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You Need Vitamin D to Live. How Could This Woman Survive With None in Her Blood?

She had a series of bone fractures, but when doctors did blood tests, the supplements she took for treatment were nowhere to be found.

By Wudan Yan

In 1992, a 33-year-old Lebanese woman had just immigrated to Canada and went to see a doctor. She was hunched over, and had limited mobility in her lower back, neck, shoulders and hips. Her doctor, Raymond Lewkonia at the University of Calgary, diagnosed her with ankylosing spondylitis, a medical condition that causes vertebrae in her spine to fuse, and thought that was it.

Then, about eight years later, the woman had a series of fractures in her ribs, feet, left arm and right hip. Her doctor had her take vitamin D supplements, but they had no effect: Lab tests revealed that she didn't have any vitamin D circulating around in her blood.

That seemed impossible. Some vitamin D, after all, is thought to be essential for maintaining bone health, and taking supplements after a bone injury or fracture is commonly used to expedite the healing process. Why was none of this vital substance in the woman's system?

A medical geneticist who looked at this case, Dr. Patrick Ferreira, suspected that a binding protein that partners with vitamin D to get in and around the body — or a lack of it — might have something to do with this medical mystery. But losing the ability to transport vitamin D would be lethal to humans, according to what doctors conventionally know.

Dr. Ferreira set out to test his hypothesis, but had trouble confirming that the vitamin D binding protein was indeed missing in the woman's system. He and others sent blood samples to labs in Europe and Vancouver, but these tests — which can be unreliable — came back saying that binding protein levels were normal. When Dr. Ferreira retired, he passed the patient's case to his colleague, Dr. Julien Marcadier, a clinical geneticist at Alberta Children's Hospital Research Institute, now the lead author of a case report published last month in The New England Journal of Medicine.

Fortunately for Dr. Marcadier, researchers at the University of Washington in Seattle had just developed a more sensitive method of detecting the protein.

Dr. Andrew Hoofnagle and his colleagues agreed to examine the blood sample, and found that there was no vitamin D in her blood, or any vitamin D binding protein.

"When you think about the biology of vitamin D," Dr. Hoofnagle said, "that shouldn't work. That person should not be alive."

Martin Hewison, a molecular endocrinologist at the University of Birmingham in England, who was not involved in the study, says that this case is the first of its kind.

How could this woman have lived nearly six decades without a substance considered essential to human life?

While vitamin D binding protein sequesters vitamin D in the body, it's the unbound molecules of vitamin D that are ultimately important for bone growth.

"The amount of vitamin D that is needed may vary by organ," said Dr. JoAnn Manson, an endocrinologist and principal investigator of the Vitamin D and Omega-3 Trial at Brigham and Women's Hospital in Boston. In this case, the amount of free vitamin D that this woman received from her diet or exposure to sun may have been sufficient to develop her bones and keep them alive.

And there's still a question of exactly how much vitamin D our bodies need, although some recent research suggests that the dose of vitamin D might not matter much for bone mineral density, fractures or falls for the elderly.

"I don't think this makes a strong case for the need for less vitamin D, but simply how well the body can adapt to limited vitamin D binding protein," said Ellen Fung, director of the Bone Density Clinic at Children's Hospital Oakland Research Institute in California, "although ultimately it caught up with her."

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Some patients with imminently fatal cancer still receive treatment

American Cancer Society study highlights need to better identify who may not benefit from aggressive treatment

Some patients who died within one month of being newly diagnosed with metastatic cancer in the United States received ineffective surgery, chemotherapy, radiation, and hormonal therapy according to a new American Cancer Society study. The authors say the findings highlight the need to better identify patients with imminently fatal metastatic cancer who may not benefit from aggressive and expensive therapies. The study appears early online in JNCI Cancer Spectrum.

Little is known about patterns of and factors associated with treatment of newly-presented (de novo) metastatic cancer patients who die soon after diagnosis. For the new study, a team led by Helmneh Sineshaw, MD, MPH, and including researchers from the American Cancer Society, Dana-Farber Cancer Institute (Boston, Mass.), Baptist Cancer Center (Memphis, TN), and Mayo Clinic College of Medicine (Rochester, MN), examined treatment patterns for 100,848 adult patients in the National Cancer Data Base. All were newly-diagnosed with metastatic lung, colorectal, breast, or pancreatic cancer and died within one month of diagnosis.

They found wide variations in treatment by cancer type, over time, age, insurance, and type of treatment facility. Surgery rates ranged from 0.4% of pancreatic cancer patients to 28.3% of colorectal cancer patients. Chemotherapy use ranged from 5.8% of colorectal cancer patients to 11% of lung and breast cancer patients. Radiotherapy rates ranged from 1.3% in pancreatic cancer patients to 18.7% of lung cancer patients. Use of some treatment, for example surgery for colorectal and breast cancer, declined over time. Lung cancer patients treated at community cancer centers had 48% lower odds of radiation than those treated at National Cancer Institute-designated cancer centers.

Those variations indicated to the authors that more research is warranted to better identify patients with imminently fatal de novo metastatic cancer who may not benefit from attempted life-prolonging aggressive and expensive therapies.

Article: Treatment patterns among de-novo metastatic cancer patients who died within one month of diagnosis Helmneh M. Sineshaw; Ahmedin Jemal; Kimmie Ng; Raymond U. Osarogiagbon; K. Robin Yabroff; Kathryn J. Ruddy; Rachel A. Freedman, JNCI Cancer Spectrum DOI: 10.1093/jncics/pkz021

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Drug reduces risk of kidney failure in people with diabetes, study finds

A new landmark clinical trial shows that a drug lowers the risk of kidney failure by a third in people with Type 2 diabetes and kidney disease.

"For the first time in 18 years, we have a therapy for patients with Type 2 diabetes and chronic kidney disease that decreases kidney failure," said Kenneth Mahaffey, MD, professor of medicine at the Stanford University School of Medicine and co-principal investigator of the trial. "Now, patients with diabetes have a promising option to guard against one of the most severe risks of their condition."

The trial involved 4,401 participants in 34 countries.

The drug, canagliflozin, improves on a nearly two-decades-old therapy that is currently the only treatment approved to protect kidney function in people with Type 2 diabetes. In the trial,

canagliflozin also was found to reduce the risk of major cardiovascular events.

Canagliflozin increases the excretion of glucose through the kidneys. It has already been approved by the Food and Drug Administration to lower blood glucose in patients with Type 2 diabetes and to reduce the risk of major adverse cardiovascular events in patients with Type 2 diabetes and existing heart disease.

A paper describing the findings of the CREDENCE trial was published today in The New England Journal of Medicine and presented at the International Society of Nephrology's World Congress of Nephrology in Melbourne. Mahaffey, who is director of the Stanford Center for Clinical Research, is the study's senior author. The lead author is Vlado Perkovic, MBBS, PhD, executive director of The George Institute for Global Health Australia, and a professor of medicine at the University of New South Wales in Sydney.

'Definitive trial result'

"People with diabetes and kidney disease are at extremely high risk of kidney failure, heart attack, stroke and death," Perkovic said. "With this definitive trial result, we now have a very effective way to reduce this risk using a once-daily pill."

Participants in the trial received the best care available for kidney disease under current guidelines, a type of therapy called renin-angiotensin-aldosterone system, or RAAS, blockade. In addition, half were randomly selected to receive canagliflozin, while the other half were given a placebo.

The primary results of the study found that participants who took canagliflozin were 30 percent less likely than the placebo group to develop kidney failure or die from either renal failure or cardiovascular disease. Their risk of kidney failure or death from kidney failure was reduced by 34 percent, and the risk of hospitalization for heart failure or death due to cardiac causes decreased by 31 percent.

'Eagerly sought' treatment

People with diabetes can develop kidney disease because prolonged high blood sugar harms blood vessels in the kidney. In addition, diabetes often causes high blood pressure, which can stretch and weaken blood vessels in the organ.

For the past two decades, physicians have largely relied on RAAS blockade to prevent the deterioration of kidney function in diabetic patients. Although RAAS blockade lowers blood pressure and delays progression of kidney disease, patients undergoing this treatment remain at a high risk for renal failure and cardiovascular disease, as well as death from these conditions.

Given that the number of people with Type 2 diabetes worldwide is estimated to rise by 20 percent to 510 million in 2030, "a drug like canagliflozin that improves both cardiovascular and renal outcomes has been eagerly sought by both patients with Type 2 diabetes and clinicians caring for them," Mahaffey said.

Other Stanford researchers assisting in the trial were Glenn Chertow, MD, professor of medicine, and Tara Chang, MD, assistant professor of medicine, who were national co-leads; and Sun Kim, MD, associate professor of medicine, who was a site investigator.

The work was funded by Janssen, which manufactures canagliflozin, and led by an independent steering committee.

Stanford's Department of Medicine and the Stanford Center for Clinical Research also supported the work.

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One side of your brain might be giving you nightmares

Study explores what controls emotions while we sleep.

Nick Carne reports.

What your brain does while you sleep might be the cause of angry dreams, research suggests.

Researchers believe they have identified a pattern of brain activity that predicts anger experienced during dreaming.

It they are right, this might help explain the neural basis of the emotional content of nightmares, which are associated with mental and sleep disorders such as anxiety, depression and insomnia.

While humans experience emotions both while awake and while dreaming, there has been only limited research into the brain mechanisms underlying the affective component of dreams.

In the recent study, Pilleriin Sikka and colleagues at University of Turku, Finland, University of Skövde, Sweden, and University of Cambridge, UK, discovered a shared emotional mechanism between the two states of consciousness.

The researchers obtained electroencephalography recordings from 17 healthy individuals during two separate nights in a sleep laboratory.

After participants reached rapid eye movement (REM) sleep – the point where dreams are most vivid – they were woken and asked to describe their dreams and rate the emotions they experienced.

It was discovered that those who displayed greater alpha-band brain activity in the right frontal cortex, as compared to the left, both during evening wakefulness and during REM sleep experienced more anger in dreams.

This neural signature – called frontal alpha asymmetry (FAA) – has been linked to anger and self-regulation during wakefulness.

"We show that individuals with greater FAA (i.e. greater right-sided alpha power) during rapid eye movement (REM) sleep, and during evening wakefulness, experience more anger in dreams," the researchers write in a paper published in the journal *JNeurosci*.

"FAA may thus reflect the ability to regulate emotions not only in the waking but also in the dreaming state."

There were limitations to the study – notably that it was carried out under laboratory conditions – but the researchers suggest their findings "provide support for theories according to which dreaming is a realistic simulation of waking life".

They stress, however, that on the strength of this study alone it is not possible to say whether the particular neural activation accompanying dream anger supports a certain function, such as to experience threatening situations or negative affective states in order to better deal with them in waking life.

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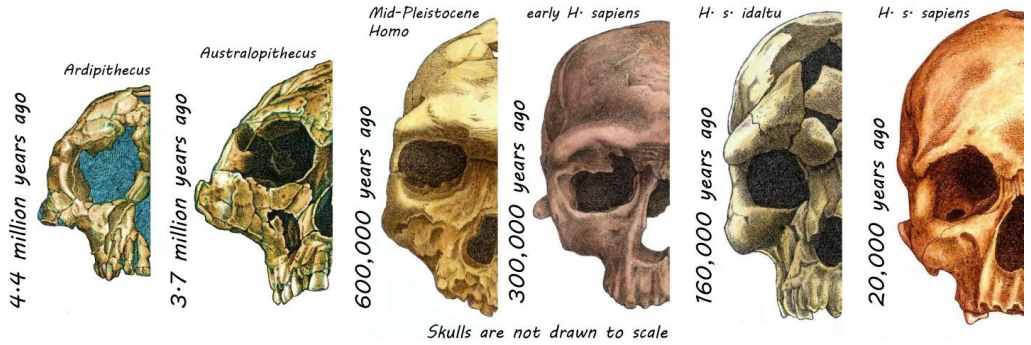
Need for social skills helped shape modern human face

The modern human face is distinctively different to that of our near relatives and now researchers believe its evolution may have been partly driven by our need for good social skills

The modern human face is distinctively different to that of our near relatives and now researchers believe its evolution may have been partly driven by our need for good social skills.

As large-brained, short-faced hominins, our faces are different from other, now extinct hominins (such as the Neanderthals) and our closest living relatives (bonobos and chimpanzees), but how and why did the modern human face evolve this way?



These are skulls of hominins over the last 4.4 million years. **Rodrigo Lacruz**

A new review published in Nature Ecology and Evolution and authored by a team of international experts, including researchers from the University of York, traces changes in the evolution of the face from the early African hominins to the appearance of modern human anatomy.

They conclude that social communication has been somewhat overlooked as a factor underlying the modern human facial form. Our faces should be seen as the result of a combination of biomechanical, physiological and social influences, the authors of the study say.

The researchers suggest that our faces evolved not only due to factors such as diet and climate, but possibly also to provide more opportunities for gesture and nonverbal communication - vital skills for establishing the large social networks which are believed to have helped Homo sapiens to survive.

"We can now use our faces to signal more than 20 different categories of emotion via the contraction or relaxation of muscles", says Paul O'Higgins, Professor of Anatomy at the Hull York Medical School and the Department of Archaeology at the University of York. "It's unlikely that our early human ancestors had the same facial dexterity as the overall shape of the face and the positions of the muscles were different."

Instead of the pronounced brow ridge of other hominins, humans developed a smooth forehead with more visible, hairy eyebrows capable of a greater range of movement. This, alongside our faces becoming more slender, allows us to express a wide range of subtle emotions - including recognition and sympathy.

"We know that other factors such as diet, respiratory physiology and climate have contributed to the shape of the modern human face, but to interpret its evolution solely in terms of these factors would be an oversimplification," Professor O'Higgins adds.

The human face has been partly shaped by the mechanical demands of feeding and over the past 100,000 years our faces have been getting smaller as our developing ability to cook and process food led to a reduced need for chewing.

This facial shrinking process has become particularly marked since the agricultural revolution, as we switched from being hunter gatherers to agriculturalists and then to living in cities - lifestyles that led to increasingly pre-processed foods and less physical effort.

"Softer modern diets and industrialised societies may mean that the human face continues to decrease in size", says Professor O'Higgins. "There are limits on how much the human face can change however, for example breathing requires a sufficiently large nasal cavity."

"However, within these limits, the evolution of the human face is likely to continue as long as our species survives, migrates and encounters new environmental, social and cultural conditions."

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Study: Aegean farmers replaced hunters of ancient Britain

Migrants from the Aegean some 6,000 years ago virtually replaced Britain's hunter-gatherer population

by Frank Jordans

A wave of migrants from what is now Greece and Turkey arrived in Britain some 6,000 years ago and virtually replaced the existing hunter-gatherer population, according to a study published Monday in the journal *Nature*.

Scientists examining samples of ancient remains dating as far back as 8500 BC found the dark-skinned foragers who had inhabited the British Isles since the last Ice Age left comparatively little trace in the genetic record after the transition to farming, suggesting there wasn't much interbreeding with the newcomers who arrived around 4000 BC.

By contrast, the same Aegean migrants mixed extensively with local populations when they introduced farming to continental Europe about 1,000 years earlier, according to previous DNA studies.

"It is difficult to say why this is, but it may be that those last British hunter-gatherers were relatively few in number," said Mark G. Thomas, a professor of evolutionary genetics at University College

London who co-wrote the study. "Even if these two populations had mixed completely, the ability of adept continental farmers and their descendants to maintain larger population sizes would produce a significant diminishing of hunter-gatherer ancestry over time."

The researchers from Britain and the United States found that the remains of Britain's early farmers were genetically similar to those discovered in what is now Spain and Portugal, indicating this population traveled east to west through the Mediterranean, and then up to Britain. Strikingly, the newcomers appear to have arrived first on the western coast before spreading to other parts of Britain, suggesting they didn't cross the English Channel using the shortest possible course but instead braved the wilder Atlantic route.

"This route is a continuation of the Mediterranean coastal dispersal route but of course in much more complicated maritime circumstances," said Carles Lalueza-Fox of the Institute of Evolutionary Biology in Barcelona, Spain.

Lalueza-Fox, who wasn't involved with the study, said the findings match what is known about the spread of megalithic structures along Europe's Atlantic coast. Perhaps the best-known of these structures is Stonehenge in Britain.

"This work highlights the complex population turnovers affecting a rather marginal area of Northwestern Europe and points out the need to investigate all regions with ancient data to understand the shaping of modern human genetic diversity," said Laluelza-Fox.

In their paper, Thomas and his colleagues also note the "considerable variation in pigmentation levels in Europe" during the Stone Age as shown from the genetic samples they examined.

Whereas Britain's outgoing hunter-gatherers—including the oldest known Briton, "Cheddar Man"—likely had blue or green eyes and dark or even black skin, the farming populations migrating across Europe are believed to have had brown eyes and dark to intermediate skin.

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Statins 'don't work well for one in two people'

Cholesterol-lowering "statin" drugs taken by millions of Britons may not work well enough in about half of those prescribed them, research suggests.

By Michelle Roberts Health editor, BBC News online

UK investigators looked at 165,000 patients on statins and found that for one in two, the drugs had too little effect on bad cholesterol - one of the big risk factors for heart disease.

They are not sure why statins appear to help some more than others.

Patients should not stop taking the drugs without seeing their doctor.

One possible explanation is patients not taking their prescribed drugs or doctors giving them at too low doses, experts suggest.

Cardiovascular disease kills about 150,000 people in the UK each year.

"Bad" low-density lipoprotein (LDL) cholesterol is a major contributor - it can lead to furring and blockage of blood vessels.

Smoking and obesity

Cutting down on saturated fat can help lower bad cholesterol, but some people will also need medication. Millions of people in the UK are given statins for this reason.

But statins can cause side effects and there is a debate about how many patients should be prescribed them.

The study, published in the journal Heart, included 165,411 patients who had been put on statins to cut their risk of developing heart disease by lowering their cholesterol to a healthy level.

Half of the patients - 84,609 in total - did not see their cholesterol go down by enough - the required 40% or more reduction specified by guidelines - even after being on the daily treatment for two years.

Experts say the study findings are somewhat limited because they cannot prove that patients who do not respond well to statins will

necessarily fare worse as a consequence. Other factors - like smoking and obesity - also raise cardiovascular risk.

But the work does provide "real life" data and experience to draw on. Researcher Dr Stephen Weng, from Nottingham University, said: "Our research has shown that in almost half of patients prescribed statins, they are very effective and offer significant protection against cardiovascular disease.

"However, for the other half - whether it's due to your genetic make-up, having side effects, sticking to the treatment or other medications - we don't see that intended benefit."

'Mixed messaging'

In the study, a higher proportion of patients with a sub-optimal response to statins were prescribed lower potency doses, compared with those with an optimal response. He said: "We have to develop better ways to understand differences between patients and how we can tailor more effective treatment for those millions of patients who are simply blanket-prescribed statins."

Prof Metin Avkiran, associate medical director at the British Heart Foundation, advised: "Statins are an important and proven treatment for lowering cholesterol and reducing the risk of a potentially fatal heart attack or stroke.

"If you have been prescribed statins, you should continue to take them regularly, as prescribed. If you have any concerns you should discuss your medication with your GP. There are now other drugs available to help lower cholesterol levels, and it may be that another type of medication will be an effective addition or alternative for you."

Prof Helen Stokes-Lampard, chairwoman of the Royal College of GPs, said: "When we prescribe medication, we have to rely on patients to make sure that they take it, both at the recommended dose and for the duration of time that we think will benefit them most.

"There is a substantial body of research showing that statins are safe and effective drugs for most people, and can reduce the risk of heart attacks and stroke, when prescribed appropriately - but controversy remains around their widespread use and their potential side-effects.

"There are complex reasons why patients choose not to take their prescribed medication, and mixed messaging around statins could be one of these."

http://bit.ly/2IsifNd

Can You Still Get the Measles If You've Been Vaccinated?

If you've been vaccinated, can you still catch the disease?

By Rachael Rettner, Senior Writer

The number of measles cases in the U.S. continues to climb, with more than 550 cases reported from January to April, according to the Centers for Disease Control and Prevention (CDC). That's the second highest number of measles cases reported in any year since 2000, the CDC says.

Many of this year's cases occurred as part of ongoing measles outbreaks in several U.S. cities, and most infected people were unvaccinated, according to the CDC. But if you've been vaccinated, can you still catch the disease?

Although it is possible to get the measles even if you've been vaccinated, it's quite rare: Two doses of the measles, mumps and rubella (MMR) vaccine — which are given as part of the standard U.S. childhood vaccination schedule — are 97% effective at preventing measles, according to the CDC. This means that about 3% of people who receive two doses of the measles vaccine will get measles if they are exposed to the virus.

It's not clear why some fully vaccinated people get measles, but it could be that their immune system did not respond properly to the vaccine, the CDC says. (Still, if a person is fully vaccinated, and

they come down with measles, they are more likely to have a mild case of the illness.)

In addition, some people may be at a slightly higher risk of getting measles because they received only one dose of the MMR vaccine. Although the measles vaccine was developed in 1963, it wasn't until 1989 that health officials recommended that a child receive two doses, according to the CDC.

This means there are "many people who are adults now who only received one dose" of MMR, said Dr. Amesh Adalja, a senior scholar at The Johns Hopkins Center for Health Security in Baltimore. One dose of MMR is still more than 90% effective at preventing measles, but it's not quite as good as two doses, Adalja said.

Adults who received only one dose of MMR as a child could consider getting a second dose, Adalja told Live Science. In situations where there are outbreaks going on, "I don't think its a bad idea," he said.

In addition, some people who received the measles vaccine in the 1960s may need to be revaccinated. That's because, between 1963 and 1967, some people received a form of the measles vaccine known as the "inactivated" (killed) vaccine, which was not effective, according to the CDC. People who received this form of the vaccine, or were vaccinated before 1968 and don't know what vaccine type they got, should be revaccinated with the current "live attenuated" form of the vaccine, the CDC says.

Waning immunity?

Another question people may have is whether the vaccine's protection wanes over time. Generally, people who've received two doses of MMR are considered protected for life, meaning they don't need a booster shot, according to the CDC.

Still, there may be some waning that happens with age, Adalja said. There is a way to check your level of protection against measles. You can get a blood test that measures antibody levels against the measles virus. However, doctors don't routinely use this test on patients — it's more often used for health care workers who are generally at higher risk of being exposed to measles. But it may be used in other situations: for example, for college students who need to show they are immune to measles, according to University of Rochester Medical Center.

Generally, the CDC recommends that people who don't have written documentation of getting the MMR vaccine should get vaccinated. However, people who were born before 1957 are considered likely to be immune to the virus (because most people born at that time were infected naturally with the virus), and therefore don't need to be vaccinated.

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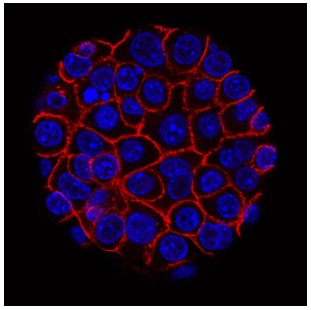
The fluid that feeds tumor cells

The substance that bathes tumors in the body is quite different from the medium used to grow cancer cells in the lab, biologists report.

CAMBRIDGE, MA -- Before being tested in animals or humans, most cancer drugs are evaluated in tumor cells grown in a lab dish. However, in recent years, there has been a growing realization that the environment in which these cells are grown does not accurately mimic the natural environment of a tumor, and that this discrepancy could produce inaccurate results.

In a new study, MIT biologists analyzed the composition of the interstitial fluid that normally surrounds pancreatic tumors, and found that its nutrient composition is different from that of the culture medium normally used to grow cancer cells. It also differs from blood, which feeds the interstitial fluid and removes waste products.

The findings suggest that growing cancer cells in a culture medium more similar to this fluid could help researchers better predict how experimental drugs will affect cancer cells, says Matthew Vander Heiden, an associate professor of biology at MIT and a member of the Koch Institute for Integrative Cancer Research.



Pancreatic cancer cells (nuclei in blue) growing as a sphere encased in membranes (red). By growing cancer cells in the lab, researchers can study factors that promote and prevent the formation of deadly tumors. **Min Yu (Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC)**

"It's kind of an obvious statement that the tumor environment is important, but I think in cancer research the pendulum had swung so far toward genes, people tended to forget that," says Vander Heiden, one of the senior authors of the study.

Alex Muir, a former Koch Institute postdoc who is now an assistant professor at the University of Chicago, is also a senior author of the paper, which appears in the April 16 edition of the journal eLife. The lead author of the study is Mark Sullivan, an MIT graduate student.

Environment matters

Scientists have long known that cancer cells metabolize nutrients differently than most other cells. This alternative strategy helps them to generate the building blocks they need to continue growing and dividing, forming new cancer cells.

In recent years, scientists have sought to develop drugs that interfere with these metabolic processes, and one such drug was approved to treat leukemia in 2017.

An important step in developing such drugs is to test them in cancer cells grown in a lab dish. The growth medium typically used to grow these cells includes carbon sources (such as glucose), nitrogen, and other nutrients. However, in the past few years, Vander Heiden's lab has found that cancer cells grown in this medium respond differently to drugs than they do in mouse models of cancer.

David Sabatini, a member of the Whitehead Institute and professor of biology at MIT, has also found that drugs affect cancer cells differently if they are grown in a medium that resembles the nutrient composition of human plasma, instead of the traditional growth medium.

"That work, and similar results from a couple of other groups around the world, suggested that environment matters a lot," Vander Heiden says. "It really was a wake up call for us that to really know how to find the dependencies of cancer, we have to get the environment right."

To that end, the MIT team decided to investigate the composition of interstitial fluid, which bathes the tissue and carries nutrients that diffuse from blood flowing through the capillaries. Its composition is not identical to that of blood, and in tumors, it can be very different because tumors often have poor connections to the blood supply.

The researchers chose to focus on pancreatic cancer in part because it is known to be particularly nutrient-deprived. After isolating interstitial fluid from pancreatic tumors in mice, the researchers used mass spectrometry to measure the concentrations of more than 100 different nutrients, and discovered that the composition of the interstitial fluid is different from that of blood (and from that of the culture medium normally used to grow cells).

Several of the nutrients that the researchers found to be depleted in tumor interstitial fluid are amino acids that are important for immune cell function, including arginine, tryptophan, and cystine.

Not all nutrients were depleted in the interstitial fluid -- some were more plentiful, including the amino acids glycine and glutamate, which are known to be produced by some cancer cells.

Location, location, location

The researchers also compared tumors growing in the pancreas and the lungs and found that the composition of the interstitial fluid can vary based on tumors' location in the body and at the site where the tumor originated. They also found slight differences between the fluid surrounding tumors that grew in the same location but had different genetic makeup; however, the genetic factors tested did not have as big an impact as the tumor location.

"That probably says that what determines what nutrients are in the environment is heavily driven by interactions between cancer cells and noncancer cells within the tumor," Vander Heiden says.

Scientists have previously discovered that those noncancer cells, including supportive stromal cells and immune cells, can be recruited by cancer cells to help remake the environment around the tumor to promote cancer survival and spread.

Vander Heiden's lab and other research groups are now working on developing a culture medium that would more closely mimic the composition of tumor interstitial fluid, so they can explore whether tumor cells grown in this environment could be used to generate more accurate predictions of how cancer drugs will affect cells in the body.

The research was funded by the National Institutes of Health, the Lustgarten Foundation, the MIT Center for Precision Cancer Medicine, Stand Up to Cancer, the Howard Hughes Medical Institute, and the Ludwig Center at MIT.

https://go.nature.com/2Xs4uSi

Millions of girls go 'missing' as a medical procedure takes hold

The advent of sex-selective abortion has ushered in changes in the sex ratio of newborns.

Some 23 million girls worldwide were never born because of the use of sex-selective abortions during the past half-century.

China and India account for the vast majority of these 'missing' girls, with 11.9 million and 10.6 million, respectively.

Fengqing Chao at the National University of Singapore and her colleagues drew on birth certificates, census data and other sources to compile a database of sex ratios at birth in more than 200 countries or other jurisdictions. Most of the information dated to 1950 or later.

For each country, the team used the decades' worth of data to estimate baseline levels of male–female birth ratios, which ranged from 1.013 in Namibia and Zambia to 1.081 in Hong Kong.

After the advent of sex-selective abortion in the 1970s, the male–female birth ratio changed significantly in 12 nations. China's reached 117.9 boys per 100 girls in 2005.

Some countries' ratios have since dropped back to normal ranges. But, as of 2017, several nations, including China and Armenia, still had more than 110 boys born per every 100 girls, according to the team's estimates.

Proc. Natl Acad. Sci. USA (2019)

http://bit.ly/2Gtu82d

As Ebola outbreak rages, vaccine is 97.5% effective, protecting over 90K people

The latest Ebola outbreak is bad—but it would be far worse without this vaccine.

Beth Mole - 4/17/2019, 12:05 AM

An experimental vaccine against the Ebola virus is 97.5 percent effective at preventing the disease, protecting well over 90,000 people in the massive, ongoing outbreak in the Democratic Republic of the Congo, according to preliminary data.

The outbreak has flared since last August, involving 1,264 cases (1,198 confirmed; 66 probable) and 814 deaths (748 confirmed, 66

probable), making it the second-largest Ebola outbreak recorded. So far the outbreak has stayed within the DRC's North Kivu and Ituri provinces, which sit on the eastern side of the country, bordering South Sudan, Uganda, and Rwanda. But, response efforts have been severely hampered by community distrust of public health campaigns. One result of this distrust has been several attacks by militants on medical facilities, injuring medical staff and, in one case, killing a police officer. Some public health experts fear the outbreak will continue to spread without new strategies and more aid, possibly across nearby borders.

Still, the outbreak could have been far worse if it had not been for an experimental vaccine. The rVSV-ZEBOV-GP Ebola vaccine, made by Merck & Co, contains a live attenuated virus harmless to humans that researchers genetically engineered to carry an Ebola glycoprotein. Ebola usually uses this protein to interact with human cells, but in the vaccine, it triggers the human immune system to generate powerful antibodies to attack the virus. Early tests of the vaccine seemed to confirm this, suggesting it is safe and effective. And a World Health Organization Strategic Advisory Group of Experts (SAGE) has given responders the greenlight to use the vaccine during outbreaks, based on an Expanded Access/Compassionate Use protocol.

As in the last outbreak, health responders are currently unleashing it in a ring vaccination strategy, which aims to immunize those in contact with known Ebola cases and contacts of those contacts—creating social rings of immunization to protect the most vulnerable and prevent the spread of disease. This was the same vaccination strategy used in the eradication of smallpox, the only human disease to ever be fully wiped out. Though Ebola spreads from animals—thus couldn't be eradicated from a human vaccination campaign alone—the strategy is considered the most effective at quickly and efficiently extinguishing any flare ups and outbreaks.

That appears to be the case in the current outbreak, according to the preliminary data released by WHO and DRC researchers (PDF). Between August 1, 2018 to March 25, health responders mapped out 679 rings around 776 of the 951 confirmed and probable cases during that time period. They vaccinated nearly 94,000 people, including nearly 29,000 healthcare and front-line responders in that time period (more have been vaccinated since then).

Of those vaccinated, only 71 people fell ill with Ebola. Most of those cases (54 of 71) were in high-risk contacts—those thought to be most likely to come down with the virus based on exposure. Moreover, most of them (56 of 71) occurred within 10 days of being immunized, before the vaccine is thought to induce full protection. Only 15 of the nearly 94,000 people vaccinated became ill after that 10-day period, and all of them survived the infection, which usually has a fatality rate of around 50 percent.

Looking at the rings overall, researchers found that Ebola was able to move through only about 9 percent of the vaccinated rings (60/679 rings), and only about two percent of those rings included cases after the 10-day period. Last, only two vaccinated people out of the 68,279 vaccinated people listed as "contacts-of-contacts" fell ill with the virus. This suggests that the vaccine and the vaccination strategy were highly effective at preventing the spread of the disease.

In all, based on calculations comparing Ebola's spread through vaccinated and unvaccinated rings in the outbreak, researchers estimated the virus' attack rate was 0.017 percent among the vaccinated and 0.656 percent among unvaccinated. That yields an estimated efficacy rate of 97.5 percent.

In a meeting late last week, WHO experts assessed the outbreak overall and determined that it did not constitute a "Public Health Emergency of International Concern," though they still expressed "deep concern" over the virus' continued spread. They called for

continued vaccination and a redoubling of efforts to work with communities to stamp out the disease.

https://wb.md/2KO6PW2

FDA Pulls All Vaginal Mesh Products Off the Market

Manufacturers ordered to stop selling and distributing their products in the US immediately

Megan Brooks

The US Food and Drug Administration (FDA) today ordered the manufacturers of vaginal mesh products to stop selling and distributing their products in the US immediately, saying the companies failed to provide reasonable assurance that the products are safe and effective.

The three vaginal mesh devices available in the United States are Boston Scientific's *Uphold LITE* and *Xenform*, and Coloplast's *Restorelle DirectFix Anterior*. The companies have 10 days to submit their plan to withdraw these products from the market.

Over the past several years, the FDA has seen a significant increase in the number of reported adverse events associated with the use of surgical mesh for transvaginal repair of pelvic organ prolapse (POP). As a result, the agency has taken a series of escalating steps, including reclassifying the devices from class II (moderate risk) to class III (high risk).

As part of this reclassification, the manufacturers were required to submit premarket approval (PMA) applications, the agency's most stringent device review pathway, in order to continue marketing their devices in the United States.

In February, the FDA convened an advisory panel to solicit input from experts on how to evaluate the safety and effectiveness of surgical mesh for transvaginal repair of POP.

As reported by *Medscape Medical News*, the panel recommended that to support a favorable benefit–risk profile, surgical mesh should be superior to native tissue repair at 36 months and the safety outcomes for surgical mesh should be comparable to native tissue repair. The FDA agreed with these recommendations, and because the manufacturers did not provide the required data in their PMAs, the FDA declined to approve them.

"In order for these mesh devices to stay on the market, we determined that we needed evidence that they worked better than surgery without the use of mesh to repair POP. That evidence was lacking in these premarket applications, and we couldn't assure women that these devices were safe and effective long term," Jeffrey Shuren, MD, director of the FDA's Center for Devices and Radiological Health, said in the statement.

The manufacturers are required to continue to follow women already enrolled in their "522" postmarketing studies.

Women who have had transvaginal mesh placed for the surgical repair of POP are advised to continue with annual and other routine check-ups and follow-up care. Women who are satisfied with their surgery and are not having complications or symptoms do not need to take any additional action. Women who experience complications or symptoms, such as persistent vaginal bleeding or discharge, pelvic or groin pain, or pain with sex, should speak with their healthcare provider.

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

Pig brains kept alive outside body for hours after death

Revival of disembodied organs raises slew of ethical and legal questions about the nature of death and consciousness.

Sara Reardon

In a challenge to the idea that brain death is final, researchers have revived the disembodied brains of pigs four hours after the animals were slaughtered. Although the experiments stopped short of restoring consciousness, they raise questions about the ethics of the approach — and, more fundamentally, about the nature of death

itself. The current legal and medical definitions of death guide protocols for resuscitating people and for transplanting organs.

Details of the pig-brain experiments appear in a paper[1] published on 17 April in *Nature*. Researchers at Yale University in New Haven, Connecticut, hooked the organs to a system that pumped in a blood substitute. The technique restored some crucial functions, such as the ability of cells to produce energy and remove waste, and helped to maintain the brains' internal structures.

"For most of human history, death was very simple," says Christof Koch, president and chief scientist of the Allen Institute for Brain Science in Seattle, Washington. "Now, we have to question what is irreversible."

In most countries, a person is considered to be legally dead when brain activity ceases or when the heart and lungs stop working. The brain requires an immense amount of blood, oxygen and energy, and going even a few minutes without these vital support systems is thought to cause irreversible damage.

Since the early twentieth century, scientists have conducted experiments that keep animals' brains alive from the moment the heart stops, by cooling the brains and pumping in blood or a substitute. But how well the organs functioned afterwards is unclear[2].

Other studies have shown that cells taken from brains long after death can perform normal activities, such as making proteins[3]. This made Yale neuroscientist Nenad Sestan wonder: could a whole brain be revived hours after death?

Sestan decided to find out — using severed heads from 32 pigs that had been killed for meat at a slaughterhouse near his lab. His team removed each brain from its skull and placed it into a special chamber before fitting the organ with a catheter. Four hours after death, the researchers began pumping a warm preservative solution into the brain's veins and arteries.

The system, which the researchers call Brain*Ex*, mimics blood flow by delivering nutrients and oxygen to brain cells. The preservative solution the team used also contained chemicals that stop neurons from firing, to protect them from damage and to prevent electrical brain activity from restarting.

Despite this, the scientists monitored the brains' electrical activity throughout the experiment and were prepared to administer anaesthetics if they saw signs that the organ might be regaining consciousness.

Time trial

The researchers tested how well the brains fared during a six-hour period. They found that neurons and other brain cells had restarted normal metabolic functions, such as consuming sugar and producing carbon dioxide, and that the brains' immune systems seemed to be working.

The structures of individual cells and sections of the brain were preserved — whereas cells in control brains, which did not receive the nutrient- and oxygen-rich solution, collapsed.

And when the scientists applied electricity to tissue samples from the treated brains, they found that individual neurons could still carry a signal.

But the team never saw coordinated electrical patterns across the entire brain, which would indicate sophisticated brain activity or even consciousness.

The researchers say that restarting brain activity might require an electrical shock, or preserving the brain in solution for extended periods to allow cells to recover from any damage they sustained while deprived of oxygen.

Sestan, whose team has used its technique to keep pig brains alive for up to 36 hours, has no immediate plans to try to restore electrical activity in a disembodied organ. Instead, his priority is to

find out how long his team can maintain a brain's metabolic and physiological functions outside the body.

"It is conceivable we are just preventing the inevitable, and the brain won't be able to recover," Sestan says. "We just flew a few hundred metres, but can we really fly?"

The Brain*Ex* system is far from ready for use in people, he adds, not least because it is difficult to use without first removing the brain from the skull.

Questions multiply

Nevertheless, the development of technology with the potential to support sentient, disembodied organs has broad ethical implications for the welfare of animals and people. "There isn't really an oversight mechanism in place for worrying about the possible ethical consequences of creating consciousness in something that isn't a living animal," says Stephen Latham, a bioethicist at Yale who worked with Sestan's team. He says that doing so might be ethically justifiable in some cases — for instance, if it enable scientists to test drugs for degenerative brain diseases on the organs, rather than people.

Gauging awareness in a brain outside a body would probably be difficult, given that the organ's surroundings would differ so radically from its natural environment. "We could imagine that brain could be capable of consciousness," says George Mashour, a neuroscientist at the University of Michigan in Ann Arbor who studies near-death experiences. "But it's very interesting to think about what kind of consciousness, in the absence of organs and peripheral stimulation."

The latest study also raises questions about whether brain damage and death are permanent. Lance Becker, an emergency-medicine specialist at the Feinstein Institute for Medical Research in Manhasset, New York, says that many physicians assume that even minutes without oxygen can cause irreversible harm.

But the pig experiments suggest that the brain might stay viable for much longer than previously thought, even without outside support. "This paper throws a hand grenade into the middle of what the common beliefs are," says Becker. "We may have vastly underestimated the ability of the brain to recover."

That could have practical and ethical consequences for organ donation. In some European countries, emergency responders who cannot resuscitate a person after a heart attack will sometimes use a system that preserves organs for transplantation by pumping oxygenated blood through the body — but not the brain.

If a technology such as Brain*Ex* becomes widely available, the ability to extend the window for resuscitation could shrink the pool of eligible organ donors, says Stuart Youngner, a bioethicist at Case Western Reserve University in Cleveland, Ohio.

"There's a potential conflict here between the interests of potential donors — who might not even be donors — and people who are waiting for organs," he adds.

Far to go

In the meantime, scientists and governments are left to confront the legal and ethical quandaries related to the possibility of creating a conscious brain without a body. "This really is a no-man's land," says Koch. "The law will probably have to evolve to keep up."

Koch wants a broader ethical discussion to take place before any researcher tries to induce awareness in a disembodied brain. "It is a big, big step," he says. "And once we do it, it's impossible to reverse it."

Nature ***568***, *283-284 (2019) doi: 10.1038/d41586-019-01216-4*

References

1 Vrselja, Z. et al. Nature https://doi.org/10.1038/s41586-019-1099-1 (2019). Article Google Scholar

2 White, R. J., Albin, M. S. & Verdura, J. Science ***141****, 1060–1061 (1963). PubMed Article Google Scholar*

3 Verwer, R. W. H. et al. FASEB J. ***16****, 54–60 (2002). PubMed Article Google Scholar*

http://bit.ly/2GoGYyB

Cervical cancer subtype rising in some sub-populations

Changing trends underscore importance of HPV prevention and early detection efforts

A new study reports that a type of cervical cancer that is less amenable to Pap testing is increasing in several subpopulations of women, pointing to the growing importance of human papillomavirus (HPV) testing and vaccination. The study appears early online in *Preventive Medicine*.

Overall trends in cervical cancer incidence have been driven by declines in squamous cell carcinoma, which account for the majority of cervical cancers. Most of the rest are adenocarcinomas, for which Pap testing is less sensitive. While overall cervical cancer rates have been dropping for decades, cervical adenocarcinomas seem to have become more common in the past 20 to 30 years. But there has been limited reporting on recent trends.

To learn more, investigators led by Farhad Islami, MD, PhD, analyzed recent cervical cancer incidence trends by histology and age in the United States. They examined trends in squamous cell carcinoma and adenocarcinoma incidence rates in the U.S. by age group, race/ethnicity, and stage at diagnosis using data from the U.S. Cancer Statistics Incidence Analytic Database.

They found squamous cell carcinoma incidence rates continued to decrease in all racial/ethnic groups except among non-Hispanic whites, in whom rates stopped dropping in the 2010s. For adenocarcinoma, after being stable between 1999 and 2002, incidence rates among non-Hispanic whites rose 1.3% per year during 2002-2015. Those increases were driven by steeper increases in women ages 40 to 49, among whom cervical adenocarcinoma rates rose 4.4% per year since 2004, and women 50 to 59?years, among whom rates rose 5.5% per year since 2011. Adenocarcinoma incidence decreased in blacks and Hispanics during 1999-2015 and was stable in Asians/Pacific Islanders.

"Increasing or stabilized incidence trends for [adenocarcinoma] and attenuation of earlier declines for [squamous cell carcinoma] in several subpopulations underscore the importance of intensifying efforts to reverse the increasing trends and further reduce the burden of cervical cancer in the U.S.," write the authors.

The authors state that "more efforts are needed to increase screening utilization according to guidelines and appropriate follow-up of positive results" to further reduce the burden of cervical cancer. They note that increasing the use of HPV testing may improve early detection of adenocarcinoma, but they also recommend research to further improve screening strategies to reduce overdiagnosis, which may be more common with HPV testing. HPV vaccination is an effective tool to prevent cervical cancer because virtually all these cancers are caused by HPV infection. "Our results also underscore the importance of HPV vaccination. Concerted efforts are needed to increase its use, which remains suboptimal" said Dr. Islami.

Article: F. Islami, S.A. Fedewa and A. Jemal, Trends in cervical cancer incidence rates by age, race/ethnicity, histological subtype, and stage at diagnosis in the United States, Preventive Medicine, *https://doi.org/10.1016/j.ypmed.2019.04.010*

http://bit.ly/2IJo1JL

Espresso yourself: Coffee thoughts leave a latte on the mind

For millions of Australians, each day begins with a hot cup of coffee in order to activate our brains for the working day.

The morning coffee run also acts a social lubricant, a creature comfort and, for some, a non-negotiable ritual.

But what if coffee aficionados could get the same effects from their morning latte by simply responding to cues that make them think of coffee - including the smells, sights and sounds?

New international research by Monash University and the University of Toronto has found that the placebo effect of coffee can heighten arousal, ambition and focus in regular drinkers without them actually consuming the beverage.

Dr Eugene Chan, Senior Lecturer in Marketing at the Monash Business School, and Sam Maglio, Associate Professor of Marketing and Psychology at the University of Toronto, explored the association between coffee and arousal to see if the brain's exposure to stimuli could deliver the same cognitive benefits as a caffeine buzz.

"As long as individuals see a connection between coffee and arousal, whatever its origin may be, mere exposure to coffee-related cues might trigger arousal in and of themselves without ingesting any form of caffeine," Dr Chan said. "Smelling coffee gives rise to the beverage's psychoactive, arousing effects. This is because the brains of habitual coffee consumers are conditioned to respond to coffee in certain ways, as per the prominent Pavlov's dog theory.

"So walking past your favourite café, smelling the odours of coffee grounds, or even witnessing coffee-related cues in the form of advertising can trigger the chemical receptors in our body enough for us to obtain the same arousal sensations without consumption."

Researchers exposed 871 participants from Western and Eastern cultures to coffee and tea-related cues across four separate experiments that would make them think of the substance without actually ingesting it.

In one study, participants had to come up with advertising slogans for coffee or tea. In another, they had to mock-up news stories about the health benefits of drinking coffee or tea. The arousal levels and heart rates were monitored by the researchers throughout the studies.

The study centred on a psychological effect called 'mental construal'. This determines how individuals think and process information, whether they focus on narrow details or the bigger picture. Results showed that priming people with coffee cues - exposing them to images and other stimuli (smells and sounds) about coffee - increased their alertness, energy levels, heart rate, and made them think narrowly.

The cognitive-altering effects of coffee were more prevalent in participants from Western countries, where coffee is more popular and has connotations related to energy, focus and ambition, compared to those from Eastern countries. Coffee was also associated with greater arousal than tea.

"Our research can offer intriguing implications, as it relies not on physiology but rather psychological associations to change our cognitive patterns," Dr Chan said.

"This study could even help to explain how drinking decaffeinated coffee can produce faster reaction times on tasks. Perhaps the mental association between coffee and arousal is so strong that it can produce cognitive changes even where there's no caffeine ingestion physiologically. "This adds to the growing amount of literature documenting that the foods we eat and the beverages we drink do more than simply provide nutrition or pleasure - mere exposure to, or reminders of them, affect how we think."

The coffee industry in Australia is worth close to $10 billion, with industry revenue growing at a rate of 2.2% annually for the past five years.

This study was published in the journal Consciousness and Cognition in April 2019.

http://bit.ly/2UqBGrn

Powerful CRISPR cousin accidentally mutates RNA while editing DNA target

New study shows base editors can also accidentally mutate the strands of RNA that help build proteins

By Jon Cohen

When researchers first reported 3 years ago that they had created base editors, a version of the powerful genome-editing tool CRISPR, excitement swirled around their distinct powers to more subtly alter DNA compared with CRISPR itself.

But the weaknesses of base editors have become increasingly apparent, and a new study shows they can also accidentally mutate the strands of RNA that help build proteins or perform other key cellular tasks. Researchers say this could complicate developing safe therapies with the technology and hamper other research applications.

Human diseases from sickle cell to Tay-Sachs are caused by a single mutation to one of the four DNA bases—adenine, guanine, cytosine, and thymine—and CRISPR has often had difficulty swapping out the bad actors.

That's in part because CRISPR cuts double-stranded DNA at targeted places and then relies on finicky cell repair mechanisms to do the heavy lifting of inserting a corrected DNA sequence for a mutation. Base editors, in contrast, chemically change one DNA base into another with enzymes called deaminases, which doesn't require a cut or help from the cell.

Base editors, which adapt key components of CRISPR to reach targeted places in the genome, have been shown to have many off-target effects on DNA. But until now, its effects on RNA, which contains three of the same bases as DNA, had escaped scrutiny. So J. Keith Joung, a pathologist and molecular biologist at the Massachusetts General Hospital in Boston, led a team that put base editors into human liver and kidney cells.

Their finding: Deaminases can also alter RNA, the group reports today in *Nature*.

Joung, a pioneering developer of base editors, was startled by the RNA changes, which had cytosines being converted to uracil, an RNA base that's related to thymine. "When a postdoc first showed me the results and we saw tens of thousands of RNA cytosines being edited, I was like, 'Wait a minute, what are we looking at here?'"

Jia Chen, who does genome editing research at ShanghaiTech University in China and was not involved in the new work, was not as surprised, noting that deaminases were originally described as having the ability to alter RNA. But he says the new work will push the field to solve the problem. "The finding will [lead to] developing novel base editors with higher editing precision," Chen says.

Joung says his lab's recent discovery of the old deaminase literature is what led his lab to do these experiments. And they've already engineered deaminases that substantially reduce the number of inadvertent RNA edits. "That was very encouraging to us," Joung says. "We're ultimately protein engineers, and we want to figure out if we can engineer the system to make the mutations go away."

David Liu, a Harvard University chemist who created the first base editor and co-founded two companies based on the technology with Joung, notes that deaminases naturally edit cellular RNA, stressing that the biological consequences of such editing are unclear. He adds that his own lab's studies of base editors have also found RNA off-target edits, but at far lower levels.

The differences between their results, says Liu, likely have less to do with the amount of off-target RNA editing that takes place than the different way Joung's group sorted its cells and analyzed the results.

Both Liu and Joung stress that their labs have found deaminases that work only on either DNA or RNA, which makes them confident that they can decouple the off-target effects seen with the current base editors. "Base editors are still incredibly powerful tools," Joung says. "This is just another parameter we need to understand."

http://bit.ly/2XBUGFt

Switch from hunting to herding recorded in ancient pee

Resolving the scale and pace of change during the first phases of animal domestication at an ancient site in Turkey

by Columbia University

The transition from hunting and gathering to farming and herding is considered a crucial turning point in the history of humanity. Scholars think the intensive food production that came along with the Neolithic Revolution, starting around 10,000 B.C., allowed cities to grow, led to technological innovation and, eventually, enabled life as we know it today.

It has been difficult to work out the details of how and when this took place. But a new study published in *Science Advances* begins to resolve the scale and pace of change during the first phases of animal domestication at an ancient site in Turkey. To reconstruct this history, the authors turned to an unusual source: urine salts left behind by humans and animals.

Whereas dung is commonly used in all sorts of studies, "this is the first time, to our knowledge, that people have picked up on salts in archaeological materials, and used them in a way to look at the development of animal management," says lead author Jordan Abell, a graduate student at Columbia's Lamont-Doherty Earth Observatory.

The team used the urine salts to calculate the density of humans and animals at the site over time, estimating that around 10,000 years ago, the density of people and animals occupying the settlement jumped from near zero to approximately one person or animal for every 10 square meters. The results suggest that domestication may have been more rapid than previously expected. They also support the idea that the Neolithic Revolution didn't have just one birthplace in the Fertile Crescent of the Mideast, but rather occurred across several locations simultaneously.

At the ancient settlement of Aşıklı Höyük in central Turkey, archaeological evidence suggests that humans began domesticating sheep and goats around 8450 BC. These practices evolved over the next 1,000 years, until the society became heavily dependent on the beasts for food and other materials.

Abell explains that it can be difficult to reconstruct the scale and pace of this evolution using bone fragments and fossilized dung. So he and his colleagues asked themselves what other clues might have been left behind by a bunch of animals onsite. "And we thought, well, humans and animals pee, and when they pee, they release a bunch of salt," says Abell. "At a dry place like this, we didn't think salts would be washed away and redistributed."

As it happened, co-authors Susan Mentzer from the University of Tübingen and Jay Quade from the University of Arizona, where Abell worked on this project as an undergraduate, had previously documented some unusually high levels of salts around Aşıklı Höyük, and were perplexed by what they meant. Using this data and others, the new study supports the idea that the salts likely came from the urine of humans, sheep and goats. The study uses the abundance of the salts over time to track the growth of the community and its animals over a period of 1,000 years.

Working with Turkish archaeologists, including Istanbul University's Mihriban Ozbasaran, who heads the Aşıklı Höyük dig, the team collected 113 samples from all across the site—from trash piles to bricks and hearths, and from different time periods—to look at patterns in the sodium, nitrate and chlorine salt levels.

They found that, overall, the urine salts at Aşıklı Höyük increased in abundance over time. The natural layers before the settlement was built contained very low levels of salts. The oldest layers with evidence of human habitation, spanning 10,400 to 10,000 years ago, saw slight increases but remained relatively low in the urine salts. Then the salts spike during a period from 10,000 to 9,700 years

ago; the amount of salts in this layer is about 1,000 times higher than in the preceding ones, indicating a rapid increase in the number of occupants (both human and animal). After that, the concentrations decrease slightly.

Abell says these trends line up with previous hypotheses based on other evidence from the site—that the settlement transitioned first from mostly hunting sheep and goats to corralling just a few, then changed to larger-scale management, and then finally shifted to keeping animals in corrals on the periphery of the site as their numbers grew. And although the timing is close to what the study authors expected, the sharp change around 10,000 years ago "may be new evidence for a more rapid transition" toward domestication, says Abell.

Using the salt concentrations, the team estimated the number and density of people plus sheep and goats at Aşıklı Höyük, after accounting for other factors that might have influenced the salt levels. They calculated that around 10,000 years ago, the density of people and animals occupying the settlement jumped from near zero to approximately one person or animal for every 10 square meters. By comparison, modern-day semi-intensive feedlots have densities of about one sheep for every 5 square meters.

Although it is not currently possible to distinguish between human and livestock urine salts, the urine salt analysis method can still provide a helpful estimate of sheep and goat abundance. Over the 1,000 year period, the team calculated that an average of 1,790 people and animals lived and peed on the settlement every day. In each time period, the estimated inhabitants were much higher than the number of people that archaeologists think the settlement's buildings would have housed. This indicates that the urine salt concentrations can indeed reflect the relative amounts of domesticated animals over time.

The researchers plan to further refine their methods and calculations in the future, and hope to find a way to differentiate between human and animal urine salts. They think the methodology could be applied in other arid areas, and could be especially helpful at sites where other physical evidence, such as bones, is lacking.

The study's results also help shed light on the geographic spread of the Neolithic Revolution. It was once thought that farming and herding originated in the Fertile Crescent, which spans parts of modern-day Iraq, Syria, Lebanon, Israel, Egypt, Jordan and the Palestinian Territories, then spread outward from there. But mounting evidence, including today's study, indicates that domestication and the transition to Neolithic lifestyles took place concurrently over a broad and diffuse swath of the region.

Anthropologist and co-author Mary Stiner from the University of Arizona said that the new method could help to clarify the larger picture of humanity's relationship to animals during this transitional period. "We might find similar trends in other archaeological sites of the period in the Middle East," she said, "but it is also possible that only a handful of long-lasting communities were forums for the evolving human-caprine relationships in any given region of the Middle East."

More information: *J.T. Abell at Lamont-Doherty Earth Observatory in New York, NY el al., "Urine salts elucidate Early Neolithic animal management at Aşıklı Höyük, Turkey," Science Advances (2019). DOI: 10.1126/sciadv.aaw0038 , advances.sciencemag.org/content/5/4/eaaw0038*

http://bit.ly/2GxRk08

How to wash your hands

Researchers suggest shorter washing time can prevent bacterial spread.

Nick Carne reports.

Advising healthcare workers to spend less time washing their hands may encourage them to do it more often, a new study suggests.

And that might ultimately help in further reducing the spread of infectious diseases in hospitals and similar settings.

The World Health Organisation recommends a 30-second, six-stage procedure with alcohol rub, but that can be pretty onerous for busy staff who have to do it many times each day.

As researchers from University Hospital Basel in Switzerland acknowledge, adherence to the whole routine is low. They believe a 15-second, three-stage procedure is no less effective, on the strength of two studies. In the first, in 2017, Sarah Tschudin-Sutter and colleagues showed that three steps are as effective as six.

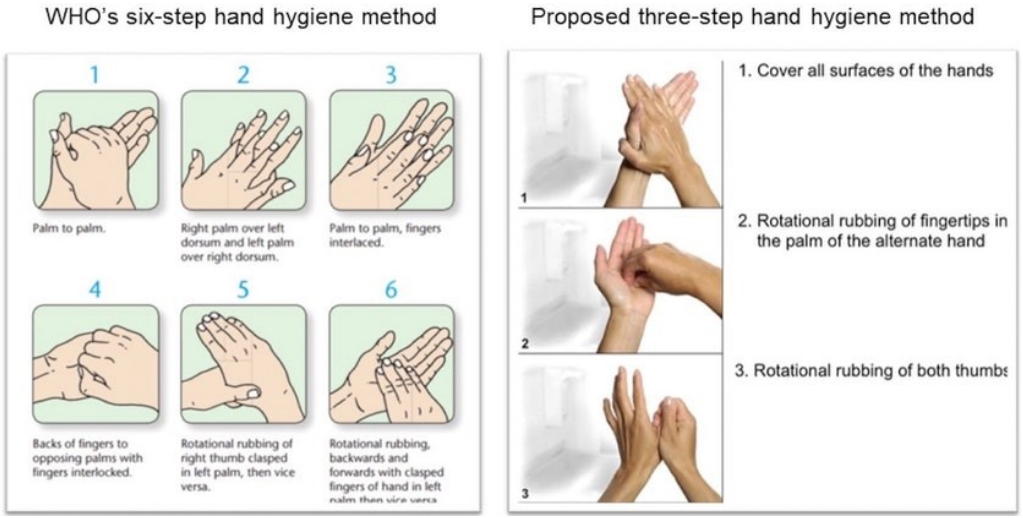
In more recent work, the same team randomly assigned 20 healthy volunteers aged 18 to 51 years to rub their hands by following four different techniques: six-step or three-step for either 30 or 15 seconds.

The "primary endpoint" – as explained in the group's poster presentation to the recent European Congress of Clinical Microbiology & Infectious Diseases in Amsterdam – was "the bacterial counts on the dominant hand as determined by the mean logarithmic reduction in bacterial counts after performance of hand hygiene".

In that context, 15 seconds was found to be "non-inferior" to 30 seconds using either technique – and might be superior in terms of helping healthcare workers comply with hygiene standards.

"Our findings suggest that shortening hand rubbing time and simplifying the technique for use of hand rub could be a safe alternative that is easier to fit into their busy routine, could enhance the overall quality of hand hygiene performance, and have a positive effect on adherence," says Tschudin-Sutter.

The researchers acknowledge that the new study was carried out in an experimental rather than a clinical setting and that, as they measured the reduction of bacterial counts, conclusions cannot be made about the impact of different hand hygiene techniques on transmission of pathogens. It's also not clear whether the suggested new regime would work on children.



WHO / Tschudin-Sutter et al

The WHO has a separate recommended procedure for washing hands with water. It "takes about as long as singing 'Happy Birthday' twice".

https://wb.md/2IJsmN3

St. Jude Doctors Claim Cure for 'Bubble Boy' Disease

Doctors at two medical centers say they have cured 10 infants of so-called bubble boy disease

By Gene Emery

Reuters Health - Relying on the trickery used by the AIDS virus to infect people, doctors at two medical centers say they have cured 10 infants of so-called bubble boy disease, a genetic defect that leaves children, typically boys, without an immune system.

The technique replaces a defective version of a gene the body needs to build cells that seek out and destroy invading germs. Earlier versions of the treatment have been less efficient and also posed a risk of triggering leukemia.

The doctors said they have skirted the leukemia problem by implanting "insulators" around the replaced gene, preventing the treatment from accidentally activating adjacent genes and causing cancer.

Three months after treatment, non-defective immune cells appeared in all but one of the treated children. That child was successfully treated with a second round of gene therapy 12 months after his initial therapy.

All have normal growth and development, and any infections they had suffered because of their disabled immune system have disappeared. There have been no signs of leukemia.

"The kids are cured because for the first time we are able to restore all three types of cells that constitute a full immune system," lead author Dr. Ewelina Mamcarz of the bone marrow transplantation and cellular therapy center at St. Jude Children's Research Hospital in Memphis, Tennessee, said at a news conference. "Our patients are able to generate a healthy, fully-functional immune system and are now responding to vaccinations, and that's a first for a gene therapy trial."

Results from the first eight babies treated at St. Jude and the University of California, San Francisco Benioff Children's Hospital through September 30 were released online April 17 in The New England Journal of Medicine.

Those children, treated when they were 2 to 14 months old, have only been followed for 7 to 25 months, so further study will be needed to determine if there are any long-term problems.

The 10th child is due to be released from the hospital this week, about four months after treatment. It typically takes three or four months for the corrected cells to sufficiently build up the immune system to allow a child to leave isolation.

Based on the results so far, said St. Jude president Dr. James Downing, "we're comfortable at this point stating this is cure."

"Only time will say if this is a durable lifelong cure," said Dr. Alain Fischer, a professor at the College of France who is also with the Unit of Pediatric Immunology, Hematology and Rheumatology at Necker Hospital for Sick Children in Paris. He was not involved in the new treatment, but helped develop an initial gene therapy for the condition 20 years ago.

The new work "is a significant step forward in the development of gene therapy and specifically for these diseases," Fischer told Reuters Health in a telephone interview. Earlier treatments were less efficient and less safe, although the first patient Fischer's team treated remains alive 20 years later and is still doing well.

Bubble boy disease, formally known as X-linked severe combined immunodeficiency or SCID-X1, is a rare genetic defect that leaves the baby defenseless against infection. Treatment usually requires getting stem cells from a donor, which can be dangerous if the donor isn't a closely-matched brother or sister. Sibling donors are usually available in fewer than 20 percent of cases.

The new technique, developed at St. Jude, involves taking some of the baby's bone marrow and using an AIDS-type virus to inject a working copy of a gene known as IL2RG into cells. The gene makes a protein essential to building a properly-functioning immune system. The treatment cannot cause AIDS.

Mamcarz noted that "any genetic disorder with a known genetic defect is amenable to this approach."

Some previous attempts to cure bubble boy disease have only produced temporary results. She said this treatment doesn't seem to have that problem.

"In previous trials, waning of the immune system was observed much, much earlier - within the first year," Mamcarz said. One patient treated with the new technique has been followed for more than two and a half years with no sign that the benefits are fading.

SOURCE: https://bit.ly/2UQI5Ar N Engl J Med 2019.

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The secret to a stable society? A steady supply of beer doesn't hurt

Archaeologists recreate ancient brewing techniques to learn how beer kept an empire afloat

A thousand years ago, the Wari empire stretched across Peru. At its height, it covered an area the size of the Eastern seaboard of the US from New York City to Jacksonville. It lasted for 500 years, from 600 to 1100 AD, before eventually giving rise to the Inca. That's a long time for an empire to remain intact, and archaeologists are studying remnants of the Wari culture to see what kept it ticking. A new study found an important factor that might have helped: a steady supply of beer.

The team worked with Peruvian brewers to recreate the ancient chicha recipe used at Cerro Baul. Donna Nash

"This study helps us understand how beer fed the creation of complex political organizations," says Ryan Williams, an associate curator and Head of Anthropology at the Field Museum and the lead author of the new study in Sustainability. "We were able to apply new technologies to capture information about how ancient beer was produced and what it meant to societies in the past."

Nearly twenty years ago, Williams, Nash, and their team discovered an ancient Wari brewery in Cerro Baúl in the mountains of southern Peru. "It was like a microbrewery in some respects. It was a production house, but the brewhouses and taverns would have been right next door," explains Williams. And since the beer they brewed, a light, sour beverage called chicha, was only good for about a week after being made, it wasn't shipped offsite--people had to come to festivals at Cerro Baúl to drink it. These festivals were important to Wari society--between one and two hundred local political elites would attend, and they would drink chicha from three-foot-tall ceramic vessels decorated to look like Wari gods and leaders. "People would have come into this site, in these festive moments, in order to recreate and reaffirm their affiliation with these Wari lords and maybe bring tribute and pledge loyalty to the Wari state," says Williams. In short, beer helped keep the empire together.

To learn more about the beer that played such an important role in Wari society, Williams and his co-authors Donna Nash (Field Museum and University of North Carolina Greensboro), Josh Henkin (Field Museum and University of Illinois at Chicago) and Ruth Ann Armitage (Eastern Michigan University) analyzed pieces of ceramic beer vessels from Cerro Baúl. They used several techniques, including one that involved shooting a laser at a shard of a beer vessel to remove a tiny bit of material, and then heating that dust to the temperature of the surface of the sun to break down the molecules that make it up. From there, the researchers were able to tell what atomic elements make up the sample, and how many--information that told researchers exactly where the clay came from and what the beer was made of.

"The cool thing about this study is that we're getting down to the atomic level. We're counting atoms in the pores of the ceramics or trying to reconstruct and count the masses of molecules that were in the original drink from a thousand years ago that got embedded into the empty spaces between grains of clay in the ceramic vessels, and that's what's telling us the new information about what the beer was made of and where the ceramic vessels were produced," says Williams. "It's really new information at the molecular level that is giving archaeologists this new insight into the past."

To check that the ingredients in chicha could indeed be transferred to the brewing vessels, the researchers worked with Peruvian

brewers to recreate the brewing process. "Making chicha is a complicated process that requires experience and expertise. The experiments taught us a lot about what making chicha would look like in the ruins of a building and how much labor and time went into the process," says Donna Nash, an adjunct curator at the Field Museum and professor at the University of North Carolina Greensboro, who led the brewing recreation. (Incidentally, the Field Museum and Chicago's Off Colour Brewing released a beer based on Nash's work, a pink ale infused with pepper berries, called Wari Ale; it's being re-released in Chicago-area stores and bars in June.)

By looking at the chemical makeup of traces of beer left in the vessels and at the chemical makeup of the clay vessels themselves, the team found two important things. One, the vessels were made of clay that came from nearby, and two, the beer was made of pepper berries, an ingredient that can grow even during a drought. Both these things would help make for a steady beer supply--even if a drought made it hard to grow other chicha ingredients like corn, or if changes in trade made it hard to get clay from far away, vessels of pepper berry chicha would still be readily available.

The authors of the study argue that this steady supply of beer could have helped keep Wari society stable. The Wari empire was huge and made up of different groups of people from all over Peru. "We think these institutions of brewing and then serving the beer really formed a unity among these populations, it kept people together," says Williams.

The study's implications about how shared identity and cultural practices help to stabilize societies are increasingly relevant today. "This research is important because it helps us understand how institutions create the binds that tie together people from very diverse constituencies and very different backgrounds," says Williams. "Without them, large political entities begin to fragment and break up into much smaller things. Brexit is an example of this fragmentation in the European Union today. We need to understand the social constructs that underpin these unifying features if we want to be able to maintain political unity in society."

http://bit.ly/2ZrvNOb

Late dinner and no breakfast is a killer combination

People who skip breakfast and eat dinner near bedtime have worse outcomes after a heart attack.

That's the finding of research published today in the European Journal of Preventive Cardiology, a journal of the European Society of Cardiology (ESC).[1]

The study found that people with the two eating habits had a four to five times higher likelihood of death, another heart attack, or angina (chest pain) within 30 days after hospital discharge for heart attack.

This was the first study to evaluate these unhealthy behaviours in patients with acute coronary syndromes. Skipping breakfast was observed in 58%, late-night dinner eating in 51%, and both behaviours in 41%.

The study enrolled patients with a particularly serious form of heart attack called ST-segment elevation myocardial infarction (STEMI). "One in ten patients with STEMI dies within a year, and nutrition is a relatively inexpensive and easy way to improve prognosis," said study author Dr Marcos Minicucci, of São Paolo State University, Brazil.

He recommended a minimum two hour interval between dinner and bedtime. "It is said that the best way to live is to breakfast like a king," he added. "A good breakfast is usually composed of dairy products (fat-free or low fat milk, yogurt and cheese), a carbohydrate (whole wheat bread, bagels, cereals), and whole fruits. It should have 15 to 35% of our total daily calorie intake."

The study included 113 patients with a mean age of 60, and 73% were men. Patients were asked about eating behaviours on admission to a coronary intensive care unit. Skipping breakfast was

defined as nothing before lunch, excluding beverages, such as coffee and water, at least three times per week. Late-night dinner eating was defined as a meal within two hours before bedtime at least three times per week.

Dr Minicucci noted that late-night dinner eating was defined by the two-hour interval between dinner and bedtime, rather than eating late at night. But nearly all participants with this habit were late-eaters.

Previous studies have found that people who miss breakfast and have a late dinner are more likely to have other unhealthy habits such as smoking and low levels of physical activity. "Our research shows that the two eating behaviours are independently linked with poorer outcomes after a heart attack, but having a cluster of bad habits will only make things worse," said Dr Minicucci. "People who work late may be particularly susceptible to having a late supper and then not being hungry in the morning."

"We also think that the inflammatory response, oxidative stress, and endothelial function could be involved in the association between unhealthy eating behaviours and cardiovascular outcomes," he added.

In this study, statin use before hospital admission was higher in the group with unhealthy eating habits and worse outcome. Dr Minicucci said: "There are some controversies regarding eating habits of patients using statins. Our study suggests that patients with STEMI perceive statins as an alternative path to health benefits. But these drugs should be an addition to healthy eating habits, not a replacement."

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Disclosures: None.

[1]Musse GNV, Moreira T, Kimura MA, et al. Skipping breakfast concomitant with late-night dinner eating is associated with worse outcomes following ST-segment elevation myocardial infarction. Eur J Prev Cardiol. 2019. doi:10.1177/2047487319839546.

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Fossils found in museum drawer in Kenya belong to gigantic carnivore

Ohio University paleontologists say mammal was larger than a polar bear

ATHENS, Ohio - Paleontologists at Ohio University have discovered a new species of meat-eating mammal larger than any big cat stalking the world today. Larger than a polar bear, with a skull as large as that of a rhinoceros and enormous piercing canine teeth, this massive carnivore would have been an intimidating part of the eastern African ecosystems occupied by early apes and monkeys.

***Simbakubwa kutokaafrika*, a gigantic carnivore known from most of its jaw, portions of its skull, and parts of its skeleton, was a hyaenodont that was larger than a polar bear. Mauricio Anton**

In a new study published in the *Journal of Vertebrate Paleontology*, the researchers name Simbakubwa kutokaafrika, a gigantic carnivore known from most of its jaw, portions of its skull, and parts of its skeleton. The 22-million-year-old fossils were unearthed in Kenya decades ago as researchers canvassed the region searching for evidence of ancient apes. Specimens were placed in a drawer at the National Museums of Kenya and not given a great deal of attention until Ohio University researchers Dr. Nancy Stevens and Dr. Matthew Borths rediscovered them, recognizing their significance.

"Opening a museum drawer, we saw a row of gigantic meat-eating teeth, clearly belonging to a species new to science," says study lead author Borths. Borths was a National Science Foundation Postdoctoral Research Fellow with Stevens in the Department of

Biomedical Sciences at Ohio University when the research was conducted, and is now Curator of the Division of Fossil Primates at the Duke Lemur Center at Duke University.

Simbakubwa is Swahili for "big lion" because the animal was likely at the top of the food chain in Africa, as lions are in modern African ecosystems. Yet Simbakubwa was not closely related to big cats or any other mammalian carnivore alive today. Instead, the creature belonged to an extinct group of mammals called hyaenodonts.

Simbakubwa kutokaafrika, an extinct hyaenodont, with a skull as large as that of a rhinoceros and enormous piercing canine teeth, would have been an intimidating part of the eastern African ecosystems occupied by early apes and monkeys. **Mauricio Anton**

Hyaenodonts were the first mammalian carnivores in Africa. For about 45 million years after the extinction of the non-avian dinosaurs, hyaenodonts were the apex predators in Africa. Then, after millions of years of near-isolation, tectonic movements of the Earth's plates connected Africa with the northern continents, allowing floral and faunal exchange between landmasses. Around the time of Simbakubwa, the relatives of cats, hyenas, and dogs began to arrive in Africa from Eurasia.

As the relatives of cats and dogs were going south, the relatives of Simbakubwa were going north. "It's a fascinating time in biological history," Borths says. "Lineages that had never encountered each other begin to appear together in the fossil record."

The species name, kutokaafrika, is Swahili for "coming from Africa" because Simbakubwa is the oldest of the gigantic hyaenodonts, suggesting this lineage of giant carnivores likely originated on the African continent and moved northward to flourish for millions of years.

Ultimately, hyaenodonts worldwide went extinct. Global ecosystems were changing between 18 and 15 million years ago as grasslands replaced forests and new mammalian lineages diversified. "We don't know exactly what drove hyaenodonts to extinction, but ecosystems were changing quickly as the global climate became drier. The gigantic relatives of Simbakubwa were among the last hyaenodonts on the planet," remarks Borths.

"This is a pivotal fossil, demonstrating the significance of museum collections for understanding evolutionary history," notes Stevens, Professor in the Heritage College of Osteopathic Medicine at Ohio University and co-author of the study. "Simbakubwa is a window into a bygone era. As ecosystems shifted, a key predator disappeared, heralding Cenozoic faunal transitions that eventually led to the evolution of the modern African fauna."

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http://www.tandfonline.com/10.1080/02724634.2019.1570222

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42,000-Year-Old Foal Entombed in Ice Still Had Liquid Blood in Its Veins

A 42,000-year-old foal discovered frozen in Siberian permafrost contained a surprise: the oldest liquid blood on record.

By Stephanie Pappas, Live Science Contributor

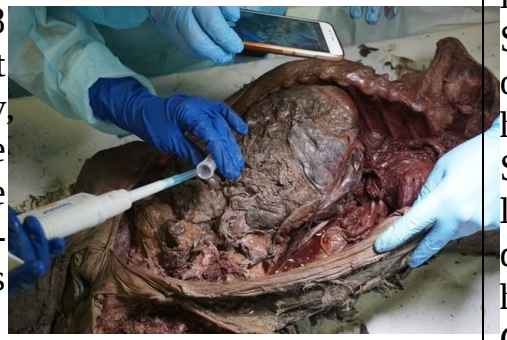
This is the second time that a defrosted Ice Age animal has turned out to contain liquid blood, said Semyon Grigoriev, the head of the Mammoth Museum at North-Eastern Federal University in Yakutsk. In 2018, Grigoriev and his colleagues extracted liquid blood from a 32,200-year-old mammoth carcass. That makes the foal's blood the oldest ever found by 10,000 years.

Grigoriev and his colleagues are set on cloning a mammoth and other Pleistocene fauna, and they're already trying to clone the foal, a member of an extinct species called the Lena horse. It's a long shot, though, Grigoriev wrote in an email to Live Science. "But," he said, "we in Russia say that hope dies last."

Called the Lena horse (*Equus caballus lenensis*), this ice age foal was found in the Batagaika Crater in eastern Siberia and is thought to have been just 2 months old when it died, likely by drowning in mud. **Semyon Grigoriev**

Lena horse

The Lena horse (*Equus caballus lenensis*) foal was found in the Batagaika Crater in eastern Siberia last year. The foal was 1 to 2 weeks old and stood 39 inches (98 centimeters) at the shoulder when it died, drowning in mud. Remarkably, the icy permafrost preserved the foal's skin and hair down to the tiniest detail. There was even well-preserved urine still inside the foal's bladder, Grigoriev said.



Researchers collect liquid blood from the ice age foal found frozen in Siberian permafrost. **Semyon Grigoriev**

The liquid blood was a surprise, he said. Typically, blood coagulates or turns to powder even in well-preserved carcasses, because fluids gradually evaporate over thousands of years, he said. In the mammoth, dubbed "Buttercup" by researchers, the blood was preserved in ice inside the carcass.

The foal autopsy should reveal a lot about Pleistocene Siberia, Grigoriev said. Not only will researchers study the biochemistry of preserved urine, gut contents and organs, but they will also study samples of the soils and paleo plants found in the layer of permafrost where the foal died.

Cloning the ice age

The blood may not help the researchers reach their goal of reviving an ice age animal. Red blood cells don't have nuclei, so they don't contain DNA, Grigoriev said.

For cloning, the researchers are focusing on muscle cells and internal organs, he said. Even there, finding DNA in good enough condition for cloning is a big challenge. DNA starts to degrade soon after an animal's death, even in excellent preservation conditions such as permafrost, Grigoriev said.

The team has been trying to extract intact cells and quality DNA from the foal for two months, Grigoriev said, without success. The researchers will continue to try both in Yakutsk and at the laboratory of their collaborator Hwang Woo-suk, the CEO of Sooam Biotech in South Korea, he said. Hwang was found guilty of embezzlement and bioethical violations in 2009 after a set of human stem-cell cloning experiments published in the journal Science in 2004 and 2005 turned out to be faked. He then kept a low profile for several years before making headlines for cloning dogs for wealthy clients. According to Vanity Fair, his company has cloned more than 1,000 dogs. He has also been working with Grigoriev and his team on attempts to clone a mammoth.

Grigoriev and his colleagues hope that if they can retrieve viable DNA from a mammoth, they can insert the DNA into an elephant embryo cleared of its genetic information, implant the embryo into an elephant and resurrect the woolly mammoth. A similar process could work for the Lena horse, using modern horses as surrogates. A recent documentary on these efforts, "Genesis 2.0," won a prize for cinematography at the Sundance Film Festival in 2018.

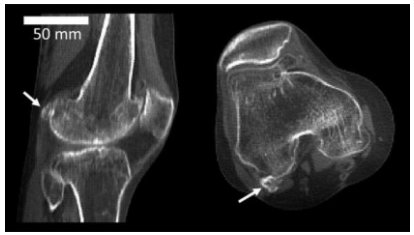
https://bbc.in/2IGXRHD

Sore knee? Maybe you have a fabella

A little bone in the knee scientists thought was being lost to evolution seems to be making a comeback, say experts from Imperial College London.

The fabella is found in some people buried in the tendon just behind their knee.

Doctors think it is entirely pointless, and you can happily live without it - many people do.



The arrow on the scan shows where the fabella is - behind the knee **Imperial College London**

However, people who have arthritis appear more likely to be in possession of a fabella. The Imperial College team has published its findings in the Journal of Anatomy.

What is it?

In medical terms, the fabella - which means little bean - is a sesamoid bone, meaning it grows in the tendon of a muscle, just like the kneecap or patella.

How common is it?

Dr Michael Berthaume and colleagues at Imperial's department of bioengineering have looked back at medical literature on knees over 150 years in 27 countries, including the UK.

Between 1918 and 2018, reports of the fabella bone's existence in the knee increased to the extent that it is now thought to be three times as common as 100 years ago.

The scientists' analysis showed that in 1918, fabellae were present in 11% of the world population, and by 2018, they were present in 39%.

The researchers made their estimations using medical scans and medical journals' findings from a growing world population.

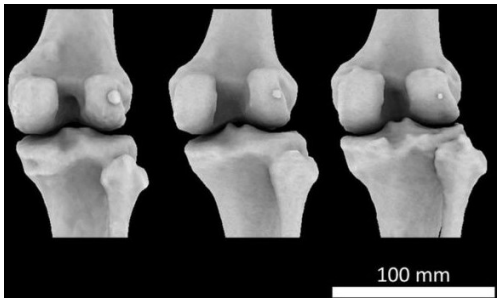
Why do some of us have it?

Dr Berthaume said that no-one really knows the answer to that, because it has never been researched. "The fabella may behave like other sesamoid bones to help reduce friction within tendons, redirecting muscle forces, or, as in the case of the kneecap, increasing the mechanical force of that muscle," he said. "Or it could be doing nothing at all."

Do we need it?

In old world monkeys, the fabella can act as a kneecap, increasing the mechanical advantage of the muscle. But when the ancestors of great apes and humans evolved, it seemed to disappear.

Now that it has returned, it is just causing us problems, according to experts. People with osteoarthritis of the knee are twice as likely to have the little bone, but there is no evidence it is actually causing the problem, or how. The fabella can also get in the way of knee replacement surgery and cause pain and discomfort on its own.



The fabella is found in the tissues behind the kneecap **Imperial College London**

So why is it making a comeback?

The theory is that it is all to do with nutrition.

The researchers came to the conclusion that better nutrition is making the average human taller and heavier, and this means we have longer shinbones and larger calf muscles.

These changes put the knee under more pressure.

Because sesamoid bones, like the fabella, are known to grow in response to the movements they make and the forces exerted on them, this could explain why the bone is more common than it used to be.

Why is it important?

Finding out about this little bone's resurgence could help doctors treat patients with knee issues. It could also give them an insight into human evolution over the past century. But first they want to find out the age, gender and location of people most likely to have a fabella, and if it occurs in one or both knees.

http://bit.ly/2Iwq8RZ

The Predator That Makes Great White Sharks Flee in Fear

Better to run than to have your liver squeezed out.

Ed Yong

The great white shark—a fast, powerful, 16-foot-long torpedo that's armed to the teeth with teeth—has little to fear except fear itself. But also: killer whales.

Even a predator like the great white shark can have a fearsome enemy. **Dave J Hogan / Getty**

For almost 15 years, Salvador Jorgensen from the Monterey Bay Aquarium has been studying great white sharks off the coast of California. He and his colleagues would lure the predators to their boats using bits of old carpet that they had cut in the shape of a seal. When the sharks approached, the team would shoot them with electronic tags that periodically emit ultrasonic signals. Underwater receivers, moored throughout Californian waters, detected these signals as the sharks swam by, allowing the team to track their whereabouts over time.

In 2009, the team tagged 17 great whites, which spent months circling Southeast Farallon Island and picking off the local elephant seals. But this period of steady hunting ended on November 2 of that year, when two pods of killer whales (orcas) swam past the islands in the early afternoon. In the space of eight hours, all 17 great whites abruptly disappeared. They weren't dead; their tags were eventually detected in distant waters. They had just fled from Farallon. And for at least a month, most of them didn't return.

Jorgensen wondered if this was a one-off, but the tags recorded similar examples in later years—orcas arrive, and sharks skedaddle. Some orcas also hunt seals, so it's possible that the sharks are just trying to avoid competition—but that seems improbable, given how quickly they bolt. The more likely explanation is that the most fearsome shark in the world is terrified of orcas.

Killer whales have a friendlier image than great white sharks. (Perhaps because of their respective portrayals in movies: *Jaws 2* even begins with the beached carcass of a half-eaten orca.) But orcas are "potentially the more dangerous predator," says Toby Daly-Engel, a shark expert at the Florida Institute of Technology. "They have a lot of social behaviors that sharks do not, which allows them to hunt effectively in groups, communicate among themselves, and teach their young."

Combining both brains and brawn, orcas have been known to kill sharks in surprisingly complicated ways. Some will drive their prey to the surface and then karate chop them with overhead tail swipes. Others seem to have worked out that they can hold sharks upside-down to induce a paralytic state called tonic immobility. Orcas can kill the fastest species (makos) and the largest (whale sharks). And when they encounter great whites, a few recorded cases suggest that these encounters end very badly for the sharks.

In October 1997, fishing vessels near Southeast Farallon Island observed a young white shark interrupting a pair of orcas that were eating a sea lion. One of the whales rammed and killed the shark, and the duo proceeded to eat its liver. More recently, after orcas passed by a South African beach, five great-white carcasses washed ashore. All were, suspiciously, missing their liver.

A great white's liver can account for a quarter of its body weight, and is even richer in fats and oils than whale blubber. It's "one of the densest sources of calories you can find in the ocean," Jorgensen says. "The orcas know their business, and they know where that organ lies."

Rather than ripping their prey apart, it seems that orcas can extract livers with surprising finesse, despite lacking arms and hands. No one has observed their technique, but the wounds on otherwise intact carcasses suggest that they bite their victims near their pectoral fins and then squeeze the liver out through the wounds. "It's like squeezing toothpaste," Jorgensen says.

An orca, then, is an apex predator's apex predator. No wonder sharks flee from them. But orcas don't actually have to kill any great whites to drive them away. Their mere presence—and most likely their scent—is enough. Many predators have similar effects. Their sounds and smells create a "landscape of fear"—a simmering dread that changes the behavior and whereabouts of their prey. The presence of tiger sharks forces dugongs into deeper waters, where food is scarcer but cover is thicker. The mere sound of dogs can keep raccoons off a beach, changing the community of animals that lives in the tide pools.

The fear of death can shape the behavior of animals more than death itself. "Lions, for example, do not eat a lot of impala, but impala fear lions more than any other predator on the landscape except humans," says Liana Zanette from Western University in Canada, who studies landscapes of fear. Similarly, killer whales don't have to kill many white sharks to radically change their whereabouts. In 2009, for example, orcas passed by Southeast Farallon for less than three hours, but the great whites stayed away for the rest of the year. For the elephant seals, the island became a predator-free zone. "The two predators faced off, and the winners were the seals," Jorgensen says.

And what about the sharks? "They had to move to find a new food source when the killer whales ruined the neighborhood," Zanette says. "This could interfere with their ability to successfully migrate, which requires a bulk-up of fat and nutrients."

"We think of white sharks as these great ocean predators, but their bag of tricks includes knowing when to pack it in," Jorgensen says. "That play might have contributed to their long-standing success."

Or, in other words: Run away, doo doo doo doo doo doo, run away, doo doo doo doo doo doo, run away, doo doo doo doo doo doo, run away.