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Maya more warlike than previously thought

Evidence of extreme warfare from Classic period disputes role of violence in civilization's decline

The Maya of Central America are thought to have been a kinder, gentler civilization, especially compared to the Aztecs of Mexico. At the peak of Mayan culture some 1,500 years ago, warfare seemed ritualistic, designed to extort ransom for captive royalty or to subjugate rival dynasties, with limited impact on the surrounding population.

Only later, archeologists thought, did increasing drought and climate change lead to total warfare -- cities and dynasties were wiped off the map in so-called termination events -- and the collapse of the lowland Maya civilization around 1,000 A.D. (or C.E., current era).

New evidence unearthed by a researcher from the University of California, Berkeley, and the U.S. Geological Survey calls all this into question, suggesting that the Maya engaged in scorched-earth military campaigns -- a strategy that aims to destroy anything of use, including cropland -- even at the height of their civilization, a time of prosperity and artistic sophistication.

The finding also indicates that this increase in warfare, possibly associated with climate change and resource scarcity, was not the cause of the disintegration of the lowland Maya civilization.

"These data really challenge one of the dominant theories of the collapse of the Maya," said David Wahl, a UC Berkeley adjunct assistant professor of geography and a researcher at the USGS in Menlo Park, California. "The findings overturn this idea that warfare really got intense only very late in the game."

"The revolutionary part of this is that we see how similar Mayan warfare was from early on," said archaeologist Francisco Estrada-Belli of Tulane University, Wahl's colleague.

"It wasn't primarily the nobility challenging one another, taking and sacrificing captives to enhance the charisma of the captors. For the first time, we are seeing that this warfare had an impact on the general population."

Total warfare

The evidence, reported today in the journal Nature Human Behaviour, is an inch-thick layer of charcoal at the bottom of a lake, Laguna Ek'Naab, in Northern Guatemala: a sign of extensive burning of a nearby city, Witzna, and its surroundings that was unlike any other natural fire recorded in the lake's sediment.

The charcoal layer dates from between 690 and 700 A.D., right in the middle of the classic period of Mayan civilization, 250-950 A.D. The date for the layer coincides exactly with the date -- May 21, 697 A.D. -- of a "burning" campaign recorded on a stone stela, or pillar, in a rival city, Naranjo.

"This is really the first time the written record has been linked to an event in the paleo data sets in the New World," Wahl said. "In the New World, there is so little writing, and what's preserved is mostly on stone monuments. This is unique in that we were able to identify this event in the sedimentary record and point to the written record, particularly these Mayan hieroglyphs, and make the inference that this is the same event."

Wahl, a geologist who studies past climate and is first author of the study, worked with USGS colleague Lysanna Anderson and Estrada-Belli to extract 7 meters of sediment cores from the lake. Laguna Ek'Naab, which is about 100 meters across, is located at the base of the plateau where Witzna once flourished and has collected thousands of years of sediment from the city and its surrounding agricultural fields.

After seeing the charcoal layer, the archaeologists examined many of Witzna's ruined monuments still standing in the jungle and found evidence of burning in all of them.

"What we see here is, it looks like they torched the entire city and, indeed, the entire watershed," Wahl said. "Then, we see this really big decrease in human activity afterwards, which suggests at least that there was a big hit to the population. We can't know if everyone was killed or they moved or if they simply migrated away, but what we can say is that human activity decreased very dramatically immediately after that event."

This one instance does not prove that the Maya engaged in total warfare throughout the 650-year classic period, Estrada-Belli said, but it does fit with increasing evidence of warlike behavior throughout that period: mass burials, fortified cities and large standing armies.

"We see destroyed cities and resettled people similar to what Rome did to Carthage or Mycenae to Troy," Estrada-Belli said.

And if total warfare was already common at the peak of Mayan lowland civilization, then it is unlikely to have been the cause of the civilization's collapse, the researchers argue.

"I think, based on this evidence, the theory that a presumed shift to total warfare was a major factor in the collapse of Classic Maya society is no longer viable," said Estrada-Belli. "We have to rethink the cause of the collapse, because we're not on the right path with warfare and climate change."

'Bahlam Jol burned for the second time'

Though Mayan civilization originated more than 4,000 years ago, the Classic period is characterized by widespread monumental architecture and urbanization exemplified by Tikal in Guatemala and Dzibanché in Mexico's Yucatan. City-states -- independent states made up of cities and their surrounding territories -- were ruled by dynasties that, archaeologists thought, established alliances and waged wars much like the city-states of Renaissance Italy, which affected the nobility without major impacts on the population. In fact, most archaeologists believe that the incessant warfare that arose in the terminal Classic period (800-950 A.D.), presumably because of climate change, was the major cause of the decline of Mayan cities throughout present day El Salvador, Honduras, Guatemala, Belize and Southern Mexico.

So when Wahl, Anderson and Estrada-Belli discovered the charcoal layer in 2013 in Laguna Ek'Naab -- a layer unlike anything Wahl had seen before -- they were puzzled. The scientists had obtained the lake core in order to document the changing climate in Central America, hoping to correlate these with changes in human occupation and food cultivation.

The puzzle lingered until 2016, when Estrada-Belli and co-author Alexandre Tokovinine, a Mayan epigrapher at the University of Alabama, discovered a key piece of evidence in the ruins of Witzna: an emblem glyph, or city seal, identifying Witzna as the ancient Mayan city Bahlam Jol.

Searching through a database of names mentioned in Mayan hieroglyphs, Tokovinine found that very name in a "war statement" on a stela in the neighboring city-state of Naranjo, about 32 kilometers south of Bahlam Jol/Witzna.

The statement said that on the day "... 3 Ben, 16 Kasew ('Sek'), Bahlam Jol 'burned' for the second time." According to Tokovinine, the connotation of the word "burned," or puluuy in Mayan, has always been unclear, but the date 3 Ben, 16 Kasew on the Mayan calendar, or May 21, 697, clearly associates this word with total warfare and the scorched earth destruction of Bahlam Jol/Witzna.

"The implications of this discovery extend beyond mere reinterpretation of references to burning in ancient Maya inscriptions," Tokovinine said. "We need to go back to the drawing board on the very paradigm of ancient Maya warfare as centered on taking captives and extracting tribute."

Three other references to puluuy or "burning" are mentioned in the same war statement, referencing the cities of Komkom, known today as Buenavista del Cayo; K'an Witznal, now Ucanal; and K'inchil, location unknown.

These cities may also have been decimated, if the word puluuy describes the same extreme warfare in all references. The earlier burning of Bahlam Jol/Witzna mentioned on the stela may also have left evidence in the lake cores -- there are three other prominent charcoal layers in addition to the one from 697 A.D. -- but the date of the earlier burning is unknown.

Mayan archaeologists have reconstructed some of the local history, and it's known that the conquest of Bahlam Jol/Witzna was set in motion by a queen of Naranjo, Lady 6 Sky, who was trying to reestablish her dynasty after the city-state had declined and lost all its possessions. She set her seven-year-old son, Kahk Tilew, on the throne and then began military campaigns to wipe out all the rival cities that had rebelled, Estrada-Belli said.

"The punitive campaign was recorded as being waged by her son, the king, but we know it's really her," he said.

That was not the end of Bahlam Jol/Witzna, however. The city revived, to some extent, with a reduced population, as seen in the lake cores. And the emblem glyph was found on a stela erected around 800 A.D, 100 years after the city's destruction. The city was abandoned around 1,000 A.D.

"The ability to tie geologic evidence of a devastating fire to an event noted in the epigraphic record, made possible by the relatively uncommon discovery of an ancient Maya city's emblem glyph, reflects a confluence of findings nearly unheard of in the field of geoarchaeology," Wahl said.

The study was supported by the National Science Foundation, USGS, Fundacion PACUNAM, National Geographic Society, Alphawood Foundation, Middle American Research Institute at Tulane University and University of Alabama.

http://bit.ly/2ZEpVkv

JHU study explains how some older brains decline before people realize it

Could reveal why some people's cognitive abilities decline with age while others remain sharp

Some older adults without noticeable cognitive problems have a harder time than younger people in separating irrelevant information from what they need to know at a given time, and a new Johns Hopkins University study could explain why.

The findings offer an initial snapshot of what happens in the brain as young and old people try to access long-term memories, and could shed light on why some people's cognitive abilities decline with age while others remain sharp.

"Your task performance can be impaired not just because you can't remember, but because you can't suppress other memories that are irrelevant," said senior author Susan Courtney, a cognitive neuroscientist at Johns Hopkins. "Some 'memory problems' aren't a matter of memory specifically, but a matter of retrieving the correct information at the right time to solve the problem at hand."

The findings were just posted in Neurobiology of Aging.

The researchers had 34 young adults (18 to 30) and 34 older adults (65-85) perform a mental arithmetic task while their brain activity was measured through functional magnetic resonance imaging, or fMRI. Other images were also collected to measure the integrity of the connections between brain areas called white matter tracts.

The task compared the participants' ability to inhibit irrelevant information automatically retrieved from long term memory. They were asked to indicate whether a proposed solution to an addition or multiplication problem was correct or not - for instance 8x4=12 or 8+4=32. These examples would create interference as participants considered the right answer because although they should answer "incorrect," the proposed solution seems correct at

first glance, based on long-term memories of basic math. This interference did not exist when participants were asked to answer clearly false equations like 8x4=22. Making the task even more complicated, the subjects were sometimes asked to switch to multiplication after they saw the addition symbol and vice versa.

Older people were a fraction of a second slower at answering the questions than younger participants, particularly when there was interference, but the more dramatic difference showed up in the brain scans. Older individuals who had more difficulty with interference also had more frontal brain activation than young adults.

The brain imaging demonstrated that in some aging participants, fibers connecting the front and back of the brain appear to have been damaged over the years. However other older individuals had fibers similar to much younger subjects. The greater the integrity of these fibers, the better the participant's task performance, said lead author Thomas Hinault, a postdoctoral fellow at Johns Hopkins.

"Everyone we studied had good functioning memory, but still we saw differences," Hinault said. "There are so many disruptions in the world and being able to suppress them is crucial for daily life."

The researchers were surprised to find that during parts of the task that were the trickiest, where participants had to switch between multiplication and addition and were asked to add after they saw a multiplication command or vice versa, the people with the strongest brain fiber connections counterintuitively performed even better. Something about deliberately exercising the mind in this fashion made the most agile minds even more so.

"If you have good connections between brain networks, that will help," Courtney said. "If not, you have interference."

Co-authors included Kevin Larcher of McGill University; Louis Bherer of the Université de Montréal; and Alain Dagher of McGill University.

http://bit.ly/2M6aVIS

Recursive language and modern imagination were acquired simultaneously 70,000 years ago

A genetic mutation that slowed down the development of the prefrontal cortex (PFC) in two or more children may have triggered a cascade of events leading to acquisition of recursive language and modern imagination 70,000 years ago.

This new hypothesis, called Romulus and Remus and coined by Dr. Vyshedskiy, a neuroscientist from Boston University, might be able to solve the long-standing mystery of language evolution. It is published in the open-science journal *Research Ideas and Outcomes (RIO)*.

Numerous archeological and genetic evidence have already convinced most paleoanthropologists that the speech apparatus has reached essentially modern configurations before the human line split from the Neanderthal line 600,000 years ago. Considering that the chimpanzee communication system already has 20 to 100 different vocalizations, it is likely that the modern-like remodeling of the vocal apparatus extended our ancestors' range of vocalizations by orders of magnitude. In other words, by 600,000 years ago, the number of distinct verbalizations used for communication must have been on par with the number of words in modern languages.

The lion-man sculpture from Germany (dated to 37,000 years ago) must have been first imagined by the artist by mentally synthesizing parts of the man and beast together and then executing the product of this mental creation in ivory. The composite artworks provide a direct evidence that by 37,000 years ago humans have acquired prefrontal synthesis. **Credit: JDuckeck [Public domain,** https://commons.wikimedia.org/wiki/File:Lion_man_photo.jpg]

On the other hand, artifacts signifying modern imagination, such as composite figurative arts, elaborate burials, bone needles with an eye, and construction of dwellings arose not earlier than 70,000 years ago. The half million-year-gap between the acquisition of the modern speech apparatus and modern imagination has baffled scientists for decades.

While studying acquisition of imagination in children, Dr. Vyshedskiy and his colleagues discovered a temporal limit for the development of a particular component of imagination. It became apparent that modern children who have not been exposed to full language in early childhood never acquire the type of active constructive imagination essential for juxtaposition of mental objects, known as Prefrontal Synthesis (PFS).

Dr. Vyshedskiy explains:

"To understand the importance of PFS, consider these two sentences: "A dog bit my friend" and "My friend bit a dog." It is impossible to distinguish the difference in meaning using words or grammar alone, since both words and grammatical structure are identical in these two sentences. Understanding the difference in meaning and appreciating the misfortune of the 1st sentence and the humor of the 2nd sentence depends on the listener's ability to juxtapose the two mental objects: the friend and the dog. Only after the PFC forms the two different images in front of the mind's eye, are we able to understand the difference between the two sentences. Similarly, nested explanations, such as "a snake on the boulder to the left of the tall tree that is behind the hill," force listeners to use PFS to combine objects (a snake, the boulder, the tree, and the hill) into a novel scene. Flexible object combination and nesting (otherwise known as recursion) are characteristic features of all human languages. For this reason, linguists refer to modern languages as recursive languages."

Unlike vocabulary and grammar acquisition, which can be learned throughout one's lifetime, there is a strong critical period for the development of PFS and individuals not exposed to conversations with recursive language in early childhood can never acquire PFS as adults. Their language is always lacking understanding of spatial prepositions and recursion that depend on the PFS ability. In a similar manner, pre-modern humans would not have been able to learn recursive language as adults and, therefore, would not be able to teach recursive language to their own children, who, as a result, would not acquire PFS. Thus, the existence of a strong critical period for PFS acquisition creates a cultural evolutionary barrier for acquisition of recursive language.

The second predicted evolutionary barrier was a faster PFC maturation rate and, consequently, a shorter critical period. In modern children the critical period for PFS acquisition closes around the age of five. If the critical period in pre-modern children was over by the age of two, they would have no chance of acquiring PFS. A longer critical period was imperative to provide enough time to train PFS via recursive conversations.

An evolutionary mathematical model, developed by Dr. Vyshedskiy, predicts that humans had to jump both evolutionary barriers within several generations since the "PFC delay" mutation that is found in all modern humans, but not in Neanderthals, is deleterious and is expected to be lost in a population without an associated acquisition of PFS and recursive language. Thus, the model suggests that the "PFC delay" mutation triggered simultaneous synergistic acquisition of PFS and recursive language. This model calls for:

- ***two or more children with extended critical period due to "PFC delay" mutation;***
- ***these children spending a lot of time talking to each other;***

- ***inventing the recursive elements of language, such as spatial prepositions;***
- ***acquiring recursive-conversations-dependent PFS;***
- ***teaching recursive language to their offsprings.***

The hypothesis is named after the celebrated twin founders of Rome, Romulus and Remus. Similar to legendary Romulus and Remus, whose caregiver was a wolf, the real children's caregivers had an animal-like communication system with many words, but no recursion. Their parents could not have taught them spatial prepositions or recursion; children had to invent recursive elements of language themselves. Such an invention of a new recursive language has been observed in contemporary children, for example among deaf children in Nicaragua.

"The acquisition of PFS and recursive language 70,000 years ago resulted in what was in essence a behaviorally new species: the first behaviorally modern Homo sapiens," concludes Dr. Vyshedskiy. "This newly acquired power for fast juxtaposition of mental objects in the process of PFS dramatically facilitated mental prototyping and led to fast acceleration of technological progress. Armed with the unprecedented ability to mentally simulate any plan and equally unprecedented ability to communicate it to their companions, humans were poised to quickly become the dominant species."

Humans acquired an ability to trap large animals and therefore gained a major nutritional advantage. As the population grew exponentially, humans diffused out of Africa and quickly settled in the most habitable areas of the planet, arriving in Australia around 50,000 years ago. These humans were very much like modern humans since they possessed both components of full language: the culturally transmitted recursive language along with the innate predisposition towards PFS, enabled by the "PFC delay" mutation.

Original source:

Vyshedskiy A (2019) Language evolution to revolution: the leap from rich-vocabulary non-recursive communication system to recursive language 70,000 years ago was associated with acquisition of a novel component of imagination, called Prefrontal Synthesis, enabled by a mutation that slowed down the prefrontal cortex maturation simultaneously in two or more children - the Romulus and Remus hypothesis. Research Ideas and Outcomes *5: e38546. https://doi.org/10.3897/rio.5.e38546*

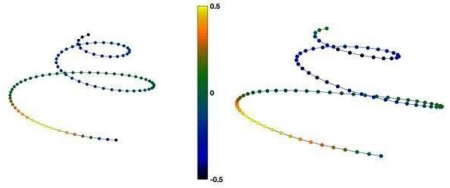
http://bit.ly/2MPUxvA

In the inner depths of the ear: The shape of the cochlea is an indicator of sex

The auditory section of the inner ear, or the "cochlea," does not have the same shape from birth depending on whether one is a man or a woman.

This is due to the torsion of the cochlear spiral, which differs based on gender, especially at its tip.

Demonstrated by a French-South African collaboration, an interdisciplinary effort evolving scientists primarily from the CNRS, UT3 Paul Sabatier, and l'Université Clermont Auvergne, these results have helped develop the first reliable method for sex determination, including among children and cases where DNA is missing or too altered.



Average female (left) and male (right) shapes for the cochlear spiral curve, whose torsion has been coded on a coloured scale. While the two forms are oriented in the same way, the geometric differences are visible. **Credit: C. Samir, A. Fradi, and J. Braga**

Until now, it was impossible to determine the sex of a child from its skeleton, while for adults this could be done reliably only from studying the pelvis, which is not always preserved. Since the cochlea is among the hardest bones in the skull—a bone that is found very frequently at archaeological sites—this technique can determine the sex of very old fossils, even when fragmentary or immature. This research was featured in an article published by *Scientific Reports*.

J. Braga et al. Cochlear shape reveals that the human organ of hearing is sex-typed from birth, Scientific Reports (2019). DOI: 10.1038/s41598-019-47433-9

http://bit.ly/31gtmye

Police use of fatal force is identified as a leading cause of death in young men

Police violence is a leading cause of death of young men in the United States with black men 2.5 times more likely to be killed by law enforcement over their lifetime than white men, according to a Rutgers study.

The study, published in *PNAS*, examined fatality risks during police encounters—some 11,456 between 2013-2017—and found that African-American men and women, American Indian/Alaska Native men and women and Latino men face a higher lifetime risk of being killed by police than do their white peers.

"The inequality is not surprising," said lead author Frank Edwards, assistant professor in the School of Criminal Justice at Rutgers University-Newark, noting the police killings of black men like Michael Brown and Eric Garner and boys like Tamir Rice and the protests that followed bringing national attention to the racialized character of police violence against civilians.

"All you have to do is turn on the news to see that people of color are at a much greater risk of police-related harm. What we lack in this country are the solid estimates of police related deaths because there is no official database where this information is stored."

The Rutgers study used data compiled by the National Vital Statistic System's mortality files and Fatal Encounters (FE), a journalist-led database that documents deaths involving police where cases are identified through public records and news coverage. Edwards said the unofficial media-based methods provide more comprehensive information on police violence than the limited official data collected.

The aim of the research, Edwards said, is to highlight the need to create a database that would accurately reflect the police violence that occurs.

"We haven't really known for sure how often these killings have been happening because the data hasn't been good enough," said Edwards. "But if we are going to try and change police practices that aren't working, we need to track this information better."

While statistics show that police in the United States kill more people than police in other advanced industrial democracies, researchers say real estimates of how often this occurs are not available. Official data is needed because these violent encounters, they insist, have profound effects on health, neighborhoods, life chances and politics, and have resulted in structural inequalities in the United States between people of color and white people.

The study found that the risk of death for each group peaks between the ages of 20 and 35 and declines with age. The highest mortality rate for men is between the ages of 25-29 when police use-of-force is deemed to be one of the leading causes of death, behind accidents—including drug overdoses, motor vehicle traffic death and other accidental fatalities—suicide, other homicides, heart disease and cancer.

Black men face a 1 in 1,000 chance of being killed by police over their lifetime compared to about 1 in 2,000 for men in general and about 1 in 33,000 for women—about 20 times lower than men.

This new research found that American Indian men were 1.5 times more likely to be killed by police than white men and American Indian women were about 1.5 times more likely to be killed by police than white women. While Latino men were 1.4 times more likely to be killed than their white counterparts, Latina women were about 1.2 times less likely to be killed than white women. Black women, however, were 1.4 times more likely to be killed by police than white women.

Edwards says the study reinforces calls to treat police violence—which has increased by as much as 50 percent since 2008—as a public health issue. While black people are disproportionately more

likely than white people to be killed by police, the rate of white deaths by police have also been increasing in recent years, according to the research.

"The Bureau of Justice Statistics needs to develop a comprehensive system that would track police-related deaths," said Edwards. "We need to increase transparency of police use-of-force if we are going to decrease the number of civilian deaths in this country as a result of these encounters."

The study stops short in evaluating current policy but says reforms are needed, including the creation of more social welfare and public health programs, adequate funding of community-based services and restricting the use of armed officers as first responders to mental health and other crisis situations where police killings have taken place.

"Our work should examine how race, gender, age, social class, disability and where someone lives exposes them to this type of violence and death," Edwards said.

More information: *Frank Edwards el al., "Risk of being killed by police use of force in the United States by age, race–ethnicity, and sex," PNAS (2019).* *www.pnas.org/cgi/doi/10.1073/pnas.1821204116*

http://bit.ly/2TaEWbi

Blood pressure recording over 24 hours is the best predictor of heart and vascular disease

Blood pressure recorded over 24 hours more accurately predicts cardiovascular complications

High blood pressure is the most important treatable risk factor for diseases of the heart and the arterial system. Blood pressure recorded over 24 hours predicts these complications more accurately than blood pressure measured on a single occasion. That is the conclusion of an international study coordinated by Professors Jan A. Staessen and Zhen-Yu Zhang of KU Leuven in Belgium. Dr. Gladys Maestre from the University of Texas, Rio Grande Valley School of Medicine, supervised the study in Venezuela, one of the participating countries. The study was published in the Journal of the American Medical Association.

An international consortium of scientists followed 11,135 individuals for 14 years. Study participants included residents of twelve countries in Europe, East Asia, and Latin America. The researchers compared the predictive accuracy of blood pressure measurements made by a healthcare provider in an office setting, to repeated blood pressure measurements recorded for 24 hours, during both day and night. The results showed that the probability of heart and vascular disease during follow-up was closely associated with the blood pressure measured over a 24-hour period.

"Although heart and vascular disease are strongly associated with blood pressure, irrespective of how it is measured, until now we did not know which type of blood pressure measurement captured risk in the most accurate way," Dr. Maestre said.

At the start of the study, investigators made individual blood pressure measurements using all available approaches, and determined other risk factors. Blood pressure was also recorded over a 24-hour period using automated portable blood pressure monitors. The number of blood pressure measurements averaged 30 during daytime and 10 during sleep. One of the advantages of measuring blood pressure during sleep, with individuals lying down in bed, is that the results are not influenced by daytime activities or meals. This at least partly explains the accuracy of nighttime blood pressure in predicting cardiac and vascular illness.

High blood pressure is the leading treatable risk factor for diseases of the heart and vascular system. Worldwide, high blood pressure causes 10 million deaths each year, with more than half of that mortality attributable to cardiovascular disease. The present study is unique in its large sample size and long follow-up period. The characteristics of participants were similar to those of the

populations from which they were enrolled, so the results can be generalized.

"Our research highlights the necessity of using 24-hour measurements to diagnose high blood pressure and to institute and fine tune its treatment," said Dr. Maestre. "Nevertheless, most health insurers in the US reimburse 24-hour ambulatory blood pressure monitoring only when blood pressure is found to be high in the clinical setting, but is suspected to be normal otherwise, or if undetected or masked hypertension is suspected. However, 24 hour ambulatory blood pressure monitoring is cost effective: It enables the prevention of cardiovascular disease by starting treatment in a timely manner."

Prevention and improved control of high blood pressure is also cost effective, because hospital-based treatment of the complications of high blood pressure, such as chest pain caused by narrowing of the arteries of the heart, myocardial infarction, and stroke, is expensive. Furthermore, prevention reduces the risk of premature disability and death, thereby avoiding suffering of patients and their families. About 30% of all adults and 60% of people age 60 and over have high blood pressure. Therefore, ambulatory blood pressure monitoring should be available at all levels of the healthcare delivery chain.

http://bit.ly/2MGKtVT

Dietary choline associates with reduced risk of dementia

Dietary intake of phosphatidylcholine is associated with a reduced risk of dementia

A new study by researchers at the University of Eastern Finland is the first to observe that dietary intake of phosphatidylcholine is associated with a reduced risk of dementia. Phosphatidylcholine was also linked to enhanced cognitive performance. The main dietary sources of phosphatidylcholine were eggs and meat. The findings were published in the *American Journal of Clinical Nutrition*.

Choline is an essential nutrient, usually occurring in food in various compounds. Choline is also necessary for the formation of acetylcholine, which is a neurotransmitter. Earlier studies have linked choline intake with cognitive processing, and adequate choline intake may play a role in the prevention of cognitive decline and Alzheimer's disease. In fact, choline is nowadays used in a multinutrient medical drink intended for the treatment of early Alzheimer's.

The new study now shows that the risk of dementia was 28% lower in men with the highest intake of dietary phosphatidylcholine, when compared to men with the lowest intake. Men with the highest intake of dietary phosphatidylcholine also excelled in tests measuring their memory and linguistic abilities. These findings are significant, considering that more than 50 million people worldwide are suffering from a memory disorder that has led to dementia, and the number is expected to grow as the population ages. Alzheimer's disease is the most common cause of dementia, for which no cure currently exists. The new findings may, therefore, play a vital role in the prevention of dementia. Successful dementia prevention is a sum of many things and in this equation, even small individual factors can have a positive effect on the overall risk, possibly by preventing or delaying the disease onset.

"However, this is just one observational study, and we need further research before any definitive conclusions can be drawn," Maija Ylilauri, a PhD Student at the University of Eastern Finland points out.

The data for the study were derived from the Kuopio Ischaemic Heart Disease Risk Factor Study, KIHD. At the onset of the study in 1984-1989, researchers analysed approximately 2,500 Finnish

men aged between 42 and 60 for their dietary and lifestyle habits, and health in general.

These data were combined with their hospital records, cause of death records and medication reimbursement records after an average follow-up period of 22 years. In addition, four years after the study onset, approximately 500 men completed tests measuring their memory and cognitive processing. During the follow-up, 337 men developed dementia.

The analyses extensively accounted for other lifestyle and nutrition related factors that could have explained the observed associations. In addition, the APOE4 gene, which predisposes to Alzheimer's disease and is common in the Finnish population, was accounted for, showing no significant impact on the findings. The key sources of phosphatidylcholine in the study population's diet were eggs (39%) and meat (37%).

Associations of dietary choline intake with risk of incident dementia and with cognitive performance: the Kuopio Ischaemic Heart Disease Risk Factor Study
Maija P.T. Ylilauri, Sari Voutilainen, Eija Lönnroos, Heli E.K. Virtanen, Tomi-Pekka Tuomainen, Jukka T. Salonen, Jyrki K. Virtanen American Journal of Clinical Nutrition, *published online July 30, 2019, https://doi.org/10.1093/ajcn/nqz148*

http://bit.ly/2KmXHp8

Researchers Concocted an Ancient Egyptian Perfume Perhaps Worn by Cleopatra

One archaeologist describes the spicy, musky scent as "the Chanel No. 5 of ancient Egypt."

by Sabrina Imbler

If Cleopatra wanted to woo you, you'd smell her before you ever saw her. Legend has it that when she first visited Marc Antony in Tarsus, she coated the purple sails of her golden boat in a fragrance so pungent that it wafted all the way to shore.

As Shakespeare wrote, Cleopatra's sails were "so perfumèd that the winds were lovesick with them." It does sound a bit extra, but, honestly, who wouldn't want to catch a whiff of Egypt's most famous queen?

Now, a team of four researchers have recreated a perfume they believe Cleopatra might have worn, based on residue found in an ancient amphora. "This was the Chanel No. 5 of ancient Egypt," says Robert Littman, an archaeologist at the University of Hawai'i at Mānoa. "It was the most prized perfume of the ancient world."

Littman and his colleague Jay Silverstein came up with the idea during their ongoing excavation of the ancient Egyptian city Thmuis, located north of Cairo in the Nile Delta and founded around 4500 BC.

The region was home to two of the most famous perfumes in the ancient world: Mendesian and Metopian. So when the researchers uncovered what seemed to be an ancient fragrance factory—a 300 BC site riddled with tiny glass perfume jars and imported clay amphoras—they knew they had to try to recover any scent that had survived.

The amphoras did not contain any noticeable smell—but they did contain an ancient sludge. After conducting a residue analysis, Littman took it to two experts on ancient Egyptian perfumes, Dora Goldsmith and Sean Coughlin, who tried to replicate the Thmuis scent using formulas found in ancient Greek *materia medica* texts.

Both Mendesian and Metopian perfumes contain myrrh, a natural resin extracted from a thorny tree. The experts also added cardamom, green olive oil, and a little cinnamon—all according to the ancient recipe.

The reproduced scent smells strong, spicy, and faintly of musk, Littman says. "I find it very pleasant, though it probably lingers a little longer than modern perfume."

In ancient Egypt, people used fragrance in rituals and wore scents in unguent cones, which were like wax hats that dripped oil into one's hair over the course of the day. "Ancient perfumes were

much thicker than what we use now, almost like an olive oil consistency," Littman says.

Though the modern-day Mendesian offers an intriguing approximation of an ancient Egyptian perfume, the jury's out on whether Cleopatra would have worn it. "Cleopatra made perfume herself in a personal workshop," says Mandy Aftel, a natural perfumer who runs a museum of curious scents in Berkeley, California. "People have tried to recreate her perfume, but I don't think anybody knows for sure what she used."

Aftel is no stranger to the concocted scents of ancient Egypt. In 2005, she reproduced the burial fragrance of a 2,000-year-old mummified Egyptian child, a girl dubbed Sherit.

Since her mummification, the perfume had shriveled into a thick black tar around Sherit's face and neck, according to a Stanford press release.

On the left, a musician wears an unguent cone. **British Museum/Public Domain**

Aftel identified frankincense and myrrh as the primary ingredients in the perfume and reconstructed a copy. "I smelled the mummy," Aftel says. "As a natural perfumer, it's a very beautiful way to connect to the past."

If you're in D.C., you can smell this most recent recreation yourself: the scent is on display at the National Geographic Museum's exhibition "Queens of Egypt" until September 15. There's not enough perfume to coat an entire sail, but you can dab a little on your arm.

http://bit.ly/33o6EWX

Dark Chocolate Consumption May Reduce Depression Symptoms

A new study, published recently in the journal* Depression and Anxiety, *provides evidence that consumption of chocolate, particularly dark chocolate, may be associated with reduced odds of clinically relevant depressive symptoms.

by News Staff / Source

Chocolate is widely reported to have mood-enhancing properties and several mechanisms for a relationship between chocolate and mood have been proposed.

Principally, chocolate contains a number of psychoactive ingredients which produce a feeling of euphoria similar to that of cannabinoid, found in cannabis. It also contains phenylethylamine, a neuromodulator which is believed to be important for regulating people's moods.

Experimental evidence suggests that mood improvements only take place if the chocolate is palatable and pleasant to eat, which suggests that the experience of enjoying chocolate is an important factor, not just the ingredients present.

Dr. Sarah Jackson of University College London and colleagues set out to examine the relationship between chocolate consumption and symptoms of depression in a large, nationally-representative sample of adults living in the US. They analyzed data from 13,626 adults participating in the US National Health and Nutrition Examination Survey. Participants' chocolate consumption was assessed against their scores on the Patient Health Questionnaire, which assesses depressive symptoms.

In the cross-sectional study, a range of other factors including height, weight, marital status, ethnicity, education, household income, physical activity, smoking and chronic health problems

were also taken into account to ensure the study only measured chocolate's effect on depressive symptoms.

After adjusting for these factors, it was found that individuals who reported eating any dark chocolate in two 24-hour periods had 70% lower odds of reporting clinically relevant depressive symptoms than those who reported not eating chocolate at all.

The 25% of chocolate consumers who ate the most chocolate (of any kind, not just dark) were also less likely to report depressive symptoms than those who didn't eat chocolate at all.

However, the scientists found no significant link between any non-dark chocolate consumption and clinically relevant depressive symptoms.

"Further research is required to clarify the direction of causation — it could be the case that depression causes people to lose their interest in eating chocolate, or there could be other factors that make people both less likely to eat dark chocolate and to be depressed," Dr. Jackson said.

"Should a causal relationship demonstrating a protective effect of chocolate consumption on depressive symptoms be established, the biological mechanism needs to be understood to determine the type and amount of chocolate consumption for optimal depression prevention and management."

Sarah E. Jackson et al. *Is there a relationship between chocolate consumption and symptoms of depression? A cross-sectional survey of 13,626 US adults.* Depression and Anxiety, *published online July 29, 2019; doi: 10.1002/da.22950*

http://bit.ly/31oPG8U

Is Ebola Evolving Into a More Deadly Virus?

Around half of all Ebola patients admitted to treatment centers in eastern Congo aren't part of any known chain of transmission

By Richard Preston

This July, the World Health Organization declared that an outbreak of Ebola in the provinces of Ituri and North-Kivu, in the eastern Democratic Republic of the Congo, was a "public health emergency of international concern." This particular strain of the virus, which first appeared in the region in 2018 and hasn't been given a formal name—I'll call it Kivu Ebola—is a variant of a species known as the Zaire Ebola virus. As of last Saturday, 2,753 cases of Kivu Ebola have been reported, with 1,843 deaths. There appear to be many undiscovered cases in the region, too. Ella Watson-Stryker, a social scientist with Doctors Without Borders, who has been studying the outbreak, said that around half of all Ebola patients admitted to treatment centers in eastern Congo aren't part of any known chain of transmission. In other words, the infected person has caught Ebola from somebody whom disease investigators haven't yet identified. "A lot of transmission is not being seen, but nobody knows the exact amount," Watson-Stryker told me.

Ebola virus is a microscopic parasite that replicates inside the cells of a host. The outbreak in eastern Congo began more than a year ago, in or near a town called Mangina, when a few particles of Ebola virus apparently moved out of some wild creature, Ebola's natural host—in this case, probably a bat—and entered the bloodstream of an as yet unidentified person. From that person, the virus began spreading through the local population. Ebola can overwhelm the human immune system in a matter of days. Symptoms typically include vomiting, diarrhea, coughing, rash, dementia, hemorrhages, and hiccups. Death occurs like the slamming of a door, when the patient abruptly goes into shock.

The Kivu Ebola outbreak area is in a conflict zone, beset by armed militias and ethnic violence. Local people often don't trust the international medical organizations that run the Ebola treatment centers. There have been at least a hundred and ninety-four attacks on local health workers, seven of whom have been killed. Watson-Stryker, the researcher, said that social media complicates containment and treatment efforts. Conspiracy theories about medical workers and false information about how the virus is

spread are ricocheting around popular platforms like WhatsApp. “The problem is the post-factual reality that exists in social media,” she said.

An effective experimental vaccine for Ebola exists, and more than a hundred and seventy-five thousand people have received it. Even so, the virus is finding new victims and extending its geographic range. Three cases of Ebola recently appeared in Uganda, and there have now been four cases in the Congolese city of Goma, which has roughly two million residents and is situated on the border with Rwanda. The W.H.O. recently estimated that more than two hundred million dollars in emergency funding would be needed to bring the virus under control. That money hasn’t been raised yet.

An Ebola particle is a very small, filament-shaped object, made of six different structural proteins. Ebola’s genetic code, or genome, is contained in a strand of ribonucleic acid, or RNA, that is coiled tightly in the core of the particle. The genome, which has some nineteen thousand letters in it, holds the master designs of Ebola’s proteins.

RNA viruses—which range from Ebola to measles and influenza—tend to produce errors, or mutations, in their code when they copy themselves. Most mutations are either bad for the virus or have no effect on it. Every now and then, however, a virus gets a mutation that benefits it. In fact, the production of errors during copying plays an important role in the long-term survival of viruses. As time goes by and the virus makes inaccurate copies of itself, slightly different varieties of the virus arise. The different varieties are called lineages. They can be imagined as moths of the same species whose wings are slightly different colors. Some wing colors help a moth camouflage itself more effectively, be eaten less often by predators, and survive longer than moths of other colors. Those types of moths go on to reproduce successfully, while moths of other colors eventually die out, until the population of moths has changed color entirely. This is the process of evolution.

Considered as a life-form, the Kivu Ebola isn’t a single organism but, rather, an immense swarm of particles that jumps from victim to victim. Each particle in the swarm possesses a biological drive to copy itself. As the particles copy themselves, they compete with all the other particles for survival. Ebola particles copy themselves every eighteen hours. This is the generation time of the virus—the time it takes for a particle of Ebola to get inside a human cell and potentially create thousands of identical copies of itself in the cell. The copies then exit the infected cell and drift into the bloodstream, infecting more cells. Early in the disease, Ebola patients tend to get sicker in downward lurches. In some patients, the lurches are spaced roughly eighteen hours apart, as each new generation of particles floods the body. An infected person’s bodily fluids are lethally infectious, because they are filled with Ebola particles. If some of those particles get into new people, the virus spreads.

By now, the Kivu Ebola swarm has been going through its eighteen-hour replication cycle in humans for more than a year. Some virologists wonder whether Kivu Ebola could start evolving, or whether it has already started to evolve, in a way that makes it more dangerous to people—perhaps by becoming more contagious, in which case it would get much harder to control. These questions introduce a new aspect to the international emergency.

During the Ebola epidemic that ravaged West Africa in 2014 and 2015, that form of Ebola showed possible signs of evolving. Virologists are still trying to determine the significance of what happened. The epidemic began in a village in Guinea, in December, 2013, when some particles of Ebola apparently went from a bat into a small boy. That strain of the virus, now referred to as Makona Ebola, killed the boy and most of his family, and then began spreading. In the end, around thirty thousand people were infected

and more than eleven thousand died before Makona Ebola was finally brought under control and eliminated from the human population. (There were eleven cases in the United States.)

As the epidemic progressed, a team of researchers, led by Pardis Sabeti, a genomic scientist at Harvard and the Broad Institute, studied the genetic code of various samples of Ebola taken from the blood of people who had been infected. They found that the virus began mutating as soon as it got into people. “From the outset, I was intrigued by the large number of mutations we found,” Sabeti told me. Makona Ebola quickly developed into several basic varieties. Then, in late May, 2014, one of the lineages took off like a wildfire and spread rapidly all over Sierra Leone and Liberia. This lineage is named the A82V Makona Variant of Ebola. For simplicity, I’ll call it the Makona mutant. The majority of patients in the epidemic were infected with the Makona mutant, including all eleven individuals in the United States. Meanwhile, the other lineages of Ebola died out. It seemed that the Makona mutant had somehow beaten them in a contest for survival.

Sabeti and other research groups noted that the change in the code of the Makona mutant happened in a single letter, which was part of the genetic recipe that causes the Ebola particle to be covered in roughly three hundred soft, squishy knobs. The knobs, called glycoproteins, are essential for the particle’s survival; they help it stick to cells and get inside cells, where it can reproduce. Sabeti wondered if the change in the knob protein could help this particular lineage of Ebola survive and prosper. “The mutation showed up at an inflection point in the outbreak, just as the outbreak exploded,” Sabeti said. “This was really intriguing.” It seemed that there might be something different about the knobs on the outside of the Makona mutant.

In 2016, a research team at the University of Massachusetts Medical School, led by a doctor named Jeremy Luban, ran some experiments on the Makona-knob protein. The team found that the knobs on the Makona mutant were four to five times better at invading human cells than those on the earlier strain of Makona. The Makona mutant stuck to human cells like a magnet, and the knobs seemed able to open a cell’s outer membrane, with the ease of a slide opening the teeth of a zipper, to allow the virus inside. “But what the significance of this mutation is for the outbreak, and how deadly this virus is, are still open questions,” Luban told me. “In biology, there is almost no such thing as proof.” Luban is planning more experiments to try to find out whether the Makona mutant was, in fact, more devastating or contagious than its predecessor.

A British team led by a virologist at the University of Nottingham named Jonathan Ball found that the Makona mutant seemed to be around twice as infectious in human cells than the earlier version of the virus had been. It also was less infectious in bat cells. The Makona mutant seemed to be evolving away from bats and turning into a virus suited for human cells. “I wasn’t at all surprised by this,” Ball said. “If you put a virus in a different system, you quickly see that the virus adapts to the new environment. I was surprised that other people were surprised.” Ball stressed that the experiments had been done in test tubes, using knobs of Ebola grafted onto a harmless virus. “We can’t show how the [real] virus will actually behave in a human,” he said. “You can’t do that experiment.” Many scientists, including Ball and Luban, aren’t so sure that the Makona mutant was any more dangerous than any other form of Ebola. The Makona mutant most likely spread far and wide because of social and behavioral factors, but it may have spread faster and more widely than it would have otherwise because of a change in one part of its genome.

What about the Kivu Ebola? The violence in the outbreak area makes doing scientific research there difficult. Nevertheless, a

Congolese team of genomic researchers at the National Institute for Biomedical Research, at the University of Kinshasa, working with international colleagues, has been collecting blood samples from the outbreak and reading the genetic code of the Ebola. The Kivu Ebola, so far, has mutated into four lineages. Three of the four are active in the population. The swarm is exploring people's immune systems and jumping from one victim to the next. So far, none of the three active varieties has become dominant. "The virus has been brewing in that area for a while," Sabeti said. "If you give Ebola enough time to transmit from human to human, then an unpredictable event can occur. How likely is it that Ebola could change suddenly? We don't have a good answer to that question."

Right now, there may be around six hundred people in eastern Congo who have Kivu Ebola particles replicating in their bodies. As Ebola re-creates itself, many of the resulting particles are deformed duds and can't replicate further. The ones that can copy themselves are infective. The Kivu swarm, with its three new lineages of Ebola, may amount to about one or two quadrillion infective particles of the virus. If these particles were collected in one place, they would fill three teaspoons and would weigh about fifteen grams. That small space contains numberless genetic possibilities. The longer the outbreak is allowed to continue, the greater the chances that Ebola will mutate, get better at spreading in humans, and vastly enlarge its circle of victims.

http://bit.ly/33lxKxK

Internet can be valuable tool for people with undiagnosed rare disorders

Internet can serve as a pathway to diagnosis and care for those who suspect they have a rare condition

WINSTON-SALEM, N.C. - The internet can serve as a pathway to diagnosis and care for people who suspect they have a rare condition that has not been identified by their physicians, according to a study by researchers at Wake Forest School of Medicine, part of Wake Forest Baptist Health.

"Rare diseases, especially inherited ones, are often not correctly diagnosed by primary care physicians and even specialists because they are so uncommon, and a provider who does have expertise may be located very far from the patient," said the study's lead author, Anthony J. Bleyer, M.D., professor of nephrology at the medical school. "While online searches can frequently fail to provide relevant or correct health information, the internet does offer those with rare disorders a way to find the rare specialists interested in a particular condition and obtain accurate information about it."

The study, published in the current issue of the Genetics in Medicine, the official journal of the American College of Medical Genetics and Genomics, analyzed 665 referrals made from 1996 to 2017 to a Wake Forest School of Medicine research center specializing in autosomal dominant tubulointerstitial kidney disease (ADTKD), a group of rare inherited conditions that gradually cause kidneys to stop working.

Among the referrals, 40 percent were from health care providers at academic medical centers, 33 percent were from non-academic practitioners and 27 percent were self-referrals from individuals or family members with concerns about but no diagnosis of inherited kidney disease who contacted the center directly through its website without guidance or assistance from a health care provider.

Genetic testing results were positive (indicating the presence of ADTKD) in 27 percent of the cases referred by academic centers, 25 percent of those referred by non-academic providers and 24 percent of those who contacted the center directly.

"The similar percentages of positive results from the three types of referrals indicate that actively pursuing self-diagnosis using the internet can be successful," Bleyer said. "One-quarter of the

families found to have ADTKD were diagnosed as result of direct contact with the center through the internet, which represents 42 families and 116 individuals who otherwise would have gone undiagnosed if a family member had not contacted us."

One of the study's limitations is that it examined data from only one center specializing in a single rare disorder.

Nonetheless, Bleyer said, the study highlights the importance of the internet as a resource for people with rare conditions.

"The availability of focused information about rare disorders on the internet may lead to increased diagnoses of these conditions," he said. "Centers interested in rare disorders should consider improving their online accessibility to the public."

The research was supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health under the award number R21DK106584 and by the Ministry of Health and Ministry of Education of the Czech Republic; Charles University, Prague; and the Carlos Slim Foundation.

Collaborators in the research are co-investigator Stanislav Kmoch, Ph.D., First Faculty of Medicine, Charles University, Prague, Czech Republic, and Anna Greka, M.D., Ph.D., at the Broad Institute of Harvard Medical School and MIT, Cambridge, Massachusetts.

http://bit.ly/2TdOQcc

Home births as safe as hospital births: International study

No clinically important or statistically different risk between home and hospital groups

Hamilton, ON - A large international study led by McMaster University shows that low risk pregnant women who intend to give birth at home have no increased chance of the baby's perinatal or neonatal death compared to other low risk women who intend to give birth in a hospital. The results have been published by The Lancet's EClinicalMedicine journal.

"More women in well-resourced countries are choosing birth at home, but concerns have persisted about their safety," said Eileen Hutton, professor emeritus of obstetrics and gynecology at McMaster, founding director of the McMaster Midwifery Research Centre and first author of the paper. "This research clearly demonstrates the risk is no different when the birth is intended to be at home or in hospital."

The study examined the safety of place of birth by reporting on the risk of death at the time of birth or within the first four weeks, and found no clinically important or statistically different risk between home and hospital groups.

The study, which is the first systematic review and meta-analyses to use a previously published, peer-reviewed protocol for the research, used data from 21 studies published since 1990 comparing home and hospital birth outcomes in Sweden, New Zealand, England, Netherlands, Japan, Australia, Canada and the U.S. Outcomes from approximately 500,000 intended home births were compared to similar numbers of births intended to occur in hospital in these eight countries.

"Our research provides much needed information to policy makers, care providers and women and their families when planning for birth," said Hutton.

The study was supported in part by a grant from the Association of Ontario Midwives.

Read the paper here: https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(19)30119-1/fulltext

http://bit.ly/2TqVEpG

Dark matter may be older than the big bang, study suggests

Study now suggests that dark matter may have existed before the Big Bang

Dark matter, which researchers believe make up about 80% of the universe's mass, is one of the most elusive mysteries in modern physics. What exactly it is and how it came to be is a mystery, but a new Johns Hopkins University study now suggests that dark matter may have existed before the Big Bang.

The study, published August 7 in Physical Review Letters, presents a new idea of how dark matter was born and how to identify it with astronomical observations.

"The study revealed a new connection between particle physics and astronomy. If dark matter consists of new particles that were born before the Big Bang, they affect the way galaxies are distributed in the sky in a unique way. This connection may be used to reveal their identity and make conclusions about the times before the Big Bang too," says Tommi Tenkanen, a postdoctoral fellow in Physics and Astronomy at the Johns Hopkins University and the study's author.

While not much is known about its origins, astronomers have shown that dark matter plays a crucial role in the formation of galaxies and galaxy clusters. Though not directly observable, scientists know dark matter exists by its gravitation effects on how visible matter moves and is distributed in space.

For a long time, researchers believed that dark matter must be a leftover substance from the Big Bang. Researchers have long sought this kind of dark matter, but so far all experimental searches have been unsuccessful.

"If dark matter were truly a remnant of the Big Bang, then in many cases researchers should have seen a direct signal of dark matter in different particle physics experiments already," says Tenkanen.

Using a new, simple mathematical framework, the study shows that dark matter may have been produced before the Big Bang during an era known as the cosmic inflation when space was expanding very rapidly. The rapid expansion is believed to lead to copious production of certain types of particles called scalars. So far, only one scalar particle has been discovered, the famous Higgs boson.

"We do not know what dark matter is, but if it has anything to do with any scalar particles, it may be older than the Big Bang. With the proposed mathematical scenario, we don't have to assume new types of interactions between visible and dark matter beyond gravity, which we already know is there," explains Tenkanen.

While the idea that dark matter existed before the Big Bang is not new, other theorists have not been able to come up with calculations that support the idea. The new study shows that researchers have always overlooked the simplest possible mathematical scenario for dark matter's origins, he says.

The new study also suggests a way to test the origin of dark matter by observing the signatures dark matter leaves on the distribution of matter in the universe.

"While this type of dark matter is too elusive to be found in particle experiments, it can reveal its presence in astronomical observations. We will soon learn more about the origin of dark matter when the Euclid satellite is launched in 2022. It's going to be very exciting to see what it will reveal about dark matter and if its findings can be used to peak into the times before the Big Bang."

http://bit.ly/2Yt9k6y

Cancer Patients Get Rare Blood Infection After Nurse Dilutes Opioids with Tap Water

Half a dozen cancer patients in New York developed a rare infection after they received injectable opioids that a nurse had diluted with tap water, according to a new report.

By Rachael Rettner 14 hours ago Health

It appears that the nurse tampered with the syringes to remove some of the narcotics for her own use, replacing the drugs with water, the report said.

The patients became infected with a bacterium called *Sphingomonas paucimobilis* and were treated with antibiotics. No deaths resulted from the infections, but some patients later died from unrelated causes, including complications of cancer, according to the report, published today (Aug. 7) in the The New England Journal of Medicine.

The issue came to light in the summer of 2018, when six patients at Roswell Park Comprehensive Cancer Center in Buffalo, New York, developed bloodstream infections with *S. paucimobilis*. This bacterium lives naturally in soil and water, but it rarely causes bloodstream infections, even among people with weakened immune systems, the report said.

Because these infections are so rare, doctors suspected a contaminated medication was behind the outbreak. Indeed, an investigation revealed that syringes of hydromorphone, an opioid medication, tested positive for *S. paucimobilis*.

What's more, hydromorphone syringes that were stored in a locked drawer that was part of the hospital's automated medication-dispensing system also tested positive for *S. paucimobilis* and other waterborne bacteria.

Records showed that a nurse had "repetitively and inappropriately" accessed this storage drawer, the report said. Although the syringes showed no overt signs of tampering, tests revealed that the medications in the syringes had been diluted with water.

"We concluded that a portion of the narcotic had been removed and replaced with an equal volume of tap water, which contaminated the [medication] with waterborne bacteria," the report said.

In other words, the outbreak was tied to "drug diversion," which happens when a person illegally uses medications meant for someone else — in this case, medication meant for cancer patients.

"We share our experience to alert health care providers that, in this age of profound prevalence of opioid addiction, drug diversion is an important consideration when a cluster of waterborne bacteremia [bloodstream infection] is identified," the report concluded.

The hospital notified staff about the outbreak and contacted patients who were at risk for exposure. Roswell Park also notified the N.Y. State Department of Health as well as law enforcement, so it could conduct an investigation.

The new report did not identify the nurse. But in June of this year, James P. Kennedy Jr., the U.S. attorney of the Western District of New York, announced that a former nurse at Roswell Park had been charged with stealing pain medications and so faces up to 10 years in prison and a $250,000 fine.

According to the criminal complaint, that nurse, Kelsey Mulvey, is accused of using her position to tamper with and steal vials of medication, including hydromorphone. Mulvey allegedly accessed the hospital's automated medication-dispensing system even on her days off and in hospital wings where she was not assigned patients. Mulvey is accused of failing to properly give medications to 81 patients between February and June 2018. She resigned her position in July 2018. Prosecutors allege that the nurse had an addiction and took the narcotics for personal use, according to The Buffalo News, a local newspaper.

"Once again, this case illustrates the destructive power of opioid addiction," Kennedy said in a statement. "In this case, however, the harm caused by defendant's actions resulted not only in harm to herself but in harm to some of the most compromised and vulnerable individuals in our community — those members of our community receiving cancer treatments."

Roswell Park first disclosed the incident to the public in September 2018, The Buffalo News reported.

Since that time, the hospital has taken more steps to prevent drug diversion, including enhancing security surveillance with video monitoring, reviewing current hospital policies, and increasing staff training and education on drug diversion, according to The Buffalo News.

In April of this year, the Centers for Disease Control and Prevention reported that a nurse in Washington state likely infected at least a dozen patients with hepatitis C after she used injectable opioid drugs that were meant for patients.

http://bit.ly/2TeWDXc

Some Fish Are Still Full of Mercury, for a Worrying Reason

Emissions of mercury have declined, but levels in fish could still increase thanks to overfishing and a changing climate.

Ed Yong

Environmental success stories are seemingly in short supply, but the fall of mercury is one of them. Released by coal-burning power plants and other industries, mercury—a toxic metal—circulates in the atmosphere, enters the ocean, worms up the food web and, via the seafood we eat, ends up in our bodies.

Because of their diet, tuna tend to accumulate mercury in their bodies. **Kim Kyung Hoon, Reuters**

For decades mercury in seafood has been a health scourge, because it inflicts long-term harm on the brain and increases the risk of heart disease. It's especially risky for developing fetuses, and mothers-to-be have long been warned away from mercury-rich tuna and swordfish.

But from 1995 to 2010, mercury concentrations in the Northern Hemisphere fell by 30 percent, thanks to aggressive regulations, falling coal use, and phaseouts of mercury in commercial goods. And in 2017, the first global treaty on reducing mercury emissions came into force.

You'd expect, then, that mercury levels in fish would have also fallen, and would continue to fall. But Amina Schartup and Elsie Sunderland of Harvard University have found that in some cases, tomorrow's seafood will contain *more* mercury, not less.

That's thanks to two unlikely culprits—overfishing and climate change, both of which could nudge fish toward pursuing more heavily contaminated prey. Although there's less mercury in the environment, our actions mean that fish like tuna are more likely to concentrate what's already in their bodies. The carbon we pump into the atmosphere ends up affecting the amount of neurotoxin on our dinner plate.

Climate change "is not just about what the weather is like in 10 years," Schartup says. "It's also about what's on your plate in the next five."

Once mercury enters the ocean, microbes convert it to a compound called methylmercury, which then enters the food web. Each animal accumulates all the methylmercury in all of its prey, and all of its prey's prey, and so on. So predatory fish, such as tuna, cod, and swordfish, accumulate the highest levels of the toxin, which they then bequeath to humans who eat them. In the U.S., 80 percent of methylmercury exposure comes from seafood, and 40 percent is from tuna alone.

This simple pattern hides a more complex one. Researchers have noted that trends in mercury levels can vary considerably between different species of fish, even those that live in similar environments. "And when people looked at trends, some would go up, some would go down, and some would be flat," Schartup says. "Why, if they're all experiencing the same declining mercury levels in seawater?" That's especially confusing for regulators, who reasonably expect to see their emissions-curbing work lead to consistent benefits.

To find out, Schartup and her colleagues collated three decades of data on fish stocks and mercury levels from the Gulf of Maine. They plugged that info into a model that simulated the region's food webs, in which virtual fish grow up in virtual seas, eating virtual plankton, and accumulating virtual mercury. And by tweaking the model to account for changing environments over the past half century, they showed how human activities radically shaped the amount of mercury that gets into different fish.

In the 1970s, the gross overfishing of herring, the favored prey of Atlantic cod and spiny dogfish, forced these predators to switch to different targets. Cod moved on to other small fish, such as shad and sardines, which contain less mercury. Dogfish, however, moved to squid, which scavenge the bodies of animals further out on the food web, and so contain *more* mercury than expected for creatures of their size. As the herring recovered, both cod and dogfish returned to eating them. So since the ’70s, mercury levels have increased in cod, and decreased in dogfish. “Everyone who’s looking at those different trends in fish: You’re not all crazy,” Schartup says.

Temperature matters, too. The water in the Gulf of Maine has warmed considerably since the 1960s, and more so than most other parts of the world’s oceans. Because most fish are cold-blooded, their physiology is yoked to the warmth of their surroundings. As oceans get hotter, they become faster and more active, they eat more prey, and they consume more mercury. (Even tuna, which can partly control their body temperatures, experience this effect, because everything else they eat has already built up more of the toxin.)

What will happen in the future if mercury emissions stay low but temperatures continue rising and herring are overfished again? It depends on the fish. Schartup and Sunderland’s model reveals that mercury levels will likely go down in cod, and go up in dogfish. And for Atlantic bluefin tuna, among the most significant current sources of mercury exposure, the outlook is poor. While mercury levels in this species have indeed fallen thanks to reduced emissions, warming temperatures will almost entirely reverse those gains by 2030. Recent data from actual tuna show that the team’s model is correct, and that this reversal is already under way. “Even if we maintain mercury emissions at a constant rate, we’ll see an increase in mercury levels in tuna just due to seawater temperatures,” Schartup says.

“It’s important for regulators to know that if they’re not seeing as fast a decline [in mercury within food] as they expected, that’s not because regulation isn’t working,” she adds. “It would be worse if they hadn’t reduced emissions in the first place.”

While other studies have focused on mercury levels in predatory fish, this one is unique in considering the entire ecosystem. “It’s an important study, showing how the quality of our seafood is intimately connected to a healthy, balanced ocean and that human behaviors—fishing and climate change—directly affect the contamination profiles of that seafood,” says Anela Choy of the Scripps Institution of Oceanography.

Of course, the dose makes the poison. Are mercury levels in fish, current or future, relevant to human health? The answer, Sunderland says, is yes—and always yes. Epidemiological studies have shown that mercury exposures are linked to impaired brain development and cognitive abilities, especially when people are exposed in the womb. (Mercury can cross from a pregnant mother’s bloodstream into her fetus.) “It doesn’t look like there’s a threshold,” Sunderland says. “Everyone would like to see less methylmercury in their seafood. It’s never beneficial for human health.”

Eating less fish might seem like an obvious solution, but many populations around the world subsist on seafood. “We’re not saying people shouldn’t eat fish, because when people substitute it, it tends to be for a less nutritious choice,” Sunderland says. “We’re saying that we can make that food even healthier. But it also requires action on climate.”

Even the existing guards against mercury pollution might be weakening, though. Under the Trump administration, the Environmental Protection Agency has been trying to loosen

Obama-era regulations that protect the environment from mercury. Arguing that such protections are too costly for the coal industry, the EPA (now under the direction of the former coal lobbyist Andrew Wheeler) proposed a rule that would change how regulators evaluate the benefits and costs of mercury restrictions. The rule would take several environmental and health benefits out of consideration, skewing the calculus in favor of industry. "It would dramatically weaken the regulations and open the door to lax regulation in the future," Sunderland says. "And that's to no one's benefit."

A rollback of existing regulations would be enormously wasteful, because it has cost $18 million to fully implement them—a process that's now complete. It would also be a counterproductive way of snatching defeat from the jaws of victory. As Schartup and Sunderland have shown, mercury regulations need to be *strengthened*, not weakened.

http://bit.ly/2OMSLOJ

Researchers discover gel reduces scar tissue after surgery in animals

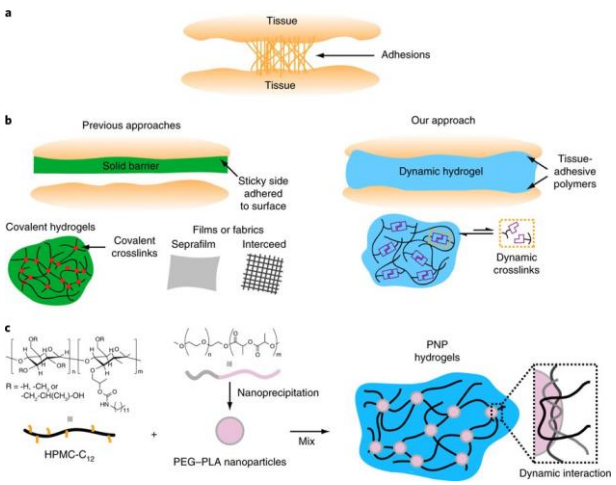
Spraying a gel on internal tissues of animals after cardiac surgery greatly reduces adhesions, fibrous bands that form between internal organs and tissues

Researchers at Stanford University have found that spraying a gel on the internal tissues of animals after cardiac surgery greatly reduces adhesions, fibrous bands that form between internal organs and tissues. Adhesions can cause serious, even fatal, complications.

The gel, developed at Stanford to deliver medications, was far more effective than adhesion prevention materials currently on the market, the researchers said. It appeared to be safe in the animal study.

"The difference between what we saw after using the gel and what we normally see after surgery was drastic," said Joseph Woo, MD, professor and chair of cardiothoracic surgery and the Norman E. Shumway Professor.

A paper describing the research published August 7 in *Nature Biomedical Engineering*. Woo and Eric Appel, Ph.D., an assistant professor of materials science and engineering, are the senior authors. Lyndsay Stapleton, a graduate student in bioengineering, is the lead author.



***a, Schematic representation of adhesion formation between two tissues. b, Schematic representation of previous approaches to prevent adhesions using solid adhesion barriers to physically separate organs and tissues. Such stationary adhesion barriers include the two best-known commercial products, Seprafilm (film) and Interceed (fabric), and covalently crosslinked hydrogels formed by in situ polymerization of precursor macromers. Our approach uses dynamically crosslinked, shear-thinning, self-healing and viscoelastic polymer hydrogels that are placed between organs and tissues, allowing these structures to move naturally. c, Our materials exploit multivalent and dynamic non-covalent interactions between hydrophobically modified HPMC-C12 and PEG–PLA to form hydrogels that can be sprayed with standard equipment, adhere to tissue (HPMC-C12 is tissue adhesive) and provide a viscoelastic barrier between organs and tissues to inhibit adhesion formation.* Credit: Nature Biomedical Engineering (2019). DOI: 10.1038/s41551-019-0442-z**

Adhesions form after 95% of surgeries. Some are harmless, but after abdominal surgeries, they can twist or compress the intestines, causing life-threatening blockages.

Gynecological surgery can also lead to adhesions that cause infertility. In cardiac re-operations, common for those born with heart defects, adhesions increase the risk of complications.

Previous methods, lot of failures

Methods to prevent adhesions—including animal membranes, sheets of rubber and mineral oil—have existed for more 100 years, but they have mostly failed.

Current adhesion barriers approved by the Food and Drug Administration are rarely used; they are difficult to deploy and are considered ineffective.

The Stanford researchers had long pondered a solution to the adhesion problem.

But one day, when Stapleton was working with lab rats to develop an injectable therapy to reduce tissue damage following a heart attack, Appel suggested she try spraying a polymer-nanoparticle hydrogel onto the hearts and surrounding tissue after surgery to see if it reduced the formation of adhesions. Weeks later, when she operated on the animals again, she saw that no adhesions had formed.

"It was pretty striking," she said. "I thought, 'Oh wow, we could be onto something here.'"

The researchers decided to conduct a study. First, they formulated four additional gels with a range of properties. Then, after inducing heart attacks in rats, they randomly divided the animals into eight treatment groups: five that each received a different gel, two that received commercially available adhesion barriers and one that received no treatment.

Four weeks later, the rats that had received no treatment or either of the two commercial adhesion barriers had formed dense adhesions: Their hearts were connected to their chest walls.

The rats that were treated with two of the five gels had formed moderate to dense adhesions.

The rats treated with the other three gels fared much better, with very few adhesions. PNP 1:10, the gel Stapleton initially tried, completely prevented adhesions.

The researchers then tested PNP 1:10 in sheep, whose hearts are similar in size and shape to human hearts; they found similar results.

Like mayonnaise

PNP 1:10 was stiff enough to stick, but not so stiff it detached from the organs, Appel said. "It was sort of a Goldilocks sweet spot." He compared PNP 1:10 to mayonnaise: thick, but easily spreadable. That property allows it to be sprayed onto an organ but then immediately reform its original strength.

The gel also has the ideal tension between stickiness and slipperiness: "It covers all of the irregular surfaces of the heart, adhering to the tissues, but not to itself," Woo said.

And it's flexible, allowing the heart to beat: "The gel doesn't prevent tissues from moving around," Appel said. "It simply provides a physical barrier to keep them from sticking to each other."

PNP 1:10 dissolves and is absorbed by the body about two weeks after its application—enough time for healing to occur, Appel said.

PNP 1:10 is not approved for use in patients, but it is made of components that the Food and Drug Administration has approved.

As part of the study, the researchers tested the rats to see if they showed any reaction to the gel; they saw no abnormalities in the surrounding tissues or in the blood.

The researchers next plan to try PNP 1:10 in abdominal surgery in rats. They hope to conduct human trials soon.

More information: *Lyndsay M. Stapleton et al. Use of a supramolecular polymeric hydrogel as an effective post-operative pericardial adhesion barrier, Nature Biomedical Engineering (2019).* *DOI: 10.1038/s41551-019-0442-z*

http://bit.ly/2OK1ml9

New study in Science: Why humans in Africa fled to the mountains during the last ice age

People in Ethiopia did not live in low valleys during the last ice age. Instead they lived high up in the inhospitable Bale Mountains.

There they had enough water, built tools out of obsidian and relied mainly on giant rodents for nourishment. This discovery was made by an international team of researchers led by Martin Luther University Halle-Wittenberg (MLU) in cooperation with the Universities of Cologne, Bern, Marburg, Addis Ababa and Rostock. In the current issue of "Science", the researchers provide the first evidence that our African ancestors had already settled in the mountains during the Palaeolithic period, about 45,000 years ago.

The Fincha Habera rock shelter in the Ethiopian Bale Mountains served as a residence for prehistoric hunter-gatherers. Credit: Götz Ossendorf

At around 4,000 metres above sea level, the Bale Mountains in southern Ethiopia are a rather inhospitable region. There is a low level of oxygen in the air, temperatures fluctuate sharply, and it rains a lot. "Because of these adverse living conditions, it was previously assumed that humans settled in the Afro-Alpine region only very lately and for short periods of time," says Professor Bruno Glaser, an expert in soil biogeochemistry at MLU. Together with an international team of archaeologists, soil scientists, palaeoecologists, and biologists, he has been able to show that this assumption is incorrect. People had already begun living for long periods of time on the ice-free plateaus of the Bale Mountains about 45,000 years ago during the Middle Pleistocene Epoch. By then the lower valleys were already too dry for survival.

For several years, the research team investigated a rocky outcrop near the settlement of Fincha Habera in the Bale Mountains in southern Ethiopia. During their field campaigns, the scientists found a number of stone artefacts, clay fragments and a glass bead. "We also extracted information from the soil as part of our subproject," says Glaser. Based on the sediment deposits in the soil, the researchers from Halle were able to carry out extensive biomarker and nutrient analyses as well as radiocarbon dating and thus draw conclusions as to how many people lived in the region and when they lived there. For this work, the scientists also developed a new type of palaeothermometer which could be used to roughly track the weather in the region - including temperature, humidity and precipitation. Such analyses can only be done in natural areas with little contamination, otherwise the soil profile will have changed too much by more recent influences. The inhospitable conditions of the Bale Mountains present ideal conditions for such research since the soil has only changed on the surface during the last millennia.

Using this data, the researchers were not only able to show that people have been there for a longer period of time. The analyses may also have uncovered the reasons for this: during the last ice age the settlement of Fincha Habera was located beyond the edge of the glaciers. According to Glaser, there was a sufficient amount of water available since the glaciers melted in phases. The researchers are even able to say what people ate: giant mole rats, endemic rodents in the region the researchers investigated. These were easy to hunt and provided enough meat, thereby providing the energy required to survive in the rough terrain. Humans probably also settled in the area because there was deposit of volcanic obsidian rock nearby from which they could mine obsidian and make tools

out of it. "The settlement was therefore not only comparatively habitable, but also practical," concludes Glaser.

The soil samples also reveal a further detail about the history of the settlement. Starting around 10,000 years before the Common Era, the location was populated by humans for a second time. At this time, the site was increasingly used as a hearth. And: "For the first time, the soil layer dating from this period also contains the excrement of grazing animals," says Glaser.

According to the research team, the new study in "*Science*" not only provides new insights into the history of human settlement in Africa, it also imparts important information about the human potential to adapt physically, genetically and culturally to changing environmental conditions. For example, some groups of people living in the Ethiopian mountains today can easily contend with low levels of oxygen in the air.

This research was funded by the German Research Foundation (DFG) in the framework of the joint Ethio-European DFG Research Unit 2358 "The Mountain Exile Hypothesis." Additional funding was provided by the Swiss National Science Foundation (SNSF grant no. 200021E-165446/1).

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Existing anti-parasitic drug could offer treatment for Ebola

Study in human cells shows it counteracts Ebola's defenses

BOSTON - Amid the worsening Ebola outbreak in the Congo, now threatening to spill into Rwanda, a new study suggests that an existing, FDA-approved drug called nitazoxanide could potentially help contain this deadly, highly contagious infection. In meticulous experiments in human cells, led by Boston Children's Hospital, the drug significantly amplified immune responses to Ebola and inhibited Ebola replication.

The study, published in the Cell Press journal *iScience*, also showed how the drug works: It enhances the immune system's ability to detect Ebola, normally impeded by the virus.

Nitazoxanide, or NTZ, is currently used to treat gastrointestinal infections caused by parasites such as Giardia and Cryptosporidium. It has been shown to be safe and even comes in a formulation for children. Study leader Anne Goldfeld, MD, of the Program in Cellular and Molecular Medicine at Boston Children's, hopes that, with further testing and validation, it could be part of the solution for Ebola.

"Currently, there is no easily deployable therapy for Ebola virus," she says. "There are some very promising vaccines, but there is no oral, inexpensive medication available."

Outsmarting Ebola

The Ebola virus caused more than 10,000 deaths in the 2014-2016 West African epidemic and more than 1,800 lives (as of August 6th) in the current outbreak in the Democratic Republic of the Congo. The virus is very good at evading human immune defenses. Though very small, it has two genes devoted to blocking immune responses.

Goldfeld and collaborators Chad Mire, PhD and Thomas Geisbert, PhD at the University of Texas Medical Branch, Galveston, showed in Biosafety Level 4 laboratory experiments that NTZ inhibits the Ebola virus (isolated from an earlier outbreak). Additional experiments performed in collaboration with Sun Hur, PhD of Boston Children's showed that NTZ works by broadly amplifying the interferon pathway and cellular viral sensors, including two known as RIG-I and PKR. By deleting RIG-I and PKR in human cells through CRISPR editing, Goldfeld and University of Texas colleagues showed that NTZ works through these molecules to inhibit Ebola virus.

"Ebola masks RIG-I and PKR, so that cells don't perceive that Ebola is inside," explains Goldfeld. "This lets Ebola get a foothold in the cell and race ahead of the immune response. What we've

been able to do is enhance the host viral detection response with NTZ. It's a new path in treating Ebola."

Goldfeld hopes to move into animal studies soon, especially given that NTZ has already been used in millions of people with minimal side effects. If effective, it could thus be easily repurposed for Ebola treatment or prevention.

Luke Jasenosky, PhD, of Boston Children's Hospital (now at Profectus Biosciences) was the study's first author. The study was funded by the Annenberg Foundation, John Moores, the National Institutes of Health (AI125075, AI106912, AI111784, U19AI109711), and the Ragon Institute. The paper can be accessed at https://doi.org/10.1016/j.isci.2019.07.003.

http://bit.ly/2ThoshH

Electromagnetic fields may hinder spread of breast cancer cells

Early findings in lab show reduced ability of cells to migrate

COLUMBUS, Ohio -- Electromagnetic fields might help prevent some breast cancers from spreading to other parts of the body, new research has found.

The study showed that low intensity electromagnetic fields hindered the mobility of specific breast cancer cells by preventing the formation of long, thin extensions at the edge of a migrating cancer cell. The research was done on cells in a lab, and the concept hasn't yet been tested in animals or humans. The study was published today in the journal Communications Biology.

"A cancer cell has a tendency to do the most destructive thing imaginable," said Jonathan Song, lead author of the study. Song is an assistant professor of mechanical and aerospace engineering at The Ohio State University and a member of the molecular biology and cancer genetics program at Ohio State's Comprehensive Cancer Center.

That ability to not only proliferate locally but spread throughout the body is what makes cancer so devastating -- and what prompted the research team to examine individual cancer cells to understand what makes them so harmful, Song said.

"One very destructive thing these cells do is migrate to distant areas of the body," he said. "And what we learned here is that it seems by treating them with a certain class of electric field we are altering their potential to spread somehow."

The research team, which included engineers and cancer biologists, found that cancer cells appeared to sense both the presence of the electromagnetic fields, and also the direction from which the fields were coming.

To study these effects, the researchers built an instrument called a Helmholz coil that allowed them to apply uniform electromagnetic energy to different types of breast cancer cells. In addition, the researchers engineered an apparatus that enabled them to track continuously the trajectories of migrating breast cancer cells while viewing them under a microscope. This apparatus, Song said, "recreates and mimics what actually happens in the body in a controllable environment that we can easily test and observe." Their goal was to see if and how the cells responded to that energy, and what role electromagnetic fields might play in treating breast cancer in the future.

They found that metastatic triple-negative breast cancer cells -- cancer cells that, by their nature, do not respond to hormonal therapy or to treatments that target a gene commonly expressed in breast cancer cells -- were the most sensitive to electromagnetic fields.

And, in their tests, they found that certain drug therapies -- and specifically one that targets a pathway for cancer called AKT -- could enhance the ability of the electromagnetic fields to block the cancer cells from spreading.

Because this research took place in a laboratory using a model the researchers designed to mimic the environment in which breast cancer cells form, the consequences of these findings for patients are still to be validated.

"But what we showed, biologically, is that these cancer cells are becoming profoundly less metastatic, which is a very important finding," Song said.

Their findings represent a significant step for researchers working to isolate the ways cancer cells couple with other cells and spread. Song said future research could expand to test electromagnetic fields and targeted molecular therapies in mice and, if those tests prove promising, to humans.

Other senior authors from Ohio State on the study were Ramesh Ganju, professor and vice chair of experimental pathology; Vish Subramaniam, professor and chair of mechanical and aerospace engineering; and Ayush Garg, a mechanical engineering PhD student. Additional Ohio State researchers are: in the Song lab, Sarah Moss, Jessica Ferree and Prabhat Kumar; in the Subramaniam lab, Travis Jones and Deepa Subramaniam; and in the Ganju lab, Sanjay Mishra, Kirti Kaul and Dinesh Ahirwar.

http://bit.ly/2yLaviF

Myth about how science progresses is built on a misreading of the story of penicillin

Myths often tell more about how professions want to be seen than about the historic events they are based on

Andrew George *

Many professions have creation myths about much-revered pioneers. For nursing, it is Florence Nightingale in Scutari, flitting between beds bearing her lamp. For engineers, it is Isambard Kingdom Brunel, driving railway lines across the countryside and building ships. These myths often tell us more about how professions want to be seen than about the historic events on which they are based.

One of the myths in medical science is the discovery of penicillin. It has been retold to generations of school children: Alexander Fleming came back from his holidays in 1928 to his laboratory at St Mary's Hospital in London and looked at some petri dishes before throwing them away. On one of the dishes he sees a mould growing, with a clearing around it where the bacteria had been killed. A eureka moment allows him to deduce that the fungus is releasing a molecule that kills the bacteria.

The action then moves to Oxford where Howard Florey and Ernst Chain discover how to isolate the molecule, now called penicillin. They realise the importance of the drug for the war effort, and with the help of American companies, large amounts of penicillin arrive just in time to treat wounded allied soldiers during World War II. The curtain call is taken by Fleming, Chain and Florey when they win a Nobel Prize in 1945.

Fleming receiving the Nobel Prize from King Gustaf V of Sweden in 1945. Wikimedia Commons

This is a very satisfying story. It includes the serendipity of a contaminated culture dish (the Fountains Abbey pub in nearby Praed Street makes unlikely claims that the mould came from their beer, tying the discovery of penicillin into British culture). It involves a moment of effortless brilliance, with Fleming seeing the implications of the clearing. It describes research working out in a predictable and rapid manner; once Fleming saw the dish, it was just a matter of time before the wonder drug started saving lives.

Not a priority

Much of this is wrong. The story of Fleming seeing the clearing first appeared in 1944. It is not supported by the notes he wrote at the time and is difficult to reconcile with the growth of *Penicillium* and *Staphylococcus aureus*, nor by how penicillin works. It appeared at a time of great tension and competition between St Mary's and Oxford scientists.

What is often missed is the time and effort it took to get from Fleming's initial discovery to production of the drug. In part this is because it was not a priority for Fleming. It was not obvious that

penicillin was of any interest, when results were presented at scientific meetings, they were often met with indifference.

It was very hard to isolate the active ingredient of the "mould juice" – several scientists tried and failed. It needed the biochemical skills and inventiveness of the Oxford scientists to solve this problem.

The Oxford group made superhuman efforts to make enough penicillin to treat patients, initially growing the mould in bedpans.

The first person treated was a policeman, Albert Alexander, who had an uncontrolled bacterial infection following a rose scratch. He responded dramatically to penicillin, seeming to recover.

But ten days later, he relapsed, and despite having recycled penicillin from his urine, supplies ran out and he died of his infection.

The final step was the scaling up and industrialisation. This stage is often forgotten. UK companies did not have the capacity, resources or vision to manufacture penicillin.

Florey turned to US industries who developed new ways to isolate penicillin. This was not trivial, and by 1945 US companies were making 6.8 trillion units – slightly more than 4,000kg of the drug a year.

By 1945, penicillin was finally being mass produced. Wikimedia Commons

Long and winding road

It took 16 years from initial observation to useful production of penicillin, and it would have been much longer without the impetus given by the war. Exploitation of scientific results takes time, persistence and different skills.

But is the final part of the story true? Did penicillin help win the war?

It certainly saved thousands of soldiers from dying of gangrene and sepsis. But its greatest contribution to the war effort may have been the treatment of gonorrhoea, helping keep the army at full strength.

During the invasion of Sicily, when penicillin was still in short supply, some argued that it should be reserved for wounded soldiers, rather than to relieve "scallywags" of the consequences of their own indiscretions. This was overruled by Churchill, who said it was to be used to obtain the "best military advantage".

What are the dangers of the penicillin myth? I suggest that it emphasises a model of scientific discovery that is effortless and dependent on individual genius. That is not fair on Fleming, he was prepared for his discovery by years of hard work, and it involved a series of difficult experiments.

It also suggests that, once the discovery is made, science proceeds down a predictable path to exploitation. This is not the case, the reason it took time to develop penicillin is because it was a hard thing to do and its potential was not obvious.

Finally, the myth concentrates on individuals, in particular Fleming. While his contribution was vital, that of Florey and Chain was equally important. The contribution of Norman Heatley was key to the biochemical isolation.

Countless other scientists and industrialists were involved. Edward Mellanby, the secretary of the Medical Research Council, saw the potential and sorted much of the funding. Patients, doctors, nurses and technicians, including the "penicillin girls" who prepared the penicillin, all played their role. Science is a shared enterprise.

Myths are important, but sometimes it is useful to look behind them to understand how science really works.

[*]*Emeritus Professor, Brunel University London*

Disclosure statement

Andrew George is Chair of Imperial College Health Partners, he is a Non-Executive Director of the Health Research Authority.

http://bit.ly/2Mbs0kO

Big Pharma is using faux generics to keep drug prices high, critics say

Drug makers have mastered gaming the system to beat generic competition, critics say.

Beth Mole

Brand-name drug makers are using "authorized generics" to keep drug prices high and stifle competition, according to a report by Kaiser Health News.

Authorized generics are defined by the US Food and Drug Administration as brand-name drugs that are simply repackaged and marketed without the brand name. They're made by the same company that makes the brand-name drug and usually sold at a discount relative to the brand-name version.

Traditional generic drugs, on the other hand, are versions of a drug that are equivalent to a brand-name drug in active ingredients and effects but may have slight variations, such as in inactive ingredients like fillers and flavors. Generics are made by different companies from those that make the brand-name versions.

High-profile examples of authorized generics include Mylan's cheaper form of its EpiPen, a life-saving epinephrine autoinjector that curbs deadly allergic reactions. In 2016, under political and public pressure to lower drug prices, Mylan introduced the authorized generic of EpiPen priced at $300 for a two-pack. That's half the price of a two-pack of the brand-name version, which has a list price of around $600. But it's still a staggering hike from EpiPen's original cost of around $50 per injector in 2007. That year, Mylan bought the rights to EpiPen and then raised the price more than 400% in the years that followed. The authorized generic is essentially triple the price of what two injectors used to cost.

Drug companies argue that because authorized generics are priced lower than brand-name drugs, the faux generics lower overall prices and spur competition. But critics note that the prices can still be inflated, as in the EpiPen case. Moreover, because brand-name drugs' list prices are often subject to rebates and discounts by middlemen, the authorized generics' lower prices sometimes have no impact on how much drug companies net for their drugs.

Tricks and games

Another example is Eli Lilly's authorized generic form of Humalog insulin, as Kaiser Health News points out. In March, Eli Lilly announced it would sell the authorized generic for $137 a vial, about half the price of the brand-name version's $275 price. The company's CEO reportedly said that seemingly compassionate move was made to address the "many patients [who] are struggling to afford their insulin."

But the slashed price won't affect Lilly's bottom line, according to a senior pharmacy benefits executive who spoke to KHN under the condition of anonymity. After rebates, $137 is about what Eli Lilly gets for Humalog now, the executive said.

"It's a parlor trick," the executive added. "They're bending to political pressure, but are they taking any money out of the system? They're not."

And, as others have noted, the price is still wildly inflated. A vial of brand-name Humalog has a list price of $55 in Germany, for instance. In 2001—before Lilly began hiking the price—the list price for a vial of Humalog in the US was $35.

While authorized generics help maintain high prices and profits for drug makers, they also choke back competition from actual generics, critics say.

When Congress set up the modern generic drug market in 1984—with the "Drug Price Competition and Patent Term Restoration Act of 1984" (aka the Hatch-Waxman Amendments)—lawmakers intended to give the first generic maker the lucrative incentive of a

180-day period of market exclusivity. That is, the FDA holds back on approving additional generic versions of a drug for that period.

But with authorized generics, brand-name drug makers can time the release of their faux generics to match the release of generic competition. That's exactly what PDL BioPharma did with the release of an authorized generic version of its blood-pressure drug, Tekturna (generic name aliskiren).

Further Reading

Drug companies are sitting on generics—43% of recently approved aren't for sale

In 2017, PDL got wind that Anchen Pharmaceuticals was planning to come out with a generic version of the blood pressure pill. PDL then cut a deal with Anchen that, in part, had Anchen agree to delay the release of its generic until at least March 1, 2019. On March 4, 2019, PDL announced the release of its authorized generic.

In the announcement, PDL's president and CEO, Dominique Monnet, noted that "We believe being first-to-market with a generic version of aliskiren provides [PDL subsidiary] Noden with a distinct competitive advantage."

Robin Feldman, a pharmaceutical policy expert at the University of California Hastings College of the Law, echoed the point to KHN, saying that such moves can "stave off generic competition and make sure that generics can't get much of a foothold when they do get to market." "That's the game," she added. "And drug companies have become masters at this."

As of July 2019, there are nearly 1,200 authorized generics on the market in the US.

http://bit.ly/2YBYZFx

It's All Greek to You and Me, So What Is It to the Greeks?

A close look at a strangely global idiom about how little we understand each other.

by Dan Nosowitz August 08, 2019

It's a curious thing when there is an idiom—structured roughly the same way and meaning essentially the same thing—that exists in a large number of languages. It's even more curious when that idiom, having emerged in dozens of different languages, is actually … about language. That's the case with "It's Greek to me."

In a wide-ranging number of languages, major and minor, from all different branches of the language family tree, there is some version of "It's Greek to me." These idioms all seek to describe one person's failure to understand what the other is trying to say, but in a particular, dismissive way. It's not just, "Sorry, I can't understand you." It's saying, "The way you're speaking right now is incomprehensible." And it specifically compares that incomprehensibility to a particular language, a language agreed upon in that culture to be particularly impenetrable.

Sometimes that original cultural peg has been lost. In English, the phrase doesn't really indicate anything about the way modern English-speakers feel about the Greek language or Greece in general. It's just an old, tired idiom. In fact, polls show that native English speakers don't even think about Greek when asked to name the hardest language to learn. So where did the phrase come from, and why is its sentiment so universal?

As with far too many linguistic questions like this, there is no definitive answer. One theory ties it to medieval monks. In Western Europe at this time, the predominant written language was Latin, but much of the writing that survived from antiquity was in Greek. The theory holds that these monks, in transcribing and copying their texts, were not necessarily able to read Greek, and would write a phrase next to any Greek text they found: "Graecum est; non legitur." Translated: "It is Greek; it cannot be read."

This phrase seems to have been embedded in parts of Western Europe, and examples appear in plays starting in the 16th century. William Shakespeare, in his 1599 *Julius Caesar*, used it, and he is

widely credited with bringing a long-latent phrase into the mainstream. Interestingly, Shakespeare's version is a lot more literal than most of the uses of this idiom. In *Julius Caesar*, the Roman character Casca describes a speech made by Cicero, a Greek scholar. Casca, one of the conspirators who assassinates Caesar, does not speak Greek. So he says, "Those that understood him smiled at one another and shook their heads; but, for mine own part, it was Greek to me."

Though Greece is nominally part of Europe, its deep ties with the Middle East, North Africa, and the Slavic countries have meant that Greek culture has never really been fully of a part with Western Europe. The alphabet used there today, called the Euclidean alphabet, was ironed out just after the Peloponnesian War, in around 400 B.C. But there were several versions of the Greek alphabet and language before then, and one of those, it's generally believed, was used by a Greek colony in southern Italy. That one was adopted by people who inhabited early Rome, and steadily evolved on its own into Latin. By Shakespeare's time, the Greek alphabet looked like a weird fifth cousin to the Latin alphabet. That continues today. Some letters look similar and have similar sounds, such as "A." "B," on the other hand, is the second letter both alphabets, but in modern Greek sounds like the English letter "V." Then there are "Φ" and "Λ," which don't particularly resemble any letter used to convey Latin or English. (These are all upper case; the lower-case ones look even more different.)

English is not the only language to rely on Greek as a shorthand for gobbledygook. Spanish, Portuguese, Swedish, Norwegian, Dutch, and Afrikaans do as well. You'll notice those are all European languages except for Afrikaans, and Afrikaans is Germanic in origin.

Harry Foundalis, a cognitive scientist who studies Greek linguistics, says many Greek people know that in English and other languages, Greek serves as an indecipherable tongue, and many Greek people, especially young ones, speak English anyway, so they've encountered it before. "How do we feel about it? We find it funny," says Foundalis. "Those of us who know it make jokes with it. For example, I've noticed that every time I talk to an English-speaking audience and I use the phrase 'That's all Greek to me,' and the audience knows I'm Greek, I get a thunderous laughter as a response. So, the phrase works well for me."

There are, however, an awful lot of other languages that have some version of this phrase that doesn't use Greek. Some of these are weird in their own right. What's up with the Baltic countries, which think Spanish is so impenetrable? Why do the Danish use Volapük, a short-lived Esperanto-type constructed language created by a German in 1880? When a Bulgarian says "Все едно ми говориш на патагонски," which uses "Patagonian" instead of Greek, what the hell are they talking about? Do they mean some extinct indigenous Chonan language, or Spanish, which is the dominant language there, or Patagonian Welsh, which also apparently exists?

And what, you might ask, do the Greeks say?

"Εμένα, αυτά μου φαίνονται Κινέζικα."

"To me, this appears like Chinese."

Chinese happens to be the most common replacement for Greek in the idiom around the world—and the language that tops polls as the most difficult natural language to learn.

"Chinese is considered a level-four foreign language—the most difficult—for native English learners in the field of second-language acquisition," says Janet Xing, a professor of Chinese and linguistics at Western Washington University. Different organizations have different rankings for the difficulty of learning languages; the Foreign Service Institute (FSI), the U.S. government's department for training foreign diplomats, has five

levels, based on roughly how long it will take a native English speaker to learn a given language.

The Romance languages are rated level one, the easiest, along with Dutch and Afrikaans, both Germanic, like English. (Strangely, German itself is a level two.) Level one languages take, according to the FSI, 23 to 24 weeks of study before a student attains general proficiency.

China has hundreds of languages, but both of its two most widely spoken languages—Mandarin and Cantonese—are rated level five (specifically on the FSI scale, which differs from the one Xing describes). To attain general proficiency, the FSI says it'll take 88 weeks of study. The only language considered more difficult is Japanese.

Most of the variations on "It's Greek to me" use "Chinese," though they don't specify which Chinese language. In the Philippines, in Poland, in France, in Albania, and in many, many other places, people say some variation on, "That's Chinese to me."

There are many reasons why Chinese has this reputation, some of which are based on cultural conceptions, and some of which are based on the structural differences between Chinese and Western languages. For the former, China is the most dominant Asian culture in the minds of most Westerners, and that tends to make it an emblem of foreignness. In a way that is either ignorant (a generous view) or racist (a harsh one), China is too incomprehensible to be understood in any capacity.

On the linguistic side, Chinese is legitimately very, very different from Romance, Germanic, and Slavic languages. The FSI doesn't declare Mandarin wildly difficult because its language experts are racist; they rank it a level five language because they have taught thousands of English-speaking diplomats to speak Mandarin, and it is very, very difficult.

David Moser, a linguist currently at Yenching Academy of Peking University, wrote a book about the development of standard Chinese. He's lived in China for years, teaches at a university there. And he also wrote a truly excellent article about why Chinese is, in his words, "so damn hard."

For one thing, he explains, Mandarin is a tonal language, meaning that changes in pitch can totally change the meanings of words. "How is it possible that shùxué means 'mathematics' while shūxuě means 'blood transfusion,' or that guòjiǎng means 'you flatter me' while guǒjiàng means 'fruit paste'?" he writes. Tonal languages are not really that uncommon, especially in Asia and Africa, and among North America's indigenous languages. But European languages and those based on them, very rarely have any tonal qualities. (Some, like Swedish and Serbo-Croatian, are considered "pitch-accent" languages, which is an ill-defined term basically meaning "a few very small tonal elements of some sort.")

The idea that the tone of your voice can totally alter the meaning of a word is a wrinkle for English speakers trying to learn Mandarin (four tones) or Cantonese (between six and nine tones, depending on how you count). Add to that the writing system in Mandarin, which Moser characterizes as truly nuts, at least to Western eyes. Mandarin as it's typically written does not use an alphabet, but rather logograms: symbols, sometimes very detailed and elaborate, that represent a word or even a whole phrase. Western-style alphabets—in which symbols correspond, more or less, to sounds—exist, but they're aftermarket solutions. Pinyin, one of the most used Mandarin alphabets, has only been around since 1958.

To learn Mandarin you have to learn thousands of individual characters, and those characters, writes Moser, are only barely phonetic. In English, if you generally understand the alphabet, you can get often get pretty close to being able to spell a word you've only heard before. In Spanish, which is a completely phonetic

language, it's even easier. Mandarin? Good luck. Some elements of an individual symbol may show up in the symbol of a similar-sounding word—say, "president" and "present"—but that's about as helpful as it gets. And Chinese logograms could have a dozen or more such elements in each one.

"I have seen highly literate Chinese people forget how to write certain characters in common words like 'tin can,' 'knee,' 'screwdriver,' 'snap' (as in 'to snap one's fingers'), 'elbow,' 'ginger,' 'cushion,' 'firecracker,' and so on. And when I say 'forget,' I mean that they often cannot even put the first stroke down on the paper," he writes. This doesn't happen in languages that rely on alphabets, no matter how bad your spelling might be.

In Chinese, for what it's worth, there are a couple of different sayings in the "It's Greek to me" family. A Mandarin speaker might describe incomprehensible speech as Martian, or being like the sound of birds. The way you can tell you've reached the peak of language difficulty is when you don't even bother with a human language in your version of the phrase.

https://go.nature.com/2MTH8CQ

Scientists glimpse oddball microbe that could help explain rise of complex life

'Lokiarchaea', previously known only from DNA, is isolated and grown in culture.

Jonathan Lambert

Archaea are often found in extreme environments, such as these chimneys on the summit of Giggenbach underwater volcano, off New Zealand.Credit: New Zealand-American Submarine Ring of Fire 2005 Exploration, NOAA Vents Program

Biologists have for the first time captured and grown an elusive type of microbe that is similar to those that might have given rise to all complex life on Earth.

In a preprint posted to the bioRxiv repository[1], scientists in Japan report that they have isolated and grown microbes from an ancient lineage of archaea — single-celled microbes that look, superficially, like bacteria but are quite distinct — that was previously known only from genomic sequences.

It took the researchers 12 years to cultivate pure laboratory cultures of these microbes from deep-sea mud. The effort gives scientists their first look at the kind of organisms that could have made the jump from simple, bacteria-like cells to eukaryotes — the group of organisms whose cells have nuclei and other structures, and which includes plants, fungi, and humans and other animals.

"This is a monumental paper that reflects a tremendous amount of work and perseverance," says Thijs Ettema, an evolutionary microbiologist at Wageningen University in the Netherlands. "It's a major step forward in understanding this important lineage."

Muddy origins

The mysterious group, called Lokiarchaea, rose to prominence from microbial muck dredged up not far from Loki's Castle, a sea-floor hydrothermal vent field off the coast of Greenland. In 2015, Ettema and his colleagues sequenced genetic fragments from the mishmash of microbes in the sediment and assembled them into fuller genomes of individual species[2], a method called metagenomics.

One genome stood out. It was clearly a member of the archaea. But dotted throughout this genome were eukaryotic-like genes, suggesting to Ettema that this oddball could help to bridge the evolutionary gap between simpler microbes and eukaryotes. The researchers called it Lokiarchaea, after Loki, the trickster of Norse mythology.

Soon, other labs found additional Loki-like archaea, and together these formed the Asgard archaea, named after a mythological region inhabited by Norse gods. Although the organisms' precise place in the tree of life remains contentious, many analyses pair

Asgards and eukaryotes together, which could mean that some distant Asgard-like ancestor gave rise to all eukaryotes — everything from panda bears to portabello mushrooms.

Two become one

Proponents of this view think that, some 2 billion years ago, an Asgard-like archaeon gobbled up a bacterium. Instead of providing a meal, the ingestion sparked a mutually beneficial relationship, a phenomenon known as endosymbiosis. Eventually, according to this hypothesis, the bacterium evolved into mitochondria, the 'powerhouse' organelles of the cell that helped to fuel eukaryotes' rise. A similar merger could have led to the first nucleated cells.

Not all researchers agree that Asgards made this jump. Some have argued that the eukaryotic-like genes that make Asgards special are just contamination from other sediment microbes. And without an actual organism to study in the lab, it was hard to know what the eukaryotic-like genes actually do, or begin to understand how endosymbiosis might have progressed. "We've learnt a lot from the genome, but without a lab culture, we can only learn so much," says Ettema.

Because Asgards hail from extreme environments and have very slow growth rates, no one has previously succeeded in growing them in the lab. "The whole field has been waiting for this moment for a long time," says Simonetta Gribaldo, an evolutionary microbiologist at the Pasteur Institute in Paris.

Twelve years of work

Years before anyone knew Asgard archaea even existed, Hiroyuki Imachi, a microbiologist at the Japan Agency for Marine-Earth Science and Technology in Yokosuka and his collaborators began the painstaking work that would eventually bring Asgards to the lab. To cultivate microbes from deep-sea sediments, Imachi and his colleagues built a bioreactor that mimicked the conditions of a deep-sea methane vent. Over the course of 5 years, the researchers waited for the slow-growing microbes in the reactor to multiply.

They then took samples from the reactor and placed these, along with nutrients, in glass tubes, which sat for another year before showing any signs of life. Genetic analysis revealed a barely perceptible population of Lokiarchaea. The researchers patiently coaxed the Lokiarchaea — which took 2–3 weeks to undergo cell division — into higher abundance and purified the samples. "It's one of the slowest-dividing organisms I know of," says Ettema.

Finally, after 12 years of work, the researchers produced a stable lab culture containing only this new Lokiarchaeon and a different methane-producing archaeon. Together, the two microbes formed a symbiotic relationship (similar colonies of bacteria and archaea have been observed before). The scientists named the cultured Lokiarchaeon *Prometheoarchaeum syntrophicum*. The authors declined requests for interviews from *Nature*'s news team while their paper was under review at a journal.

"It's a tremendous effort," says Gribaldo. "And it's a really nice story because they started out before the Asgard frenzy even started. Halfway through their experiment they must've realized they had gold in their hands."

'An organism from outer space'

Under the microscope, that gold took the form of round cells less than one micrometre wide. Like other archaea and bacteria, they have relatively simple interiors, but their external surface can produce wisp-like protrusions that extend from their bodies. "I don't think anyone predicted that it would look like this," says Ettema. "It's sort of an organism from outer space."

The researchers report that the cultured Lokiarchaeon produces energy by breaking down amino acids and that it can exchange molecules used to carry energy with symbiotic partners. Ettema

says the Asgard genomes hinted at these capabilities, but without a lab culture they weren't confirmed.

Finally, because the researchers could extract and sequence DNA from a pure sample, rather than sediment containing a multitude of organisms, their findings would confirm that Lokiarchaea do, in fact, contain numerous eukaryote-like genes. "It puts to rest any concerns about contamination," says Gribaldo.

Ettema says this research opens the door to the next stage of Asgard research, although he stresses that many more Asgards will need to be cultured for researchers to work out whether, and how, Asgard-like archaea gave rise to eukaryotes.

"We can't just go back in time and observe what happened," says Ettema. The Asgards we see today are not the same as the microbe that gave rise to eukaryotes. But he says that culturing more Asgards and studying what their eukaryotic-like genes actually do will give a fuller picture of the evolutionary tree, and help researchers to better infer how simple, single-celled organisms made the first giant leap towards complexity.

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http://bit.ly/2yN8aUe

How huge forest of 'art deco streetlamps' sparked transformation of life on Earth – and carries a message for us today

Oldest large forest yet found on Earth represents a pivotal step in the history of forest growth

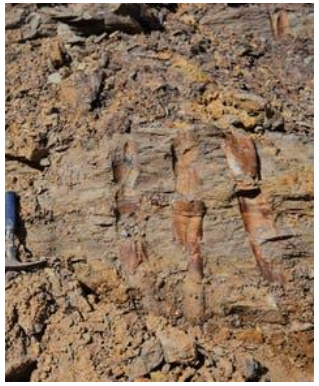
Jan Zalasiewicz *

If you were to step back in time some 365m years, you might see a landscape more akin to the wilder shores of science fiction than earthly reality. Imagine a forest made up only of one kind of tree. A thin, straight, leaf-covered trunk just a few metres tall, dividing at the very top into four short hanging branches. A little like a green, living version of an art deco streetlamp.

The extinct guangdedendron tree. **Zhenzhen Deng**

These bizarre plants made up the oldest large forest yet found on Earth, which was recently unearthed in Xinhang, in the Anhui province of China. Researchers discovered 250,000 square metres of fossilised lycopsid trees in two clay quarries dating to the Devonian period, making it the oldest known fossil forest in Asia. It represents a pivotal step in the history of forest growth that marked a true transformation, and enormous expansion, of life on Earth.

The ancient forest-forming tree has been named Guangdedendron, a new genus of the extinct lycopsid plants. It had no flowers and no seeds (those were mainly later features of the plant world) but shed spores from bottle-like structures at the ends of its branches. Primitive by comparison with the trees of modern forests, it had nevertheless evolved enough to survive the harsh conditions of life on land, subject to sharp temperature swings and frequent dry spells. This was a much more challenging environment than the more constant (and constantly hydrated) conditions of the sea, where complex multicellular life had already flourished for hundreds of millions of years. But life was slowly conquering the land as well. Ankle-high, simple land plants inhabited the preceding Silurian Period, some 430m years ago. The first known forest (more a copse, about the area of few tennis courts) grew around 385m years ago in what is now Gilboa in New York state in the US.



Fossilised guangdedendrons. **Deming Wang and Le Liu**

However, the often densely packed Xinhang trees form the earliest truly large forest that we know of. It marks a transition to the gigantic, worldwide swamp forests of the succeeding Carboniferous period that developed some 320m years ago.

These pioneering land plants, and the food and shelter they provided, allowed animals ranging from millipedes to amphibians to invade the land as well.

Even rivers changed their form as the vegetation took hold and stabilised their banks. This made single, meandering channels more common than the multiple shifting arteries that had characterised the landscape for billions of years prior to its greening.

The sheer biological scale of this landscape invasion was shown in a recent study that calculated the mass of the modern biosphere, that is, the weight of all of life on Earth today.

They arrived at a figure of 550 billion tons of carbon (which represents one fifth of all the mass in organic molecules). Over 80% of that biomass is land plants. This underlines just how significant the spread of forests was in the history of life on Earth.

Origins of climate change

The super-charged plant growth of the late Devonian and Carboniferous periods had another planet-wide consequence. It locked up huge amounts of carbon from the atmosphere, first in the living plants and then as the buried fossils that became deposits of coal and gas we still rely on for energy today.

The resulting fall in atmospheric carbon dioxide plunged the world into a glaciation that lasted some 50m years, causing fluctuations in climate and sea level that had worldwide effects and was a major event in paving the way for life as we know it today.

Now, we have dug up the compressed remains of those fossil forests, and in using them to power the industrial transformation of the last two centuries, have returned their carbon to the atmosphere in enormous amounts.

This is what has precipitated the global warming – or more accurately global heating – climate crisis that we have today.

What can be done about humanity's ongoing massive ground-to-air carbon transfer? The global biomass study noted that the estimate of 550 billion tons of living carbon is likely about only half the size of the Earth's biomass that was present before humans began cutting down trees. So a rapid Xinhang-style re-expansion of the forests may be one way of taking some of the heat out of global warming.

Professor of Palaeobiology, University of Leicester

Disclosure statement

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More Nuts Improve Men's Orgasmic Function, Sexual Desire

Adding nuts to a regular diet significantly improves orgasmic function and sexual desire in healthy young men, according to the FERTINUTS study.

Becky McCall

The randomized controlled trial, which was recently published in *Nutrients*, showed a significant increase in the orgasmic function (P = .037) and sexual desire (P = .040) of men of reproductive age who received the nut intervention in comparison with an age-matched control group.

The researchers found no significant between-group differences in changes during the intervention in erectile function (P = .192), intercourse satisfaction (P = .473), and overall satisfaction (P = .333). In addition, there were no significant correlations between changes in erectile dysfunction parameters and in biochemical

parameters during the intervention, write Albert Salas-Huetos, PhD, from University Rovira i Virgili, Reus, Spain, and colleagues.

"None of the possible mechanisms explored (nitric oxide and E-selectin, as surrogate markers of endothelial function) seem to explain the beneficial effects observed on orgasmic function and sexual desire," they write. They add that the study "did not provide enough evidence to support the main mechanism for these improvements, however, an absence of evidence does not mean evidence of no effect."

Commenting on the study, Kevin McEleny, FRCS (Urol), consultant urologist from Newcastle upon Tyne NHS Hospitals Foundation Trust, United Kingdom, said, "The study is interesting but not conclusive." He highlighted some marked methodologic flaws: "Self-reported consumption is imperfect in being based on handing back empty packets as proof of consumption, while dietary habits recorded with a diary are subjective."

In addition, he said, the number of participants involved was small, and the authors could not explain why there is a difference in sexual desire and orgasmic function between the groups. "The researchers really needed to look at the psychosexual and hormonal parameters to make a complete comment, but they did not do this," McEleny said.

Erectile dysfunction occurs in only 2% of men younger than 40 years. Prevalence increases markedly with age, to around 52% in men aged 40 to 70 years. Prior studies have shown that nut consumption has beneficial effects on endothelial function, which is implicated in erectile function.

Nuts are nutrient-dense foods that have a relatively high amount of the nonessential amino acid arginine, a precursor of nitric oxide, which is a potent neurotransmitter that plays an important role in erectile action, according to the authors.

Study in Young Men Without Erectile Dysfunction

To better understand the possible role of nut consumption in the primary prevention of erectile dysfunction, the investigators explored the effects of nut supplementation on erectile function and endothelial function by measuring peripheral concentrations of nitric oxide and E-selectin, a marker of endothelial dysfunction.

In the 14-week study, healthy men aged 18 to 35 years were randomly assigned to consume either a usual Western-style diet with an added 60 g/day of a mixture of raw walnuts, almonds, and hazelnuts (nuts group), or a usual Western-style diet in which nuts were avoided (control group).

The primary outcome, which was reported previously, showed improved sperm count and quality among men assigned to the intervention group.

In this secondary analysis, Salas-Huetos and colleagues assessed the intervention's effect on self-reported erectile function parameters using the 15-question validated International Index of Erectile Function (IIEF). They also analyzed concentrations of peripheral endothelial biomarkers (nitric oxide and E-selectin) during the study period.

Of the 98 participants who successfully completed the study, 83 (43 in the nuts group and 40 in the control group) completed the IIEF questionnaire and were included in the secondary analysis. Participants were matched for age, and there were no significant differences in baseline parameters between the two groups.

The researchers note that the study findings are consistent with a previous study that reported an increase in all five IIEF domains after consumption of 100 g/day of pistachios for 3 weeks, although that study was conducted in patients who had erectile dysfunction at baseline.

"Our study extends the findings to a healthy population without erectile dysfunction supplemented with a mixture of nuts like hazelnuts, almonds, and walnuts," they write.

As a possible explanation for the lack of effect on E-selectin, the researchers note that serum E-selectin appears to be more important with respect to patients with diabetes. "E-selectin...plays an important role in inflammation," they write. "Because consuming between 60 and 90 g of nuts has proven effective in improving inflammation, it could have been reasonable to detect some differences in this marker due to the nut's supplementation."

The lack of effect on E-selectin "could be explained not only because of a lack of power but also because our participants were healthy and therefore without having type 2 diabetes."

The study was designed to assess erectile function with respect to the theory that nuts improve vascular endothelial function, but no difference was found between groups, McEleny noted. He recognized that a difference was found in the orgasm domain and the sexual desire domain of the IIEF.

"Looking at the box plot graphs for orgasmic function, there is no box with whiskers for the control group, which automatically means that orgasmic function in the nuts group will be more likely to be significant," he said.

"If you like nuts, then eat them, but I don't think they'll improve your sex life," McEleny concluded.

The authors note that large studies are warranted to confirm these results and to elucidate possible mechanisms for these benefits.

The study work was partially supported by the International Nut and Dried Fruit Council, a nonprofit organization registered with the Register of Foundations of Catalonia, Spain; and by Human Nutrition Unit. The authors and McEleny have disclosed no relevant financial relationships.

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http://bit.ly/2GXBGv9

Questions Surround Canadian Shipment of Deadly Viruses to China

The same Winnipeg lab that sent Ebola and Henipah viruses to Beijing recently removed a number of researchers for an "administrative issue."

Nicoletta Lanese

Canada's National Microbiology Laboratory shipped Ebola and Henipah viruses to Beijing on March 31, raising suspicions from experts in biochemical warfare, who say they think China may use the pathogens to develop offensive biological agents.

The Public Health Agency of Canada (PHAC) and the Royal Canadian Mounted Police (RCMP) report that the incident has not introduced any known risk to public health, according to the *Winnipeg Free Press*.

The same lab is the focus of an ongoing investigation by the RCMP. The inquiry began following the recent dismissal of the head of the National Microbiology Laboratory's (NML) Vaccine Development and Antiviral Therapies section in the Special Pathogens Program, virologist Xiangguo Qiu. Qiu, her colleague and husband Keding Cheng, and a number of her international students lost security clearance to their lab on July 5.

In 2018, Govenor General Julie Payette presented Qiu with an innovation award for her helping to lead the development of the Ebola vaccine ZMapp, according to the *Winnipeg Free Press*. There are no reports as to whether she was involved in the March shipment.

Ebola and Henipah viruses—classified as Category A and C bioterrorism agents by the US Centers for Disease Control and Prevention, respectively—pose a threat to national security because of their potential to be easily disseminated, cause high morbidity and mortality rates, and deliver lasting blows to public health. They

are also categorized as Risk Group 4 pathogens, meaning they can only be handled in a lab with the highest level of biosafety control, according to *CBC News*.

"All transfers of Risk Group 4 samples follow strict transportation requirements and are authorized by senior officials at the lab and the NML tracks and keeps electronic records of all shipments of samples in accordance with the HPTA," PHAC spokesman Eric Morrissette writes in a statement, as reported by *CBC News*. "On the specific shipments to China earlier this year, we can confirm that we have all records pertaining to the shipment, and that all protocols were followed as directed by the above Acts and Standards."

Although health officials insist all protocols were met, anonymous sources report that the shipment lacked an agreement spelling out intellectual property rights, known as a "material transfer agreement," according to the *Winnipeg Free Press*. The document would protect Canada's claim over the viruses, assuming they had been patented through the Budapest Treaty deposit, an internationally recognized system for patenting intentions involving microorganisms.

"If China was leveraging these scientists in Canada to gain access to a potentially valuable pathogen or to elements of a virus without having to license the patent . . . it makes sense with the idea of China trying to gain access to valuable IP without paying for it," says Leah West, an expert in national security law at the Norman Paterson School of International Affairs, in an interview with *CBC News*.

China agreed to the Biological Weapons Convention in 1984, but both academics and government agencies have recently asserted that the country is a world leader in bio-weapon production, according to the *Edmonton Journal*.

"I would say this Canadian 'contribution' might likely be counterproductive. I think the Chinese activities . . . are highly suspicious, in terms of exploring [at least] those viruses as BW [biological warfare] agents," says Dany Shoham, a biological and chemical warfare expert at Israel's Bar-Ilan University, in an interview with the *Edmonton Journal*.

"Frankly, if it's already in China, cat's out of the bag," adds China intellectual property expert Mark Cohen in an interview with the *Winnipeg Free Press*. "They're probably culturing it already."

The March shipment took place during a dispute between the US and China, which led to the arrest of an executive of Huawei Technologies and the later detainment of two Canadians in China, according to the *Winnipeg Free Press*.

Given the tension between the two countries, Chinese-Canadian researchers and academics are starting to worry they may be singled out and targeted, says Jia Wang, deputy director of the University of Alberta's China Institute, in an interview with *CBC News*. "As China observers, we'd like to perhaps gently remind people not to jump into any conclusions too quickly."