the Yamnaya lacked the genetic ability to metabolize milk sugars—in other words, they were lactose intolerant. It's possible, Wilkin says, that—much like modern Mongolians—the Yamnaya consumed fermented dairy products like yogurt or hard cheeses, which contain virtually no lactose. Whatever form of dairy they consumed, she adds, "I don't know how you would have moved that far that fast [without it]."

https://bit.ly/3hGZbuA

SARS-like viruses may jump from animals to people hundreds of thousands of times a year

Study pinpoints Asian regions that could spark the next coronavirus pandemic

By Kai Kupferschmidt

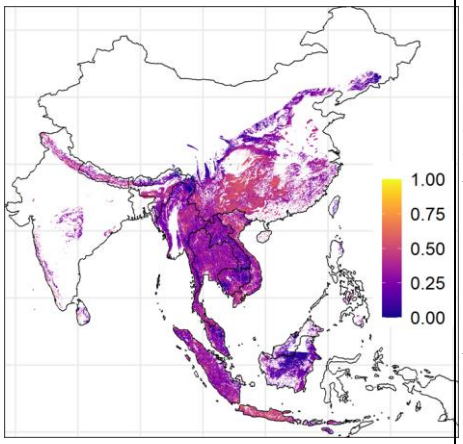
Only two new coronaviruses have spread globally the past 2 decades: SARS-CoV, which caused an outbreak of severe acute respiratory syndrome (SARS) in 2003, and SARS-CoV-2, the virus that causes COVID-19. But that may just be the tip of the iceberg of undetected infections with related viruses emerging from bats, a new paper claims. In a preprint published yesterday researchers estimate that an average of 400,000 people are likely infected with SARS-related coronaviruses every year, in spillovers that never grow into detectable outbreaks.

Although that number comes with big caveats, "It should be eye-opening to the entire scientific community that we don't know very much about the frequency of zoonotic spillover," says virologist Angela Rasmussen of the University of Saskatchewan, who was not involved in the work. That needs to change, she says, "because otherwise we grossly underestimate it."

The researchers, including Peter Daszak from the EcoHealth Alliance and Linfa Wang from Duke-NUS Medical School in Singapore, created a detailed map of the habitats of 23 bat species known to harbor SARS-related coronaviruses, the group to which SARS-CoV and SARS-CoV-2 belong, and then overlaid it with data on where humans live to create a map of potential infection hot spots. They found that close to 500 million people live in areas where spillovers can occur, including northern India, Nepal, Myanmar, and most of Southeast Asia. The risk is highest in southern China, Vietnam, Cambodia, and on Java and other islands in Indonesia (see map, below).

"This is a definitive analysis of where on the planet the next SARS- or COVID-like virus is most likely to emerge," Daszak says. The maps could guide efforts to reduce the likelihood of spillover by changing behaviors in high-risk communities and targeting surveillance to detect new outbreaks earlier, he says. Daszak, a vocal advocate of the hypothesis that SARS-CoV-2 came from the wild instead of a research lab, says the maps could also guide efforts to find the virus' natural origin. (Several studies are underway or being planned to look for SARS-CoV-2 and its relatives in *Rhinolophus* [horseshoe] bats and other animals.)

But the researchers went one step further. Small surveys done before COVID-19 erupted have suggested some people in Southeast Asia harbor antibodies against SARS-related coronaviruses. Combining those data with data on how often people encounter bats and how long antibodies remain in the blood, the researchers calculated that some 400,000 undetected human infections with these viruses occur each year across the region.



A map in a new paper shows the relative spillover risk for severe acute respiratory syndrome–related coronaviruses. China and countries in Southeast Asia are potential hot spots for human infections. **C. A. Sánchez et al., medRxiv (2021) 10.1101/2021.09.09.21263359**

Daszak says interactions with bats are much more common than people think: "Just living there means you're exposed: People are sheltering in caves, they're digging guano out of caves, they're hunting and eating bats." The paper does not even address how many people work in the wildlife trade and may be infected indirectly when a bat virus infects another animal first, he says.

Although 400,000 infections annually sounds like a lot, Rasmussen says, "in a region with likely hundreds of millions of bats and nearly half a billion people it isn't that many." The confidence interval stretches from one to more than 35 million hidden infections per year, however—big enough to "fly the entire population of Rhinolophid bats through," Rasmussen quips. Models are only as good as the data that are fed into them, says Vincent Munster, a virologist at the U.S. National Institute of Allergy and Infectious Diseases who studies coronaviruses. The data on antibodies only include a few thousand people, he notes, and the assays used to test for antibodies can easily lead to false positives.

"I think if the seroprevalence estimate is way off, the whole thing collapses," says David Fisman, an epidemiologist at the University of Toronto, who calls the modeling "shaky." The high number of hidden infections "doesn't ring true," Fisman says, because you would expect regular spillovers to be recognized, as they are for rabies and the Nipah virus.

But Rasmussen says many infections could remain hidden if they are short-lived and don't lead to onward transmission because the viruses are not well adapted to humans. They might not infect enough cells—or cells of the right type—to be transmitted to another person, or they might not be able to escape humans' immune defenses. In cases when the virus does spread, sheer chance may keep it confined to a small, isolated community.

"A lot of the viruses are probably unable to be transmitted from one person to another, but I have very little doubt that there have been illnesses due to these viruses that get misdiagnosed or never diagnosed," Daszak says. "A rural farmer in Myanmar is hardly likely to go to the clinic because they've got a bit of a cough."

The work is part of a nascent effort to try to understand the risk factors for viral spillover from animals into humans, Munster says. Already, one message is clear, he says: "I think for virtually any

zoonotic pathogen from wildlife, spillover is more frequent than previously recognized."

***Update, 16 September, 3:20 p.m.:** Comments from Davis Fisman have been added to this story.*

https://bit.ly/3CremQB

Nanoengineered Plant Virus Could Protect and Save Your Lungs From Metastatic Cancer

New treatment developed using a virus that grows in black-eyed pea plants could keep metastatic cancers from the lungs

Using a virus that grows in black-eyed pea plants, nanoengineers at the University of California San Diego developed a new treatment that could keep metastatic cancers at bay from the lungs. The treatment not only slowed tumor growth in the lungs of mice with either metastatic breast cancer or melanoma, it also prevented or drastically minimized the spread of these cancers to the lungs of healthy mice that were challenged with the disease.

The research was published on September 14, 2021, in the journal *Advanced Science*.

Cancer spread to the lungs is one of the most common forms of metastasis in various cancers. Once there, it is extremely deadly and difficult to treat. Researchers at the UC San Diego Jacobs School of Engineering developed an experimental treatment that combats this spread. It involves a bodily injection of a plant virus called the cowpea mosaic virus. The virus is harmless to animals and humans, but it still registers as a foreign invader, thus triggering an immune response that could make the body more effective at fighting cancer. The idea is to use the plant virus to help the body's immune system recognize and destroy cancer cells in the lungs. The virus itself is not infectious in our bodies, but it has all these danger signals that alarm immune cells to go into attack mode and search for a pathogen, said Nicole Steinmetz, professor of nanoengineering at UC San Diego and director of the university's Center for Nano-ImmunoEngineering.

To draw this immune response to lung tumors, Steinmetz's lab engineered nanoparticles made from the cowpea mosaic virus to target a protein in the lungs. The protein, called S100A9, is expressed and secreted by immune cells that help fight infection in the lungs. And there is another reason that motivated Steinmetz's team to target this protein: overexpression of S100A9 has been observed to play a role in tumor growth and spread.

"For our immunotherapy to work in the setting of lung metastasis, we need to target our nanoparticles to the lung," said Steinmetz. "Therefore, we created these plant virus nanoparticles to home in on the lungs by making use of S100A9 as the target protein. Within the lung, the nanoparticles recruit immune cells so that the tumors don't take."

"Because these nanoparticles tend to localize in the lungs, they can change the tumor microenvironment there to become more adept at fighting off cancer—not just established tumors, but future tumors as well," said Eric Chung, a bioengineering Ph.D. student in Steinmetz's lab who is one of the co-first authors on the paper.

To make the nanoparticles, the researchers grew black-eyed pea plants in the lab, infected them with cowpea mosaic virus, and harvested the virus in the form of ball-shaped nanoparticles. They then attached S100A9-targeting molecules to the surfaces of the particles.

The researchers performed both prevention and treatment studies. In the prevention studies, they first injected the plant virus nanoparticles into the bloodstreams of healthy mice, and then later injected either triple negative breast cancer or melanoma cells in these mice. Treated mice showed a dramatic reduction in the cancers spreading to their lungs compared to untreated mice.

In the treatment studies, the researchers administered the nanoparticles to mice with metastatic tumor in their lungs. These

mice exhibited smaller lung tumors and survived longer than untreated mice.

What's remarkable about these results, the researchers point out, is that they show efficacy against extremely aggressive cancer cell lines. "So any change in survival or lung metastasis is pretty striking," said Chung. "And the fact that we get the level of prevention that we do is really, really amazing."

Steinmetz envisions that such a treatment could be especially helpful to patients after they have had a cancerous tumor removed. "It wouldn't be meant as an injection that's given to everyone to prevent lung tumors. Rather, it would be given to patients who are at high risk of their tumors growing back as a metastatic disease, which often manifests in the lung. This would offer their lungs protection against cancer metastasis," she said.

Before the new treatment can reach that stage, the researchers need to do more detailed immunotoxicity and pharmacology studies. Future studies will also explore combining this with other treatments such as chemotherapy, checkpoint drugs, or radiation.

Reference: "S100A9-Targeted Cowpea Mosaic Virus as a Prophylactic and Therapeutic Immunotherapy against Metastatic Breast Cancer and Melanoma" by Young Hun Chung, Jooneon Park, Hui Cai and Nicole F. Steinmetz, 14 September 2021, Advanced Science.
DOI: 10.1002/advs.202101796

In addition to Young Hun (Eric) Chung, co-first authors of the study include Jooneon Park and Hui Cai. Nicole Steinmetz serves as the corresponding author of this work.

This work was supported in part by the National Institutes of Health (R01 CA224605, R01 HL137674 and U01-CA218292).

Disclosure: Nicole Steinmetz is a co-founder of and has a financial interest in Mosaic ImmunoEngineering Inc. The other authors declare no conflict of interest.

https://bit.ly/2Z0as2D

Coffee cells produced in a bioreactor through cellular agriculture

VTT Technical Research Centre of Finland has successfully produced coffee cells in a bioreactor through cellular agriculture.

The innovation can help to make the production of coffee more sustainable. The first batches produced by VTT in a laboratory in Finland smell and taste like conventional coffee.

With increasing demand and numerous sustainability challenges concerning traditional coffee agriculture, there is a pressing need for alternative ways of producing coffee. Due to the high demand of coffee, more acreage is required to produce enough coffee beans, leading to deforestation –particularly in sensitive rainforest areas.

VTT Technical Research Centre of Finland is developing coffee production through plant cells in its laboratory in Finland. In the process, cell cultures floating in bioreactors filled with nutrient medium are used to produce various animal- and plant-based products.

"At VTT, this project has been part of our overall endeavor to develop the biotechnological production of daily and familiar commodities that are conventionally produced by agriculture. For this, we use many different hosts, such as microbes, but also plant cells," says Research Team Leader, Dr. Heiko Rischer from VTT.

The work was started by initiating coffee cell cultures, establishing respective cell lines in the laboratory and transferring them to bioreactors to begin producing biomass. After analyses of the biomass, a roasting process was developed, and the new coffee was finally evaluated by VTT's trained sensory panel.

The whole procedure required input from several disciplines and experts in the fields of plant biotechnology, chemistry, and food science.

"In terms of smell and taste, our trained sensory panel and analytical examination found the profile of the brew to bear similarity to ordinary coffee. However, coffee making is an art and involves iterative optimization under the supervision of specialists with dedicated equipment. Our work marks the basis for such work," says Rischer.

Currently all coffee material produced in laboratory conditions

represents experimental food and would require regulatory approval by the FDA to be marketed and sold to consumers in the United States. In Europe, the lab-grown coffee should first be approved as Novel Food before being marketed.

Technically the production process is based on existing and established technology such as conventional bioreactor operation. In fact, the idea that coffee cells could be used to make coffee was already presented in the 1970s by P.M. Townsley.

"The experience of drinking the very first cup was exciting. I estimate we are only four years away from ramping up production and having regulatory approval in place. Growing plant cells requires specific expertise when it is time to scale and optimize the process. Downstream processing and product formulation together with regulatory approval and market introduction are additional steps on the way to a commercial product. That said, we have now proved that lab-grown coffee can be a reality," says Rischer.

The project links to VTT's strategic research targets to solve the world's biggest challenges. Cellular agriculture is one of the routes towards more sustainable food production.

"The true impact of this scientific work will happen through companies who are willing to re-think food ingredient production and start driving commercial applications. VTT collaborates and supports large enterprises and small companies in adopting opportunities in their product development. Ultimately, all efforts should result in more sustainable and healthy food for the benefit of the consumer and the planet," concludes Rischer.

https://bit.ly/2ZcfGsn

Evidence of Fur and Leather Clothing, Among World's Oldest, Found in Moroccan Cave

Humans likely sported clothes made of jackal, fox and wildcat skins some 120,000 years ago

Brian Handwerk

Fur is a controversial fashion statement these days. But stepping out in a wildcat cape or jackal wrap was de rigueur for Pleistocene humans, according to the recent discovery of a 120,000-year-old leather and fur production site that contains some of the oldest archaeological evidence for human clothing.

Homo sapiens at the site first made and wore clothes around the onset of an Ice Age which may suggest that, even in relatively mild Morocco, clothes were adopted as a way to keep warm. But the invention of animal-based apparel also corresponds with the appearance of personal adornments, like shell beads, which hints that prehistoric clothing, like today's styles, could have been about style as well as functionality.

Emily Hallett, of the Max Planck Institute for the Science of Human History in Germany, didn't set out to investigate where and when humans started wearing clothes, which decompose and vanish after a few thousand years at most. Initially interested in diet, she was examining bones to see which animals Pleistocene humans ate, and how they butchered them, in Contrebandiers Cave on Morocco's Atlantic Coast.

But Hallett found bones she wasn't expecting: dozens of tools carefully shaped, smoothed and polished into implements ideal for scraping hides clean to make leather, and scraping pelts to produce furs. "They look like the tools that people still use today to process hides for leather and fur," Hallett says, noting that similar tools have also been found associated with the same tasks in far younger archaeological sites. Hallett, who co-authored a study on the findings in the September 16 issue of the journal *iScience*, worked with a team that included the late Harold Dibble, an influential archaeologist from the University of Pennsylvania.

The researchers found 62 different bone tools in Middle Stone Age layers dated to 90,000 to 120,000 years ago. Despite their age the implements represent relatively specialized instruments for the

tasks at hand, which suggests that humans first started using more crude versions of such implements to process fur and skins at an even earlier date.

Oddly a single marine mammal tooth was also found in the cave, dated to about 113,000 years ago, which represents a first for Pleistocene archaeological sites in North Africa. Future molecular analysis should identify the species but the shape strongly suggests that it's from an ancient sperm whale. Signs of wear on the tooth might have happened while the animal was alive, but it might have also been used as some type of flaking tool, used to sharpen another tool's edge by applying careful pressure.

But the bone tools tell only half of the story. Hallett also noticed that a lot of carnivore bones piled in the cave still bore the telltale marks of being cut by humans.

The remains of sand foxes, golden jackals and wildcats clearly showed marks like those still created in skinning techniques. Incisions were made to detach the skin at each of the animal's four paws, so that the skin could be pulled in one piece to the animal's head. Skin at the head was then removed by cutting around the lips, which is also evidenced by ancient cut marks. These carnivore species show no marks of butchery that would suggest they were eaten, only the cuts necessary to remove skin. On the other hand, the remains of other animals including bovids akin to ancient cows, show clear signs that they were processed to produce meat for the Pleistocene dinner table.

"Once those two pieces were there, bone tools used to prepare leather and fur and carnivore bones that have marks for fur removal, we put that together and realized that it's most likely this was evidence for the making of clothing," notes Hallett.

The evidence suggests that North African cave dwellers were making and wearing clothing long before the great migrations of humans to which all living non-Africans can trace their roots. When those Homo sapiens left Africa to populate the corners of the globe, it appears that they likely did so adorned in an array of animal skins and furs.

The reason why our ancestors began creating those clothes in the first place may be more complex than it appears at first glance. It's often theorized that many human cognitive and evolutionary leaps were born of necessity—adapt or die. Early modern humans and Neanderthals needed, and seem to have produced, clothing to survive in colder times and places like Ice Age Europe (15,000 to 70,000 years ago).

But the climate around Contrebandiers Cave in Morocco was relatively mild 100,000 years ago, as it remains today. That's led some, including Hallett, to suggest that clothing might not have been needed for survival. But Ian Gilligan, author of *Climate, Clothing and Agriculture in Prehistory*, says Northern Africa can be surprisingly cold at times even in warmer eras, so that cold snaps and conditions like hypothermia would have presented a definite threat. Humans might well have adopted clothing for comfort against the chill even when conditions were not extreme, adds Gilligan, an archaeologist at the University of Sydney who was not involved with the study.

"This new study really pushes back the first good archaeological evidence for the manufacture of clothing, and it's coinciding nicely with the beginning of the last Ice Age about 120,000 years ago, so I think that's really significant," Gilligan says. "It's precisely at the time when you'd expect to see the first clothing for protection from cold in context of the glacial cycles."

The earliest previous technological evidence for clothing didn't appear until about 75,000 years ago, in Southern African sites like Blombos Cave and Sibudu Cave. There scientists found the first confirmed bone awls, with microwear on the tips suggesting they were used hide-piercing to sew garments, together with hide-cutting

stone blade tools and hide-scrapers. (Some much older sites have tools that suggest human relatives could have worn clothes hundreds of thousands of years ago, but the evidence is far less certain.)

The onset of colder climate isn't the only interesting development that corresponds with the creation of clothes in Africa. In that period of time personal ornaments appeared in the lives of Pleistocene humans. Contrebandiers Cave, for example, is littered with tiny shells that could have produced no nutritional benefit but may have been valued for other reasons.

"Some of them are pierced, and they show up all over Africa around this time," Hallett explains. "Most archaeologists believe this is personal ornamentation, a form of symbolic expression, and it's interesting that this evidence for clothing shows up at the same time in these mild habitats."

The world's oldest surviving clothing hasn't lasted nearly as long as shells or beads. The world's oldest known shoes, bark sandals, were stashed in a central Oregon cave some 9,000 or 10,000 years ago. Some of the oldest extant clothes were found on the famous mummy Ötzi some 5,000 years ago. By that same time Egyptians were producing fine linens as evidenced by the Tarkhan dress, the world's oldest woven garment.

While scientists say it's extremely unlikely that skins or fur could ever be found preserved from the far more ancient eras when humans first started wearing them, another line of indirect evidence seems to dovetail nicely with the archaeological findings at Contrebandiers. "Human lice have evolved in tandem with their hosts, and can shed light on aspects of human evolution that lack direct data. It is like having another record of our history," says David Reed a biologist at the Florida Museum of Natural History who was not involved with the study.

The lice that live in human clothing are a distinct lineage that evolved from those that live on our scalps. By using DNA sequencing to trace when these clothes-loving lice first appeared, genetically diverging from their relatives, scientists can learn when humans started wearing clothes in the first place. A decade ago Reed authored a genetic study of clothing lice that traced their lineages far back in time and suggested that H. Sapiens in Africa may have been wearing clothing as long as 170,000 years ago—a date that corresponds nicely with the facts found in the ground in Morocco.

"It is really gratifying to see that years later our prediction that clothing arose in Africa has been validated in finding clear evidence of clothing use in Pleistocene Africa," says Reed.

Hallett is planning experiments in making and using bone tools to better understand how Paleolithic clothing was sourced—a process far more involved than online ordering or even a trip to the mall on a Holiday weekend. After all, humans had to first hunt and kill dangerous predators, develop skills in crafting and using ever more specialized tools and labor through time-consuming processing of handmade fur and leather. The first clothes makers must have felt that the payoff, whether in warmth, symbolic style or a combination of the two, was worth all that effort. Hallett believes it definitely paid dividends for our species.

"Clothing and the expanded toolkits of early humans are likely parts of the package that led to the adaptive success of humans," she says, "and helped our ability to succeed globally and in climatically extreme regions."

https://bit.ly/2XvWYe9

Animals died in 'toxic soup' during Earth's worst mass extinction: A warning for today

Toxic microbial blooms lead to fish die-off events, and are becoming increasingly common in freshwater lakes.

The end-Permian mass extinction event of roughly 252 million

years ago—the worst such event in earth's history—has been linked to vast volcanic emissions of greenhouse gases, a major temperature increase, and the loss of almost every species in the oceans and on land.

Now, it seems that even the lakes and rivers were no safe havens. A recent study published by an international team of researchers including Professor and Head of the Department of Geosciences Tracy Frank and Professor Chris Fielding, both newly arrived at UConn, has identified a new cause of extinction during extreme warming events: toxic microbial blooms.

In a healthy ecosystem, microscopic algae and cyanobacteria provide oxygen to aquatic animals as a waste product of their photosynthesis. But when their numbers get out of control, these microbes deplete free oxygen, and even release toxins into the water. By studying the fossil, sediment, and chemical records of rocks near Sydney, Australia, the researchers discovered that several pulses of bloom events had occurred soon after the first volcanic rumblings of the end-Permian mass extinction. Once the bottom-feeder animals, or "detritivores," were killed off, there was no one left to keep the microbes in check. The freshwater systems then seethed with algae and bacteria, delaying the recovery of animals for perhaps millions of years.

Frank and Fielding study sediment, and Frank explains their contribution to the work, which was performed while both were at the University of Nebraska–Lincoln, was in gleaning details about the conditions of the environment, and the resulting toxic soup, from the layers of sediment.

"We are trying to understand what conditions these plants were living in, for instance were they lake deposits versus river deposits," Frank says. "Then what can we determine details about the salinity and temperatures of the waters, those details come from the geochemistry."

The three main ingredients for the toxic soup are accelerated greenhouse gas emissions, high temperatures, and abundant nutrients. The volcanic eruptions provided the first two, while sudden deforestation caused the third. When the trees were wiped out, the soils bled into the rivers and lakes, providing all the nutrients that the microbes would need. When the researchers compared the fossil records of different warming-related mass extinctions, the team found extremely similar fossil records. This implicates deadly microbial blooms as repeat offenders of freshwater extinctions during extreme warming events.

Today, humans have been following this recipe, and freshwater microbial blooms have been on the rise, illustrating how important the geosciences are in understanding the past in ways that offer crucial context for understanding contemporary changes in climate.

"We're seeing more and more toxic algae blooms in lakes and in shallow marine environments that's related to increases in temperature and changes in plant communities which are leading to increases in nutrient contributions to freshwater environments," Frank says. "So, a lot of parallels to today. The volcanism was a source of CO_2 in the past but we know that the rate of CO_2 input that was seen back then was similar to the rate of CO_2 increases we're seeing today because of anthropogenic effects.

"We can get a sense of how much climate has changed in the past, what the extremes are, how fast it can change, what the causes of climate change are and that gives us a nice backdrop for understanding what's happening today."

According to this year's report by the Intergovernmental Panel on Climate Change (IPCC), the influence of humans on the changing climate is "unequivocal," creating conditions that favor the spread of these warmth-loving microbes. In combination with an influx of nutrients from water pollution, mostly from agriculture and deforestation, this has led to a sharp increase in toxic blooms. The

results: mass fish die-offs, severe human and livestock health effects, and an annual cost measurable in billions of dollars.

"The end-Permian is one of the best places to look for parallels with what's happening now," says Fielding.

"The other big parallel is that the increase in temperature at the end of the Permian coincided with massive increases in forest fires. One of the things that that destroyed whole ecosystems was fire, and we're seeing that right now in places like California. One wonders what the longer-term consequences of events like that as they are becoming more and more widespread."

These are clear symptoms of an unbalanced ecosystem, and the present study indicates that the impacts of bloom events can echo for an extremely long time. However, unlike the species that suffered the mass extinctions of the past, we have the opportunity to prevent these toxic blooms by keeping our waterways clean and curbing our greenhouse gas emissions.

"The scary thing is we are used to thinking in terms of timescales of years, maybe tens of years, if we get really adventurous. The end-Permian mass extinction event took four million years to recover from. That's sobering," says Fielding.

More information: *Chris Mays et al, Lethal microbial blooms delayed freshwater ecosystem recovery following the end-Permian extinction, Nature Communications (2021).* *DOI: 10.1038/s41467-021-25711-3*

https://bit.ly/3lFosqh

Ancient DNA rewrites early Japanese history—modern day populations have tripartite genetic origin

A finding that refines previously accepted views of a dual genomic ancestry

Ancient DNA extracted from human bones has rewritten early Japanese history by underlining that modern day populations in Japan have a tripartite genetic origin—a finding that refines previously accepted views of a dual genomic ancestry.

Twelve newly sequenced ancient Japanese genomes show that modern day populations do indeed show the genetic signatures of early indigenous Jomon hunter-gatherer-fishers and immigrant Yayoi farmers—but also add a third genetic component that is linked to the Kofun peoples, whose culture spread in Japan between the 3rd and 7th centuries.

Rapid cultural transformations

The Japanese archipelago has been occupied by humans for at least 38,000 years but Japan underwent rapid transformations only in the last 3,000 years, first from foraging to wet-rice farming, and then to a technologically advanced imperial state.

The previous, long-standing hypothesis suggested that mainland Japanese populations derive dual-ancestry from the indigenous Jomon hunter-gatherer-fishers, who inhabited the Japanese archipelago from around 16,000 to 3,000 years ago, and later Yayoi farmers, who migrated from the Asian continent and lived in Japan from around 900 BC to 300 AD.

But the 12 newly sequenced ancient Japanese genomes—which came from the bones of people living in pre- and post-farming periods—also identify a later influx of East Asian ancestry during the imperial Kofun period, which lasted from around 300 to 700 AD and which saw the emergence of political centralisation in Japan.

Shigeki Nakagome, Assistant Professor in Psychiatry in Trinity College Dublin's School of Medicine, led the research, which brought together an interdisciplinary team of researchers from Japan and Ireland. Professor Nakagome said:

"Researchers have been learning more and more about the cultures of the Jomon, Yayoi, and Kofun periods as more and more ancient artefacts show up, but before our research we knew relatively little about the genetic origins and impact of the agricultural transition and later state-formation phase."

"We now know that the ancestors derived from each of the foraging, agrarian, and state-formation phases made a significant contribution to the formation of Japanese populations today. In short, we have an entirely new tripartite model of Japanese genomic origins—instead of the dual-ancestry model that has been held for a significant time."

Genomic insights into key Japanese transformations

In addition to the overarching discovery, the analyses also found that the Jomon maintained a small effective population size of around 1,000 over several millennia, with a deep divergence from continental populations dated to 20,000-15,000 years ago—a period which saw Japan become more geographically insular through rising sea-levels.

The Japanese archipelago had become accessible through the Korean Peninsula at the beginning of the Last Glacial Maximum, some 28,000 years ago, enabling movement between. And the widening of the Korea Strait 16,000 to 17,000 years ago due to rising sea-levels may have led to the subsequent isolation of the Jomon lineage from the rest of the continent. These time frames also coincide with the oldest evidence of Jomon pottery production.

"The indigenous Jomon people had their own unique lifestyle and culture within Japan for thousands of years prior to the adoption of rice farming during the subsequent Yayoi period. Our analysis clearly finds them to be a genetically distinct population with an unusually high affinity between all sampled individuals—even those differing by thousands of years in age and excavated from sites on different islands," explained Niall Cooke, Ph.D. Researcher at Trinity. "These results strongly suggest a prolonged period of isolation from the rest of the continent."

The spread of agriculture is often marked by population replacement, as documented in the Neolithic transition throughout most of Europe, with only minimal contributions from hunter-gatherer populations observed in many regions. However, the researchers found genetic evidence that the agricultural transition in prehistoric Japan involved the process of assimilation, rather than replacement, with almost equal genetic contributions from the indigenous Jomon and new immigrants associated with wet-rice farming.

Several lines of archaeological evidence support the introduction of new large settlements to Japan, most likely from the southern Korean peninsula, during the Yayoi-Kofun transition. And the analyses provide strong support for the genetic exchange involved in the appearance of new social, cultural, and political traits in this state-formation phase.

"The Japanese archipelago is an especially interesting part of the world to investigate using a time series of ancient samples given its exceptional prehistory of long-standing continuity followed by rapid cultural transformations. Our insights into the complex origins of modern-day Japanese once again shows the power of ancient genomics to uncover new information about human prehistory that could not be seen otherwise," added Dan Bradley, Professor of Population Genetics in Trinity's School of Genetics and Microbiology, who co-led the project. The eye-opening research has just been published in *Science Advances*.

More information: *"Ancient genomics reveals tripartite origins of Japanese populations," Science Advances (2021).* *www.science.org/doi/10.1126/sciadv.abh2419*

https://bit.ly/3tU9RuM

Serious Infections Linked to Autism: Study

In both a mouse model and the hospital records of more than 3 million children, researchers found a connection between strong immune activation in males and later symptoms of autism spectrum disorder.

Abby Olena

While researchers have found plenty of gene variants that seem to

increase the risk of an autism diagnosis, it's not clear why some people carrying these mutations develop autism spectrum disorders and some do not. In a study published today (September 17) in *Science Advances*, researchers point to a potential answer: severe infections during early childhood. After an early immune challenge, male mice with a mutated copy of the *tuberous sclerosis complex 2* (*Tsc2*) gene developed deficits in social behavior linked to changes in microglia, the immune cells of the brain. And an analysis of the hospital records of more than 3 million children showed that children, particularly boys, who were hospitalized for infections between ages 18 months and four years were more likely that healthy peers to receive a future autism spectrum disorder (ASD) diagnosis.

"We have genetic models, and we have a lot of in utero exposure models and early life stress models, but it's pretty rare that people are blending the two to find that gene [and] environment interaction," says Audrey Brumback, a pediatric neurologist at the University of Texas at Austin Dell Medical School who was not involved in the work. Plus, "we're so neuron centric in neuroscience, [but] a huge chunk of our brain is non-neuronal," she adds. "It's really exciting to see work that's exploring those non-neuronal cells."

"We knew that mutations predispose [people] for autism, but if you look in patients with genetic mutations, not everyone with that mutation has autism, and the question is why?" says neuroscientist Alcino Silva of University of California, Los Angeles (UCLA). One such type of mutation, linked to autism in about half of the people who carry the variants, are in the *tuberous sclerosis complex 1* or *2* genes and can have a range of symptoms in addition to autism. Mice with a mutation in *Tsc2* have some of the same symptoms, but until about a decade ago, the social deficits that can show up in people with the mutations had not been recreated in the mouse model. Then, in 2010, Silva's group showed that challenging the immune systems of pregnant mice caused ASD-like behavior in their *Tsc2* mutant offspring.

In the new study, Silva and colleagues further explore the interactions of genetics and environment, this time at later stages of development.

They injected either an immune stimulant known as PolyI:C or saline into wildtype mice and *Tsc2* heterozygotes at postnatal days 3, 7, and 14. After the mice reached adulthood, the researchers tested their social behaviors with the three-chamber social interaction test, in which mice are exposed to a chamber that's empty on one side and contains a new mouse on the other.

Twenty-four hours later, the chamber contains the now-familiar mouse on one side and a new mouse on the other side. All of the mice spent more time with the new mouse on the first day than on the empty side of the chamber. But only male *Tsc2* heterozygotes who'd received the immune stimulant in early childhood spent equal time with the familiar mouse and the new mouse on the second day—instead of preferring the unfamiliar mouse, as the animals normally do—indicating that their social memory was impaired.

"It was super interesting that these deficits were unique to social memory and did not result in impaired sociability—one of the key hallmark tasks used to assess social interactions in mouse models of ASD," Annie Ciernia, a neuroscientist at the University of British Columbia who was not involved in the study, writes in an email to *The Scientist.* "This suggests that postnatal viral infections (which PolyI:C mimic) could be disrupting unique neural circuits important for social memory that are vulnerable during early postnatal development."

Mice use ultrasonic vocalizations to communicate, and it's been shown before that *Tsc2* heterozygotes don't vocalize like their

wildtype siblings, instead making more short calls that mother mice may be less responsive to. Silva's group collaborated with that of Stephanie White, a UCLA biologist and vocal learning expert, to investigate the effect of infections on these vocalizations. The team showed that early immune activation exacerbated the differences in vocalizations between wildtype mice and *Tsc2* heterozygotes, and write in the paper that this "may parallel early ASD social communication deficits" seen in humans.

Then, the researchers analyzed gene expression in the brains of the adult mice and found that genes associated with microglia and interferon signaling were more active in male *Tsc2* heterozygotes that received the immune stimulant, but not in any of the other mice. Using a drug to deplete the microglia in these mice reversed the defects in social behaviors, even after microglia reappeared months later.

"This is one of the first examples of how repopulation [of microglia] opens a new opportunity to reshape microglia function in the adult and provides the potential for novel therapeutic delivery in adults with ASD," Ciernia writes.

The team also found that mice without functional interferon signaling—due to either a genetic mutation or injection of the drug rapamycin—don't develop deficits in either social memory or vocalizations after simulated infections.

Taken together, the findings point to a role for interferon signaling by microglia in the development of ASD-like symptoms in mice. The differences in the development of microglia in males and females may help explain the sex differences in the response to immune activation, Silva says, adding that autism is about four times more common in boys than in girls.

Finally, in what he calls "a Hail Mary," Silva asked a friend, computational biologist Andrey Rzhetsky of the University of Chicago, to look at dataset of more than 3.5 million health insurance claims to see if there was any relationship between severe infections and autism in humans.

"He comes back months later and says, 'That's the biggest association I've ever found in this dataset,'" says Silva. Male children, regardless of genetic status, who were hospitalized with infections between the ages of 18 months and four years were 40 percent more likely to be diagnosed with ASD later than were boys who weren't hospitalized for infections, while for girls, hospitalization for infection at this age was associated with a 30 percent greater chance of ASD diagnosis. The difference for girls was not statistically significant, however.

"This paper has to be [understood] as proof that you need to vaccinate your kids," since infectious diseases can not only be fatal, but can also raise the risk of ASD among children who survive, says coauthor Manuel López Aranda, a neuroscientist at UCLA.

The combination of basic science and the clinically relevant data analysis of more than 3 million children is "a slam dunk," says Tanjala Gipson, a pediatric neurologist at Le Bonheur Children's Hospital in Memphis, Tennessee, who did not participate in the study. Open questions include: "how do I know my child is at risk? Do I need to be worried about every fever? Do I need to be worried about every infection?" she says. Thus, one next step would be determining whether there are biomarkers that indicate when children are more at risk.

Rapamycin, the drug the authors used to ameliorate the effects of simulated infection on the mice, is already being studied for tuberous sclerosis, the genetic disorder caused by *Tsc1* and *Tsc2* mutations, she notes. "It's another reason for hope, and there's always room for hope."

Clarification (September 17): The paragraph about the association found between hospitalization for infection and autism diagnosis in children has been amended to state that the association was not statistically significant for girls.

https://bit.ly/3EzXHfx

The Surprising Reason The Moon Has Fewer Craters Than It Probably Should

New study suggests that it's survived more early asteroid hits than its surface actually shows today

David Nield

You only have to take a look at the Moon to see that it's had something of a rough time during its roughly 4.5-billion-year history, but a new study suggests that it's survived more early asteroid hits than its surface actually shows today.

The new research proposes that some of the oldest impacts on the Moon left near-invisible imprints because they were striking a softer surface: The global ocean of magma that covered the Moon in its youth before it cooled and solidified.

These relatively soft landings, leaving next to no permanent trace of ever having happened, could explain why the Moon as it currently looks doesn't match up with what scientists think happened to it in the first billion years or so. "These large impact craters, often referred to as impact basins – formed during the lunar magma ocean solidification more than four billion years ago – should have produced different looking craters, in comparison to those formed later in geologic history," says planetary scientist Katarina Miljkovic from Curtin University in Australia.

The idea of a global magma ocean on the Moon is by no means new, but the research digs deeper into the potential timeline of magma and asteroid hits – and tries to line it up with what we think we know about what was happening in the Solar System at the time.

We have multiple clues as to what's happened to the Moon since it was formed, from Solar System modeling to evidence of impact shocks in rocks that have actually been recovered from the surface by Apollo astronauts. Some studies suggest the boiling lakes of magma could have stayed around for as many as 200 million years, and this latest research shows how that would fit in with the dates suggested for an early bombardment of large asteroids.

"The timeframe for the solidification of the lunar magma ocean varies significantly between different studies, but it could have been prolonged enough to experience some of the large impact bombardment history typical for the earliest periods of the Solar System evolution," says Miljkovic. "As the Moon ages and the surface cools, it becomes harder, and the bombardment imprints are a lot more noticeable by remote sensing."

This is all hugely important in establishing how the Solar System came to be the way it is – and from that, learning more about how planets actually form and how long they stay in particular states for. Even knowing that there's an unknown involved, like how many asteroid hits could have been missed by previous assessments of the lunar cratering record, helps to improve models of what was going on billions of years ago.

And because we're such near neighbors to the Moon, anything that happened to it would have had some effect on Earth too – giving us a better understanding of how our planet and the life on it came into being. "Translating this finding will help future research understand the impact that the early Earth could have experienced and how it would have affected our planet's evolution," says Miljkovic.

The research has been published in *Nature Communications*.

https://lat.ms/3ApAOsP

Big gap between Pfizer, Moderna vaccines seen for preventing COVID hospitalizations

One is significantly less effective at preventing severe cases of disease over the long term than many experts realized

By Melissa Healy,

Amid persistent concerns that the protection offered by COVID-19 vaccines may be waning, a report released Friday by the Centers for Disease Control and Prevention finds that America's workhorse

shot is significantly less effective at preventing severe cases of disease over the long term than many experts had realized.

Data collected from 18 states between March and August suggest the Pfizer-BioNTech vaccine reduces the risk of being hospitalized with COVID-19 by 91% in the first four months after receiving the second dose. Beyond 120 days, however, that vaccine efficacy drops to 77%. Meanwhile, Moderna's vaccine was 93% effective at reducing the short-term risk of COVID-19 hospitalization and remained 92% effective after 120 days. Overall, 54% of fully vaccinated Americans have been immunized with the Pfizer shot.

The surprising findings came as a Food and Drug Administration advisory panel recommended against offering booster doses of the Pfizer vaccine to all Americans ages 16 and older. In a striking rebuke, 16 of 18 experts told the agency it had not mustered enough data to make a third shot the norm.

In lengthy briefings to the panel, representatives from Pfizer pointed to clinical trial results involving 306 mostly healthy participants to argue that a booster "restores" the 95% vaccine effectiveness rate seen earlier in the pandemic.

Company officials also touted evidence from Israel, which rolled out boosters after seeing a rise in hospitalizations among people who were fully vaccinated. Those hospitalizations dropped dramatically after third doses were given, Israeli scientists have said. But panel members made clear that despite Pfizer's aggressive stance, it had not gathered enough evidence that a third shot was safe for young people and for those at lesser risk of becoming severely ill with COVID-19.

"We need age-specific data" on the safety and protective benefits of a further booster, said Dr. Ofer Levy, a panel member who directs the Precision Vaccines program at Boston Children's Hospital.

FDA clearance for booster shots for everyone 16 and older would be seen as something "close to a mandate," said Dr. Eric Rubin, a panel member and infectious-disease expert at the Harvard T.H. Chan School of Public Health. Rubin worried that such a move could redefine what it takes to be considered fully vaccinated against COVID-19. "None of us are there yet," he said.

But others apparently are. Dr. Anthony Fauci, President Biden's top advisor on vaccines, has come out strongly in favor of booster shots, saying before Friday's vote that a failure to endorse the shots "would be a mistake."

And in mid-August, Biden himself said his administration would begin making booster shots available the week of Sept. 20 to those vaccinated for at least eight months. Biden cautioned at the time that his plan was contingent on FDA approval. But his announcement stoked concerns of political meddling in a matter that required the unhindered evaluation of scientists.

"This should demonstrate to the public that the members of this committee are independent of the FDA," Dr. Archana Chatterjee, dean of the Chicago Medical School, said after the vote. "In fact, we do bring our voices to the table when we are asked to serve on this committee."

The panel unanimously agreed that a third shot of the vaccine now sold under the brand name Comirnaty should be offered to select groups: individuals 65 and older, people at risk of developing severe disease, and those, including healthcare workers, whose occupations put them at high risk of infection.

Dr. Peter Marks, who leads the FDA's evaluation of drugs and vaccines, told panel members that the agency could give its blessing to booster shots with an emergency use authorization — a regulatory step that falls short of the full approval Pfizer had sought. The company issued no statement Friday in response to the panel's vote.

Researchers in the United States have been warning for months that the immunity afforded by COVID-19 vaccines might be waning.

The CDC reported that in late July, close to three-quarters of the 469 people swept up in a Massachusetts outbreak were fully vaccinated. And the agency has launched several studies aimed at detecting changes in vaccine effectiveness in healthcare workers and others who were vaccinated early.

But virtually all of those infections appeared to be mild. And health officials eager to induce vaccine skeptics to step up for their shot — including Fauci and Dr. Rochelle Walensky, director of the Centers for Disease Control and Prevention — have repeatedly praised the vaccines for keeping most fully vaccinated people out of hospitals.

The new report on waning vaccine efficacy challenges that expectation.

Researchers from around the country found striking differences between two mRNA vaccines long thought to be interchangeable.

When the Moderna vaccine received emergency use authorization in December, the company reported that 30 people in its clinical trial developed severe cases of COVID-19, including nine who required hospitalization. All 30 patients were in the placebo group, resulting in a vaccine efficacy against severe disease of 100%.

Ten people in Pfizer's initial clinical trial developed severe cases of COVID-19. Nine of them were in the placebo group, including seven who were hospitalized, resulting in a vaccine efficacy against severe disease of 88.9%.

Once the Moderna and Pfizer vaccines were rolled out to the public, their records of preventing COVID-19 hospitalizations in the first four months were neck and neck — 93% and 91% effective, respectively. But the degree of protection diverged after that.

When they focused specifically on the period 120 days beyond the second dose, the study authors found that the Moderna vaccine remained 92% effective at preventing COVID-19 hospitalizations. But the equivalent figure for the Pfizer vaccine was 77%.

The results were published in the CDC's Morbidity and Mortality Weekly Report.

Both the Pfizer and Moderna vaccines are based on mRNA technology, which delivers temporary instructions to the body's muscle cells that help it learn to recognize the spike protein, a key part of the coronavirus' structure. But "they're actually not necessarily interchangeable," said Dr. Timothy Brewer, a professor of medicine and epidemiology at UCLA. Each vaccine is formulated and administered differently, Brewer said, and those differences could affect the strength and duration of the two vaccines' protection.

Moderna's shot contains 100 micrograms of vaccine, more than three times the 30 micrograms in the Pfizer shot. And Pfizer's two doses are given three weeks apart, while Moderna's two-shot regimen is administered with a four-week gap.

Brewer also pointed to evidence that the Moderna vaccine seemed to elicit higher levels of a key antibody than the Pfizer vaccine.

"We know from other studies the neutralizing antibody levels will decay over time, so starting at a higher level will mean that you have farther to go before you decay to a point where efficacy drops off," he said.

Dr. Robert Murphy, who directs Northwestern University's Institute for Global Health, said the Pfizer vaccine's reduced protection against severe disease may bolster the case for boosters for all who got the vaccine, not just the specific groups identified by the FDA advisory panel.

"Based on the data I have seen, persons who received the Pfizer vaccine would benefit from a booster dose at this time," he said. "I don't see why we have to wait until the younger people get sick and become hospitalized."

But Dr. Arnold Monto, who chairs the FDA advisory panel, applauded the agency's willingness to withhold a full-throated call for boosters until a stronger case can be made. And he suggested

that as more evidence accumulates, boosters for all might still get the nod. “That’s the beauty of the emergency use authorization,” said Monto, an epidemiologist at University of Michigan. “It can be changed based on changing data.”

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More Than 1 in 10 COVID-19 Patients Were Infected After Hospital Admission in First Pandemic Wave

Over one in 10 COVID-19 patients in 314 UK hospitals were infected after admission.

More than one in ten COVID-19 patients in 314 UK hospitals caught the infection in a hospital during the first pandemic wave say researchers conducting the world’s largest study of severe COVID-19.

The research into hospital-acquired infections (HAIs) was led by Dr. Jonathan Read from Lancaster University with colleagues from other UK universities including the Universities of Liverpool, Edinburgh, Birmingham and Imperial College London, and was recently published in *The Lancet*.

The researchers examined records of COVID-19 patients in UK hospitals enrolled in the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC) Clinical Characterisation Protocol UK (CCP-UK) study, who became ill before 1st August 2020.

They found that at least 11.1% of COVID-19 patients in 314 UK hospitals were infected after admission. The proportion of COVID-19 patients infected in hospital also rose to between 16% and 20% in mid-May 2020, long after the peak of admissions in the first wave.

The researchers said: “We estimate between 5,699 and 11,862 patients admitted in the first wave were infected during their stay in hospital. This is, unfortunately, likely to be an underestimate, as we did not include patients who may have been infected but discharged before they could be diagnosed.”

Dr. Jonathan Read, lead author at Lancaster University, said “Controlling viruses like SARS-CoV-2 (the virus that causes COVID-19) has been difficult in the past, so the situation could have been much worse. However, infection control should remain a priority in hospitals and care facilities.”

Dr. Chris Green, University of Birmingham, said: “There are likely to be a number of reasons why many patients were infected in these care settings. These include the large numbers of patients admitted to hospitals with limited facilities for case isolation, limited access to rapid and reliable diagnostic testing in the early stages of the outbreak, the challenges around access to and best use of PPE, our understanding of when patients are most infectious in their illness, some misclassification of cases due to presentation with atypical symptoms, and an under-appreciation of the role of airborne transmission.”

There were marked differences in the numbers of patients infected in hospital according to the type of care provided. Hospitals providing acute and general care had lower proportions of hospital acquired infections (9.7%) than residential community care hospitals (61.9%) and mental health hospitals (67.5%), which reflects the outbreaks seen in care-homes.

Professor Calum Semple, University of Liverpool, said: “The reasons for the variation between settings that provide the same type of care requires urgent investigation to identify and promote best infection control practice. Research has now been commission to find out what was done well and what lessons need to be learned to improve patient safety.”

Dr. Anne Marie Docherty, University of Edinburgh, said: “The underlying reasons for these high rates of transmission in hospitals at the peak of the first wave must be investigated, so that we can improve safety and outcomes for our patients. Rates are

considerably lower a year on, and people should not be deterred from attending hospital if they are unwell."

Reference: "Hospital-acquired SARS-CoV-2 infection in the UK's first COVID-19 pandemic wave" by Jonathan M Read, Chris A Green, Ewen M Harrison, Annemarie B Docherty, Sebastian Funk, Janet Harrison, Michelle Girvan, Hayley E Hardwick, Lance Turtle, Jake Dunning, Jonathan S Nguyen-Van-Tam, Peter JM Openshaw, J Kenneth Baillie, Malcolm G Semple and theISARIC4C investigators, 12 August 2021, The Lancet. DOI: 10.1016/S0140-6736(21)01786-4

https://bit.ly/3zr66hJ

COVID-19 vaccine's impact on menstrual cycles needs to be investigated after 30,000 women report changes, says top scientist

Women have reported their periods being altered after getting the COVID-19 vaccine - research is needed to understand why this is happening

Bethany Dawson

Since the rollout of COVID-19 vaccines, thousands of women in the UK have been saying that their periods have been disrupted, say experts. More than 30,000 women said their menstrual cycle being somewhat altered after getting the COVID-19 vaccine, reported Sky News.

The UK's Yellow Card scheme, where people can voluntarily report their side effects to any medication - including vaccinations - has shown that many women have seen a disruption in their periods.

Dr. Victoria Male, a reproductive immunologist from Imperial College London, wrote in the British Medical Journal that while these changes are safe and short-lived, has stated that an investigation as to why this happens is crucial.

In the US, the National Institute of Health is investing $1.67 million into understanding how the COVID-19 vaccines impact periods.

Dr. Male states that periods can be heavier or delayed because of an immune response, and poses no danger to one's body.

"Robust research into this possible adverse reaction remains critical to the overall success of the vaccination program. One important lesson is that the effects of medical interventions on menstruation should not be an afterthought in future research," wrote Dr. Male.

Writing in The Telegraph, Caroline Criado-Perez, author of Invisible Women, said: "As with most clinical studies, the Covid-19 vaccine trials did not investigate menstrual cycle effects – in fact, in many trials women are wholesale excluded *because* of potential menstrual cycle effects."

There is no reason to be significantly concerned about menstrual changes and long-term impacts, writes Dr. Male, as the vast majority of those reporting the post-vaccine alterations state that normality ensues quickly.

Meanwhile, the data available shows that the COVID-19 vaccine has no adverse effects on fertility and pregnancy.