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Plants "Eavesdrop" on Slimy Snails

Tomato plants detect snail slime and mount preemptive defenses

By Erica Tennenhouse | Scientific American May 2018 Issue

Plants cannot run or hide, so they need other strategies to avoid being eaten. Some curl up their leaves; others churn out chemicals to make themselves taste bad if they sense animals drooling on them, chewing them up or laying eggs on them—all surefire signals of an attack. New research now shows some flora can detect an herbivorous animal well before it launches an assault, letting a plant mount a preemptive defense that even works against other pest species.

When ecologist John Orrock of the University of Wisconsin–Madison squirted snail slime—a lubricating mucus the animals ooze as they slide along—into soil, nearby tomato plants appeared to notice. They increased their levels of an enzyme called lipoxygenase, which is known to deter herbivores. "None of the plants were ever actually attacked," Orrock says. "We just gave them cues that suggested an attack was coming, and that was enough to trigger big changes in their chemistry."

Initially Orrock found this defense worked against snails; in the latest study, his team measured the slimy warning's impact on another potential threat. The investigators found that hungry caterpillars, which usually gorge on tomato leaves, had no appetite for them after the plants were exposed to snail slime and activated their chemical resistance. This nonspecific defense may be a strategy that gets the plants more bang for their buck by further improving Their overall odds of survival, says Orrock, who reported the results with his colleagues in March in *Oecologia*.

The finding that a snail's approach can trigger a plant response that affects a different animal intrigued Richard Karban, a plant communications expert at the University of California, Davis, who was not involved in the study. "It is significant that the plants are responding before being damaged and that these cues are having such far-ranging effects," Karban says. The research was comprehensive, he adds, but he wonders how the tomato plants detected chemicals in snail slime that never actually touched them.

"That's the million-dollar question," Orrock says. He hopes future research will tease out the mechanisms that enable plants to perceive these relatively distant cues.

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Eggs not linked to cardiovascular risk, despite conflicting advice

No extra risk for people with pre-diabetes or type 2 diabetes

University of Sydney researchers aim to help clear up conflicting dietary advice around egg consumption, as a new study finds eating up to 12 eggs per week for a year did not increase cardiovascular risk factors in people with pre-diabetes and type 2 diabetes.

Published in the *American Journal of Clinical Nutrition* today, the research extends on a previous study that found similar results over a period of three months.

Led by Dr Nick Fuller from the University's Boden Institute of Obesity, Nutrition, Exercise and Eating Disorders at the Charles Perkins Centre, the research was conducted with the University of Sydney's Sydney Medical School and the Royal Prince Alfred Hospital.

In the initial trial, participants aimed to maintain their weight while embarking on a high-egg (12 eggs per week) or low-egg (less than two eggs per week) diet, with no difference in cardiovascular risk markers identified at the end of three months.

The same participants then embarked on a weight loss diet for an additional three months, while continuing their high or low egg consumption. For a further six months - up to 12 months in total - participants were followed up by researchers and continued their high or low egg intake.

At all stages, both groups showed no adverse changes in cardiovascular risk markers and achieved equivalent weight loss - regardless of their level of egg consumption, Dr Fuller explained.

"Despite differing advice around safe levels of egg consumption for people with pre-diabetes and type 2 diabetes, our research indicates people do not need to hold back from eating eggs if this is part of a healthy diet," Dr Fuller said.

"A healthy diet as prescribed in this study emphasised replacing saturated fats (such as butter) with monounsaturated and polyunsaturated fats (such as avocado and olive oil)," he added.

The extended study tracked a broad range of cardiovascular risk factors including cholesterol, blood sugar and blood pressure, with no significant difference in results between the high egg and low egg groups.

"While eggs themselves are high in dietary cholesterol - and people with type 2 diabetes tend to have higher levels of the 'bad' low density lipoprotein (LDL) cholesterol - this study supports existing research that shows consumption of eggs has little effect on the levels of cholesterol in the blood of the people eating them," Dr Fuller explained.

Dr Fuller said the findings of the study were important due to the potential health benefits of eggs for people with pre-diabetes and type 2 diabetes, as well as the general population.

"Eggs are a source of protein and micronutrients that could support a range of health and dietary factors including helping to regulate the intake of fat and carbohydrate, eye and heart health, healthy blood vessels and healthy pregnancies."

The different egg diets also appeared to have no impact on weight, Dr Fuller said.

"Interestingly, people on both the high egg and low egg diets lost an equivalent amount of weight - and continued to lose weight after the three month intended weight loss phase had ended," he said.

The research was supported with a grant from Australian Eggs; they had no role in the research design, conduct, analyses or writing of the manuscript.

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Earth's orbital changes have influenced climate, life forms for at least 215 million years

Gravity of Jupiter and Venus elongates Earth's orbit every 405,000 years, Rutgers-led study confirms

Every 405,000 years, gravitational tugs from Jupiter and Venus slightly elongate Earth's orbit, an amazingly consistent pattern that has influenced our planet's climate for at least 215 million years and allows scientists to more precisely date geological events like the spread of dinosaurs, according to a Rutgers-led study.

The findings are published online today in the *Proceedings of the National Academy of Sciences*.

"It's an astonishing result because this long cycle, which had been predicted from planetary motions through about 50 million years ago, has been confirmed through at least 215 million years ago," said lead author Dennis V. Kent, a Board of Governors professor in the Department of Earth and Planetary Sciences at Rutgers University-New Brunswick. "Scientists can now link changes in the climate, environment, dinosaurs, mammals and fossils around the world to this 405,000-year cycle in a very precise way."

The scientists linked reversals in the Earth's magnetic field - when compasses point south instead of north and vice versa - to sediments with and without zircons (minerals with uranium that allow radioactive dating) as well as to climate cycles.

"The climate cycles are directly related to how the Earth orbits the sun and slight variations in sunlight reaching Earth lead to climate and ecological changes," said Kent, who studies Earth's magnetic field. "The Earth's orbit changes from close to perfectly circular to about 5 percent elongated especially every 405,000 years."

The scientists studied the long-term record of reversals in the Earth's magnetic field in sediments in the Newark basin, a prehistoric lake that spanned most of New Jersey, and in sediments with volcanic detritus including zircons in the Chinle Formation in Petrified Forest National Park in Arizona. They collected a core of rock from the Triassic Period, some 202 million to 253 million years ago. The core is 2.5 inches in diameter and about 1,700 feet long, Kent said.

The results showed that the 405,000-year cycle is the most regular astronomical pattern linked to the Earth's annual turn around the sun, he said.

Prior to this study, dates to accurately time when magnetic fields reversed were unavailable for 30 million years of the Late Triassic. That's when dinosaurs and mammals appeared and the Pangea supercontinent broke up. The break-up led to the Atlantic Ocean forming, with the sea-floor spreading as the continents drifted apart, and a mass extinction event that affected dinosaurs at the end of that period, Kent said.

"Developing a very precise time-scale allows us to say something new about the fossils, including their differences and similarities in wide-ranging areas," he said.

The study was conducted by National Science Foundation-funded scientists at Rutgers-New Brunswick; Lamont-Doherty Earth Observatory at Columbia University, where Kent is also an adjunct senior research scientist and where longtime research collaborator and co-author Paul E. Olsen works; and other institutions. Christopher J. Lepre, a lecturer in Rutgers' Department of Earth and Planetary Sciences, and seven others co-authored the study, and the cores were sampled at the Rutgers Core Repository.

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Alligators on the beach? Killer whales in rivers? Get used to it

Large predators once hunted to near-extinction are showing up in unexpected places

DURHAM, N.C. - Alligators on the beach. Killer whales in rivers. Mountain lions miles from the nearest mountain.

In recent years, sightings of large predators in places where conventional wisdom says they "shouldn't be" have increased, in large part because local populations, once hunted to near-extinction, are rebounding -- thanks to conservation.

Many observers have hypothesized that as these populations recover the predators are expanding their ranges and colonizing new habitats in search of food.

A Duke University-led paper published today in the journal *Current Biology* suggests otherwise.

It finds that, rather than venturing into new and alien habitats for the first time, alligators, sea otters and many other large predators -- marine and terrestrial species alike -- are re-colonizing ecosystems that used to be prime hunting grounds for them before humans decimated their populations and well before scientists started studying them.

"We can no longer chock up a large alligator on a beach or coral reef as an aberrant sighting," said Brian Silliman, Rachel Carson Associate Professor of Marine Conservation Biology at Duke's Nicholas School of the Environment. "It's not an outlier or short-term blip. It's the old norm, the way it used to be before we pushed these species onto their last legs in hard-to-reach refuges. Now, they are returning."

By synthesizing data from recent scientific studies and government reports, Silliman and his colleagues found that alligators, sea otters, river otters, gray whales, gray wolfs, mountain lions, orangutans and bald eagles, among other large predators, may now be as abundant or more abundant in "novel" habitats than in traditional ones.

Their successful return to ecosystems and climatic zones long considered off-limits or too stressful for them upends one of the most widely held paradigms of large animal ecology, Silliman said.

"The assumption, widely reinforced in both the scientific and popular media, is that these animals live where they live because they are habitat specialists. Alligators love swamps; sea otters do best in saltwater kelp forests; orangutans need undisturbed forests; marine mammals prefer polar waters. But this is based on studies and observations made while these populations were in sharp decline. Now that they are rebounding, they're surprising us by demonstrating how adaptable and cosmopolitan they really are," Silliman said.

For instance, marine species such as sting rays, sharks, shrimps, horseshoe crabs and manatees now make up 90 percent of alligators' diet when they're in seagrass or mangrove ecosystems, showing that gators adapt very well to life in a saltwater habitat.

The unanticipated adaptability of these returning species presents exciting new conservation opportunities, Silliman stressed.

"It tells us these species can thrive in a much greater variety of habitats. Sea otters, for instance, can adapt and thrive if we introduce them into estuaries that don't have kelp forests. So even if kelp forests disappear because of climate change, the otters won't," he said. "Maybe they can even live in rivers. We will find out soon enough."

As top predators return, the habitats they re-occupy also see benefits, he said. For instance, introducing sea otters to estuarine seagrass beds helps protect the beds from being smothered by epiphytic algae that feed on excess nutrient runoff from inland farms and cities. The otters do this by eating Dungeness crabs, which otherwise eat too many algae-grazing sea slugs that form the bed's front line of defense.

"It would cost tens of millions of dollars to protect these beds by re-constructing upstream watersheds with proper nutrient buffers," Silliman said, "but sea otters are achieving a similar result on their own, at little or no cost to taxpayers."

Co-authors on the new study were Lindsay Gaskins, Qiang He and Andrew Read of Duke's Nicholas School; Brent Hughes of the University of California Santa Cruz (UCSC); Tim Tinker of UCSC and the U.S. Geological Survey; James Nifong of Kansas State University; and Rick Stepp of the University of Florida.

Funding came from the Stolarz Foundation, a National Science Foundation Graduate Research Fellowship, a David H. Smith Conservation Fellowship, the U.S. Geological Survey, and the California Coastal Conservancy

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http://bit.ly/2jLSp8D

Understanding how DNA is selectively tagged with 'do not use' marks

Chemical equivalent of a "do not use" sign keeps genetic elements under control

LA JOLLA - Not all of your genome needs to be active at any given time. Some regions are prone to hopping around the genome in problematic ways if left unchecked; others code for genes that need to be turned off in certain cells or at certain times. One way that cells keep these genetic elements under control is with the chemical equivalent of a "do not use" sign. This chemical signal, called DNA methylation, is known to vary in different cell types or at different stages of cellular development, but the details of how cells regulate exactly where to put DNA methylation marks have remained unclear.

Salk scientists studying plants discovered a small family of proteins that control where in the genome DNA methylation marks are added. Their work on this aspect of genetic regulation is highly relevant for processes that range from normal development to cellular defects and diseases, which can arise due to erroneous DNA methylation patterns in plants and/or humans, respectively. Their paper appeared in *Nature Genetics* on May 7, 2018.

"If we want to understand how differences in DNA methylation patterns can cause developmental defects in plants, or diseases like cancer in humans, we need to understand how DNA methylation is targeted to specific regions of the genome under normal conditions," says Salk Assistant Professor Julie Law, senior author of the paper. "Until now, factors able to control methylation in such a precise manner have been elusive."

Law studies an easy-to-grow weed, Arabidopsis thaliana, the first plant to have its genome sequenced. In the ensuing years, scientists, including Law, have been working to characterize and understand the plant's DNA methylation patterns, which affect gene activity without changing the DNA code itself. This process is similar in plants and animals, but investigating DNA methylation in Arabidopsis is much easier because plants can tolerate methylation defects better than animals, where global changes in methylation are often lethal.

Law was interested in understanding how the pathways that control DNA methylation are regulated not only to control global patterns of methylation but also to enable the regulation of individual regions--a critical step in generating different patterns of DNA methylation within a given organism.

Previously, it was known that a protein complex called RNA polymerase IV (Pol-IV) played a global role in establishing DNA methylation patterns. This polymerase makes small molecular messages called siRNAs that act like a molecular GPS system, indicating all the locations within the genome where methylation should be targeted. However, how this polymerase might be regulated to control DNA methylation at individual genomic locations was unclear.

To address this question, Law's lab used a combined genetic-genomic approach to investigate the functions of four related proteins, the CLASSY family, that they thought might regulate Pol-IV. It turned out that disruption of each CLASSY gene resulted in different sets of genomic regions--in different locations--losing their siRNA signals, resulting in reduced DNA methylation levels. More dramatically, when all four CLASSY genes were disrupted, the siRNA signals and DNA methylation were lost throughout the entire genome.

"In the CLASSY quadruple mutants, the Pol-IV signal completely disappears--essentially no siRNAs are made," says Ming Zhou, a Salk research associate and the paper's first author. "This is very strong evidence that CLASSYs are required for Pol-IV function."

When Law's team probed further, they discovered that the DNA methylation defects in the CLASSY mutants caused some genes to be erroneously turned on and resulted in global decreases in methylation at mobile DNA elements, increasing their potential to move around and disrupt essential gene activity.

"The CLASSYs are a part of a large superfamily that is common to both plants and animals," adds Law, who holds the Hearst Foundation Development Chair. "We hope that by understanding how specific methylation patterns are generated in plants, we can provide insights into how DNA methylation is regulated in other organisms."

Knowledge of this mechanism for regulating DNA methylation could help scientists develop strategies for correcting epigenetic defects that are associated with reduced yields in crops, or diseases--such as cancer-in humans. In the future, the lab is interested in exploring how DNA methylation patterns are controlled during development and in response to the environment.

The work was funded by the National Institutes of Health (GM112966), the Hearst Foundation, a Pioneer Fund Postdoctoral Award, the Glenn Center for Aging Research at the Salk Institute, the National Cancer Institute (CCSG: P30 014195), L. and C. Greenfield, the Chapman Foundation and the Helmsley Charitable Trust.

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Breast cancer: Discovery of a protein linked to metastasis

Treatment targeting AXL could reduce the risk of metastasis

Jean-François Côté, a researcher at the Montreal Clinical Research Institute (IRCM) and professor at Université de Montréal's Faculty of Medicine, studies metastasis, the leading cause of cancer-related death. Recently, his team uncovered a protein that, once deactivated, could prevent the development of metastases in an aggressive type of cancer, HER2-positive breast cancer.

One in eight women will be diagnosed with breast cancer in her lifetime and one in 30 is expected to die from it. The findings, published in the journal Cell Reports, could improve this prognosis.

'Cunning' cells

A cancerous tumour develops when cells proliferate at an abnormally high rate and agglomerate in healthy tissue. Some of these cells are even more cunning. "Sometimes, cancer cells manage to leave the tumour to spread in the body, which complicates the evolution of the disease," said Côté, director of the IRCM's Cytoskeletal Organization and Cell Migration Research Unit.

These cells move more easily than most of their peers. They detach from the tumour, enter the bloodstream and reach other organs, for example the lungs, bones or the brain. Called 'metastatic cells,' they are more difficult to destroy as they spread to other parts of the body and are more resistant to current treatments; 90 per cent of breast-cancer deaths are caused by metastases. Hence, one priority in oncology is to prevent tumour cells from spreading because it has the potential of saving many lives.

A promising target

Côté and his collaborators have taken a step towards actually blocking metastases. In their study, the IRCM team demonstrated that a protein, AXL, influences the occurrence of metastasis in HER2-positive cancer, an aggressive type that accounts for 20 per cent of breast cancers. In HER2-positive breast cancers, cells with high levels of AXL are more likely to detach from tumours to form metastases.

The research was done on mice and with samples of tumour cells taken from cancer patients in Montreal. Statistical indicators about patients are also encouraging. In women with HER2-positive cancer, it was found that the less AXL is present, the better the survival rate. Previously, researchers had linked the AXL protein to another type of cancer, triple negative breast cancer, but no one had examined its presence in HER2-positive cancer before Côté and his team.

"Based on this discovery, a treatment targeting AXL could reduce the risk of metastasis," said Côté.

It has already been shown that the action of AXL can be hindered. The IRCM researchers administered an AXL-inhibiting drug therapy to mice with HER2-positive tumours and found that metastases were less prone to develop. The drug is currently being tested in clinical trials for various therapeutic uses. If subsequent studies are as successful, this treatment could also be used to treat breast cancer patients. It would act as a complement to therapies targeting the HER2-positive tumour.

Further work is already underway in the IRCM laboratory.

"At the moment, we are checking whether the tumour's environment, such as blood vessels and the immune system, is affected when AXL is inhibited," said Côté. By getting a better picture of the phenomenon, it will be one more step towards treating the disease.

About the study

The research was conducted at the IRCM Cytoskeletal Organization and Cell Migration Research Unit by Marie-Anne Goyette, Stéphanie Duhamel, Ariane Pelletier, Marie-Pier Thibault and Jean-François Côté. Léo Aubert, Philippe Roux and Louis Gaboury, of UdeM's Institute for Research in Immunology and Cancer; Paul Savage, Radia Marie Johnson, William J. Muller and Morag Park of McGill University; Peter Carmeliet of University of Leuven; and Jean-Philippe Gratton of UdeM's Department of Pharmacology and Physiology, also collaborated on the study.

The research was funded by the Transat Breast Cancer Research Chair, the Canadian Institutes of Health Research, the Fonds de recherche du Québec - Santé, the Quebec Breast Cancer Foundation, the Cole Foundation and the Diane and Sal Guerrera Chair in Cancer Genomics.

https://wb.md/2Idvs8O

Bad News for BBQ Lovers: Grill at Your Own Risk

More bad news for barbecue lovers

Charles P. Vega, MD

Hello. I'm Dr Charles Vega, and I am a clinical professor of family medicine at the University of California at Irvine. Welcome to Medscape Morning Report, our 1-minute news story for primary care.

Just as our patients are looking forward to firing up their barbecue grills, we have more bad news for them.

A high consumption of meat, poultry, or fish cooked by grilling, broiling, or roasting at high temperatures may raise blood pressure. A study of 87,000 adults showed that eating these foods more than 15 times per month was associated with a 17% higher risk for hypertension. The risk was also increased by eating more "well-done" meats.

The link between hypertension and grilled foods is a new finding. The carcinogenic potential of grilling is already known. The same hazardous chemicals that might cause cancer are also believed to cause hypertension. It may be time to tell patients to go easy on those grilled foods and well-done meats.

http://bit.ly/2KRFwpS

Can chimpanzee vocalizations reveal the origins of human language?

While closely related to humans, researchers discover that chimpanzees' vocalizations resemble human language less than you'd expect

WASHINGTON, D.C. - It's very difficult to determine when, how and why human language began. While fossil primates provide important clues about human evolution, the sounds they made and the soft tissue involved in making those sounds weren't preserved.

But chimpanzees -- one of our closest living relatives -- provide important points of comparison for inferring the sorts of sounds our early ancestors may have made. During the 175th Meeting of the Acoustical Society of America, being held May 7-11, 2018, in Minneapolis, Minnesota, Michael Wilson, an associate professor at the University of Minnesota, will present his group's work searching for similarities between the vocal communications of chimpanzees and humans.

"Chimpanzees give a range of different calls: hoots, pant-hoots, pant-grunts, pant-barks, rough-grunts, nest-grunts, alarm barks, waa-barks, wraas, screams, copulation screams, and soft panting play sounds (a.k.a. laughter)," Wilson said. "Many of these calls grade into one another, and it can be difficult to categorize particular examples of some calls."

Wilson's group works with new and archival recordings of chimpanzees from Gombe National Park in Tanzania, the site where Jane Goodall, renowned primatologist and anthropologist, began the first long-term field study of chimpanzees.

"When Jane gives public talks, she often begins by giving a pant-hoot: a loud call that begins with an introduction, followed by a build-up, a climax and a let-down. Much of the work on chimpanzee vocalizations has focused on pant-hoots because they're loud, conspicuous, and seem to be important," Wilson said.

For their work, Wilson's group records calls from chimpanzees at Gombe using hand-held directional microphones and digital recorders. And, until recently, they applied simple statistical models -- such as principal components analysis -- to small sets of features like the duration of different call components, fundamental frequency, and frequency range. "More recently, my student Nisarg Desai has adapted techniques from speech technology, such as machine learning models, to better categorize calls," Wilson said.

Chimpanzee vocal communication is also interesting because it "raises questions about the evolution of signaling and social behavior," Wilson said. "Do chimpanzee pant-hoots inform other chimpanzees about good food patches, signal community membership, or individual identity, body size, or health?"

The group's findings so far suggest that chimpanzee vocalizations resemble human language less than you'd expect. For example, Wilson's student Lisa O'Bryan studied food-associated rough-grunt calls at Gombe and in a group of captive chimpanzees in Texas. "In contrast to some previous studies, which reported that rough-grunts vary acoustically in ways that could inform other chimpanzees about food quality, she found that within rough-grunt sequences to a given food type, chimpanzees produce a range of rough-grunt variants -- suggesting there is no consistent match between acoustic features and food quality," Wilson said.

And, it turns out, "chimpanzee vocal communication isn't particularly languagelike," Wilson said. "This is surprising, given that chimpanzees resemble us in so many other ways. But it seems that the key events in language evolution occurred well after the divergence of the chimpanzee and hominin (primate) lineages. In this case, language likely evolved due to uniquely human circumstances."

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Bridgehead effect found to be a major driver for invasive species infestations

Species invading one place, surviving, and then migrating to another appears to be a major driver for new infestations

by Bob Yirka, Phys.org report

A team of researchers from Switzerland, France and New Zealand has found evidence suggesting that the bridgehead effect is a major driver for invasive species infections. In their paper published in *Proceedings of the National Academy of Sciences*, the group describes their study of global alien ant spread and how they believe it has come about.

Ants are among the most invasive species on the planet. They now exist on every continent except Antarctica. An impressive 241 species have been recorded as being transported by humans to new geographic locations, and 19 of those are considered invasive. But not all invasions

occur as the result of direct transport. Some species have managed to invade one place, survive, and then migrate to another—a process known as the bridgehead effect. These secondary invasions, the team reports, appear to be a major driver for new infestations.

To learn more about invasive species, the researchers focused only on ants. They looked at data from two major sources—both using border inspection data. One dataset came from 4,533 border interceptions in the US covering the years 1914 to 1984. The second from New Zealand covering the years 1955 to 2013. The U.S. data revealed that 51 distinct ant species were observed while the New Zealand dataset recorded 45 alien species. But what was surprising, the team noted, was that most of the alien species did not arrive from the species origin point, but from a secondary location. More specifically, they found that 75.7 percent of the ant interceptions in the U.S. came from secondary locations—the number was even higher for New Zealand at 87.8 percent. They also noticed that the interceptions increased when they came from countries that were physically closer. And they further noted that in some instances, ants that traveled the most tended to be more successful in invading a secondary location. And the more they settled elsewhere, they more they moved to other places—setting up a snowball scenario. The findings show that it is not enough simply to account for the original location of an invasive species. To better understand how plants and animals make their way across geographic spans, researchers need to follow the hops they make as well.

More information: *Cleo Bertelsmeier el al., "Recurrent bridgehead effects accelerate global alien ant spread," PNAS (2018).* *www.pnas.org/cgi/doi/10.1073/pnas.1801990115*

Abstract

Biological invasions are a major threat to biological diversity, agriculture, and human health. To predict and prevent new invasions, it is crucial to develop a better understanding of the drivers of the invasion process. The analysis of 4,533 border interception events revealed that at least 51 different alien ant species were intercepted at US ports over a period of 70 years (1914–1984), and 45 alien species were intercepted entering New Zealand over a period of 68 years (1955–2013). Most of the interceptions did not originate from species' native ranges but instead came from invaded areas. In the United States, 75.7% of the interceptions came from a country where the intercepted ant species had been previously introduced. In New Zealand, this value was even higher, at 87.8%. There was an overrepresentation of interceptions from nearby locations (Latin America for species intercepted in the United States and Oceania for species intercepted in New Zealand). The probability of a species' successful establishment in both the United States and New Zealand was positively related to the number of interceptions of the species in these countries. Moreover, species that have spread to more continents are also more likely to be intercepted and to make secondary introductions. This creates a positive feedback loop between the introduction and establishment stages of the invasion process, in which initial establishments promote secondary introductions. Overall, these results reveal that secondary introductions act as a critical driver of increasing global rates of invasions.

http://bit.ly/2I6GTDj

Simple post-surgery step reduces bladder cancer recurrence

Flushing the bladder with a common chemotherapy drug immediately after surgery significantly reduces the chances of bladder cancer returning

PORTLAND, OR - Flushing the bladder with a common chemotherapy drug immediately after surgery significantly reduces the chances of bladder cancer returning, according to a major study by SWOG, an international clinical trials network funded by the National Cancer Institute.

The research was led by Edward M. Messing, M.D., a SWOG investigator and professor of urology, and a professor of oncology and pathology, at the University of Rochester School of Medicine and Dentistry and a physician at the Wilmot Cancer Institute.

Published in the May 8 edition of the *Journal of the American Medical Association* (JAMA), the study notes this may be the first phase III trial in the U.S. to show a benefit from this treatment strategy in two decades. European and Canadian urologists have been using it for years, with their own clinical trial data to support the procedure.

"The real importance of this study is that we now have a readily available drug that's fairly inexpensive, well-tolerated, and effective," Messing said. "One of the biggest issues with low-grade bladder cancer is that it frequently returns. I know some patients who have to undergo four surgeries a year, and if we can cut down on these recurrences, we will save a lot of people a lot of pain, money, and time lost to recovery."

The JAMA study says the findings "support using this therapy," but adds that further research is needed to compare various chemotherapy agents for their effectiveness. About 80,000 Americans a year are diagnosed with bladder cancer, and the low-grade non-muscle invasive form makes up about half of the new cases annually.

The SWOG team conducted the randomized, double-blind clinical trial involving 406 eligible patients at 23 cancer centers.

Surgeons removed all cancerous tissue with a procedure known as TURBT, or transurethral resection of bladder tumor. Then, 201 patients received the chemotherapy drug, gemcitabine, mixed with saline, administered via catheter to the bladder area within three hours after surgery. Gemcitabine works by blocking new DNA and killing any dividing cells. It's used to treat several other cancers, including advanced bladder cancer, but had not been studied in this setting among low-grade cancer patients. The second group of 205 patients received saline alone.

Researchers followed all patients for four years -- the time period when most bladder cancers return -- seeking to discover which treatment strategy worked better. The results were clear: A 34 percent reduction in the risk of recurrence for patients receiving the gemcitabine infusion. Sixty-seven patients in the gemcitabine group, or 35 percent, experienced a recurrence, compared with 91 patients in the saline group, or 47 percent.

Messing is a former president of the Society of Urologic Oncology, and later this month will receive the American Urological Association (AUA) Ramon Guiteras Award, honoring 35 years of accomplishments that have improved care for patients with urologic cancers. He presented this data in 2017 at the AUA annual meeting.

The trial, S0337, was supported by the NCI of the National Institutes of Health under Award Numbers CA180888 and CA180819. Eli Lilly and Company also supported the work. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or Eli Lilly and Company.

Messing's SWOG study team includes: Cathy Tangen, DrPH, of Fred Hutchinson Cancer Research Center; Deepak Sahasrabudhe, MD, of University of Rochester; Theresa Koppie of Oregon Health & Science University; David Wood Jr., MD, of Beaumont Health; Philip Mack, PhD, of UC Davis Cancer Center; Robert Svatek, MD, of UT Health San Antonio; Christopher Evans, MD, UC Davis Cancer Center; Khaled Hafez, MD, of University of Michigan; Daniel Culkin, MD, of University of Oklahoma; Timothy Brand, MD, of Madigan Army Medical Center; Lawrence Karsh, MD, of The Urology Center of Colorado; Jeffrey Holzbeierlein, MD, of University of Kansas Cancer Center; Shandra Wilson, MD, of University of Colorado; Guanming Wu, PhD, of Oregon Health & Science University; Melissa Plets, MS, Fred Hutchinson Cancer Research Center; Seth Lerner, MD, Baylor College of Medicine; Nicholas Vogelzang, MD, Comprehensive Cancer Centers of Nevada; and Ian Thompson, Jr., MD, of CHRISTUS Santa Rosa Medical Center.

http://bit.ly/2wvd2it

Does HPV vaccination prevent the development of cervical cancer?

Are there harms associated with being vaccinated?

New evidence published today in the Cochrane Library shows that human papilloma virus (HPV) vaccines protect against cervical lesions in young women, particularly in those who are vaccinated between the ages of 15 and 26. It also summarizes findings on harms that have been assessed in randomized controlled trials.

Most people who have sexual contact at some point in their life will be exposed to the human papilloma virus (HPV). In the majority of women, HPV infection will be cleared by the immune system. When the immune system does not clear the virus, persistent HPV infection can cause abnormal cervical cells. These lesions are known as cervical 'precancer' because over time they can progress to cervical cancer if left untreated.

There are many different types of HPV. Some are associated with the development of cervical lesions that can become cancerous and are considered as high-risk HPV types. Two of these high-risk types (HPV16 and HPV18) account for about 70% all cases of cervical cancer worldwide. Vaccines have been developed that help the immune system to recognize certain HPV types. Because cervical cancer can take several years to develop, regulatory bodies and international health

agencies such as the World Health Organization (WHO) regard cervical lesions as the preferred outcome measure for HPV vaccine trials.

A team of Cochrane researchers has summarized results of 26 studies in 73,428 women conducted across all continents over the last eight years. Most women in the studies were under the age of 26 years old, although three trials recruited women between 25 and 45 years. The studies were well-designed, randomizing the women to either HPV vaccine or a placebo. The review evaluates evidence for two vaccines: the bivalent vaccine targeting HPV16 and 18, and the quadrivalent vaccine targeting HPV16/18 and two low-risk HPV types causing genital warts. The newer vaccine that targets nine HPV types was not included in the review since it has not been compared against a placebo in a randomized controlled trial.

The review looked at two groups of people: women who are free of high-risk HPV at the time of vaccination and all women regardless of HPV status at vaccination. The effects of the vaccine were measured as precancer associated with HPV16/18 and precancer irrespective of HPV type. The review looked at data from ten trials assessing cervical lesion data at between three and a half to eight years after vaccination.

None of the studies have followed up participants for long enough to detect an effect on cervical cancer. The researchers looked at precancer cervical lesions instead. They found that in young women who did not carry HPV, vaccination reduced the risk of developing precancer. About 164 per 10,000 women who got placebo and 2 per 10,000 women who got the vaccine went on to develop cervical precancer.

The researchers also looked at data from all enrolled women regardless whether they were free of high-risk HPV at vaccination or not. Among women aged 15 to 26 years, vaccines reduced the risk of cervical precancer associated with HPV16/18 from 341 to 157 per 10,000. HPV vaccination reduced also the risk for any precancer lesions from 559 to 391 per 10,000.

In older women vaccinated between 25 to 45 years the HPV vaccine does not work as well. This might be because older women are more likely to have been exposed already.

The evidence also shows that the vaccines do not appear to increase the risk of serious side effects which was about 7% in both HPV vaccinated or control groups. The researchers did not find increased risk of miscarriage in women who became pregnant after vaccination. However, they emphasize that more data are required to provide greater certainty about very rare side effects and the effect vaccines have on rates of stillbirth, and babies born with abnormalities in those who became pregnant around the time of vaccination.

Cochrane lead author, Dr. Marc Arbyn, of the unit Cancer Epidemiology, Belgian Cancer Centre, Sciensano, said: "The findings of this review should be viewed within the context of multiple global surveillance studies, which have been conducted by the Global Advisory Committee on Vaccine Safety from the WHO since the vaccinations were licensed. The committee concluded that the risk-benefit profile of prophylactic HPV vaccines remains favourable and expressed its concerns about unjustified claims of harm that lack biological and epidemiological evidence, and which may affect the confidence of the public. At the same time, the Committee encouraged health authorities to continue surveillance and examination for potential adverse events."

Dr. Jo Morrison, Consultant in Gynaecological Oncology at the Musgrove Park Hospital, Somerset, UK, said: "Vaccination aims to prime the immune system to produce antibodies that can block subsequent natural HPV infection. These data show that immunizing against HPV infection protects against cervical precancer, and it is very likely that this will reduce cervical cancer rates in the future. However, it cannot prevent all cervical cancer and it is still important to have regular screening, even if you have been vaccinated."

She added: "Cervical cancer can take many years to develop following HPV infection and development of precancer lesions, therefore long-

term follow-up studies are needed to find out the effects of HPV vaccination on cervical cancer rates."

Editor's notes:

Full citation: Arbyn M, Xu L, Simoens C, Martin-Hirsch PPL. Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors. Cochrane Database of Systematic Reviews 2018, Issue 5. Art. No.: CD009069. DOI: 10.1002/14651858.CD009069.pub3.

Breakdown of results by sub-groups of women:

Women who are hrHPV DNA negative (only efficacy data for women aged 16-26y)

HPV vaccines reduce hgCIN associated with HPV16/18 from 164/10,000 to 2/10,000 (high certainty). They reduce also any precancer irrespective of HPV types from 287/10,000 to 106/100,000 (high certainty). HPV vaccination protects also against AIS associated with HPV16/18 (from 9 to 0 per 10,000) and any AIS (from 10 to 0/10,000) - moderate certainty for both AIS outcomes.

Women who are HPV16/18 DNA negative

The effect of HPV vaccines on risk of precancer differ by age group. In younger women, HPV vaccines reduce precancer associated with HPV16/18 from 113 to 6/10,000 (high certainty). HPV vaccines lower any precancer from 231 to 95/10,000 (high certainty). In females older than 25, the vaccines probably reduce precancer associated with HPV16/18 from 45 to 14/10,000 (moderate certainty).

Women unselected by HPV DNA status

In women vaccinated at 15 to 26 years of age, HPV vaccination reduces precancer associated with HPV16/18 from 341 to 157/10,000 (high certainty) and any precancer from 559 to 391/10,000 (high certainty).

In older women vaccinated between 25 to 45 years, the effects of HPV vaccine on precancer are smaller, and this may be due to previous exposure to HPV. The risk of precancer associated with HPV16/18 is probably lowered from 145/10,000 in unvaccinated women to 107/10,000 following HPV vaccination (moderate certainty). The risk of any precancer is probably similar between unvaccinated and vaccinated (341/10,000 compared with 356/10,000, moderate certainty).

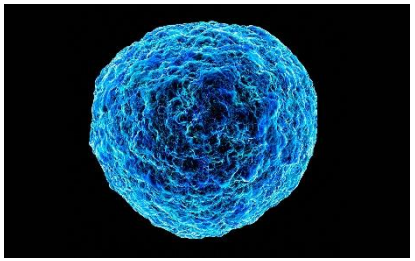
http://bit.ly/2KfXLEu

HIV Has a 'Long Lost' Cousin: What You Should Know About This Virus

It's related to HIV, yet you've probably never heard of it: a virus called human T-cell leukemia virus type 1, or HTLV-1.

But now, high rates of HTLV-1 in parts of Australia are prompting some scientists to call for increased efforts to prevent the spread of the disease, according to news reports.

In remote regions of central Australia, rates of HTLV-1 infection exceed 40 percent among adults, with indigenous communities most affected, according to CNN. "The prevalence is off the charts" in Australia, Dr. Robert Gallo, co-founder and director of the Institute of Human Virology at the University of Maryland School of Medicine, who helped discover HTLV-1 in 1979, told CNN. Yet there's been little research to develop treatments or a vaccine for the disease, Gallo said.



An illustration of human T cell leukemia virus (HTLV). **Science Photo Library/Alamy**

HIV vs. HTLV-1

But what exactly is HTLV-1, and how is it different from HIV?

HTLV-1 is a "distant cousin" of HIV that's found primarily in parts of sub-Saharan Africa, Latin America, the Caribbean, Japan and central Australia, according to Imperial College London. The virus infects white blood cells known as T cells, and in rare cases, it can cause aggressive leukemia, a cancer of white blood cells, according to the National Institutes of Health's Genetic and Rare Diseases Information Center (GARD). People infected with HTLV-1 can also develop a neurological condition that often results in losing the ability to walk, GARD said.

HTLV-1 shares some similarities with HIV, but there are also some key differences between the viruses. Like HIV, HTLV-1 can be spread through sexual activity, blood transfusions and the sharing of needles, and it can also pass from mother to child during birth or breastfeeding, according to GARD.

However, HTLV-1 is not as easily transmitted as HIV, and only a small proportion of people who get HTLV-1 will ever get sick, said Dr. William Schaffner, an infectious-disease specialist at Vanderbilt University Medical Center in Nashville, Tennessee. "Unlike HIV, which almost invariably makes you ill, only 2 to 6 percent of [people infected with HTLV-1] will ever develop an illness," Schaffner told Live Science.

This means that although an estimated 20 million people worldwide are infected with HTLV-1, the vast majority of those people will remain asymptomatic for their entire lives, according to a 2010 review paper on HTLV-1. (These infections are centered in certain parts of the world, meaning the infection is not very common outside of those areas. In the United States, a 2014 study of HTLV-1 and the related HTLV-2 among blood donors found that the rates of these infections were about 22 per 100,000 people, or 0.02 percent.)

In addition, people who do get sick from HTLV-1 usually don't show symptoms until about 20 to 30 years after they were infected, Schaffner said. For comparison, the median time from HIV infection to the development of AIDS is about 10 years, although it can be sooner for certain populations, according to the University of California, San Francisco.

These differences between HIV and HLTV-1 likely played a role in why the latter is less well-known, and less studied, Schaffner said.

But now "we have to make up for what we didn't do before," said Gallo, who also helped discover HIV after his work on HTLV. "We have to get attention to HTLV-1 quick," Gallo told CNN.

Schaffner noted that work done by Gallo and colleagues on HTLV was beneficial to studying HIV, and now the "work in HIV could cycle back … and help research in HTLV." In particular, the development of an HIV vaccine may help accelerate research into an HTLV vaccine.

"If we could solve the HIV vaccine puzzle, I think the results of that research" could perhaps be translated to help with the development of an HTLV vaccine, Schaffner said.

http://bit.ly/2IwGR6Z

Nutmeg's hidden power: Helping the liver

Nutmeg has been used for years in traditional Chinese medicine to treat gastrointestinal illnesses

Smelling nutmeg evokes images of fall, pumpkin pie and hot apple cider. But the spice has been used for years in traditional Chinese medicine to treat gastrointestinal illnesses. Now one group reports in ACS' *Journal of Proteome Research* that they have figured out how nutmeg helps other organs, specifically the liver.

According to the Food and Agriculture Organization of the United Nations, the world consumes 9,000 tons of nutmeg annually. Nutmeg is the seed of the *Myristica fragrans* tree, which is commonly found in Indonesia, and has been used to treat asthma, rheumatic pain, toothaches and infections. In the laboratory, researchers have shown that nutmeg can fight hyperlipidaemia, hyperglycemia, heart tissue damage and hepatotoxicity. Inspired by these studies, Xiu-Wei Yang, Frank Gonzalez, Fei Li and colleagues wanted to see how nutmeg prevents damage to the liver.

The researchers used a mouse animal model of liver toxicity to test the mechanism behind nutmeg's protective effects. Metabolomics analyses showed that nutmeg likely protected against liver damage by restoring the mice to more healthy levels of various lipids and acylcarnitines. Gene expression studies showed that peroxisome proliferator-activated receptor alpha (*PPARα*) was modulated by nutmeg, and the spice didn't protect mice from liver injury if the *PPARα* gene was deleted. In addition, the team found that a specific compound in nutmeg, myrislignan, had a strong protective effect against liver damage.

The authors acknowledge funding from the Nan-jing University, Yunnan Province, the National Key Research and Development Program of China, the U.S.-China Program for Biomedical Collaborative Research, the State Key Laboratory of Phytochemistry and Plant Resources in West China and the Thousand Young Talents Programs of China.

The abstract that accompanies this study is available here.

http://bit.ly/2KRVT5K

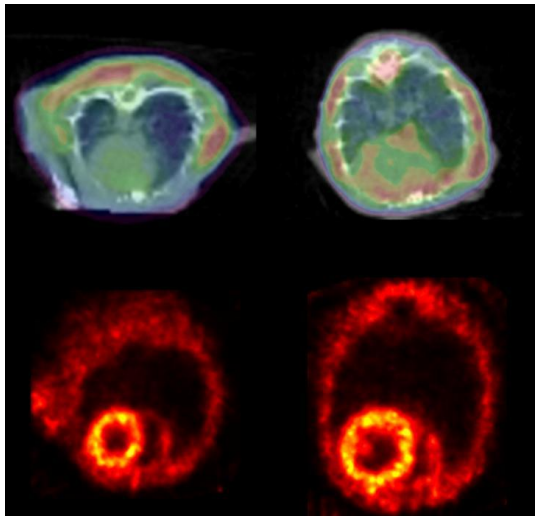
Heart failure: The Alzheimer's disease of the heart?

Protein clumping may contribute to heart failure development and could be used as a diagnostic tool for testing therapies or disease progression

Similar to how protein clumps build up in the brain in people with some neurodegenerative diseases such as Alzheimer's and Parkinson's diseases, protein clumps appear to accumulate in the diseased hearts of

mice and people with heart failure, according to a team led by Johns Hopkins University researchers.

In experiments described in the May 11 issue of the journal *Circulation Research*, the investigators report identifying in diseased hearts the form of the protein that tends to clump, and visualizing it in the heart using a noninvasive positron emission tomography (PET) scan could, they say, lead to advances in monitoring disease progression and testing new therapies.



A PET scan detects clumping proteins in rat hearts (top). The enlarged heart (right) is one with heart failure. Other PET scans showing blood flow in the rat hearts (bottom) show that the protein clumps aren't due to circulation problems.
Courtesy of Circulation Research, May 11, 2018

Heart failure is a chronic condition in which the heart doesn't fill or pump blood as well as it should, leading to excessive fatigue. About 5.7 million people in the U.S. have heart failure, and about half of people diagnosed will die within five years, according to the U.S. Centers for Disease Control and Prevention.

"From a molecular standpoint there's not a unified, clear mechanism for why the heart goes into failure," says Giulio Agnetti, Ph.D., assistant professor of medicine at the Johns Hopkins University School of Medicine and University of Bologna. "But by figuring out this mechanism, we may be able to devise better treatments and diagnostic tools."

Current drugs used to treat heart failure -- such as those that lower blood pressure by relaxing blood vessels -- reduce stress on the heart and symptoms associated with heart failure without necessarily fixing the underlying cause. Once the heart fails to pump, the only treatment in the end is a heart transplant.

Previous work by this team, published in 2014, showed that the protein desmin accumulates in clumps called amyloid in the hearts of dogs with heart failure. Desmin is a protein found in the cell's "skeleton," or supporting structure, and is known as intermediate filaments. Why it clumps in diseased heart cells isn't known, Agnetti says.

To see if desmin protein clumps are also found in human heart failure, the researchers studied the proteins from heart tissue biopsies from people with or without heart failure. They used a fluorescent antibody commonly used in Alzheimer's disease research and a new fluorescent stain for amyloid developed by Agnetti to visualize and quantify the desmin protein clumps. They observed twice as many desmin clumps in heart failure patients than those without heart failure.

The team used a common mouse model of heart failure to look for desmin clumps. In this model, the aorta -- the main artery coming from the heart -- is surgically constricted, which noticeably raises pressure and stress, and causes heart failure. After four weeks of pressure on the aorta, the mice develop symptoms of heart failure such as an enlarged heart and lung congestion. Desmin amyloid was more than doubled in the heart failure mice when using the same antibody and staining techniques used for the human tissue samples.

Then the researchers treated proteins from the mice hearts with epigallocatechin gallate (EGCG) -- a chemical from green tea known to break up amyloid. The treatment cut by half the amount of protein clumps.

"Interestingly, green tea has already been demonstrated to curb the incidence of cardiovascular disease as well as improve cognitive impairment in Alzheimer's models, though the mechanism for such action is unclear," says Agnetti. "EGCG's ability to 'de-clump' these sticky proteins could be one of green tea's healthy effects. Knowing how this chemical works could open new avenues for designing a new class of drugs that target protein clumping."

Next, the researchers wanted to identify the form of desmin that tended to clump. Based on their earlier work, they thought that one or more

chemical phosphate groups added to the 27th or 31st building blocks in desmin's protein structure might affect how the protein clumps. They genetically engineered versions of desmin with one, both or none of the phosphate groups attached to desmin, tagged them with a green fluorescent signal to make them visible, and put them in heart cells using a virus.

A week later, using a microscope to track the green glow, the cells with desmin and two phosphate groups were still pumping, and this form of desmin was incorporated in the muscle fibers. The researchers say they believe this shows that the desmin with two phosphate groups is most likely the normal, healthy version of the protein.

The cells that had a single phosphate on desmin at the 31st position in the protein's chain of amino acids contracted more rapidly and had more green clumps, leading the researchers to believe that this behaves as the diseased version of the protein.

Agnetti learned from Richard O'Brien, M.D., Ph.D., a former Johns Hopkins neuroscientist now at Duke University, that PET is used to detect protein clumps in the brains of Alzheimer's and Parkinson's disease patients and can detect the clumps in certain genetic heart conditions that cause excessive protein clump formation. Following O'Brien's advice, the researchers tested if they could use this noninvasive technique to detect desmin clumps in mice with heart failure. Healthy and heart failure mice were injected with Amyvid, a radioactive dye that allows the researchers to see the protein clumps by PET. The heart failure mice had 13 percent more of the Amyvid taken up in their hearts than the healthy mice.

"PET imaging of protein clumps may be eventually used in patients to identify structural changes in the heart as the disease progresses, and this information likely holds prognostic value," says Peter Rainer, M.D., Ph.D., a former postdoctoral fellow at Johns Hopkins who is now at the Medical University of Graz in Austria. "It could be used as a nice measure of the effect of an intervention to halt or reverse disease progression."

In future experiments, the research team plans to confirm its results in more human tissue samples. The investigators also hope to identify a drug or small molecule to prevent desmin from forming clumps.

"There is a lot of emphasis placed on the role of genes in modern times, but we're born with our genes and at present we can do very little about the ones we have," says Agnetti. "I think the next step is to follow up with the proteins that are dynamically modified in response to environment, which places a larger emphasis on lifestyle intervention to help prevent diseases. Natural compounds like EGCG in green tea and modified dietary interventions could play a role in keeping us healthy."

Additional authors include Nazareno Paolocci, Peihong Dong, Yuchuan Wang, Catherine Foss, Steven An, Martin Pomper and Gordon Tomaselli of Johns Hopkins; Matteo Sorge of the University of Turin; Justyna Fert-Bober, Ronald Holewinski and Jennifer Van Eyk of Cedars-Sinai; Alessandra Baracca and Giancarlo Solaini of the University of Bologna and Charles Glabe of the University of California, Irvine.

The study was funded by grants from the National Heart, Lung, and Blood Institute (R01 HL107361 and P01 HL107153), the American Heart Association (2SDG9210000 and 16IRG27240002) and the Magic That Matters Foundation.

https://bbc.in/2rz6Gc4

Ditch cranberry juice for urine infections

Drinking lots of cranberry juice is no way to fix a urine infection, say new draft guidelines from health body the National Institute for Health and Care Excellence.

Although some studies have claimed it may help, NICE says there is not enough good evidence to recommend it. Instead, people should drink plenty of water or fluids and take painkillers. They can also speak to their doctor who might prescribe antibiotics, but these drugs will not always be necessary.

Urinary tract infections (UTIs) are caused by bacteria. Sometimes the body can fight a mild infection alone without medication. When antibiotics are needed, the shortest course that is likely to be effective should be prescribed to reduce the risk of antimicrobial resistance, says NICE.

It might be more appropriate to get a back-up prescription to be used only if symptoms do not improve within 48 hours or if they worsen rapidly or significantly at any time.

Signs and symptoms of a UTI include:

- ***pain, burning or stinging when you urinate***
- ***needing to urinate more often or urgently than normal***
- ***dark, cloudy or smelly urine***
- ***pain in the lower abdomen***
- ***feeling generally unwell, achy, sick and tired***

Prof Mark Baker, director for the centre of guidelines at NICE, said: "We recognise that the majority of UTIs will require antibiotic treatment, but we need to be smarter with our use of these medicines. "Our new guidance will help healthcare professionals to optimise their use of antibiotics. "This will help to protect these vital medicines and ensure that no one experiences side effects from a treatment they do not need."

A consultation on the draft guidelines for England will close on 5 June.

https://bbc.in/2I7DjJ7

Potential new cure found for baldness

A potential new cure for baldness has been discovered using a drug originally intended to treat osteoporosis.

By Ian Westbrook Health reporter, BBC News

Researchers found the drug had a dramatic effect on hair follicles in the lab, stimulating them to grow. It contains a compound which targets a protein that acts as a brake on hair growth and plays a role in baldness. Project leader Dr Nathan Hawkshaw told the BBC a clinical trial would be needed to see if the treatment was effective and safe in people.

Only two drugs are currently available to treat balding (androgenetic alopecia):

- ***minoxidil, for men and women***
- ***finasteride, for men only***

Neither is available on the NHS and both have side-effects and are not always very effective, so patients often resort to hair transplantation surgery instead.

The research, published in PLOS Biology, was done in a lab, with samples containing scalp hair follicles from more than 40 male hair-transplant patients.

The researchers, from the University of Manchester, first latched onto an old immunosuppressive drug, cyclosporine A, used since the 1980s to prevent transplant organ rejection and reduce symptoms of autoimmune disease. The scientists found that the drug reduced the activity of a protein called SFRP1, a key growth regulator that affects many tissues including hair follicles. But because of its side effects, CsA was unsuitable as a baldness treatment.

The team went on to look for another agent that targeted SFRP1 and found that WAY-316606 was even better at suppressing the protein.

Dr Hawkshaw said the treatment could "make a real difference to people who suffer from hair loss".

What causes hair loss?

Hair loss is a daily occurrence and generally nothing to worry about. Some types are temporary and some are permanent.

You should see a doctor because of:

- ***sudden hair loss***
- ***developing bald patches***
- ***losing hair in clumps***
- ***head itching and burning***
- ***worry about hair loss***

Source: NHS Choices

http://bit.ly/2KSNsas

Study about 'shock therapy' for depression suggests more patients should try it sooner

After trying two other options and failing to get relief, ECT could provide cost-effective option, according to U-M researchers' analysis

ANN ARBOR, MI - Right now, very few depression patients receive the treatment once known as 'shock therapy', which today uses far milder electrical impulses than decades ago.

But a new study suggests that the modern form of the approach -- called ECT --should be made more available to patients who fail to get relief

from two other types of treatment, such as antidepressant medications and talk therapy.

The study, published in JAMA Psychiatry by a team from the University of Michigan Department of Psychiatry, looks at the cost-effectiveness of ECT. Its findings could inform depression care decisions by insurers and policy makers, as well as conversations between doctors and patients.

The researchers used data from recent, highly regarded clinical studies to create a simulation of patients' potential journeys through many depression treatment strategies.

The model found that for patients getting depression treatment for the first time, medication, psychotherapy or a combination of the two is more cost-effective than ECT. This also held true for patients whose first depression treatment choice didn't help them.

But for patients whose depression symptoms didn't ease after trying two different treatments - what psychiatrists call "treatment resistant" depression -- ECT emerged as a cost-effective choice.

Short for electroconvulsive therapy, ECT delivers brief, mild electrical impulses to the brain under short-term anesthesia. Although it may require more specialized care, opting for ECT as a third-line option could be cost-effective compared to other treatments, and it may significantly reduce the time that patients spend with depression symptoms, the study finds.

"Although choosing a depression treatment is a very personal choice that each patient must make with their physician based on their preferences and experience, our study suggests that ECT should be on the table as a realistic option as early as the third round of care," says lead author Eric L. Ross, a U-M Medical School student who will graduate with his M.D. just after the paper's publication and enter a psychiatry residency program this summer.

"ECT is often considered a last resort by patients and providers," says senior author Daniel Maixner, M.D. "Unfortunately, research shows that with multiple medication failures and long duration of illness -- sometimes many years -- the chance that patients can achieve remission drops quickly to very low numbers. ECT is the best treatment to produce remission. So, in addition to the clinical idea that ECT should be used sooner, our study adds another perspective highlighting that ECT is also cost-effective earlier in the treatment course of depression."

Maixner, an associate professor of psychiatry at U-M, directs the ECT program at Michigan Medicine, U-M's academic medical center.

More about the study

Ross and Maixner worked on the study with Kara Zivin, Ph.D., an associate professor of psychiatry, mental health services researcher and member of the U-M Institute for Healthcare Policy and Innovation, and the Veterans Affairs Center for Clinical Management Research.

In 2011, Zivin, Maixner and their U-M and VA colleagues showed that just 0.16 percent of VA patients who had depression nationwide received ECT. Their study also revealed wide variations in use of ECT by region, and by the race and medical health status of the patient. Other more recent studies have shown that patients receive ECT only after trying five to seven different antidepressants, and other medications.

Ross brought his experience in cost-effectiveness research to the project. He and his colleagues created a model that used data from the gold-standard national STAR*D study of drug- and psychotherapy-based depression treatment, and from randomized controlled studies and observational studies of ECT's initial effects, long-term maintenance and risk of relapse.

The model also used data from ECT clinical trials. It took a conservative approach based on those findings that assumed that half of patients who try ECT would get immediate and full relief, also called remission, though one-third might relapse after a year. ECT treatment regimens start with multiple sessions in the first few weeks, followed often by a brief or longer-term maintenance schedule.

By comparison, the STAR*D study showed that 33 percent of patients experienced remission after trying their first antidepressant, and only 25 percent of those who went on to try a second antidepressant

experienced remission. After that, STAR*D found diminishing returns: a third antidepressant-based treatment only helped about 15 percent of those who failed to get relief from the first two options they tried, and a fourth option only helped 7 to 10 percent of patients.

The U-M team's model suggests that instead of spending half of the four years after diagnosis with active depression symptoms, patients could be symptom-free two-thirds of the time.

The study predicts ECT as a third-line treatment would have an incremental cost-effectiveness ratio of $54,000 per quality-adjusted life year. This ratio, which measures the value received for the dollars spent to restore patients' quality of life, falls well below the $100,000 threshold usually considered worthwhile for health spending. The cost-effectiveness analysis focused on health care related costs, and did not take into account lost productivity by the individual due to depression, or time or travel costs for ECT or clinic appointments.

Next steps

Ross notes that the team had not expected ECT to come out as cost-effective for third-line use - they had expected this to be true for fifth- to sixth-line treatment. The findings suggest that if patients and physicians decide to try a third, fourth or fifth antidepressant or psychotherapy course, or combinations of medicine and therapy before they opt for ECT, the latter would will still be most cost-effective the sooner they decide to try it.

The new findings might also help physicians make the case to patients' insurers that ECT should be covered earlier in a treatment-resistant depression patient's course, Zivin notes.

"Coverage for ECT varies widely, and it's not clear why it should, since it's one of the most effective treatments we have," she says. "We shouldn't allow the stigma attached to the past incarnations of this approach to prevent its modern form from being seriously considered for appropriate patients. Increased coverage could also help address the widespread ECT service-area gaps that we've found in other research."

The study was funded by Zivin's grant from Veterans Affairs Health Services Research and Development Services.

Zivin and Maixner are members of the U-M Depression Center.

DOI: 10.1001/jamapsychiatry.2018.0768

http://bit.ly/2Iv2HI7

Words matter: Stigmatizing language in medical records may affect the care a patient receives

A Johns Hopkins study found that physicians who use stigmatizing language in their patients' medical records may affect the care those patients get for years to come.

When doctors read notes and descriptions from previous medical visits, says the study, published in the May edition of *The Journal of General Internal Medicine*, the language in those notes may play a role in how that patient is treated, as well as how aggressively the patient's pain is managed.

Mary Catherine Beach, M.D., M.P.H., designed the study to determine whether the language and descriptions used in patient records can perpetuate bias among physicians. More than 400 physicians-in-training -- medical students and residents -- were presented with one of two vignettes about a hypothetical patient, a 28-year-old man with sickle cell disease and chronic hip pain.

While the vignettes contained medically identical information, one used neutral language to describe the patient and his condition, while the other vignette contained nonessential language that implied various value judgements.

Beach and her research colleagues found that physicians-in-training who read the stigmatizing patient chart notes were significantly more likely to have a negative attitude toward the patient than those who read the chart containing more neutral language.

And not only did their attitudes change -- so did their treatment plans. Those physicians-in-training who had read the stigmatizing chart note decided to treat the patient's pain less aggressively.

Every clinician encounter with a patient is documented in a chart note. Symptoms, patient history, vital signs, test results, clinicians' assessments and treatment plans are all part of the medical record.

"This record may be the only source of information a new clinician has about some patients," says Beach. "We have to question the assumption that the medical record always represents an objective space."

The study's participants were introduced to the hypothetical Mr. R., an African-American man whose condition necessitates the use of a wheelchair. Both vignettes begin with Mr. R. visiting the hospital emergency department with a painful condition known as a vaso-occlusive crisis, common among patients with sickle cell disease. Among the standard treatments for this condition are opioids to treat pain and oxygen to combat the effects of sickled red blood cells' inability to oxygenate organs.

Examples of the differing notes on the hypothetical patient:

Examples of the differing notes on the hypothetical patient:

- ***"He has about 8-10 pain crises a year, for which he typically requires opioid pain medication in the ED."***
- ***"He is narcotic dependent and in our ED frequently."***
- ***"He spent yesterday afternoon with friends and wheeled himself around more than usual, which caused dehydration due to the heat."***
- ***"Yesterday afternoon, he was hanging out with friends outside McDonald's where he wheeled himself around more than usual and got dehydrated due to the heat."***
- ***"The pain is not alleviated by his home pain medication regimen."***
- ***"The pain has not been helped by any of the narcotic medications he says he has already taken."***
- ***"He is in obvious distress."***
- ***"He appears to be in distress."***
- ***"His girlfriend is by his side but will need to go home soon."***
- ***"His girlfriend is lying on the bed with shoes on and requests a bus token to go home."***

Even physicians-in-training who recognized the language as stigmatizing were more likely to form more negative opinions about the patient and to treat that patient's pain less aggressively.

"There is growing evidence that the language used to communicate in health care reflects and influences clinician attitudes toward their patients," says Anna Goddu, a Johns Hopkins University School of Medicine student who co-authored the study. "Medical records are an important and overlooked pathway by which bias may be propagated from one clinician to another, further entrenching health care disparities."

Goddu and her co-authors are encouraged by one particular result of the study.

"When prompted, the participants seemed able to reflect on how the words used in the chart notes communicated respect and empathy for the patient," she says. "To us, this seems like a promising point of intervention."

Beach adds that, in the study, medical residents had more negative attitudes than medical students toward the hypothetical patient.

"Attitudes seem to become more negative as trainees progress," she says. "It may be that trainees are influenced by negative attitudes and behaviors among their peers and seniors in the clinical setting."

Participants who identified as black or African-American generally had more positive attitudes toward the patient.

"That affirms what some other studies have shown," says Beach, "specifically, that African-American clinicians have more positive attitudes toward patients with sickle cell disease."

Goddu says that, while the topic deserves more research, she hopes this study opens some eyes.

"I hope our study makes clinicians think twice before including certain, nonessential points about a patient's history or demeanor in the medical record," she says.

In addition to Beach and Goddu, the study's authors are Katie O'Conor, Sophie Lanzkron, Mustapha Saheed and Carlton Haywood Jr., of the Johns Hopkins University School of Medicine, Somnath Saha, of the Oregon Health and Science University, and Monica Peek of the University of Chicago.

This work was supported by the Johns Hopkins University School of Medicine AMWA Dr. Elizabeth Small Grant for Urban Primary Care and the National Heart, Lung, and Blood Institute (R01HL088511).

COI: The authors declare they have no conflicts of interest.

http://bit.ly/2rDmhaM

Large clinical trials change experts' minds on prostate cancer screening

For men 55 to 69, it should be an individual choice. For 70 and older, don't bother.

Beth Mole - 5/10/2018, 1:22 AM

Prostate cancer screening is now something to consider for men aged 55 to 69, according to the federal panel tasked with making recommendations for such preventative care options. In a finalized recommendation released Tuesday, the US Preventive Services Task Force (USPSTF) revealed that it has officially warmed to the screening—ever so slightly.

Back in 2012, the task force famously recommended *against* the then-common blood screening for elevated levels of PSA protein, which can indicate prostate cancer as well as other conditions. But, given new data from large, randomized clinical trials showing that routine screening can save a small number of lives, the USPSTF now says the scales have tipped in screening's favor.

The USPSTF doesn't offer an emphatic endorsement, but rather, a cautious consideration:

"For men aged 55 to 69 years, the decision to undergo periodic prostate-specific antigen (PSA)–based screening for prostate cancer should be an individual one. Before deciding whether to be screened, men should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and preferences in the decision."

The task force still has the same recommendation for men aged 70 and over, which is against screening. The benefits still don't outweigh the risks for this age group, the panel says.

These latest recommendations are mostly in line with those of the American Urological Association, American College of Physicians, and the American Cancer Society, all of which stress informed, individual decision-making with the patient. The latter two organizations say men should consider the screening at 50, not 55, however. The American Academy of Family Physicians and the Canadian Task Force on Preventive Health Care, on the other hand, continue to recommend against screening.

Still, while no organization offers a resounding endorsement, and some advise against screening, the USPSTF's earlier recommendation was considered "controversial" at the time. The USPSTF has a knack for getting this label. This may be due in part to how it comes up with its recommendations. While some doctors and health experts may tend to focus on screening benefits and overall public health gains—i.e., the chance to catch a rare or unexpected cancer and the chance to save some number of lives over time, however small—the USPSTF carefully weighs evidence based on quality and the patient's individual benefits and harms, even taking into consideration intangible harms, such as stress and anxiety from false-positive test results. It also doesn't factor in costs. This includes the costs of an individual screening and may also extend to long-term costs such as how much individuals or healthcare systems overall might pay for future disease treatments—with or without screenings.

A bum rap

For prostate cancer screening, the USPSTF focused on the benefits and harms of screening and treatment. Prostate cancer is one of the most common types of cancers affecting men. In the US, the lifetime risk of getting a diagnosis is 13 percent, and the risk of dying from the disease is 2.5 percent. In 2013, approximately 172,000 US men were diagnosed, and almost 28,000 died.

Elevated PSA levels in the blood are most often used to catch the cancer early, but this screening can also pick up the benign condition of an enlarged prostate and inflammation. One trial found that men screened every two to four years for a 10-year period had a 15-percent chance of getting a false positive result. This can cause stress, anxiety, and lead to unnecessary diagnostic tests and biopsies, which come with their own set of harms and risks, including infection and pain.

A diagnosis may also pick up slow-developing prostate cancers that may otherwise have never been symptomatic or posed a danger to health—aka, "overdiagnosis." Follow-up from one large trial suggested that overdiagnosis was the case for 20 percent to 50 percent of the men diagnosed through routine screening. And treatments for prostate cancer, such as prostate removal and radiation therapy, have significant and common potential harms, such as long-term erectile dysfunction, urinary incontinence, and bothersome bowel symptoms. Even the more conservative "active surveillance" strategy for treatment—a sort of wait-and-see approach—comes with the anxiety and stress from sustained vigilance and repeated exams and screenings.

For these reasons (and others), the USPSTF recommended against routine screening in the past. But a new set of large clinical trials, including two in Europe, have highlighted the benefits of the screening. They suggested that for men aged 55 to 69 years, screening may avert about 1.3 deaths from prostate cancer over roughly 13 years per 1,000 men screened. The screening may also prevent about three cases of metastatic prostate cancer per 1,000 men screened.

This was enough to sway the USPSTF for the 55 to 69 age group. It assessed the quality of the data overall as "moderate" and upgraded its recommendation from a "D" (recommend against) to a "C" (provide screening for select patients based on individual circumstances.)

But, the new recommendations and existing data still leave a lot of unanswered questions. For instance, it's still not clear what screening intervals might be best and for whom—every two or four years? More frequently for African-Americans or people with a family history, both of which have higher risks of prostate cancer? There's simply not enough data to make good or clear calls on these specifics yet.

JAMA, *2018. DOI: 10.1001/jama.2018.3710 (About DOIs).*

http://bit.ly/2KYtqLR

A hangover pill? Tests on drunk mice show promise

Keep the buzz. Lose the hangover.

Yunfeng Lu *

"Civilization begins with distillation," said William Faulkner, a writer and drinker. Although our thirst for alcohol dates back to the Stone Age, nobody has figured out a good way to deal with the ensuing hangover after getting drunk.

As a chemical engineering professor and wine enthusiast, I felt I needed to find a solution. As frivolous as this project may sound, it has serious implications. Between 8 and 10 percent of emergency room visits in America are due to acute alcohol poisoning. Alcohol is the leading risk factor for premature deaths and disability among people aged 15-49 and its abuse leads to serious health problems, including cardiovascular and liver cancer. Despite these sobering facts, current treatments for alcohol overdose largely rely on the body's own enzymes to break down this drug.

I decided to design an antidote that could help people enjoy wine or cocktails or beer without a hangover, and at the same time create a lifesaving therapy to treat intoxication and overdose victims in the ER. I chose to create capsules filled with natural enzymes usually found in liver cells to help the body process the alcohol faster.

Together with professor Cheng Ji, an expert in liver diseases from Keck School of Medicine at the University of Southern California, and my graduate student Duo Xu, we developed an antidote and tested it in mice. Inspired by the body's approach for breaking down alcohol, we chose three natural enzymes that convert alcohol into harmless molecules that are then excreted. That might sound simple, because these enzymes were not new, but the tricky part was to figure out a safe, effective way to deliver them to the liver.

To protect the enzymes, we wrapped each of them in a shell, using a material the U.S. Food and Drug Administration had already approved for pills. We then injected these nanocapsules into the veins of drunk mice where they hurtled through the circulatory system, eventually arriving in the liver where they entered the cells and served as mini–reactors to digest alcohol.

We showed that in inebriated mice (which fall asleep much faster than drunk humans), the treatment decreased the blood alcohol level by 45 percent in just four hours compared to mice that didn't receive any. Meanwhile, the blood concentration of acetaldehyde – a highly toxic compound that is carcinogenic, causes headaches and vomiting, makes people blush after drinking, and is produced during the normal alcohol metabolism – remained extremely low. The animals given the drug woke from their alcohol-induced slumber faster than their untreated counterparts – something all college students would appreciate.

The ability to efficiently break down alcohol quickly should help patients wake up earlier and prevent alcohol poisoning. It should also protect their liver from alcohol–associated stress and damage.

We are currently completing tests to ensure that our nanocapsules are safe and don't trigger unexpected or dangerous side effects. If our treatments prove effective in animals, we could begin human clinical trials in as early as one year.

This sort of antidote won't stop people from going too far when consuming alcohol, but it could help them recover quicker. In the meantime, we plan on drinking responsibly, and hope that you do too.

*Professor Chemical and Biomolecular Engineering, University of California, Los Angeles

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http://bit.ly/2Gd5fFB

Kenyan cave sheds new light on dawn of modern man

Forty-eight thousand year-old crayons and shell beads were among a treasure trove of items unearthed by archaeologists at a cave in Kenya.

Archaeologists have discovered more than 30,000 items at the site which is shedding new light on the crucial time period when Homo sapiens first started showing signs of modern behaviour.

The research was led by archaeologist Dr Ceri Shipton of The Australian National University (ANU) School of Culture, History and Language, who said the Panga ya Saidi cave sequence dates back 78,000 years and is the only known site in East Africa with an unbroken archaeological record of human inhabitation. "It is the most beautiful site I have ever worked on. As soon as I saw it I knew it was special," Dr Shipton said. "It has a continuous record with people there right up until 500 years ago.

"The site has amazing levels of preservation with so many of the artefacts in mint condition."

Dr Shipton said the site, on the Kenyan south coast just north of Mombasa, was providing new insights into the Later Stone Age - a period of time beginning about 67,000 years ago associated with the rise of modern human behaviour and culture in Africa.

Items found in Panga ya Saidi cave. 1. A decorated bone 2. A broken bone arrow point 3. An awl made of tusk 4. An ochre crayon. 5-9. Ostrich egg shell beads, 10-13 are marine shell beads. Other items: miniaturized stone tools. **Francesco d'Errico and Africa Pitarch Marti.**

"You start to see things like decorated bones, beads made from marine shell or ostrich eggs, miniaturized stone tools, and bones carved into things like arrow points. This is the oldest date we have for when this behaviour is first observed," he said.

"Previous sites relating to this early period of modern human behaviour have all been in South Africa and the East African Rift Valley, this is the first site on the coast of East Africa and the first with such a continuous record."

Dr Shipton said it was highly unusual to find a site where early *Homo sapiens* were living in a tropical forest. "Early humans liked to be on open grassland where there is a lot of large animals for hunting," Dr Shipton said.

"These people were living in tropical forest hunting smaller animals like monkeys and small deer, animals you may need more sophisticated technology to catch."

"What is striking about this record is the innovations you see in technology and material culture, and the ability to exploit both forest and savannah environments. It is this kind of behavioural flexibility that allowed our species to populate the rest of the world outside of Africa."

Professor Andy Herries from La Trobe University Archaeology undertook archaeomagnetic analysis of the cave sediments which showed that the transition in stone tool technology took place during a particularly cold and dry glacial period.

"the site documents the earliest evidence of this style of microlithic Later Stone Age technology and shows how early modern humans were able to adapt to a range of new environments at this time," Professor Herries said. "It is a small precursor to our eventual habitation of every corner and environment on the planet."

Of more than 30,000 items found at the site, some of the most remarkable include 48,000 year old red ochre crayons and engraved bones. Dr Shipton was struck by the high-level preservation of the artefacts. "The stone tools are still sharp. The beads and engraved bones have survived intact which is really rare," he said.

"On the crayons we can still see the grooves where they have been used. They're in the same condition now as when people discarded them."

The study was published on Wednesday in the *Nature Communications* journal. The project was led by the Max Planck Institute for the Science of Human History.

http://bit.ly/2jR3mG2

Body's 'natural opioids' affect brain cells much differently than morphine

Study may help explain addictive nature of synthetic opioid drugs

A new study led by UC San Francisco scientists shows that brain cells, or neurons, react differently to opioid substances created inside the body - the endorphins responsible for the "natural high" that can be produced by exercise, for example - than they do to morphine and heroin, or to purely synthetic opioid drugs, such as fentanyl. The researchers say their findings may help explain why the use of synthetic opioids can lead to addiction.

Since both synthetic opioids and the natural, "endogenous" opioids produced in the brain bind to and activate opioid receptors on the surface of nerve cells, scientists have long assumed that both types of molecules target the same cellular systems. But the new research reveals that these molecules also activate opioid receptors inside cells, and that the locations of these activated intracellular receptors differ between natural and synthetic opioids.

In the new study, published in the May 10, 2018 issue of *Neuron*, the researchers report that this difference could help explain why the effects of synthetic opioid drugs are more rewarding than those produced by endogenous opioids.

"There has been no evidence so far that opioid drugs do anything other than what natural opioids do, so it's been hard to reconcile the experiences that drug users describe - that opioid drugs are more intensely pleasurable than any naturally rewarding experience that they've ever had," said Mark von Zastrow, MD, PhD, a professor of psychiatry at UCSF and senior author on the new paper. "The possibility that these opioid drugs cause effects that natural opioids cannot is very intriguing because it seems to parallel this extremely rewarding effect that users describe."

Researchers in von Zastrow's lab collaborated with Aashish Manglik, MD, PhD, assistant professor of pharmaceutical chemistry, to create a "biosensor" that binds to the opioid receptors along with an opioid drug or natural opioid. The tool allowed the scientists to see what's happening inside cells, giving them a closer look than ever before at opioids' effects. "It's a way of sniffing out where these receptors are active in the particular types of neurons in which opioids work," explained von Zastrow, a member of the UCSF Weill Institute for Neurosciences.

It has generally been thought that all opioid molecules, natural or synthetic, impart their signal only from receptors on the surface of the

cell. Opioid-bound receptors are then taken inside the cell to compartments called endosomes, but receptors were thought not to signal from this location. Overturning this long-held view, the research team discovered that receptors actually remain active in endosomes and they use the endosome to sustain the signal within cells.

But in the most intriguing twist, the research team discovered that morphine and synthetic opioids activate receptors in yet another internal location called the Golgi apparatus, where endogenous opioids are unable to produce any activation at all.

"It really surprised us that there was a separate location of activation for drugs in the Golgi apparatus that could not be accessed by endogenous opioids," said first author Miriam Stoeber, PhD, a postdoctoral researcher in von Zastrow's lab. "Drugs, which we generally thought of as mimics of endogenous opioids, actually produce different effects by activating receptors in a place that natural molecules cannot access."

Moreover, morphine and synthetic opioids crossed cell membranes without binding receptors or entering endosomes. They traveled directly to the Golgi apparatus, reaching their target much more quickly than endogenous opioids got into endosomes, taking only 20 seconds compared to over a minute. This time difference could be important in the development of addiction, the researchers said, because typically the faster a drug takes effect, the higher its addictive potential.

The scientists hope to apply their findings to create new types of opioid-based pain medications that have a lower risk for addiction. They also plan to screen other existing medications to see if they act more like natural or synthetic opioids.

"We're very excited about the possibility of leveraging these principles to develop better or more selective drugs that have the ability to get into the brain, but then differ in their activities at internal locations within individual neurons," says von Zastrow. "This is an area that hasn't been explored in drug development because people haven't been thinking about it, but the potential is there."

Other authors on the study were Damien Jullie and Braden Lobingier of UCSF; Toon Laeremans and Jan Steyaert of Vrije Universiteit Brussel, in Brussels, Belgium; and Peter Schiller of the Clinical Research Institute of Montreal, in Canada.

The research was supported in part by funding from the National Institute of Drug Abuse (DA10711, DA012864, DA004443, and DP5 OD 02304801), the Canadian Institutes of Health Research (MOP-89716), and the Swiss National Science Foundation (P2EZP3_152173 and P300PA_164712).

http://bit.ly/2rFaYPu

Simple walking test helps predict risk for cognitive issues after heart surgery

Research highlights the need for a more comprehensive evaluation of patient readiness for surgery

Chicago - The distance a patient can walk in 6-minutes before a heart operation may be a clue to whether that patient will develop problems with memory, concentration, and attention after the procedure, according to a study published online today in *The Annals of Thoracic Surgery*.

Broadly speaking, a decline in cognitive performance after surgery is known as postoperative cognitive dysfunction (POCD). With POCD, a patient's mental aptitude is weaker after surgery, resulting not only in a greater risk of complications, but also a lesser quality of life. Cognitive deterioration is increasingly recognized as a common occurrence after major surgery, especially among older adult patients.

"This study indicates that the easy and inexpensive 6-minute walk distance (6MWD) is a valuable assessment for identifying patients at a high risk for POCD," said Kazuhiro Hayashi, PT, MSc, of Nagoya University Hospital in Japan. "If we are able to identify patients who are at risk for POCD, we can provide early treatment and encourage them to better understand the dysfunction."

For this study, Hayashi and colleagues identified 181 patients who were undergoing non-emergency heart surgery between March 2014 and August 2015 at Nagoya University Hospital. The mean age of the patients was 71.4 years.

Patients performed the 6MWD test upon admission for their operations. Functional exercise capacity was measured by having patients walk the

length of a predetermined course at their own pace while attempting to cover as much ground as possible in 6 minutes. The distance covered in that duration was measured to the nearest meter. According to the results of this study, a low 6MWD was an associated risk factor for POCD after cardiac surgery. In fact, the lower the 6MWD was, the more significant the reduction in cognitive function postoperatively was. Of the study participants, 51 (28 percent) developed POCD.

"It is increasingly recognized that a patient's fitness level has an impact on how well he/she does after a surgical procedure," said Rakesh C. Arora, MD, PhD, of St. Boniface Hospital in Winnipeg, Canada, who was not involved with this research. "This study further highlights the need for the health care team to undertake a more detailed assessment of patients' physical fitness before the operation. The 6MWD is an important component of this evaluation."

According to Dr. Arora, the identification of patients at risk for POCD and other cognitive disorders should alert the health care team to consider modifying anesthetic and medication choices during-and-after the operations, as well as assist with discharge planning as patients transition to home. In addition, the health care team should consider strategies, such as prehabilitation, to optimize the patients' fitness before their operations. Dr. Arora explained that prehabilitation includes a combination of exercise training, education, and social support intended to improve patients' physical and psychological readiness for surgery.

"Prehabilitation may be of benefit to patients with poor physical fitness by improving postoperative recovery and post-discharge functional survival," said Dr. Arora. "Patient self-management and follow-through are essential, however, as is the patient's understanding of their health issues and their proposed plan of care."

Dr. Hayashi agrees that a multidisciplinary approach, which includes elements such as prehabilitation, is key to a better assessment and treatment outcome. "Precise preoperative risk assessment for postoperative complications is critical, and when indicated, supervised exercise before an operation should be recommended to improve functional exercise capacity before heart surgery," he said.

Notes for editors

The article is "Preoperative 6-Minute Walk Distance Is Associated With Postoperative Cognitive Dysfunction," by Hayashi K, Oshima H, Shimizu M, Kobayashi K, Matsui S, Nishida Y, and Usui A. It appears in The Annals of Thoracic Surgery, *published by Elsevier.*

http://bit.ly/2KjVtEa

Patients who have had an irregular heart beat can't ever be considered 'cured'

Patients with abnormal heart rhythm are at at a higher risk of stroke and need treatment even after heart rhythm seems normal

Patients with an abnormal heart rhythm that can leave them at a higher risk of suffering from stroke still need treatment even after their heart rhythm seems to have returned to normal, say researchers at the University of Birmingham.

Atrial fibrillation is the most common heart rhythm disturbance, affecting around 1.6 million people in the UK. Those with atrial fibrillation may be aware of noticeable heart palpitations, where their heart feels like it's pounding, fluttering or beating irregularly. Sometimes atrial fibrillation does not cause any symptoms and a person who has it is completely unaware that their heart rate is irregular.

People with atrial fibrillation are much more likely to develop blood clots and suffer from strokes. To avoid strokes it is important for them to take drugs to prevent blood clotting. Sometimes atrial fibrillation seems to go away and the heart goes back to its normal rhythm -the condition may then be deemed to have 'resolved'. Up until now it has been unclear as to whether the clot-prevention drugs can be safely stopped when the condition is 'resolved'.

Now a study by researchers at the University of Birmingham, published today in *The BMJ*, has found that people whose heart rhythm returns to normal continue to be at high risk of stroke and should continue to be treated.

Researchers looked at patient records from 640 general practices throughout the UK and compared the frequency of strokes in three

groups of people: those with ongoing atrial fibrillation; those whose records said that atrial fibrillation had resolved; and those who never had atrial fibrillation.

Dr Nicola Adderley, of the University of Birmingham's Institute of Applied Health Research, said: "What we found was that strokes were least common in people who never had atrial fibrillation, and much more common in people whose records said their atrial fibrillation had been resolved.

"Significantly, in recent years we found that strokes were nearly as common in people whose atrial fibrillation had resolved as in those with ongoing atrial fibrillation.

"Therefore, we can conclude that people with resolved atrial fibrillation continue to be at high risk of stroke."

The researchers also looked at patient treatment. What they found was that, while most people deemed to have atrial fibrillation as an ongoing condition continue to get the clot-prevention drugs they need, the vast majority of those whose atrial fibrillation had 'resolved' do not.

Dr Krish Nirantharakumar, of the University of Birmingham's Institute of Applied Health Research, added: "Our research demonstrates that although people with resolved atrial fibrillation continue to be at high risk of stroke, they are not getting their prevention drugs.

"Worryingly, we found that the problem seems to be becoming more common, with our research showing an increasing number of people are recorded as having atrial fibrillation as resolved and are highly unlikely to be given medication to prevent stroke."

The researchers said that in 2016 one in 10 people with atrial fibrillation - around 160,000 people in the UK - were classed to have had their condition resolved.

Professor Tom Marshall, of the University of Birmingham's Institute of Applied Health Research, added: "One possibility as to why people whose atrial fibrillation has resolved continue to be at high risk of stroke is that it had not really resolved in the first instance.

"Atrial fibrillation can be present one day and absent the next, so giving someone the all-clear may be a mistake. Another possibility is that it can come back. Many people don't know when they have this condition and it can come back without them or their doctor realising.

"GPs keep a register of people with atrial fibrillation, this means they are reviewed regularly and are prescribed clot-preventing drugs.

"But if the atrial fibrillation seems to have resolved they are taken off the register and rarely continue their treatment. It is as if they fall off the radar.

"We have shown they are still at high risk of stroke and should still be treated. We cannot ever safely consider atrial fibrillation to have resolved."

What causes atrial fibrillation?

When the heart beats normally, its muscular walls contract (tighten and squeeze) to force blood out and around the body.

They then relax so the heart can fill with blood again. This process is repeated every time the heart beats.

In atrial fibrillation, the heart's upper chambers (atria) contract randomly and sometimes so fast that the heart muscle cannot relax properly between contractions. This reduces the heart's efficiency and performance.

Atrial fibrillation occurs when abnormal electrical impulses suddenly start firing in the atria.

These impulses override the heart's natural pacemaker, which can no longer control the rhythm of the heart. This causes a sufferer to have a highly irregular pulse rate. Read more here:

https://www.nhs.uk/conditions/atrial-fibrillation/

http://bit.ly/2Izi2aG

How 250 Siberians Became the First Native Americans

The Americas are a big place, but the Native American group that first settled it was small — just about 250 people, according to a new genetic study.

By Laura Geggel, Senior Writer | May 10, 2018 02:42pm ET

These people, known as a founding group because they "founded" the first population, migrated from Siberia to the Americas by about 15,000

years ago, said study co-lead researcher Nelson Fagundes, a professor in the Department of Genetics at Federal University of Rio Grande do Sul, in Brazil.

Figuring out the size of founding groups is key, because it determines the amount of genetic diversity that gets passed on to the group's descendants, Fagundes said. That, in turn, could alter how effectively natural selection weeds out bad genes, Fagundes said.

"Large populations have very efficient selection, while in small populations, mildly deleterious alleles [versions of genes] can spread, which may increase genetic susceptibility to some diseases," Fagundes told Live Science in an email.

To investigate the size of the original Native American founding group, Fagundes and his colleagues studied DNA samples from 10 Native American individuals scattered across Central and South America, 10 people from different Siberian groups and 15 people from China. (The Native American groups included the Aché of Paraguay; the Bribri, Guatuso and Guaymi of Costa Rica; the Lengua of Argentina; The Quechua of Peru; and the Arara, Waiwai, Xavante and Zoró of Brazil.)

The researchers didn't include Native Americans from North America for the simple reason that many of them formed unions with people from later migrations, which would make the original founding group more challenging to pinpoint, Fagundes said.

Once they had the individuals' DNA, the researchers looked at nine regions, each containing about 10,000 base pairs, or letters, on each person's genome.

Researchers know that genetic variation within a sample (such as Native Americans) is directly related to population size, Fagundes said. That, combined with the fact that genetic divergence between two populations (such as the Native Americans and Siberians) increases with time, allowed the researchers to plug the DNA data into computer simulation models and work backward to figure out the original size of the founding group.

The models found that between 229 and 300 people were in the original group, which led to the final estimate of 250 people, the researchers said. This number is so small, it would have created a "genetic bottleneck," meaning there was little genetic variation associated with the first major migration wave into the Americas, Fagundes said.

However, so much time has passed since that original group arrived in the Americas, that Native Americans as a whole have had time to recover their genetic diversity through new genetic mutations, he noted. Moreover, some Native Americans in North America formed unions with people from later migrations, which also increased genetic diversity, Fagundes said.

Just a guess

It's important to note that the 250 number is just an estimate, Fagundes said. "One must keep in mind that it is very hard (not to say impossible) to estimate how many real individuals correspond to this figure of about 250 effective individuals," Fagundes wrote in the email.

Even so, the estimate is similar to the findings of other studies. "This bottleneck probably involved less than 1,000 effective individuals, even though lower values (say between 150-700 effective individuals) seem more likely," Fagundes said. "There have been some even lower estimates around, but our data doesn't support them."

Estimating the size of the genetic bottleneck is important because it helps scientists figure out how many genetic markers are needed to capture the genetic diversity of Native American populations in studies, as well as to evaluate how harmful or beneficial different versions of genes are in this population, the researchers said.

The genetic data illustrates how ancient migration unfolded in the Americas, said study co-researcher Michael Crawford, a professor of anthropology at Kansas University.

Native Americans would settle in a new place, and as the population — and thus, fertility — grew, people from one population would break off and form another population in a neighboring area, Crawford said. "After 15,000 years, you can put them all the way down in Argentina,"

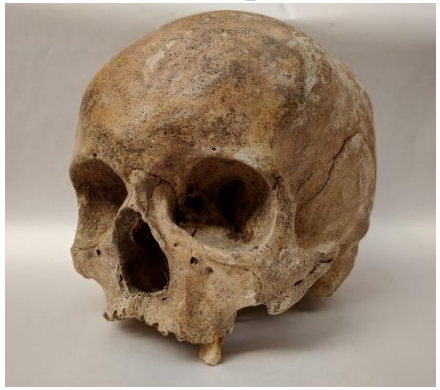
Crawford said in a statement. The study was published May 1 in the journal Genetics and Molecular Biology.

http://bit.ly/2wIO6V4

A European origin for leprosy?

The largest study to date on ancient leprosy DNA reveals previously unknown diversity of strains in Medieval Europe

New research by an international team including scientists from the Max Planck Institute for the Science of Human History, the University of Tübingen, EPFL Lausanne and the University of Zurich has revealed that there was much more diversity in the leprosy strains circulating in Medieval Europe than previously thought.



Skeletal remains showing evidence of leprosy from the Odense St. Jørgen cemetery in Denmark, which was established in 1270 and existed until 1560.
Dorthe Dangvard Pedersen

This finding, based on the sequencing of 10 new ancient genomes from the leprosy-causing bacterium *Mycobacterium leprae*, complicates prior assumptions about the origin and spread of the disease, and also includes the oldest *M. leprae* genome sequenced to date, from about 400 AD in the United Kingdom.

Leprosy is one of the oldest recorded and most stigmatized diseases in human history. The disease was prevalent in Europe until the 16th century and is still endemic in many countries, with over 200,000 new cases reported annually. The bacterium *Mycobacterium leprae* is the main cause of leprosy. Previous research on the bacterium suggested that it clusters into several strains, only two of which were present in Medieval Europe. The present study, published in the journal PLOS Pathogens, aimed to further investigate the history and origin of *M. leprae* by looking for genetic evidence from a large number of ancient samples from throughout Europe.

10 new ancient genomes of *M. leprae* dating from approximately 400-1400 AD

The current study examined approximately 90 individuals with skeletal deformations that were characteristic of leprosy, from across Europe and from time periods ranging from approximately 400 AD to 1400 AD. From these samples, 10 new medieval *M. leprae* genomes were fully reconstructed. These genomes represent all known strains, including strains that are today associated with different locations around the globe, including Asia, Africa and the Americas. Additionally, in this study multiple strains were often found in the same cemetery, illustrating the diversity of the leprosy strains circulating throughout the continent at the time.

"We found much more genetic diversity in ancient Europe than expected," explains Johannes Krause, senior author of the study and a director at the Max Planck Institute for the Science of Human History. "Additionally, we found that all known strains of leprosy are present in Medieval Europe, suggesting that leprosy may already have been widespread throughout Asia and Europe in antiquity or that it might have originated western Eurasia."

Oldest leprosy genome to date

One *M. leprae* genome reconstructed by the team was from Great Chesterford, England, and dates to between 415-545 AD. This is the oldest *M. leprae* genome sequenced to date and comes from one of the oldest known cases of leprosy in the United Kingdom. Interestingly, this strain is the same found in modern-day red squirrels and supports the hypothesis that squirrels and the squirrel fur trade were a factor in the spread of leprosy among humans in Europe during the medieval period.

"The dynamics of *M. leprae* transmission throughout human history are not fully resolved. Characterization and geographic association of the most ancestral strains are crucial for deciphering leprosy's exact origin" states lead author Verena Schuenemann of the University of Zurich. "While we have some written records of leprosy cases that predate the

Common Era, none of these have yet been confirmed on a molecular level."

The abundance of ancient genomes in the current study has resulted in a new and older estimate for the age of *M. leprae* than previous studies, placing its age at least a few thousand years old. "Having more ancient genomes in a dating analysis will result in more accurate estimates," explains Krause. "The next step is to search for even older osteological cases of leprosy than currently available, using well-established methods for identification of potential cases."

http://bit.ly/2rGrv6k

Discovery of novel biomarker with remarkable specificity to rheumatoid arthritis

University of Tsukuba-centered researchers first in world to identify citrullinated ITIH4 protein with high specificity in patients with rheumatoid arthritis

Tsukuba, Japan - Rheumatoid arthritis (RA) is an autoimmune disorder that occurs when the immune system mistakenly attacks the body's tissues. Unlike the wear-and-tear damage of osteoarthritis, rheumatoid arthritis affects the lining of the joints, causing painful swelling that can eventually result in bone erosion and joint deformity.

Most RA patients are positive for anticitrullinated protein antibodies (ACPA), and these antibodies are highly specific for RA diagnosis. ACPA recognizes various citrullinated proteins, such as fibrinogen, vimentin and glucose- 6-phosphate isomerase. Citrullinated proteins are proteins that have the amino acid arginine converted into the citrulline, which is not one of the 20 standard amino acids encoded by DNA in the genetic code. Autoreactivity to citrullinated protein may increase susceptibility to RA.

While many candidate citrullinated antigens have been identified in RA joints, the involvement of citrullinated proteins in blood serum remains mostly uninvestigated. To that end, a team of University of Tsukuba-centered researchers set out to explore the expression and commonality of citrullinated proteins in peptide glucose-6-phosphate isomerase-induced arthritis (pGIA) and patients with RA, and went one step further to investigate its correlation with RA disease activity. The researchers recently published their findings in Arthritis Research & Therapy.

"We examined serum citrullinated proteins from pGIA by western blotting, and the sequence was identified by mass spectrometry. With the same methods, serum citrullinated proteins were analyzed in patients with RA, primary Sjögren's syndrome, systemic lupus erythematosus, and osteoarthritis as well as in healthy subjects," study corresponding author Isao Matsumoto explains. "In patients with RA, the relationship between the expression of the identified protein inter-alpha-trypsin inhibitor heavy chain 4 (ITIH4) and clinical features was also evaluated, and the levels of citrullinated ITIH4 were compared before and after biological treatment."

The researchers found that citrullinated ITIH4 was highly specific to patients with RA, compared with patients with other autoimmune and arthritic diseases or in healthy subjects, indicating a potential role for citrullinated ITIH4 in RA pathogenesis. Notably, its levels were decreased in correlation with the reduction of disease activity score after effective treatment in patients with RA. Moreover, antibody response to citrullinated epitope in ITIH4 was specifically observed in patients with RA.

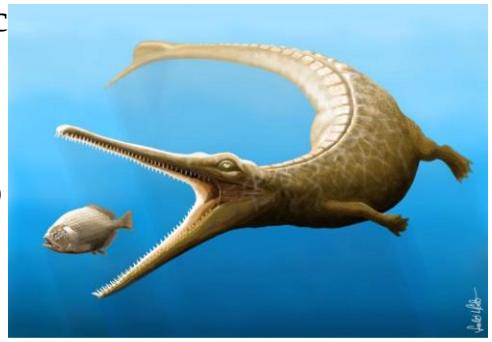
"Our results suggest that citrullinated ITIH4 might be a novel biomarker to distinguish RA from other rheumatic diseases and for assessing disease activity in patients with RA," Matsumoto says. "To our knowledge, this is the first report of its kind in the literature."

http://bit.ly/2Ga5Vvz

Jurassic fossil tail tells of missing link in crocodile family tree

A 180 million-year-old fossil has shed light on how some ancient crocodiles evolved into dolphin-like animals.

The specimen - featuring a large portion of backbone - represents a missing link in the family tree of crocodiles, and was one of the largest coastal predators of the Jurassic Period, researchers say.



The newly discovered species was nearly five metres long and had large, pointed teeth for grasping prey. It also shared key body features seen in two distinct families of prehistoric crocodiles, the team says.

This is an artist's impression of Magyarosuchus fitosi. **Marton Szabo**

Some Jurassic-era crocodiles had bony armour on their backs and bellies, and limbs adapted for walking on land. Another group had tail fins and flippers but did not have armour.

The new species was heavily armoured but also had a tail fin, suggesting it is a missing link between the two groups, researchers say.

It has been named *Magyarosuchus fitosi* in honour of the amateur collector who discovered it, Attila Fitos.

The fossil - unearthed on a mountain range in north-west Hungary in 1996 and stored in a museum in Budapest - was examined by a team of palaeontologists, including a researcher from the University of Edinburgh. It was identified as a new species based on the discovery of an odd-looking vertebra that formed part of its tail fin.

The study, published in the journal *PeerJ*, also involved researchers in Hungary and Germany. It was supported by the Leverhulme Trust and the SYNTHESYS project, part of the European Commission's Seventh Framework Programme.

Dr Mark Young, of the University of Edinburgh's School of GeoSciences, who was involved in the study, said: "This fossil provides a unique insight into how crocodiles began evolving into dolphin and killer whale-like forms more than 180 million years ago. The presence of both bony armour and a tail fin highlights the remarkable diversity of Jurassic-era crocodiles."

http://bit.ly/2wz6uiS

Preliminary research shows noninvasive therapy may reverse atherosclerosis

An injection may one day be able to reverse atherosclerosis

SAN FRANCISCO - An injection may one day be able to reverse atherosclerosis, according to emerging research presented at the American Heart Association's Vascular Discovery: From Genes to Medicine Scientific Sessions 2018, a premier global exchange of the latest advances in vascular biology for researchers and clinicians.

Atherosclerosis is characterized by a narrowing of arteries and blood vessels caused by a build-up of a hard, waxy substance called plaque, which is rich in cholesterol.

Drugs such as statins are used to control low density lipoprotein (LDL) the so-called bad cholesterol and thus decrease "plaque burden", explained Neel A. Mansukhani, M.D. lead author of the study and an integrated vascular surgery fellow at Northwestern University Feinberg School of Medicine in Chicago. "But statins have not been proven to reverse the disease." Mansukhani said.

Other treatment approaches for atherosclerosis, which can narrow blood vessels and arteries throughout the body, include bypass surgery and stenting, but neither reverses the disease and each can cause damage to the vessel wall, he said.

"Our aim was to develop a non-invasive, non-surgical, novel therapy to halt and reverse the disease by actually targeting the vessel wall with peptide-based nanofibers developed in the laboratory," Mansukhani said. The tiny fibers contained particles that helped remove cholesterol deposits from the plaque in the artery walls.

Researchers synthesized self-assembling peptide amphile nanofibers that targeted areas of plaque and could be delivered by intravenous injection. Importantly these synthetically engineered nanofibers

contained an amino acid sequence that promotes the cholesterol to dissolve.

To test the concept, mice were genetically modified to rapidly develop atherosclerosis, then fed high fat diets for 14 weeks and after which the mice received biweekly injections of either the peptide amphile nanofiber or saline for 8 weeks.

"It was important that we were able to achieve reproducible results in this model in the lab, so first we wanted to confirm that the therapy actually targeted areas of atherosclerosis," Mansukhani said.

They used imaging techniques -- fluorescent microscopy and pixel quantification -- to determine optimum dose, concentration, binding duration and biodistribution and found they could observe the targeting effect after 24 hours, and after 48 to 72 hours the nanofiber would dissipate and it was cleared in 7 to 10 days.

After 8 weeks of treatment, plaque area in the arteries of the male mice was reduced by 11 percent and in the female mice by 9 percent.

The results "demonstrate that a novel targeted nanofiber binds specifically to atherosclerotic lesions and reduces plaque burden after a short treatment duration," Mansukhani said.

He noted, however, that this is preliminary research, and more is needed before this approach can be tested in humans.

Co-authors are Miranda So, M.S.; Mazen; S. Albgaghdadi, M.D.; Zheng Wang, B.A.; Samuel I. Stupp, Ph.D.; Erica B. Peters, Ph.D. and Melina R. Kibbe, M.D.

The study was funded by the National Institutes of Health/National Heart Lung and Blood Institute; Northwestern Memorial Foundation Dixon Translational Sciences Award.

http://bit.ly/2jTDwRG

Genghis Khan's Mongol horde probably had rampant Hepatitis B

Viral DNA recovered from ancient human remains sheds light on HBV's evolutionary past.

Kiona N. Smith - 5/12/2018, 12:22 AM

Next time you picture a Mongol horde sweeping across the Asian steppes on horseback, imagine that about two-thirds of them have liver disease. Hepatitis B is a virus that attacks the liver, causing scarring, organ failure, and sometimes cancer. Its origins and evolutionary history are still a bit of an enigma, but viral DNA left behind in the bones and teeth of ancient people from the Asian steppe may help reconstruct part of our long history with the disease.

The battle of Liegnitz, 1241. From a medieval manuscript of the Hedwig legend.
Wikimedia Commons

The virus showed up in what have been considered extraneous sequences of DNA that are associated with DNA samples but not part of the human genome. Typically, software gets rid of these sequences and uses what's left to assemble the human genome.

Viruses and genomes

While DNA sequencing has focused on the human portion of human genome data, that's starting to change. "Originally, this was nothing we paid much attention to. It was just expensive and kind of a waste product, but now we've started investigating this waste product for possible positives," said Copenhagen University evolutionary geneticist Eske Willerslev. It's how his team found evidence that Mongol warriors from the steppe carried an early form of the pathogen that would later become the 541-542 CE Justinian Plague.

Viruses show up during DNA sequencing for two reasons. About eight percent of the human genome is made up of fragments of viral DNA that we've acquired over the last 1.8 million years or so. One category of this viral DNA, the so-called endogenous retroviruses, have actually worked themselves into our chromosomes, and they're passed from parent to child with all the rest of our genetic makeup.

But most viruses don't integrate into the genome as part of their life cycle. The hepatitis B DNA that Cambridge University pathogen evolution researcher Barbara Mühlemann and her colleagues have extracted from Bronze Age and Iron Age samples is like this; it remains

separate from the host's genome. But that doesn't mean there's no hepatitis B DNA in the cells of infected individuals. As a result, it's picked up during genome sequencing and can be identified as viral DNA that happened to be in a person's cells when they died but wasn't part of their chromosomes. Researchers call this exogenous viral DNA. A 4,500-year-old sample from the group is the oldest exogenous viral DNA ever recovered so far, beating out a 450-year-old hepatitis B sample found in an earlier study.

The unromantic past

When Mühlemann and her colleagues sequenced 304 genomes from the skeletons of people who lived on the steppe during the Iron and Bronze Ages (from about 4,500 years ago up until about 800 years ago) they checked the waste sequences for possible evidence of ancient infections. Twenty-five people out of 304 had DNA from the hepatitis B virus in their bones.

"The samples that are sequenced are obviously either teeth or bones, and we think that the reason why we find viruses in those samples is because those are tissues that have blood flow going through them, and the virus gets to a high concentration in the blood, which is why we find them in those tissues," said Mühlemann. "That essentially means that we're only able to find viruses that cause infections with high titers in the blood, and the individual has to die in the state like that."

That means that HBV on the ancient steppes may have been as prevalent as it is in some of the most heavily impacted areas of the world today—or more so. In South Sudan, for instance, about 22.38 percent of people are infected. And in areas where prevalence is over about 8 percent, a surprisingly high majority of adults, 70 to 90 percent, show signs of having been infected at some point in their lives.

"About 10 percent or so of the samples of the individuals we are studying have nasty pathogens in them, and when we use teeth, you also find that 50 percent of the individuals have all kinds of oral infections that you might not die of but it's not nice that you have. So the picture that emerged from this line of work is that a lot of people were running around with diseases in the past," said Willerslev. "It certainly kind of cracked my romantic picture of the Bronze Age and Iron Age."

The more you know

They sequenced 12 of the best-preserved ancient viral genomes and combined them with modern genomes to analyze the evolutionary relationships between different strains of the virus. What they found is that hepatitis B was part of life on the Eurasian steppes for thousands of years, and its evolutionary story is more complicated than anyone thought. Mühlemann and her colleagues found at least one strain of hepatitis B that's now extinct, having apparently faded out of existence sometime in the last 4,500 years. And according to a phylogenetic tree mapping the evolutionary relationship between the genomes, one of the nine major genotypes circulating today was the product of an ancient recombination between two strains of the hepatitis B virus.

"Based on the observation that genotypes go extinct and can be created by recombination, the ancient sequence data show that the diversity that we observe today is only a subset of the diversity that has ever existed," Mühlemann and her colleagues wrote. Most of the genetic diversity in hepatitis B viruses today probably arose sometime between 25,000 and 13,400 years ago, when the genetic lineages of Old World hepatitis B strains and New World hepatitis B strains split, according to Mühlemann and her colleagues.

Understanding some of that long-lost genetic diversity and how the virus evolved into the strains we see today may equip us to fight it more effectively in the future. By looking at genetic variants of the virus in the past, researchers can get a preview of the kinds of mutations that are likely to arise in the future. The World Health Organization has set a goal of significantly reducing the worldwide burden of hepatitis B by 2030. The best hope for that, at the moment, rests on a combination of vaccines to protect the uninfected and antiviral drugs to treat the infected, but the wrong mutation in the virus' genome could render those weapons useless. Knowing which mutations may be coming could give us an advantage.

"It's good to have a very in-depth look at those sequences, also potentially in the lab, to see if the variation that we see can tell us anything about the changes that the virus could make in the future, and if such changes occur, whether our vaccines and our antivirals and our diagnostic tests still work," said Mühlemann. "In case of the arising of that variant of the virus in the future, that might help us to know how we have to adapt or change our diagnostic tests or our vaccines."

People and pathogens

The 12 hepatitis B genomes may also help tell us where the virus came from. We still don't know where hepatitis B first evolved, for instance, and while it's going to take more viral genomes and a lot more analysis to answer that question, Mühlemann and her colleagues say there's already reason to think that some current hypotheses about where hepatitis B arose and how it spread around the world may need some revision.

"Some ideas that have been around over the years, [such as] that hepatitis B came from America and very recently entered Europe some 500 years ago, are certainly wrong, because of course these are going much further back in time," said Willerslev.

One modern strain, genotype A, was previously thought to have emerged in Africa and spread to the Americas and India within the last few centuries via the slave trade. But Mühlemann and her colleagues found some ancestral strains of type A in people living on the steppe as early as 4,300 years ago: some from the Sintasha culture in what is now southwest Russia, and one in a person from the Scythian culture in what is now Hungary.

That, according to Natural History Museum of Denmark paleogeneticist Peter de Barros Damgaard, "suggests that it's kind of the other way around, that it came from Europe, but it was introduced to South Asian populations historically recently, without having a massive human population admixture."

And Damgaard says that's an important point about tracking the movement of diseases through human history. Paleogenomicists use changes in human genomes to track large-scale population movements and interactions between cultures, but DNA can only capture the kind of intercultural relations that leave a genetic signature, which means interbreeding on a fairly large scale for a period of time. The exchange of diseases can provide an independent line of evidence for paleogenomicists to check their work against, but diseases spread between populations much more easily than genes do.

"While it's super exciting to try to correlate the human dispersals with the dispersal of pathogens, there for sure are limitations to doing that, because the pathogen can also spread without you having massive population admixture," he said. "Once the pathogen is introduced, it can also spread horizontally without you having to have a human population admixture that's so considerable that you actually see it."

But that may mean that some pathogens can help track other kinds of interactions between groups of people.

"There's now a number of cases emerging where you can say we don't see much of that sexual contact [between populations]," said Willerslev. Bronze Age Scythian culture, for example, was pretty uniform across a wide swath of the steppe, but the Scythians themselves actually consisted of several genetically distinct populations.

"So how did that kind of similar culture come about? What kind of processes? And there I think maybe some of the pathogens can be one way to address some of these questions," said Willerslev.

Searching for ancient diseases

Answering some of those remaining questions will require more ancient viral genomes, not just from hepatitis B but from other pathogens. Hepatitis B is particularly easy to find in ancient DNA samples because infected people carry lots of the virus in their blood for several years, increasing the chances its DNA will be preserved in bone cells. The virus particle itself is very stable over time. But other viruses, including influenza and variola (pox) have been found in archaeological human remains as much as 400 years old, and Mühlemann says that others like

herpes viruses, parvoviruses, and adenoviruses might be good candidates.

The team has set up dedicated systems to scan what was once considered waste DNA for sequences that match known viruses and bacteria (except for RNA viruses like influenza, whose genes won't be preserved in human DNA), and they're still working through the sequences from samples they've already taken from ancient bones.

"We haven't even completed that yet, but obviously also for future samples we will be screening for all known viruses and all known bacteria," said Willerslev.

And it's possible that in one of those future samples, they may find even older traces of hepatitis B or another virus. "In a number of cases, you will find that it has survived, in time," said Willerslev.

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https://wapo.st/2rHLsJa

A pioneering vaccine is being sent to Congo in hopes of containing a new Ebola outbreak

Hopes a vaccine can help contain a new outbreak of the virus in Congo

by Siobhán O'Grady May 11 Email the author

When the Ebola virus swept through West Africa in 2014, it hit capital cities so quickly that medical professionals were left with few options to prevent its spread. Soon, health-care workers and those who touched the bodies of the dead were coming down with the virus themselves and then passing it to others. By the time the outbreak was finally contained, more than 11,000 people had died.

Now, experts hope a vaccine can help contain a new outbreak of the virus in Congo — a simple intervention that could have saved thousands of lives had it been ready in 2014.

On Friday, the World Health Organization announced its plan to send the experimental vaccine to northwest Congo, where there have been about 32 suspected or confirmed cases since early April and 18 deaths.

"We are very concerned and planning for all scenarios, including the worst-case scenario," Peter Salama, the WHO's deputy director-general of emergency preparedness and response, said in Geneva on Friday.

Challenges will include keeping the vaccine at low temperatures in Congo's heat and with the lack of infrastructure in the rural area, as well as getting the vaccine to those who have been exposed to the virus.

Despite it occurring outside an urban area, this particular outbreak may be harder to contain because it has already spread across 37 miles. Some of those infected are health workers, which poses an additional risk of transmission to others. Those who help bury or clean the bodies of the infected are also at high risk.

Michael T. Osterholm, director of the Center for Infectious Disease Research and Policy at the University of Minnesota, told The Washington Post that Ebola outbreaks are dangerous in an increasingly urbanizing Africa because once infections spread to a metropolitan area, they become much more difficult to control. Already, officials in Congo fear that the virus could spread to the provincial capital Mbandaka, home to about 1 million people.

"All it would take is one or two of these infected individuals to go into a larger metropolitan area," Osterholm said. When it comes to the danger of a large outbreak, "Kinshasa is a gas tanker waiting for a match to hit it," he added. The Congolese capital's population of 14 million means the disease would spread very quickly if it reaches the city, which is far from the affected area.

On Friday, Salama said he had spoken to Congo's health minister and hoped that he would soon have approval to use the vaccine, which was developed by Merck in 2016. In a trial of 11,800 people in Guinea in 2015, the vaccine had 100 percent efficacy, giving hope it could be a game-changer in preventing Ebola from spreading.

Researchers there used the same approach that was used to study smallpox, where they identified a "ring" of people who may have come into contact with an infected person and then vaccinated all of them after determining they may have been at risk. The side effects

were mostly mild. Congo has suffered a number of Ebola outbreaks in recent years but has largely managed to contain them. A 2014 outbreak killed 49 people. In this case, the vaccine's deployment is intended to assist health-care workers in ending the outbreak long before it has the possibility of turning into an epidemic.

http://bit.ly/2wCDqQ9

Existential debate in US food industry: What is meat?

Can a hamburger or steak be labeled "meat" if it is plant-based?

May 13, 2018 by Juliette Michel

That question has sparked a debate about US food labels as key US cattle industry players have sought to crack down on marketing of proteins made from soy and other plant-based substances.

Jessica Almy, policy director of the non-profit Good Food Institute, which promotes meat-alternatives, said labels must state clearly if a product is made from soy or another plant, but they usually make sense in context. "Regardless of whether it is made of beef, soy, or wheat, a burger tells you it can be cooked on a grill, placed on a bun, and served with mustard and ketchup," she said.

Almy also sees no alternative to labeling as "meat" new products made from animal cells grown in a lab. Such protein offerings are expected to hit US supermarkets and specialty shops within the next few years.

"These are muscles and fat. It would be extremely misleading to call it other than meat," said Almy said.

That stance has enraged some in the traditional meat industry, spurring the US Cattlemen's Association to file a petition to the Agriculture Department to reserving the term "meat" or "beef" to protein derived from slaughtered animals. "Labels indicating that a product is 'beef' should be limited to product from cattle that have been born, raised and harvested in the traditional manner," the petition said.

The cattle association, which represents ranchers and cattle breeders, said it wants to avoid a similar outcome to the dairy industry, which has seen alternative products made of soy, almond and other non-dairy sources take 10 percent of the "milk" market.

"We started seeing these products put into the meat shelves in the grocery stores with packaging, label and design misleading the consumers into believing that perhaps it is a healthier version of the traditional meat or perhaps this is real beef," said USCA spokeswoman Lia Biondo. "We are trying to preempt the issue, to prevent what the dairy industry is going through."

Industry split

For now, alternative meat products represent a tiny portion of US protein sales. But the items are becoming more widely used, and not just by vegetarians.

Startups in alternative food today offer products that do a much-improved job of simulating the taste, texture and smell of traditional meat. Industry players say it is only a matter of time before these options are made with animal cells, further complicating the picture.

While the USCA petition has won some support, not all in the food industry have signed on. The Farm Bureau generally supports the idea behind the petition, but does not want oversight of alternative proteins to shift outside of the Agriculture Department.

"If it is not called meat, what is it then? We want to retain the jurisdiction under the Secretary of Agriculture," said Dale Moore, who is in charge of public affairs for the Farm Bureau. The National Cattlemen's Beef Association, which counts among its members meat distributors and processors, has not signed the petition either.

Chris Kerr, investment manager at New Crop Capital, a venture capital firm investing in alternative food companies, said efforts like the USCA petition illustrate a head-in-the-sand approach to shifting tastes. "We are looking at a major behavioral shift by a whole segment of the consumer population, driven a lot by the millennials. They are very open to plant-based food, to being flexitarian," he said.

"The industry can fight this, but they are arguably fighting against themselves because ultimately most meat producers will have some stake in this and it will be a successful outcome," he added.