http://bit.ly/2aZ0uGc

New study explains why MRSA 'superbug' kills influenza patients

Secondary MRSA infection often kills because flu virus causes white blood cells to damage the patients' lungs instead of the bacterium

Researchers have discovered that secondary infection with the Methicillin-resistant Staphylococcus aureus (MRSA) bacterium (or "superbug") often kills influenza patients because the flu virus alters the antibacterial response of white blood cells, causing them to damage the patients' lungs instead of destroying the bacterium. The study, which will be published online August 15 ahead of issue in The Journal of Experimental Medicine, suggests that inhibiting this response may help treat patients infected with both the flu virus and MRSA.

Many influenza patients develop severe pneumonia as a result of secondary infections with MRSA. Over half of these patients die, even when treated with antibiotics that are usually capable of clearing MRSA infections. Keer Sun, an assistant professor at the University of Nebraska Medical Center, previously discovered that mice infected with influenza are susceptible to MRSA because the ability of their macrophages and neutrophils to kill bacteria by releasing hydrogen peroxide and other reactive oxygen species is suppressed. But it remained unclear why MRSA-infected influenza patients often die, even after receiving an appropriate antibiotic treatment.

Sun and colleagues now reveal that this may be because the patients' white blood cells cause extensive damage to their lungs. Though the macrophages and neutrophils of mice co-infected with influenza and MRSA were defective at killing bacteria, reactive oxygen species released by these cells induced the death of inflammatory cells within the lungs, lethally damaging the surrounding tissue. Inhibiting NADPH oxidase 2 (Nox2), the enzyme that produces reactive oxygen species in macrophages and neutrophils, reduced the extent of this damage and, when combined with antibiotic treatment, boosted the survival of co-infected mice.

"Our results demonstrate that influenza infection disrupts the delicate balance between Nox2-dependent antibacterial immunity and inflammation," says Sun. "This not only leads to increased susceptibility to MRSA infection but also extensive lung damage. Treatment strategies that target both bacteria and reactive oxygen species may significantly benefit patients with influenza-complicated MRSA pneumonia."

Sun, K., et al. 2016. J. Exp. Med. http://dx.doi.org/10.1084/jem.20150514

http://bit.ly/2aZ1ien

Heading for a fall

Neuroscientists reveal how overconfidence can lead to poor decision making

The link between overconfidence and poor decision making is under the spotlight in an international study by scientists from Monash University and the Max Planck Institute for Human Cognitive and Brain Sciences in Leipzig.

People vary widely in their awareness of what they do and don't know, or metacognitive ability, and in general are too confident when evaluating their performance. This often leads to poor decision making with potentially disastrous consequences, according to the report's authors.

The team has published a study in the journal Social, Cognitive and Affective Neuroscience which provides some insight into how overconfidence can lead to poor decision making.

The authors include an international group of scientists at the Department of Social Neuroscience at the Max Planck Institute, headed by Professor Tania Singer, in collaboration with Dr Pascal Molenberghs from the Monash Institute of Cognitive and Clinical Neurosciences and Fynn-Mathis Trautwein, Dr. Anne Böckler and Dr. Philipp Kanske from the Max Planck institute team.

They analysed data from the ReSource Project, which is a unique, large scale study on Eastern and Western methods of mental training performed at the Max Planck Institute. In the context of a social cognition task performed in the brain scanner, the volunteers watched a video of a person telling a story and then had to answer a difficult question about what the person said.

Subsequently, people indicated how confident they felt their response was correct. The researchers then measured how good people were in evaluating their own accuracy; a process called metacognition.

"The more confident people were about their performance, the higher the activation in brain areas such as the striatum, an area often associated with reward processing," first author Dr Molenberghs said.

"However, too much confidence was associated with lower metacognitive ability," co-first author Mr Trautwein added.

When combined, the results indicate that although being confident entails a reward-like component, it can lead to overconfidence which in turn can undermine decision making.

http://wb.md/2bmuR7w

Human Metapneumovirus: Common yet Underdiagnosed

About human metapneumovirus, an important cause of respiratory illness that affects many people every year

Eileen Schneider, MD |August 15, 2016

Hello. I am Dr Eileen Schneider, a medical epidemiologist in CDC's Division of Viral Diseases. I'm pleased to speak with you as part of the CDC Expert Commentary series on Medscape. Today I will talk about human metapneumovirus, an important cause of respiratory illness that affects many people every year.

In the United States each year, human metapneumovirus is associated with approximately 20,000 hospitalizations among children younger than 5 years.[1] It can also severely affect older adults and immunocompromised patients. Most people have a metapneumovirus infection by the age of 5 years; however all ages are at risk for infection.[1]

The clinical presentation is usually mild and can include such respiratory symptoms as cough, fever, and nasal congestion. The symptoms are often clinically indistinguishable from infection with other common respiratory viruses, such as flu and respiratory syncytial virus (RSV).[2] Human metapneumovirus infection can also progress to the lower respiratory tract and result in bronchiolitis and pneumonia.

Human metapneumovirus was recently identified, in 2001, as an important cause of respiratory illness. However, some serologic evidence suggests that the virus has been widespread since at least 1958.[2] Metapneumovirus can be detected throughout the year, but infections typically peak in the United States from late winter to early spring. Of note, metapneumovirus cocirculates with RSV and flu during the respiratory virus season, but metapneumovirus activity generally peaks later in the winter than RSV and flu.[3]

Because human metapneumovirus is relatively new and not well described, healthcare professionals might not routinely test for it or even consider it in their differential diagnosis. But CDC recommends that clinicians consider metapneumovirus testing, along with flu, RSV, and other common respiratory viruses, especially in patients with severe respiratory illness.

Test results can help identify a possible etiologic pathogen and help guide available treatment.

The most sensitive method for human metapneumovirus diagnosis is to test respiratory specimens using polymerase chain reaction (PCR) assays. Examples of respiratory specimens include upper airway specimens (such as a nasopharyngeal swab, oropharyngeal swab, or nasal wash), and lower respiratory tract specimens (such as sputum, tracheal aspirate, and bronchoalveolar lavage). In patients with clinical or radiologic evidence of lower respiratory infection, a lower respiratory specimen should be tested.

Metapneumovirus is commonly included in commercial multipathogen PCR respiratory panels. Antigen detection assays are

also available for diagnosing this infection. Healthcare providers can contact their state health departments for assistance with laboratory diagnostics or consultation.

There is currently no vaccine, and antiviral treatment is not recommended. You can help your patients reduce their risk for respiratory illnesses caused by metapneumovirus and other pathogens by reminding them to wash their hands often and practice good hygiene habits.

For additional information about human metapneumovirus, see a recent Medscape article that describes the first published summary of metapneumovirus testing data from CDC's National Respiratory and Enteric Virus Surveillance System. Also see a new CDC webpage on the clinical features of the virus.

Thank you for listening.

Web Resources ***CDC Human Metapneumovirus Clinical Features***

1. Haas LE, Thijsen SF, van Elden L, Heemstra KA. Human metapneumovirus in adults. Viruses. 2013;5:87-110.

2. van den Hoogen BG, de Jong JC, Groen J, et al. A newly discovered human pneumovirus isolated from young children with respiratory tract disease. Nat Med. 2001;7:719-724.

3. Haynes AK, Fowlkes AL, Schneider E, Mutuc JD, Armstrong GL, Gerber SI. Human metapneumovirus circulation in the United States, 2008 to 2014. Pediatrics. 2016;137.

http://bit.ly/2aYkTVJ

Humble moss helped create our oxygen-rich atmosphere

The evolution of the first land plants may explain a long-standing mystery of how Earth's atmosphere became enriched with oxygen

The evolution of the first land plants including mosses may explain a long-standing mystery of how Earth's atmosphere became enriched with oxygen, according to an international study led by the University of Exeter.

Oxygen in its current form first appeared in Earth's atmosphere some 2.4 billion years ago, in an incident known as the Great Oxidation Event. However, it was not until roughly 400 million years ago that this vital compound first approached modern levels in the atmosphere. This shift steered the trajectory of life on Earth and researchers have long debated how oxygen rose to modern concentrations.

In a study published in the journal Proceedings of the National Academy of Sciences, Professor Tim Lenton, of the University of Exeter, and his colleagues theorised that the earliest land plants, which colonised the land from 470 million years ago onwards, are responsible for the levels of oxygen that sustains our lives today. Their emergence and evolution permanently increased the flux of organic carbon into sedimentary rocks, the primary source for atmospheric oxygen, thus driving up oxygen levels in a second oxygenation event and establishing a new, stable oxygen cycle.

Earth's early plant biosphere consisted of simple bryophytes, such as moss, which are non-vascular - meaning they do not have vein-like systems to conduct water and minerals around the plant. Using computer simulations, the researchers first estimated that these plants could have generated roughly 30% of today's global terrestrial net primary productivity by about 445 million years ago.

When the properties of modern bryophytes were taken into account, including their elemental composition and effects on rock weathering, they found that modern levels of atmospheric oxygen were achieved by 420 to 400 million years ago, consistent with independent evidence. These findings therefore suggest that the first land plants, such as the humble moss, created the stable oxygen-rich atmosphere that allowed large, mobile, intelligent animal life, including humans, to evolve.

Professor Tim Lenton, of the University of Exeter, said: "It's exciting to think that without the evolution of the humble moss, none of us would be here today. Our research suggests that the earliest land plants were surprisingly productive and caused a major rise in the oxygen content of the Earth's atmosphere."

Article #16-04787: "Earliest land plants created modern levels of atmospheric oxygen" by Timothy M. Lenton et al.

The research was funded by the Leverhulme Trust, the Natural Environment Research Council, a Royal Society Wolfson Merit Award, and the VILLUM Foundation. It involved collaboration from the University of Leeds, the University of Copenhagen, the Georgia Institute of Technology, Ohio State University and Stockholm University.

http://bit.ly/2b0n3Yf

New Baker Institute charts provide picture of drug use in the United States

An extensive and easy-to-use collection of charts that present findings from decades of government survey data of drug use in the United States is now available on the website of Rice University's Baker Institute for Public Policy.

HOUSTON - The Brian C. Bennett Drug Charts provide a more accurate and illuminating picture of drug use -- from alcohol to methamphetamines and tranquilizers -- than is typically presented in popular media or reflected in the country's drug policies, said William Martin, director of the Baker Institute's Drug Policy Program.

Originally created by nonresident contributing expert Brian Bennett and updated by the Drug Policy Program, most of these charts trace the pattern of the use and abuse of individual drugs over more than 40 years.

To understand how these data can inform smarter and more effective U.S. drug policy, Martin and Katharine Neill, the Alfred C. Glassell III Postdoctoral Fellow in Drug Policy at the Baker Institute, wrote an issue brief, "Drugs by the Numbers: The Brian C. Bennett Drug Charts." A closely related policy report, "Rx for U.S. Drug Policy: A New Paradigm," by Martin and contributing expert Jerome Epstein elaborates further on the implications of these and other amply documented patterns of drug use and abuse.

Most of the charts show the percentage of people 12 and older (or in smaller groupings) who have ever used a given drug in their lifetime, in the past year and in the last month. High proportions of people who have ever used any of the drugs against which federal, state and local law enforcement agencies have waged aggressive war since the 1970s stopped using the drugs within the first year and no longer use them regularly, if at all.

"The Bennett charts graphically illustrate the natural course of the use of psychoactive drugs," Martin and Neill wrote. "Most people who ever use such drugs stop using them shortly after initiation or a period of (usually brief) experimentation. As the introduction to the collection explains, this pattern is closely correlated with age, with illicit drug use (and other risky behaviors) reaching a peak between 18 and 20, declining sharply by age 26 and then dropping gradually over the rest of the life span. This calls into question policies that levy harsh penalties and apply indelible criminal records to people for what may be experimental or incidental use likely to stop on its own in the normal course of maturation without treatment, 12-step programs or relapse. More rational and compassionate responses exist and deserve close attention."

Martin and Neill said important findings in these two publications include the following:

Alcohol causes far more personal and social damage than any other drug. Illegal drugs comprise less than 20 percent of substance-use disorders in the U.S.

Marijuana's reputation as a "gateway" drug is not supported, even for more marijuana use. More than half of respondents under 60 have used it during their lifetime, but fewer than 10 percent use it regularly.

Far fewer people progress to harder drugs. Current monthly use of cocaine is 0.6 percent; for heroin and methamphetamines, only 0.2 percent.

The vast majority of people with a "substance-use disorder" after age 26 developed it before age 18.

Problematic drug use has been stable for decades, calling into question the success of the war on drugs.

Some cities, states and countries have devised proven successful alternatives to prohibition and harsh punishment for drug use and abuse.

Now that about 90 percent of new heroin users are white, politicians and other officials are starting to treat opioid addiction as a disease and public health problem rather than a crime deserving harsh punishment.

Traumatic childhood experience, mental illness and economic insecurity are more significant predictors of substance abuse than availability of the drugs.

For more information or to schedule an interview with Martin, Bennett or Neill, contact Jeff Falk, associate director of national media relations at Rice, at jfalk@rice.edu or 713-348-6775.

Related materials:The Brian C. Bennett Drug Charts: http://bakerinstitute.org/bennett-charts

"Drugs By The Numbers: The Brian C. Bennett Drug Charts" issue brief:
http://bakerinstitute.org/media/files/files/8b79cbd3/BI-Brief-080116-DRUG_Charts.pdf
"Rx for U.S. Drug Policy: A New Paradigm," policy report:
http://bakerinstitute.org/files/9300

http://bit.ly/2bmdJQK

World's oldest ocean crust dates back to ancient supercontinent

The oldest known bit of oceanic crust is sitting at the bottom of the Mediterranean

By Emily Benson

The oldest patch of undisturbed oceanic crust on Earth may lie deep beneath the eastern Mediterranean Sea – and at about 340 million years old, it beats the previous record by more than 100 million years.

Earth's outermost shell can be billions of years old on land, but most oceanic crusts are younger than 200 million years. Understanding where they developed can help us figure out what Earth looked like as continents formed, broke apart, and shifted around the globe hundreds of millions of years ago.

Earth's crust is well-studied, but there are geologically complex places where scientists don't agree on its nature – whether it's oceanic or continental, and its age – says Roi Granot at Ben-Gurion University of the Negev in Israel. "The Mediterranean Sea is one of them," he says. "And now it seems that we know what it is."

Hidden stripes

Oceanic crust is formed when hot magma wells up at mid-ocean ridges, then slowly spreads out towards the edges of the ocean. When it collides with continents, it slides under the land, and its components are recycled within Earth's mantle, ready to rise again as new magma. That conveyor belt-like movement is why oceanic crust tends to be relatively young compared with continental crust.

When molten magma cools, magnetic minerals within it align themselves with Earth's geomagnetic field. Because the planet's north and south magnetic poles flip at irregular intervals, a distinctive, striped pattern in mineral orientation forms over millions of years.

Granot towed magnetic sensors behind a boat on four different cruises, criss-crossing the area between Turkey and Egypt. The magnetic signals revealed stripes indicating a previously unknown mid-ocean ridge.

"Here I am in the middle of the eastern Mediterranean and I see this beautiful feature that crosses the entire sea, from north to south," Granot says. "That feature can only be created by oceanic crust."

Granot estimated the age of the oceanic crust by comparing its magnetic signals with predictions based on the northward drift of the African continental plate over the past 400 million years. Because he knew where plate tectonics shifted Africa – and when – he could calculate the expected magnetic signals of the nearby oceanic crust over time. The best match between Granot's observations and the model estimates suggest the oceanic crust formed about 340 million years ago.

Supercontinental structure

"This is a nice suggestion that certainly will promote more debate," says Uri ten Brink at the US Geological Survey in Woods Hole, Massachusetts. "But it is by no means something that one can totally hang their hat on."

The thick blanket of sediment that covers the crust in the eastern Mediterranean makes it difficult to interpret magnetic signals, ten Brink says. And the basin itself is so small that it's hard to identify multiple stripes of the minerals that signify oceanic crust.

This isn't the first time that scientists have found evidence for extremely old sections of oceanic crust in the Mediterranean, ten Brink adds, although the newest age estimate is the oldest yet.

"This crust is by far the oldest crust that still lies at the sea floor," says Douwe van Hinsbergen at Utrecht University in the Netherlands.

The runner up, located east of Japan, is only about 190 million years old, van Hinsbergen says. And although older chunks of oceanic crust – some of which are billions of years old – have been partially

preserved in mountain ranges, the chemical properties of those fragments are likely to have been changed in the process.

The eastern Mediterranean basin was thought to have been created when a newly forming ocean split the supercontinent Pangaea apart, less than 300 million years ago. But the revised, older age of the oceanic crusts suggests that Pangaea might have started breaking up even before it was finished forming, or that this section of crust existed before the supercontinent arose.

"A piece of pre-Pangaea ocean may be preserved here," van Hinsbergen adds. Studying that bit of oceanic crust could help us understand the conditions that led to Pangaea's formation.

Journal reference: Nature Geoscience, DOI: 10.1038/ngeo2784

http://bit.ly/2b3xuZI

Does eating more salt prevent migraines and severe headaches?

A bit of salt might stop headaches' battery of the brain

By Jessica Hamzelou

Could a salty diet keep migraines at bay? People who eat a lot of salt report having fewer migraines and severe headaches – the first evidence that dietary sodium may affect the condition. But the researchers caution that more evidence is needed before people change their diets, given that high salt consumption is linked to heart disease and stroke.

There is growing evidence linking migraines with sodium. During a migraine, levels of sodium have been found to rise in cerebrospinal fluid, the liquid that bathes the brain and central nervous system. And sodium levels in this liquid seem to peak in the early morning and late afternoon – times of day when people commonly report experiencing migraines.

Plenty of sodium gets into our bodies via the food we eat. "I started to wonder if migraines could be affected by diet," says Michael Harrington at Huntington Medical Research Institutes in Pasadena, California. To find out, he and his colleagues turned to the National Health and Nutritional Examination Survey, a US survey of the health and diets of tens of thousands of people. Among other things, the survey asks respondents to list everything they consume over a 24-hour period, and whether they experienced a severe headache or migraine during that time.

Of 8819 adults surveyed between 1999 and 2004, the team found that those with the highest levels of sodium in their diets – in products like meat, cheese and bread as well as table salt – reported the fewest severe headaches and migraines.

Harrington says he's surprised by the results as they are counterintuitive. Given that sodium ions are known to activate neurons, we might have expected the relationship to go in the other direction. High sodium levels generally make neurons more excitable, so the idea that they in some way inhibit or prevent migraine activity is puzzling.

"I think people with migraine handle sodium differently," says Harrington.

American diets

The theory makes sense, says Svetlana Blitshteyn, who treats and studies nervous system disorders at the University at Buffalo School of Medicine and Biomedical Sciences in New York.

Blitshteyn specialises in disorders of the autonomic nervous system, which controls all our automatic functions, such as heart rate, breathing and urination. Many of her patients have migraines too, and she has noticed that, if they start consuming more salt as a treatment for a different condition, their migraine symptoms often get better – although this evidence is only anecdotal and hasn't been published yet. But it is too early to know how safe eating more salt is for people who have migraines, and who might benefit from doing so. "We need more evidence before we can make general recommendations," says Blitshteyn.

Harrington agrees. Salt has its own risks, and has been linked to heart disease and stroke. Harrington points out that almost all of the people

surveyed in his study were on typical US diets, which are already high in salt. Until we know more, the best advice for people with migraines is to eat well and regularly.

Journal reference: Headache, DOI: 10.1111/head.12792

http://s.nikkei.com/2b3JfiV

Japanese drugmakers to create screening tests alongside treatments

Following an international trend, Astellas Pharma and Kyowa Hakko Kirin are moving to develop new drugs in tandem with tests that screen out patients who do not stand to benefit.

TOKYO -- Astellas will create with a U.S. company a so-called companion diagnostic for an acute myeloid leukemia treatment the Japanese pharmaceutical giant has been working on. This marks Astellas' first time developing both products simultaneously.

By screening for mutations in proteins that affect blood cell proliferation, the test will identify patients likely to benefit from the medicine. The AML treatment is now in the final stages of clinical trials. Having received fast-track status from the Japanese health ministry thanks to the significant potential demand, the company seeks to obtain approval in Japan, the U.S. and elsewhere within three years.

At the Kyowa Hakko Kirin group, the parent will work on a rachitis medicine, while subsidiary Kyowa Medex will handle the development of a companion diagnostic. Success would result in the first effective treatment for the genetic condition. The group aims to obtain approval in Japan, the U.S. and Europe as early as 2018. This will be the group's second time developing a drug and its companion diagnostic side by side.

Advances in genetics have made it possible to gauge a medicine's effectiveness in a particular patient by checking for protein abnormalities targeted by the compound. Patients can save money and avoid suffering side effects for nothing, while governments that subsidize drug costs can reduce wasteful spending.

Draft guidance from the U.S. Food and Drug Administration aims to encourage drugmakers to proactively develop new medicines and companion diagnostics simultaneously. Similar moves are seen forthcoming in Japan and elsewhere.

http://bit.ly/2bGj3Ps

Computers trounce pathologists in predicting lung cancer type, severity, researchers find

Computers can be trained to be more accurate than pathologists in assessing slides of lung cancer tissues, according to a new study by researchers at the Stanford University School of Medicine.

The researchers found that a machine-learning approach to identifying critical disease-related features accurately differentiated between two types of lung cancers and predicted patient survival times better than the standard approach of pathologists classifying tumors by grade and stage.

"Pathology as it is practiced now is very subjective," said Michael Snyder, PhD, professor and chair of genetics. "Two highly skilled pathologists assessing the same slide will agree only about 60 percent of the time. This approach replaces this subjectivity with sophisticated, quantitative measurements that we feel are likely to improve patient outcomes."

The research will be published Aug. 16 in Nature Communications. Snyder, who directs the Stanford Center for Genomics and Personalized Medicine, shares senior authorship of the study with Daniel Rubin, MD, assistant professor of radiology and of medicine. Graduate student Kun-Hsing Yu, MD, is the lead author of the study.

Although the current study focused on lung cancer, the researchers believe that a similar approach could be used for many other types of cancer.

"Ultimately this technique will give us insight into the molecular mechanisms of cancer by connecting important pathological features with outcome data," said Snyder.

Assessing grade, severity of cancer

For decades, pathologists have assessed the severity, or "grade," of cancer by using a light microscope to examine thin cross-sections of tumor tissue mounted on glass slides. The more abnormal the tumor tissue appeared -- in terms of cell size and shape, among other indicators -- the higher the grade. A stage is also assigned based on whether and where the cancer has spread throughout the body.

Often a cancer's grade and stage can be used to predict how the patient will fare. They also can help clinicians decide how, and how aggressively, to treat the disease. This classification system doesn't always work well for lung cancer, however. In particular, the lung cancer subtypes of adenocarcinoma and squamous cell carcinoma can be difficult to tell apart when examining tissue culture slides. Furthermore, the stage and grade of a patient's cancer doesn't always correlate with their prognosis, which can vary widely. Fifty percent of stage-1 adenocarcinoma patients, for example, die within five years of their diagnosis, while about 15 percent survive more than 10 years.

The researchers used 2,186 images from a national database called the Cancer Genome Atlas obtained from patients with either adenocarcinoma or squamous cell carcinoma. The database also contained information about the grade and stage assigned to each cancer and how long each patient lived after diagnosis.

The researchers then used the images to "train" a computer software program to identify many more cancer-specific characteristics than can be detected by the human eye -- nearly 10,000 individual traits, versus the several hundred usually assessed by pathologists. These characteristics included not just cell size and shape, but also the shape and texture of the cells' nuclei and the spatial relations among neighboring tumor cells.

"We began the study without any preconceived ideas, and we let the software determine which characteristics are important," said Snyder, who is the Stanford W. Ascherman, MD, FACS, Professor in Genetics. "In hindsight, everything makes sense. And the computers can assess even tiny differences across thousands of samples many times more accurately and rapidly than a human."

Bringing pathology into the 21st century

The researchers homed in on a subset of cellular characteristics identified by the software that could best be used to differentiate tumor cells from the surrounding noncancerous tissue, identify the cancer subtype, and predict how long each patient would survive after diagnosis. They then validated the ability of the software to accurately distinguish short-term survivors from those who lived significantly longer on another dataset of 294 lung cancer patients from the Stanford Tissue Microarray Database.

Identifying previously unknown physical characteristics that can predict cancer severity and survival times is also likely to lead to greater understanding of the molecular processes of cancer initiation and progression. In particular, Snyder anticipates that the machine-learning system described in this study will be able to complement the emerging fields of cancer genomics, transcriptomics and proteomics. Cancer researchers in these fields study the DNA mutations and the gene and protein expression patterns that lead to disease.

"We launched this study because we wanted to begin marrying imaging to our 'omics' studies to better understand cancer processes at a molecular level," Snyder said. "This brings cancer pathology into the 21st century and has the potential to be an awesome thing for patients and their clinicians."

The work is an example of Stanford Medicine's focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

Stanford co-authors of the study are former postdoctoral scholar Ce Zhang, PhD; professor of pathology Gerald Berry, MD; professor of bioengineering, of genetics and of medicine Russ Altman, MD, PhD; and assistant professor of computer science Christopher Re, PhD.

The study was supported by the National Cancer Institute and the National Institutes of Health (grants U01CA142555 and 5U24CA160036-05).

Stanford's Department of Genetics also supported the work.

http://bit.ly/2b0Fc89

Scientists on the prowl for 'the ultimate Pokémon'

Researchers seek Zenkerella, an elusive scaly-tailed squirrel that has never been spotted alive by scientists

Researchers are on a real-life search for what one calls "the ultimate Pokémon": Zenkerella, an elusive scaly-tailed squirrel that has never been spotted alive by scientists. However, biologists recently found three newly dead specimens that hint at how the "living fossil" has evolved over the past 49 million years.

The second male specimen of* Zenkerella insignis *was found near the village of Ureca on Bioko, an island off the west coast of Africa. **Steven Heritage**

Zenkerella insignis, a mysterious rodent from central Africa, is among the least studied of all living mammals, said Erik Seiffert, study senior author and a professor of cell and neurobiology at the Keck School of Medicine of USC.

The last time scientists heard about Zenkerella in the wild was two decades ago. Notably, only 11 Zenkerella specimens are curated in museums around the world. The three new rodents bring the count to 14.

"Zenkerella could be seen as the ultimate Pokémon that scientists have still not been able to find or catch alive," Seiffert said. "After all, it probably only shows up in the middle of the night, deep in the jungles of central Africa, and might spend most of its time way up in tall trees where it would be particularly hard to see."

Using the three whole-body specimens, scientists sampled Zenkerella's DNA for the first time. The study, published in the journal PeerJ on Aug. 16, details how researchers analyzed Zenkerella's genes using cells from cheek swabs. Then they compared the scaly-tailed squirrels' DNA with a large sample of other rodents in an online database called GenBank, which includes all rodent suborders and families.

A family divided

Based on DNA results, the researchers determined that, contrary to expectation, Zenkerella is a very distant cousin of two scaly-tailed squirrels with webbing between their legs and elbows that allows them to glide from tree to tree.

Thus, Zenkerella, who cannot glide, should be placed in the newly named Zenkerellidae family, researchers said. All three cousins are part of the superfamily of Anomaluroidea, partially because they all have a set of scales on the bottom of their tails that reportedly provide support and traction for tree climbing.

The study adds to a growing body of evidence: Extreme anatomical adaptations that evolved and enabled some mammals to perform tasks such as gliding, flying or swimming are unlikely to be lost or reversed over the course of evolution.

One of only a few ancient 'living fossils'

Of the about 5,400 mammal species alive today, only Zenkerella insignis and five others are the "sole surviving members of ancient lineages" dating all the way back to the early part of the Eocene epoch, 49 million years ago or more, Seiffert said.

Within this select group, only Zenkerella, the monito del monte (Dromiciops gliroides) and the pen-tailed tree shrew (Ptilocercus lowii) have been given the medal "living fossil." They closely resemble what is observed in their species' fossil record. In other words, although they have evolved over time, the changes were minimal.

"It's an amazing story of survival," Seiffert said. "In strong contrast to Zenkerella, all of these five other 'sole survivor' mammal species have been fairly well studied by scientists. We are only just starting to work on basic descriptions of Zenkerella's anatomy. It's fun to think that there might be other elusive mammalian species out there, deep in the rainforests of central Africa that will be new to science."

Hunters caught the three Zenkerella specimens in ground snares near the southern tip of Bioko Island off the west coast of Africa. Villagers there said they catch Zenkerella in forest floor traps once or twice a year, but the meat is not desirable. Eyewitnesses said the rodent is nocturnally active and sleeps in tree hollows.

The mystery remains

Scientists still know almost nothing about the unique rodent's way of life: how it moves, whether it spends most of its time in the trees or on the ground, or what it eats. Future studies will detail Zenkerella's anatomy, behavior, diet, ecology and locomotion on Bioko Island.

The lack of knowledge about Zenkerella's life history and ecology has led the International Union for Conservation of Nature to categorize the species as "least concern" because it is thought to be distributed over a broad geographical region in central Africa, said Drew Cronin, study co-author and postdoctoral researcher with the Bioko Biodiversity Protection Program at Drexel University.

"This rating belies the fact that threats such as habitat loss and degradation are intense and widespread in central Africa," Cronin said. "Zenkerella may be under greater threat. The more information and visibility for the species that we can generate, the more likely we are to facilitate the research and conservation attention a unique species like Zenkerella requires."

Steven Heritage from Stony Brook University, David Fernández from the University of the West of England-Bristol, Hesham Sallam from Duke and Mansoura universities, and Jose Manuel Esara Echube from the National University of Equatorial Guinea also contributed to this research, which was supported by the U.S. National Science Foundation (BCS-1231288), the Research Foundation of SUNY, the Turkana Basin Institute and the ExxonMobil Foundation.

http://bit.ly/2bptTI1

Elbows of extinct marsupial lion suggest unique hunting style

Marsupial lion used its teeth to hold its prey, while it dispatched it with its huge claws

Scientists from the Universities of Bristol and Málaga have proposed that the long extinct marsupial lion hunted in a very unique way - by using its teeth to hold prey before dispatching them with its huge claws.

The marsupial lion, or Thylacoleo carnifex, was a predator in the Pleistocene era of Australia and was about the same size as a large jaguar. It was known to have existed from around two-and-a-half-million years ago until as recently as a few tens of thousands of years ago. The animal is depicted on native Australian cave art and some speculate it still survives as the "Queensland Tiger".

Reconstruction of Thylacoleo. **Mauricio Antón**

As its name suggests, the marsupial lion has long been presumed to be a cat-like predator, despite lacking large canine teeth - instead it had large, protruding incisors that have been suggested to be canine substitutes.

Thylacoleo was a powerful beast but, as other researchers have noted, it had limbs of different proportions to a lion, suggesting it was not a fast. It also sported a very large claw on its hand, similar to the dew claw of cats but of a much bigger size, with a bony sheath foisted on a mobile first digit (thumb).

The new study, published in Paleobiology by Christine Janis, a Marie Curie Research Fellow at the University of Bristol (currently on a leave of absence from a professorship at Brown University, USA) with colleagues Borja Figueirido and Alberto Martín-Serra from the

University of Málaga, Spain looked at the elbow joints of a large number of living mammals.

This showed a strong association between the anatomy of the humerus (upper arm bone) where it articulates with the forelimb and the locomotor behaviour of mammals.

Animals more specialized for running (like a dog) have a joint indicating movement limited for back and forwards, stabilising their bodies on the ground, while animals more specialised for climbing (like a monkey) have a joint that allows for rotation of the hand around the elbow.

Modern cats, which (unlike dogs) use their forelimbs to grapple with their prey, have an elbow joint of intermediate shape.

Christine Janis said: "If Thylacoleo had hunted like a lion using its forelimbs to manipulate its prey, then its elbow joint should have been lion-like".

"But, surprisingly, it a unique elbow-joint among living predatory mammals - one that suggested a great deal of rotational capacity of the hand, like an arboreal mammal, but also features not seen in living climbers, that would have stabilized the limb on the ground (suggesting that it was not simply a climber)."

Christine Janis and colleagues proposed that this unique elbow joint, in combination with the huge "dew claw" on a mobile thumb, would have allowed the marsupial lion to use that claw to kill its prey.

In contrast the large incisors were blunt. While Thylacoleo had massive shearing teeth in the back of its jaw, the incisors appear to have functioned better for gripping than for piercing flesh in a killing bite.

They concluded that, unlike a real lion, which holds its prey with its claws, and kills it with its teeth, the marsupial lion - unlike any living predator - used its teeth to hold its prey, while it dispatched it with its huge claws.

http://bit.ly/2b1finZ

Recently approved cholesterol medication not cost-effective; could substantially increase US health costs

Annual drug prices need to be reduced by more than 2/3 to meet a generally acceptable threshold for cost-effectiveness

Although the recently FDA approved cholesterol-lowering drugs, PCSK9 inhibitors, could substantially reduce heart attacks, strokes, and cardiovascular deaths, they would not be cost-effective for use in patients with heterozygous familial hypercholesterolemia or atherosclerotic cardiovascular disease, with annual drug prices needing to be reduced by more than two-thirds to meet a generally acceptable threshold for cost-effectiveness, according to a study appearing in the August 16 issue of JAMA.

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors were approved by the U.S. Food and Drug Administration (FDA) for use in patients with heterozygous familial hypercholesterolemia (FH; a disorder caused primarily by mutations in the low-density lipoprotein [LDL] receptor gene that causes severe elevations in levels of LDL-cholesterol [C], resulting in early atherosclerotic lesions) or pre-existing atherosclerotic cardiovascular disease (ASCVD) who require additional lowering of LDL-C despite maximally tolerated doses of statins.

If clinical benefits seen in short-term trials are sustained in the longer term, PCSK9 inhibitors could become an important option for patients at high risk of ASCVD, potentially lowering health care costs through preventing ASCVD events.

However, with an average U.S. price in 2015 of more than $14,000 per patient per year, their cost-effectiveness and effect on national health care spending are uncertain.

Kirsten Bibbins-Domingo, Ph.D., M.D., M.A.S., of the University of California, San Francisco, and colleagues used the Cardiovascular Disease Policy Model, an established simulation model of ASCVD in the U.S. population, to evaluate cost-effectiveness of PCSK9

inhibitors or the cholesterol drug ezetimibe in heterozygous FH or ASCVD. The model incorporated 2015 annual PCSK9 inhibitor costs of $14,350 (based on average wholesale acquisition costs of evolocumab and alirocumab).

Adding PCSK9 inhibitors to statins in heterozygous FH was estimated to prevent 316,300 major adverse cardiovascular events (MACE; cardiovascular death, nonfatal heart attack, or stroke) at a cost of $503,000 per quality-adjusted life-year (QALY) gained compared with adding ezetimibe to statins. In ASCVD, adding PCSK9 inhibitors to statins was estimated to prevent 4.3 million MACE compared with adding ezetimibe at $414,000 per QALY. Reducing annual drug costs to $4,536 per patient or less would be needed for PCSK9 inhibitors to be cost-effective at less than $100,000 per QALY.

At 2015 prices, PCSK9 inhibitor use in all eligible patients was estimated to reduce cardiovascular care costs by $29 billion over 5 years, but drug costs increased by an estimated $592 billion (a 38 percent increase over 2015 prescription drug expenditures), and was estimated to increase annual U.S. health care expenditures by about $120 billion (a 4 percent increase from the $2.8 trillion dollars in total U.S. health care spending in 2015).

The authors write that the high cost of PCSK9 inhibitors is uniquely challenging. "This is because PCSK9 inhibitors are meant to be lifelong therapy not only for the relatively small number of patients with FH but also for a large and growing population with ASCVD. As a result, the potential increase in health care expenditures at current or even moderately discounted prices could be staggering, despite cost savings from averted ASCVD events."

"In the face of limited health care resources, payers must consider the potential trade-off between paying for new drug treatments like PCSK9 inhibitors and investing in interventions known to improve access, physician prescription rates, and patient adherence to statin therapy among those at high ASCVD risk."

(doi:10.1001/jama.2016.11004; the study is available pre-embargo to the media at the For the Media website)

http://bit.ly/2boLfWr

A dog's dilemma: Do canines prefer praise or food?

Study explores canine reward preferences

Given the choice, many dogs prefer praise from their owners over food, suggests a new study published in the journal Social, Cognitive and Affective Neuroscience. The study is one of the first to combine brain-imaging data with behavioral experiments to explore canine reward preferences.

"We are trying to understand the basis of the dog-human bond and whether it's mainly about food, or about the relationship itself," says Gregory Berns, a neuroscientist at Emory University and lead author of the research. "Out of the 13 dogs that completed the study, we found that most of them either preferred praise from their owners over food, or they appeared to like both equally. Only two of the dogs were real chowhounds, showing a strong preference for the food."

Dogs were at the center of the most famous experiments of classical conditioning, conducted by Ivan Pavlov in the early 1900s. Pavlov showed that if dogs are trained to associate a particular stimulus with food, the animals salivate in the mere presence of the stimulus, in anticipation of the food.

"One theory about dogs is that they are primarily Pavlovian machines: They just want food and their owners are simply the means to get it," Berns says. "Another, more current, view of their behavior is that dogs value human contact in and of itself."

Berns heads up the Dog Project in Emory's Department of Psychology, which is researching evolutionary questions surrounding man's best, and oldest friend. The project was the first to train dogs to voluntarily enter a functional magnetic resonance imaging (fMRI) scanner and remain motionless during scanning, without restraint or sedation. In previous research, the Dog Project identified the ventral caudate region of the canine brain as a reward center. It also showed how that region of a dog's brain responds more strongly to the scents of familiar

humans than to the scents of other humans, or even to those of familiar dogs.

For the current experiment, the researchers began by training the dogs to associate three different objects with different outcomes. A pink toy truck signaled a food reward; a blue toy knight signaled verbal praise from the owner; and a hairbrush signaled no reward, to serve as a control.

The dogs then were tested on the three objects while in an fMRI machine. Each dog underwent 32 trials for each of the three objects as their neural activity was recorded.

All of the dogs showed a stronger neural activation for the reward stimuli compared to the stimulus that signaled no reward, and their responses covered a broad range. Four of the dogs showed a particularly strong activation for the stimulus that signaled praise from their owners. Nine of the dogs showed similar neural activation for both the praise stimulus and the food stimulus. And two of the dogs consistently showed more activation when shown the stimulus for food.

The dogs then underwent a behavioral experiment. Each dog was familiarized with a room that contained a simple Y-shaped maze constructed from baby gates: One path of the maze led to a bowl of food and the other path to the dog's owner. The owners sat with their backs toward their dogs. The dog was then repeatedly released into the room and allowed to choose one of the paths. If they came to the owner, the owner praised them.

"We found that the caudate response of each dog in the first experiment correlated with their choices in the second experiment," Berns says. "Dogs are individuals and their neurological profiles fit the behavioral choices they make. Most of the dogs alternated between food and owner, but the dogs with the strongest neural response to praise chose to go to their owners 80 to 90 percent of the time. It shows the importance of social reward and praise to dogs. It may be analogous to how we humans feel when someone praises us."

The experiments lay the groundwork for asking more complicated questions about the canine experience of the world. The Berns' lab is currently exploring the ability of dogs to process and understand human language.

"Dogs are hypersocial with humans," Berns says, "and their integration into human ecology makes dogs a unique model for studying cross-species social bonding."

http://bit.ly/2b1i4t2

Tube-feeding in dementia nursing home residents drops dramatically

Decreased by approximately 50% between 2000 and 2014

BOSTON - The proportion of nursing home residents with advanced dementia and eating dependency who received feeding tubes decreased by approximately 50% between 2000 and 2014 according to a new study published in the Journal of the American Medical Association (JAMA).

Researchers from the Harvard affiliated Hebrew SeniorLife Institute for Aging Research (IFAR), Brown University's Center for Gerontology and Health Care Research and University of Washington's Cambia Palliative Care Center of Excellence conducted the study.

Investigators reviewed data on more than 71,000 advanced dementia residents in nursing homes across the U.S. From 2000 - 2014, researchers found that the proportion of residents receiving feeding tubes declined from 11.7% in 2000 to 5.7% in 2014. Among white patients, insertion rates declined from 8.6 to 3.1% while rates in black patients declined from 37.6-17.5%. For both cohorts, the proportion of residents with advanced dementia and eating dependency who received feeding tubes decreased by approximately 50% between 2000 and 2014.

According to Susan L. Mitchell MD, MPH, lead author of the study and HSL title, "This decline parallels the emergence of research, expert opinion, and recommendations by national organizations

discouraging this practice." In the future, to ensure that expert recommendations are disseminated and racial disparities are reduced, researchers argue that fiscal and regulatory policies are needed to discourage tube-feeding and promote a palliative approach to feeding problems for people with dementia.

This study was supported by NIH-NIA P01AG02729. Dr. Mitchell is supported by NIH-NIA K24AG033640.

http://bit.ly/2b6sJin

NIH explores connection between Ebola survival and co-infection with malaria parasites

People infected with Ebola 20% more likely to survive if co-infected with Plasmodium

People infected with Ebola virus were 20 percent more likely to survive if they were co-infected with malaria-causing Plasmodium parasites, according to data collected at an Ebola diagnostic laboratory in Liberia in 2014-15. Moreover, greater numbers of Plasmodium parasites correlated with increased rates of Ebola survival, according to a dozen collaborating research groups in the new study, published in Clinical Infectious Diseases. The survival difference was evident even after controlling for Ebola viral load and age. Scientists from the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health (NIH), led the project.

At a joint diagnostic laboratory established in Liberia by NIH and the Centers for Disease Control and Prevention, the scientists tested 1,868 blood samples. The samples were from people seeking care for possible Ebola virus infection at the ELWA3 Ebola Treatment Unit in Monrovia. Testing confirmed Ebola virus infection in 1,182 samples; 956 of them were tested for Plasmodium parasites, and 185 were positive. Fifty-eight percent with both infections survived, compared to 46 percent who were infected with Ebola virus alone. Of the people with the highest Plasmodium levels, 83 percent survived.

Anti-malaria drugs were routinely administered to all patients seen at the Treatment Unit during the Ebola outbreak and had no bearing on the increased survival in Plasmodium-infected patients in the study, the researchers say. Moreover, in separate experiments conducted in the United States, treatment with antimalarials did not affect survival in laboratory mice infected with Ebola virus.

The research group is working to pinpoint a mechanism that could explain the association between Plasmodium infection and surviving an Ebola infection. If a connection is found, they say it might improve understanding of disease caused by Ebola and open possibilities for developing new treatments.

ARTICLE: K Rosenke et al. Plasmodium parasitemia associated with increased survival in Ebola virus-infected patients. Clinical Infectious Diseases DOI: 10.1093/cid/ciw452 (2016).

http://bbc.in/2bpIsLB

Neonic pesticide link to long-term wild bee decline

Species that fed regularly on oil seed rape such as the buff tailed bumblebee showed more serious declines

By Matt McGrath Environment correspondent

The large-scale, long-term decline in wild bees across England has been linked to the use of neonicotinoid insecticides by a new study.

Over 18 years, researchers analysed bees who forage heavily on oilseed rape, a crop widely treated with "neonics". The scientists attribute half of the total decline in wild bees to the use of these chemicals. Industry sources say the study shows an association, not a cause and effect.

Weighing the evidence

In recent years, several studies, conducted in the lab and in the field, have identified a negative effect on honey bees and bumble bees from the use of neonics. But few researchers have looked at the long term impacts of these substances.

This new paper examined the impacts on populations of 62 species of wild bees across England over the period from 1994-2011.

The team, from the Centre for Ecology and Hydrology (CEH), used distribution data on wild bees, excluding honey and bumblebees collected by the bees, ants and wasps recording scheme.

They were able to compare the locations of these bees and their changing populations with growing patterns of oilseed rape across England over 18 years. The amount of this crop being sown has increased significantly over the period of the study, from around 500,000 hectares in 1994 to over 700,000 in 2011.

A key innovation was the commercial licensing of neonicotinoid insecticides for the crop in the UK in 2002. Seeds are coated with the chemical and every part of the plant becomes toxic to pests.

Manufacturers hailed the development as a major advance, reducing the need for leaf spraying with other insecticides. Around 85% of the oilseed rape crop in England now uses this method for pest protection.

'Long term, large scale'

But this new work suggests, for the first time, that the detrimental impacts seen in the lab can be linked to large scale population extinctions of wild bees, especially for those species of bees that spend longer foraging on oilseed rape.

"The negative effects that have been reported previously do scale up to long-term, large-scale multi-species impacts that are harmful," said Dr Nick Isaac, a co-author of the new paper. "Neonicotinoids are harmful, we can be very confident about that and our mean correlation is three times more negative for foragers than for non-foragers."

There was a decline in the number of populations of 10%, attributable to neonicotinoids, across the 34 species that forage on oilseed rape. Five of the species showed declines of 20% or more, with the worst affected declining by 30%. Overall, half the total decline in wild bees could be linked to the chemicals.

"Historically, if you just have oilseed rape, many bees tend to benefit from that because it is this enormous foraging resource all over the countryside," said lead author Dr Ben Woodcock from the CEH.

"But this co-relation study suggests that once its treated with neonicotinoids up to 85%, then they are starting to be exposed and it's starting to have these detrimental impacts on them." "What we can't say is what these detrimental impacts are but what it does suggest is you can have these population declines and they can be big - I mean 30% is a big decline."

The authors acknowledge that their study finds an association and doesn't prove a cause and effect link between the use of neonicotinoids and the decline of bee populations.

Intensive farming at fault?

The manufacturers of the chemicals agree that it is an interesting statistical study, but they argue that intensive farming and not just a single insecticide might be the real cause of the decline.

"Since most of the oilseed rape grown in the UK was treated with a neonicotinoid seed treatment during the years that this study looked at, we believe its findings would be more correctly headlined that intensive agriculture is causing some issues with pollinators," said Dr Julian Little, from Bayer Crop Science in the UK. "Whether this is due to the use of insecticides is not clear; a lack of nesting sites and pollen and nectar sources in these areas may also be critical factors."

Other scientists, though, believe that the new study is some of the strongest data yet for the impact of these substances over the long term.

"This is the first good evidence that bees are affected at the population level by the widespread use of neonicotinoids," said Prof Henrik Smith from Lund University in Sweden, who was not involved with the research. "It is the combination of evidence that is persuasive, that the effect depends on neonicotinoid exposure and affect species known to forage on oilseed rape more than other species."

The European Food Safety Authority is currently conducting a review of the scientific evidence about neonicotinoids.

An EU-wide moratorium on their use was implemented in 2013 and is still in place. This new work is likely to be part of that review, along with another, major field study due out in the Autumn. However, the National Farmers Union (NFU) say that it doesn't make a convincing case about the extinction of bees in England.

"While this study claims to provide an important contribution to the evidence base underpinning the current EU moratorium on some uses of neonicotinoids, experts reviewing all the evidence have concluded that there are still major gaps in our knowledge and a limited evidence base to guide policymakers," said Dr Chris Hartfield from the NFU.

The scientists involved in the wild bee study caution against "simplistic solutions" to the problems of pollinators. They say a "holistic" approach to the use of insecticides must be taken and they are lukewarm about the idea of banning chemicals.

"When you grow oilseed rape you can't do it without pesticides, there's an underlying reality to this," said Dr Woodcock.

"Just because you say 'don't use neonicotinoids anymore', the likelihood is that another pesticide is going to have to be used to compensate for that, that is going to have impacts on runoffs into waterways and on other species that you can control for."

"It needs to be taken in a very holistic perspective, you can't just say as long as we can save the bees everything else can go to hell, that's not where you want to be at."

The study has been published in the journal Nature Communications.

http://nyti.ms/2boUbeu

Flooding in the South Looks a Lot Like Climate Change

Climate change is never going to announce itself by name. But this is what we should expect it to look like.

By JONAH ENGEL BROMWICHAUG. 16, 2016

That's what many scientists, analysts and activists are saying after heavy rains in southern Louisiana have killed at least 11 people and forced tens of thousands of residents from their homes, in the latest in a series of extreme floods that have occurred in the United States over the last two years.

That increase in heavy rainfall and the resultant flooding "is consistent with what we expect to see in the future if you look at climate models," said David Easterling, a director at the National Centers for Environmental Information, which is operated by the National Oceanic and Atmospheric Administration. "Not just in the U.S. but in many other parts of the world as well."

The flooding in Louisiana is the eighth event since May of last year in which the amount of rainfall in an area in a specified window of time matches or exceeds the NOAA predictions for an amount of precipitation that will occur once every five hundred years, or has a 0.2 percent chance of occurring in any given year.

Louisiana joins five other states, most of them in the South, that have experienced deadly flooding in the last 15 months, including Oklahoma, Texas, South Carolina and West Virginia.

In the last three months alone, floods in Maryland, West Virginia and Louisiana have combined to kill dozens of people and damage tens of thousands of homes and vehicles.

The National Weather Service reports that parts of Louisiana have received as much as 31 inches of rain in the last week, a number Dr. Easterling called "pretty staggering," and one that exceeds an amount of precipitation that his center predicts will occur once every thousand years in the area.

Dr. Easterling said that those sorts of estimates were predicated on the idea that the climate was stable, a principle that has become outdated.

The third National Climate Assessment, released in 2014 by the United States Global Change Research Program, showed that "the amount of rain falling in very heavy precipitation events" had been significantly above average since 1991.

However, the research did not identify the South as one of the areas of greatest concern; the increase was found to be greatest in the Northeast, Midwest and Upper Great Plains regions of the United States.

Some climate researchers warned Tuesday that it was too early to explain why so much of the country has faced sudden flooding.

"It's really hard to attribute things like this without a larger body of evidence," said Barry D. Keim, the Louisiana state climatologist.

“And, of course, the question keeps coming up: How large does that body of evidence have to get?”

But others said that the situation was quite clear.

“This is exactly what scientists have been predicting,” said the climate activist Bill McKibben. “The basic physics are simple: Warm air holds more water vapor, something that is turning out to be one of the most important facts of the 21st century.”

“And while Louisiana was flooding, there were also huge flood events underway in Moscow (biggest rains in 129 years of record-keeping), the Sudan, Manila, and probably plenty of other places,” he added.

For the last four years, the American Meteorological Society has attempted to explain how climate change has influenced individual extreme weather events. However, that type of analysis, known as event attribution, is not yet available for the flooding in Louisiana.

Rob Moore, a senior policy analyst at the Natural Resources Defense Council, an environmental nonprofit, who focuses on climate change’s effect on water resources, said that state and local governments would have to change their approaches to keeping citizens safe from flooding.

“If you look across all our natural disaster policies, they’re predicated on the wrong assumption that our flood risk in the future looks identical to our flood risk in the past,” he said.

He said that initiatives like the National Flood Insurance Program, which focuses on helping people rebuild in areas that have been flooded, were increasingly “untenable,” given sea level rise.

A report released earlier this month by the real estate sales company Zillow predicted that almost 1.9 million homes, worth a combined $882 billion, would be lost to the rising sea levels — and the flooding likely to follow — that climate scientists expect to see by the year 2100.

“When Zillow starts warning about sea level rise, it may be time to start worrying about sea level rise,” Mr. Moore said.

http://bbc.in/2bfq4Va

Meningitis W: Students urged to get vaccine

Young people starting university or college this autumn are being urged to get a vaccine against meningitis.

By Smitha Mundasad Health reporter

Public Health England says the jab will help protect against meningitis W in particular - a sometimes deadly strain that is on the rise. Officials say new students are at risk as they often mix closely with groups of unfamiliar people - some who may unknowingly carry the bug.

Wales has also renewed calls for school-leavers to take up the jab.

The injection - known as the Men ACWY vaccine - was first introduced for new university students in the UK last year.

'Highly aggressive'

It protects against the A, C, Y and W strains of the disease - all forms that can cause death or disability. But health experts say they are particularly concerned about "a highly aggressive strain" of meningitis W bacteria. Some 22 people got meningitis W in 2009 in England, compared with almost 200 people in the last 12 months.

Meningitis W infection is fatal in one in 10 cases and can lead to long-term health problems including deafness, epilepsy and amputations.

'Horrific side-effects'

Amy Davis, 24, from Surrey, got meningitis W when she was 18 years old, a few months before she was due to start college.

She said: "At first I thought I had the flu and felt very tired. But by the next day, I was covered in a rash, felt extremely unwell and was rushed to hospital. "I spent three weeks in intensive care on life-support. My organs failed, and my family was told I was the most unwell person in the hospital."

The infection spread to her bloodstream and bones and damaged her feet. She had toes on both feet amputated, and later her left leg was also amputated. She added: "The jab was not available when I was 18. I would encourage everyone to get the vaccine who can. "It takes just

five minutes, and is just one injection that can save your life or save you from getting horrific side-effects."

GPs in England are inviting 17 and 18-year-olds to come for a vaccine. First-time students under the age of 25 are eligible too. People who missed out on the jab last year should also see their doctor, experts say.

'Save lives'

And though students are the focus of the campaign, other young people are strongly advised to get the jab - whether they are planning on attending university or college or not.

Dr Mary Ramsay, at Public Health England, said students needed to remain vigilant to signs of the disease. She added: "Protecting young people from this potentially deadly disease as they embark upon one of the most important periods of their lives is vitally important. "The vaccination will save lives and prevent lifelong devastating disability."

Meningitis

- ***Meningitis is an infection of the meninges - the membranes that surround the brain and spinal cord***
- ***Meningococcal bacteria are common and carried harmlessly in the nose or throat by about one in 10 people***
- ***They are passed on through close contact***
- ***Symptoms can include a fever, tiredness, and general aches at first. These can get rapidly worse, with agitation, confusion, vomiting and headaches***
- ***People should seek help as soon as possible and should not wait for a rash to appear before getting advice***

Vinny Smith, of the Meningitis Research Foundation, said: "By getting this free meningitis vaccine students are not only protecting themselves from a potentially deadly disease, but also protecting others by stopping the spread.

"It is also vital to watch out for friends if they are unwell. If they have meningitis it can be like a very bad hangover that quickly gets worse. It can be deadly so it is important to act fast and get medical help."

Meanwhile Liz Brown, at the charity Meningitis Now, said people must not get complacent about the threat of meningitis.

She added: "Up to a quarter of students carry the bacteria that can cause meningitis compared to one in 10 of the general population. "In the UK, every university could experience at least one case of meningitis amongst its students within the first term."

Since 2015 the vaccine has also been rolled out for younger teenagers at schools across the UK. The ultimate aim is to ensure teenagers are offered the vaccine before they leave school. In the meantime officials in Scotland and Wales say any school-leavers who have not had the vaccine should speak to their doctor.

http://bit.ly/2bpeqZx

Isotope research opens new possibilities for cancer treatment

Computer models supporting spectroscopy unlock behavior of actinium-225

LOS ALAMOS, N.M. - A new study at Los Alamos National Laboratory and in collaboration with Stanford Synchrotron Radiation Lightsource greatly improves scientists' understanding of the element actinium. The insights could support innovation in creating new classes of anticancer drugs.

"The short half-life of actinium-225 offers opportunity for new alpha-emitting drugs to treat cancer, although very little has been known about actinium because all of its isotopes are radioactive and have short half-lives," said Maryline Ferrier, a Seaborg post-doctoral researcher on the Los Alamos team. "This makes it hard to handle large enough quantities of actinium to characterize its chemistry and bonding, which is critical for designing chelators."

The insights from this new study could provide the needed chemical information for researchers to develop ways to bind actinium so that it can be safely transported through the body to the tumor cell. "To build an appropriate biological delivery system for actinium, there is a clear need to better establish the chemical fundamentals for actinium," Ferrier said. "Using only a few micrograms (approximately the weight of one grain of sand) we were able to study actinium-containing

compounds at the Stanford Synchrotron Radiation Lightsource and at Los Alamos, and to study actinium in various environments to understand its behavior in solution."

Medical Isotopes at Los Alamos

Medical isotopes have long been a product of the Los Alamos specialty facilities, which create strontium-82, germanium-68 and other short-lived isotopes for medical scans. Taking advantage of the unique multidisciplinary capabilities of the Laboratory, researchers use the linear particle accelerator at the Los Alamos Neutron Science Center (LANSCE) to provide rare and important isotopes to the medical community across the United States. The expansion into actinium exploration moves the research forward toward treatment isotopes, as opposed to only diagnostic materials, says Ferrier.

For the actinium work, a spectroscopic analysis called X-ray Absorption Fine Structure (XAFS) was used, a sensitive technique that can determine chemical information such as the number of atoms surrounding actinium, their type (i.e., oxygen or chlorine) and their distances from each other. To help understand actinium's behavior in solution and interpret the data obtained with XAFS, these experimental results were compared with sophisticated computer model calculations using molecular-dynamics density functional theory (MD-DFT).

The study showed that actinium, in solutions of concentrated hydrochloric acid, is surrounded by three atoms of chlorine and six atoms of water. Americium, another +3 actinide often used as a surrogate for actinium, is surrounded only by one chlorine atom and eight water molecules. It has been assumed in the past that actinium would behave similarly to americium.

"Our study shows that the two are different in a way that could help change how actinium ligands are designed," Ferrier said. "We're actively working to gather more fundamental data that will help understand how actinium chemically behaves."

Actinium Useful for Targeted Alpha Therapy

Perhaps the most potent impact of these studies will be on the application of the isotope actinium-225, which is used in a novel, attractive cancer treatment technique called targeted alpha therapy (TAT). TAT exploits alpha emissions from radioisotopes to destroy malignant cells while minimizing the damage to healthy surrounding tissue. "Our determination that actinium's behavior in solution is different than other nearby elements (such as americium) is directly relevant to TAT in a biological environment, which is always a complex solution," said Ferrier.

Actinium-225 has a relatively short half-life (10 days) and emits four powerful alpha particles as it decays to stable bismuth, which makes it a perfect candidate for TAT. However, TAT with actinium can only become a reliable cancer-treatment if actinium is securely bound to the targeting molecule, as the radioisotope is very toxic to healthy tissue if it is not brought quickly to the site of disease.

Nature Communications Paper: "Spectroscopic and Computational Investigation of Actinium Coordination Chemistry," by authors M. G. Ferrier, E. R. Batista, J. M. Berg, E. R. Birnbaum, J. N. Cross, J. W. Engle, H. S. La Pierre, S. A. Kozimor, J. S. Lezama-Pacheco, B. W. Stein, S. C. E. Stieber and J. J. Wilson. Nature Communications .

Funding: Support for portions of this research was provided by the Los Alamos LDRD program and the U.S. Department of Energy (DOE) Office of Science. Related work was supported by a postdoctoral fellowship from the Glenn T. Seaborg Institute and the Los Alamos National Laboratory's Director's postdoctoral fellowship. The Stanford Synchrotron Radiation Lightsource is a DOE Office of Science User Facility at the Department's SLAC National Accelerator Laboratory.

http://bit.ly/2bfRkCZ

Fluoride consumption linked to diabetes using mathematical models

Regression analyses suggest association between increases in consumption of fluoridated water and type 2 diabetes

Water fluoridation prevents dental cavities, which are a costly public health concern. But despite the benefits supplemental water fluoridation remains a controversial subject. Some indicate it may cause long term health problems, but studies reporting side effects

have been minimal or inconclusive. The long-term effects of ingested fluoride remain unclear.

A recent study published in the Journal of Water and Health examined links between water fluoridation and diabetes. Type 2 diabetes is a growing epidemic in the United States. Incidence rates have nearly quadrupled in the past 32 years and show no signs of stopping. According to the study, fluoridation with sodium fluoride could be a contributing factor to diabetes rates in the United States, as the chemical is a known preservative of blood glucose.

The sole author of the paper, Kyle Fluegge, PhD, performed the study as a post-doctoral fellow in the Department of Epidemiology and Biostatistics at Case Western Reserve University School of Medicine. Fluegge now serves as health economist in the Division of Disease Control for the New York City Department of Health and Mental Hygiene and co-director of the Institute of Health and Environmental Research in Cleveland, Ohio.

In the study, Fluegge used mathematical models to analyze publicly available data on fluoride water levels and diabetes incidence and prevalence rates across 22 states. He also included adjustments for obesity and physical inactivity collected from national telephone surveys to help rule out confounding factors. Two sets of regression analyses suggested that supplemental water fluoridation was significantly associated with increases in diabetes between 2005 and 2010.

"The models look at the outcomes of [diabetes] incidence and prevalence being predicted by both natural and added fluoride," said Fluegge.

Fluegge reported that a one milligram increase in average county fluoride levels predicted a 0.17% increase in age-adjusted diabetes prevalence. Digging deeper revealed differences between the types of fluoride additives used by each region. The additives linked to diabetes in the analyses included sodium fluoride and sodium fluorosilicate. Fluorosilicic acid seemed to have an opposing effect and was associated with decreases in diabetes incidence and prevalence. Counties that relied on naturally occurring fluoride in their water and did not supplement with fluoride additives also had lower diabetes rates.

The positive association between fluoridation and diabetes was discovered when Fluegge adjusted fluoride exposure levels to account for estimated per capita tap water consumption.

"The models present an interesting conclusion that the association of water fluoridation to diabetes outcomes depends on the adjusted per capita consumption of tap water," explained Fluegge. "Only using the concentration [of added fluoride] does not produce a similarly robust, consistent association." For this reason, Fluegge adjusted his calculations to incorporate tap water consumption, instead of sticking to calculations that rely on "parts per million" measurements of fluoride in the water.

Fluegge used several estimations in his study, including calculations of county-level water fluoride levels; per capita county tap water consumption; and county measures of poverty, obesity and physical inactivity. Although he doesn't suggest the study should trigger policy changes, he does indicate it should serve as a call for additional research on the important association between fluoridation and diabetes.

"This is an ecological study. This means it is not appropriate to apply these findings directly to individuals," explained Fluegge. "These are population-level associations being made in the context of an exploratory inquiry. And water is not the only direct source of fluoride; there are many other food sources produced with fluoridated water."

In addition to being found in food like processed beverages or produce exposed to specific pesticides, fluoride is found naturally in water in the form of calcium fluoride. Supplemental fluoride was first added to community water supplies in the 1940s.

Said Fluegge, "The models indicate that natural environmental fluoride has a protective effect from diabetes. Unfortunately, natural fluoride is not universally present in the water supply."

Residents can learn more about fluoride levels in their communities through the Centers for Disease Control My Water's Fluoride database.

This work was supported by a National Institutes of Health National Heart Lung and Blood Institute (NIH NHLBI) training grant T32HL007567.

http://bit.ly/2b69aYu

Giant ancient supervolcanoes threw rock right across Australia

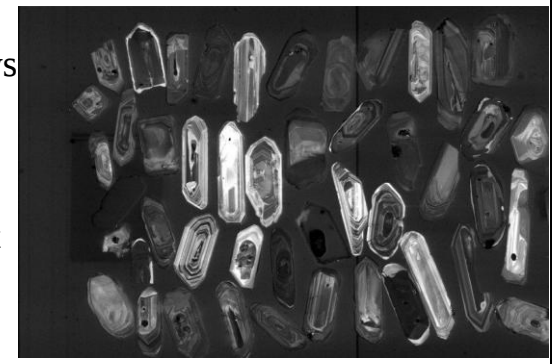
A blast from the past? The east coast of Australia was once lined by volcanoes that were so explosive they could shoot sand-sized particles 2300 kilometres – all the way across to the west coast.

By Alice Klein

The volcanic activity occurred 100 million years ago, at a time when New Zealand began tearing away from Australia's eastern edge.

Until recently, the only evidence of the scale of these eruptions were the 20-kilometre-wide dormant craters and the solidified lava flows left behind.

But now, Milo Barham at Curtin University in Western Australia and his colleagues have found that these eastern Australian volcanoes flung material to the other side of the country.



Well travelled: these zircon crystals took a 2300-kilometre trip **Milo Barham, Curtin University**

Crystal clues

The researchers were drilling beneath the Nullarbor plain in remote Western Australia when they discovered sand-sized zircon crystals that did not match any of the region's typical rock compositions.

Instead, the crystals matched volcanic rock in the Whitsundays area on the country's north-east coast in both age and geochemical make-up.

"We didn't find anything else from the east coast – just these very distinctive grains," says Barham. "Initially, we thought there might be some volcanism in Western Australia, but we couldn't find any evidence."

Two clues ruled out the possibility that river systems had carried the zircon crystals across the country: they were so well preserved and fossils in the rocks indicated that the crystals were of an identical age.

Staggering power

The finding points to the sheer force of the east coast volcanoes, says Barham.

The eruptions would have been tens to hundreds of times more powerful than any documented in human history. An equivalent eruption today would be heard in the west coast city of Perth.

Tremendous volcanic activity was happening all around the world 100 millions of years ago due to the disintegration of the supercontinent Gondwana, says Scott Bryan at Queensland University of Technology in Brisbane.

Modern volcanoes can spew fine particles of ash that are carried by winds over large distances, as happened in 2010 when Iceland's Eyjafjallajökull volcano released an ash plume that grounded flights across Europe.

But they lack the power to hurl larger particles thousands of kilometres.

The biggest known super-eruption occurred from Toba volcano in Indonesia 75,000 years ago. This propelled sand-sized particles over a 2700-kilometre radius.

Barham's work hints that Australia's east coast volcanoes may have been in a similar league, says Bryan. "It reinforces the potential scale of these eruptions." ***Journal reference:*** Geology, *DOI: 10.1130/G38000.1*

http://bit.ly/2bCY4da

Bunnies helped a great civilisation in ancient Mexico thrive

The trade in bunnies helped power an ancient economy.

By Conor Gearin

Teotihuacan, an ancient city in central Mexico, was an advanced metropolis where most people lived in apartment complexes. The city reached its peak between the first century and 550 AD. With about 100,000 residents, it was the largest urban area in the Americas at the time, of a similar scale and sophistication as other ancient centres like Alexandria and Rome.

But until now, it has been a mystery what kinds of animals supported this complex society. “One of the big puzzles for the pre-Colombian Americas has always been the lack of domesticated animals,” says David Carballo at Boston University. Other than managing dogs and turkeys, Mesoamericans didn’t appear to have the close relationships with animals that sustained ancient peoples in Africa and Europe.

Now it seems that raising cottontails and jackrabbits may have given the city a reliable source of meat and fur. Linda Manzanilla at the National Autonomous University of Mexico in Mexico City and colleagues have uncovered an apartment compound that seems to have belonged to rabbit breeders and butchers. The team found rooms littered with rabbit bones, as well as obsidian blades for butchering and for scraping skins.

The remains of baby rabbits and a low-walled room that appears to have been a pen indicate that the inhabitants were breeding and rearing the animals, Manzanilla says. A stone rabbit sculpture on top of a household courtyard temple (see illustration below) suggests that the residents specialised in the rabbit trade.

The carbon within the rabbit bones gave another clue, says Andrew Somerville at the University of California in San Diego. Animals eating maize and other common Mexican crops like agave cactus tend to have higher levels of an isotope of carbon with an extra neutron. Analysing the bones showed that up to 74 per cent of the animals’ diet came from human-grown foods rather than wild plants.

“This study does a great job of showing the innovations in this urban society for cultivating their own protein sources,” says Carballo. “It gives you a good idea of what regular folks were up to in this city.”

Illustration of rabbit sculpture **Manzanilla ed.1993; drawing by Fernando Botas**

The rabbits could have served a few different uses, such as a source of meat and fur or ritual purposes, says Heather Lapham at the University of North Carolina at Chapel Hill.

Michael Smith at Arizona State University in Tempe says we shouldn’t overestimate the importance of the meat, because the diet of beans and maize available at the time was already a complete protein source. “It’s not as if, ‘oh my gosh, they’re starving if they don’t get some rabbit meat.’” Still, the study gives more evidence that Teotihuacan had a highly organised economy with specialised workers, Smith says.

Palatial housing

The city’s tradespeople, like the rabbit butchers, were well off. Nearly everyone lived in large multifamily apartment buildings that would have matched royal palaces in other ancient cities. “I don’t know of any other ancient society where the bulk of the population lived in such luxury,” he says.

There’s also a conspicuous lack of royal tombs or paintings of powerful leaders amid the city’s abundant murals, says Carballo. This suggests that there were no kings; instead, government was probably a more collective affair.

It seems one of the ancient city's traditions remains. "Some of the delicacies of the Teotihuacan valley today involve rabbit," says Carballo. "It continues to be an important food for the area."

Journal reference: PLoS One, DOI: 10.1371/journal.pone.0159982

http://bit.ly/2b6dtTQ

Menopause supplements may raise dementia risk after stroke

Calcium supplements have been linked to a dramatic increase in the risk of developing dementia in women who have had a stroke or other conditions that affect the flow of blood to the brain.

By New Scientist staff and Press Association

The pills are taken by thousands of women in the UK to stave off osteoporosis after going through menopause. A study of 700 women between the ages of 70 and 92 has now revealed that women who take these pills have a seven-fold increase in their chances of developing dementia, if they have already experienced a stroke.

Only a small proportion – 98 women – were taking calcium supplements when the study began. Although none of the participants had dementia at the start of the study, 59 went on to develop it.

Silke Kern, at the University of Gothenburg in Sweden, and her team found that calcium supplements were only associated with dementia in women who had a history of cerebrovascular disease – disorders involving the brain's blood supply.

Women who hadn't had strokes, but who had lesions in their white matter – damage related to cerebrovascular disease – were three times more at risk of developing dementia if they took calcium pills.

However, Kern stresses that the study was small, and more work is needed to confirm these findings.

"While this research does not show a direct link between calcium supplements and increased dementia risk, it does warrant further investigation," says Doug Brown, at UK charity Alzheimer's Society.

But Reynolds says people should not worry about eating and drinking calcium as part of a normal diet. "This study looked at calcium supplements only, which have a different effect in the body to dietary calcium."

Journal reference: Neurology, DOI: 10.1212/WNL.0000000000003111

http://bit.ly/2bsOCud

The Cosmos Might Be Mostly Devoid of Life

We still have no idea how easy it is for life to arise—and it may be incredibly difficult

By Paul Davies on September 1, 2016

When I was a student in the 1960s, almost all scientists believed we are alone in the universe. The search for intelligent life beyond Earth was ridiculed; one might as well have professed an interest in looking for fairies.

The focus of skepticism concerned the origin of life, which was widely assumed to have been a chemical fluke of such incredibly low probability it would never have happened twice.

"The origin of life appears at the moment to be almost a miracle" was the way Francis Crick described it, "so many are the conditions which would have had to have been satisfied to get it going." Jacques Monod concurred; in his 1976 book Chance and Necessity he wrote, "Man knows at last that he is alone in the indifferent immensity of the universe, whence which he has emerged by chance."

Today the pendulum has swung decisively the other way. Many distinguished scientists proclaim that the universe is teeming with life, at least some of it intelligent. Biologist Christian de Duve went so far as to call life "a cosmic imperative." Yet the science has hardly changed. We are almost as much in the dark today about the pathway from nonlife to life as Charles Darwin was when he wrote, "It is mere rubbish thinking at present of the origin of life; one might as well think of the origin of matter."

There is no doubt that SETI—the search for extraterrestrial intelligence—has received a huge fillip from the recent discovery of

hundreds of extrasolar planets. Astronomers think there could be billions of Earth-like planets in our galaxy alone. Clearly, there is no lack of habitable real estate out there. Yet because we do not know the process that transformed a mishmash of chemicals into a living cell, with all its staggering complexity, it is impossible to calculate the probability that life has actually arisen on these planets.

Carl Sagan once remarked that the origin of life cannot be that hard, or it would not have popped up so quickly once Earth became hospitable. It is true that we can trace the presence of life on Earth back 3.5 billion years. But we cannot draw any statistical significance from a sample of one.

Another common argument is that the universe is so vast, there just has to be life out there somewhere. But what does that statement mean? If we restrict attention to the observable universe, there are probably 1023 planets. Yes, that is a big number. But it is dwarfed by the odds against forming even simple organic molecules by random chance alone. If the pathway from chemistry to biology is long and complicated, it may well be that fewer than one in a trillion trillion planets ever spawns life.

Affirmations that life is widespread are founded on a tacit assumption that biology is not the upshot of random chemical reactions but the product of some kind of directional self-organization that favors the living state over others—a sort of life principle at work in nature. There may be such a principle, but if so we have found no evidence for it yet.

Maybe we do not need to look far. If life really does pop up readily, as Sagan suggested, then it should have started many times on our home planet. If there were multiple origins of life on Earth, the microbial descendants of another genesis could be all around us, forming a possible shadow biosphere. Nobody has seriously looked under our noses for life as we do not know it. It would take the discovery of just a single “alien” microbe to settle the matter.

http://bit.ly/2bPqVyl

Common cold viruses originated in camels -- just like MERS

One of the four common cold coronaviruses also originates from camels

There are four globally endemic human coronaviruses which, together with the better known rhinoviruses, are responsible for causing common colds. Usually, infections with these viruses are harmless to humans. DZIF Professor Christian Drosten, Institute of Virology at the University Hospital of Bonn, and his research team have now found the source of "HCoV-229E", one of the four common cold coronaviruses--it also originates from camels, just like the dreaded MERS virus.

The Middle East respiratory syndrome (MERS) coronavirus was identified in humans for the first time in 2012. It causes severe respiratory tract infections that are often fatal. Dromedaries were confirmed to be its animal source some time ago.

"In our MERS investigations we examined about 1,000 camels for coronaviruses and were surprised to find pathogens that are related to 'HCoV-229E', the human common cold virus, in almost six percent of the cases," says Drosten. Further comparative molecular genetic analysis of common cold viruses in bats, humans and dromedaries suggests that this common cold virus was actually transmitted from camels to humans.

Common cold virus evolution could provide a scenario for MERS emergence

Drosten and his team isolated live camel common cold viruses and discovered that these could principally also enter human cells--via the same receptor used by the common cold virus "HCoV-229E". However, the human immune system is able to defend itself against the camel viruses, just as it can against common cold viruses. Furthermore, tests with human serum and animal common cold viruses showed that there is no immediate risk of an epidemic in

humans, because largest part of the human population already has immunity, owing to the widespread immunity against the common cold virus HCoV-229E.

So is this the all-clear for MERS viruses too? "The MERS virus is a strange pathogen: smaller, regionally restricted outbreaks, for example in hospitals, keep occurring. Fortunately, the virus has not adapted well enough to humans, and has consequently been unable to spread globally up to now," says Drosten. The results of the current investigations on predecessors of the human HCoV-229E virus in camels depict a situation that is similar to the current situation with MERS. These predecessor viruses are also not optimally adapted to humans.

The global spread of HCoV-229E through human-to-human transmission, which is highly likely to have occurred during a past pandemic, gives rise to concern. "Our current study gives us a warning sign regarding the risk of a MERS pandemic--because MERS could perhaps do what HCoV-229E did." So there is need for action: DZIF researchers are working intensively on researching a vaccine against MERS; it will go into clinical testing early next year.

Publication

V M Corman, I Eckerle, Z A Memish, A M Liljander, R Dijkman, H Jonsdottir, K J Z Juma Ngeiywa, E Kamau, M Younan, M Al Masri, A Assiri, I Gluecks, B E Musa, B Meyer, M A Müller, M Hilali, S Bornstein, U Wernery, V Thiele, J Jores, J F Drexler, and C Drosten

Link of a ubiquitous human coronavirus to dromedary camels

PNAS, Early Edition, DOI: 10.1073/pnas.1604472113. bit.ly/2bwMjrW

http://bit.ly/2b83YAK

Synthetic supermicrobe will be resistant to all known viruses

It's not finished yet. But if it is, it will be the greatest feat of genetic engineering by far.

By Michael Le Page

A team in the US is part-way towards recoding the *E. coli* bacterium to work with a different genetic code from all other organisms on Earth. That means making more than 62,000 changes to its genome.

"We take on projects other groups say are impossibly expensive – or just plain impossible," says the team leader George Church at Harvard Medical School in Boston, for whom this project is one step towards even more ambitious creations.

Don't mess with me: a supermicrobe might look like this **Chris Bickel/Science**

The recoded *E. coli* could have all kinds of industrial uses. It should be better in several ways: resistant to all existing viruses, unable to swap genes with other organisms and capable of producing proteins unlike any found in nature.

Building blocks

Normal proteins have the 20 natural amino acids as their building blocks. The recoded *E. coli* will make proteins with up to four additional artificial amino acids. "That's going to challenge the creativity of the scientific community," says team member Marc Lajoie at the University of Washington, Seattle.

Making an organism virus-resistant gives it a huge advantage. But the recoded *E. coli* will be unable to grow unless fed one of those artificial amino acids, so it shouldn't spread in the wild. "Biocontainment is our number one priority," says Church.

Church ultimately wants to make farm animals and human stem cells that are resistant to all viruses. Such cells could be used for producing vaccines and for transplants. It is very difficult to make people resistant to viruses, cancer and ageing, Church says, but we could create tissues and organs for transplant with these properties.

Genetically engineered microbes are ever more widely used in industry. At first, only simple changes could be made. In the 1970s, for instance, a human gene was added to *E. coli* so it could be used to "brew" insulin for people with diabetes. Nowadays, brewers are adding or tweaking dozens of genes, to create microorganisms that

can churn out everything from saffron and vanilla flavouring to antimalarials and opium.

Trouble brewing?

But the worry is that drastically modified microbes will escape from factories or swap genes with wild microbes. Imagine, for instance, if a microbe churning out a drug like opium started colonising the guts of people. Viruses can also wreck batches of growing microbes if they infect the vats. "Companies don't like to talk about it," Church says.

In theory at least, changing microbes' genetic code could solve these problems. In a gene coding for a protein, each sequence of three DNA letters – called a triplet codon – either specifies which amino acid should be added to the chain next, or tells the protein-making machinery to stop when a protein is complete.

There are four different DNA letters (A, T, G and C) so there are 64 different triplet codons (AAA, AAT and so on). But because there are only 20 amino acids, there's a lot of redundancy. For instance, the codons TAG, TAA and TGA all mean stop. If every TAG in a genome was altered to TAA or TGA, it wouldn't alter any of the protein recipes. But it would free up the TAG codon, so it could be used for specifying an artificial amino acid.

Church was part of a group that has already done this. In 2013, they finished editing the genome of one strain of *E. coli* to replace every one of the 314 instances of TAG.

Last year, the biologists went on to show that the freed-up TAG could be made to specify any one of several artificial amino acids. What's more, they altered genes so that essential proteins would work only if they included the artificial amino acid at certain points. This meant these strains of *E. coli* could only grow if their culture medium contained those artificial amino acids. In other words, these bacteria cannot escape from labs or factories.

Piece by piece

Now Church's team has revealed their progress towards on a far more ambitious project: changing seven codons in *E. coli*. Because this requires making more than 62,000 DNA changes, it cannot be done by gene editing. Instead, the team designed the genome on a computer and then synthesised the DNA in short pieces around 2000 DNA letters long.

These short segments have been stitched together to make 87 longer segments 50,000 DNA letters long. The final step will be to put them together to create a complete, 4-million-letter long *E. coli* genome. But before they do that, Church and his team are checking that all the genes still work, by inserting these segments into a living bacterium and deleting the equivalent sequence.

As expected, changing codons sometimes has lethal effects. For instance, one change to an essential gene altered the binding of a protein that controls gene activity. But so far only 13 deadly flaws have been found in the 2200 genes that have been checked so far – just over half the total – and these have all been fixed.

When will it be finished? The betting pool among the team ranges from 4 months to 4 years, says Church. But unexpected problems could yet put a spanner in the works.

If it does succeed, Church's team won't be the first to create a bacterium with a genome synthesised by scratch. That honour goes to a team at the J. Craig Venter Institute in La Jolla, California.

Minimal genome

But Venter's team created a microbe with a stripped down, minimal genome. Altering the genetic code as Church's team are doing is far more challenging. Although seven codons have been altered, the peculiarities of the genetic code mean only four could be used to specify artificial amino acids. "The genetic code is weird," says Lajoie.

The recoded *E. coli* will be made freely available to other researchers. Companies will be able to license it on a non-exclusive basis, Church says.

And many may want this since changing seven codons should be enough to make it completely resistant to all viruses. Viruses cannot make their own proteins, but instead hijack the machinery of the cells

they infect. A recoded *E. coli* will still start producing viral proteins if it is infected, but there will be so many errors in those proteins that no new viruses will be produced.

Making animals resist viruses in the same way will be a far greater challenge. The human genome is 6 billion letters long compared to the 4 million of *E. coli*, for instance. But a group of biologists including Church are trying to raise $100 million to synthesise the entire human genome from scratch. The initial plans do not include altering the genetic code, but if this Human Genome Project-Write goes ahead, it would pave the way for doing so.

Journal reference: Science, *DOI:* 10.1126/science.aaf3639

http://bit.ly/2bbsX7E

Nivolumab in advanced lung cancer: Indication of major added benefit

Advantages for overall survival and for side effects

Nivolumab has been approved since April 2016 as a checkpoint inhibitor for the treatment of adults with locally advanced or metastatic nonsquamous non-small-cell lung cancer (NSCLC) who have already undergone chemotherapy. In an early benefit assessment, the German Institute for Quality and Efficiency in Health Care (IQWiG) has now examined whether in these patients this monoclonal antibody offers advantages over the appropriate comparator therapy.

According to the findings, there is an indication of a major added benefit of nivolumab over docetaxel. An added benefit over the appropriate comparator therapy (best supportive care) is not proven in patients for whom treatment with docetaxel or similar drugs is not indicated.

Approval study stopped early due to survival advantage

The Federal Joint Committee (G-BA) specified docetaxel, pemetrexed or - depending on the mutation status - gefitinib, erlotinib or crizotinib as the appropriate comparator therapy. Patients for whom these drugs are not indicated were to be treated in the control arm with best supportive care instead, that is, treatment tailored to the individual patient's needs in order to alleviate pain and improve quality of life. The manufacturer did not present data on this second research question.

For the first research question, the manufacturer cited the approval study CA209-057, in which nivolumab was compared with docetaxel. After an interim analysis, all patients in the docetaxel arm were offered the option of further treatment with nivolumab, as the new drug showed clear advantages for overall survival. However, only PD-L1-positive patients had a statistically significant survival advantage. In contrast, an added benefit for overall survival is not proven in patients with a negative PD-L1 status.

Also advantages for side effects

Nivolumab also has advantages over docetaxel with regard to several outcomes from the category "side effects" (severe and serious adverse events, discontinuation due to adverse events, alopecia, and blood and lymphatic system disorders).

Overall, for patients who can be treated with docetaxel and similar drugs the data provide an indication of a major added benefit of nivolumab over the appropriate comparator therapy. Due to a lack of data, an added benefit is not proven for patients for whom such drugs are not indicated.

G-BA decides on the extent of added benefit

The dossier assessment is part of the early benefit assessment according to the Act on the Reform of the Market for Medicinal Products (AMNOG) supervised by the Federal Joint Committee (G-BA). After publication of the dossier assessment, the G-BA conducts a commenting procedure and makes a final decision on the extent of the added benefit.

An overview of the results of IQWiG's benefit assessment is given by a German-language executive summary. In addition, the Website gesundheitsinformation.de, published by IQWiG, provides easily understandable German-language information.

More English-language information will be available soon (Sections 2.1 to 2.6 of the dossier assessment as well as subsequently published health information on informedhealth.org). If you would like to be informed when these documents are available, please send an e-mail to » info@iqwig.de.

http://bit.ly/2bHvpCW

Flesh-eating infections in rheumatoid arthritis patients spur new discovery

Patient data reveals the crucial role immune molecule interleukin-1beta plays in sensing streptococcal infections and provides new insights for the development of targeted autoimmune disease therapies with fewer side effects

Rheumatoid arthritis patients taking medications that inhibit interleukin-1beta (IL-1beta), a molecule that stimulates the immune system, are 300 times more likely to experience invasive Group A Streptococcal infections than patients not on the drug, according to University of California San Diego School of Medicine researchers. Their study, published August 19 in Science Immunology, also uncovers a critical new role for IL-1beta as the body's independent early warning system for bacterial infections.

"The more we know about each step in the body's immune response to bacterial infections, the better equipped we are to design more personalized, targeted therapies for autoimmune diseases -- therapies that are effective, but minimize risk of infection," said senior author Victor Nizet, MD, professor of pediatrics and pharmacy at UC San Diego School of Medicine and Skaggs School of Pharmacy and Pharmaceutical Sciences.

IL-1beta is a molecule that stimulates an immune response, calling white blood cells to the site of an infection so they can engulf and clear away invading pathogens. The body first produces the molecule in a longer, inactive form that must be cleaved to be activated. The scientific community long believed that only the body itself could cleave and activate IL-1beta, by employing a cellular structure known as the inflammasome. But in experiments using cell cultures and mouse models of infection, Nizet and team found that SpeB, an enzyme secreted by strep bacteria, also cleaves and activates IL-1beta, triggering a protective immune response.

"This finding may explain why some of the more invasive, flesh-eating strep strains have a genetic mutation that blocks SpeB production -- it helps them avoid tripping the alarm and setting off an immune response," said first author Christopher LaRock, PhD, a postdoctoral researcher in Nizet's lab.

The researchers hypothesize that for less invasive strains, like those that cause strep throat, producing SpeB and activating IL-1beta might be advantageous -- the resulting immune response may wipe out competing bacteria and help strep establish a foothold in the body.

While the human immune system can quickly recognize and respond to bacterial infections, sometimes this reaction can go overboard, leading to autoimmune diseases such as rheumatoid arthritis. In this case, a person's own immune system attacks "self" proteins instead of just foreign invaders.

In their efforts to investigate IL-1beta function, Nizet, LaRock and team analyzed a U.S. Food and Drug Administration (FDA) database on adverse events in rheumatoid patients who took anakinra, a drug that dampens autoimmunity by inhibiting IL-1beta. They found that patients receiving anakinra were more than 300 times more likely to experience invasive, flesh-eating strep infections than patients not taking the drug.

"A likely explanation for this increased risk is that with IL-1beta out of the picture, as is the case with patients taking anakinra, strep strains can progress to invasive infection even while producing SpeB, which goes unnoticed by the immune system," LaRock said.

This finding underscores IL-1beta's importance as an early warning system that's triggered not only by the host, but also directly by bacterial enzymes, essentially "taking out the middle man," Nizet said.

The UC San Diego researchers believe this capacity for direct

pathogen detection represents IL-1beta's original role in immunity, going all the way back in evolution to simpler animals, such as fish.

"Inhibiting the body's bacterial sensor can put a person at risk for invasive infection," Nizet said, "but just the fact that we now know that this patient population is at higher risk and why means we can take simple steps -- such as close monitoring and prophylactic antibiotics -- to prevent it from happening. "

A video on this research can be found here.

Co-authors of this study include: Jordan Todd, Doris L. LaRock, Joshua Olson, Anthony J. O'Donoghue, and Hal M. Hoffman, UC San Diego; Avril A. B. Robertson, and Matthew A. Cooper, University of Queensland.

http://bit.ly/2boo64U

Study shows standing up for beliefs in face of group opposition is worth the effort

Going with the flow might appear easier than sticking up for yourself when confronted with unanimous disagreement.

BUFFALO, N.Y. - But a new study from the University at Buffalo that assessed bodily responses suggests that standing up for your beliefs, expressing your opinions and demonstrating your core values can be a positive psychological experience.

There can be a clear divergence between what people do and say and how they feel, according to Mark Seery, an associate professor in UB's Department of Psychology.

"People can show conformity, but going along with the group doesn't mean they're going along happily," he says. "The external behavior isn't necessarily a good indication of their internal experience."

The findings, published in the journal Psychophysiology, provide new insights into what it's like being alone against the group, investigating the experience as it happens.

Methodologically this is a hard thing to capture, according to Seery.

He says there is a long tradition in social psychology investigating how people are affected by pressure to conform to a group. The vast majority of the work has focused on behavior and self-reported attitudes, with the assumption that it's uncomfortable being the lone dissenter, and that people are motivated to conform because it relieves their discomfort.

Questioning study subjects during the experience can be disruptive, while waiting to interview them later demands that they recall feelings that aren't always accurately reported.

"But we can tap into the experience using psychophysiological measures, which is what we did in this case by assessing cardiovascular responses," says Seery. "That's where this study started. To try to understand what that momentary experience of conformity pressure is like."

By measuring cardiovascular responses, Seery and the other researchers - UB colleague Shira Gabriel, Daemen College's Shannon Lupien and Southern Illinois University's Mitsuru Shimizu - get a sense for how people are evaluating personal resources versus the demands of the situation while in the act of potentially conforming.

When trying to reach a goal, evaluating high resources and low demands leads to a mostly positive, invigorating experience called challenge, which corresponds with feeling confident. Low resources and high demands lead to a much less confident state called threat, which may produce feelings of anxiety.

The researchers assigned participants into one of four experimental conditions, each with a goal to either fit in with a group's political opinion or assert their individuality, and with a group that either agreed or disagreed with participants' opinion on the issue.

"When participants' goal was to fit in with a group of people who disagreed with them, their cardiovascular responses were consistent with a psychological threat state," says Seery. "In contrast, when the goal was to be an individual among a group of people who disagreed with them, their cardiovascular responses were consistent with challenge.

"You may have to work to reach a goal, but when you experience challenge, it is more like feeling invigorated than overwhelmed. It is

consistent with seeing something to gain rather than focusing on what can be lost," he says.

The results have interesting implications, especially in an election year, when someone can be surrounded by family members, coworkers or even neighborhood lawn signs that run contrary to personal opinions.

"It could easily be overwhelming to face a group on the other side of an issue or candidate, but this study suggests that reminding yourself of wanting to be an individual can make it a better experience, challenging instead of threatening, invigorating instead of overwhelming," says Seery.

http://bit.ly/2belTqZ

Quantum trick sees two things happen before and after each other

Alice sent a present to Bob. No wait, Bob sent the present to Alice. Actually… they kind of sent it to each other at the same time.

By Jacob Aron

A new experiment shows how gift-giving gets confusing when you're using quantum mechanics to muck about with causality.

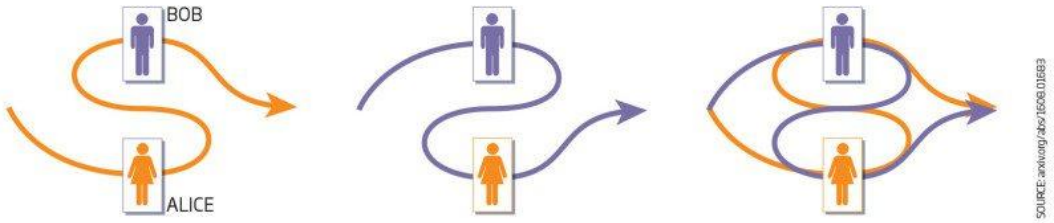
You may have heard of the double-slit experiment, in which a single particle fired at two small gaps appears to interfere with itself, as if it had passed through both slits at once. That happens because, until it is measured by a detector on the other side, the particle is in a quantum superposition of two states. In some sense it is able to take both paths.

It's weird, and difficult to wrap your head around, but now a team at the University of Vienna in Austria have performed a different kind of experiment that is even more mind-bending: putting the order of events into a superposition.

Normally, it's easy for us to say that event A happens before event B, or vice versa. But Giulia Rubino and her colleagues have created a superposition in which these seemingly contradictory scenarios are in superposition. "If you put together quantum mechanics and causal relations, a situation arises in which there is no pre-defined causal order," she says. "It's counter-intuitive."

Who's on first? It's hard to say...

Alice and Bob can both alter the quantum state of a photon as it passes them by, producing a different result depending on the order they act. But if the path of a photon is in a quantum superposition, it's impossible to say who went first



Their experiment involves sending a photon through two collections of optical devices, labelled Alice and Bob. These devices transform the quantum state of the photon in different ways, so that going through Alice, then Bob produces a different outcome to Bob, then Alice. "The fact that A is applied before B or B is applied before A actually changes the results," says Rubino.

To picture how that works, imagine the photon is a present intended for a third party. Alice likes to wrap presents, while Bob prefers a simple ribbon tied into a bow. If Alice gets her hands on the present first, she wraps it and then passes it to Bob, who puts a bow on. If Bob gets it first, Alice's wrapping covers the bow, resulting in a different outcome. Things are slightly more complicated for the photon, as Alice and Bob can perform different actions with a certain probability, so there are more than two possible outcomes.

Who's first?

In the team's experiment, a kind of quantum switch controls which path the photon takes, and thus the order in which Alice and Bob act. To mess with causality, they place this switch itself in a superposition, meaning that in a sense, both act first.

Of course, that's not quite what's happening, just as the particle in the double slit experiment doesn't truly go through both slits at once – it's just we don't have the language to describe the truly weird nature of the quantum realm that bubbles beneath our layer of reality.

"Time itself might be undefined in these situations," says team member Mateus Araújo. "The whole confusion with quantum mechanics is unfamiliarity, something that just doesn't match our macroscopic, classical experience."

What's reality, any way

"We're really pushing the mysteries and confusion of quantum physics to the absolute limit," says Matty Hoban at the University of Oxford. "We don't have a good picture of what reality is."

But this experiment isn't just a neat quantum party trick. We already know that causality confusion could theoretically help with some kinds of quantum communications and computation, reducing the number of resources needed to send messages or solve certain problems. In the future, the team want to realise this in an experiment. "We want to recreate the gain proposed in many theoretical papers and demonstrate this advantage," says Rubino.

Whether that turns out to be useful remains to be seen, says Hoban, as the computational problems in question are fairly esoteric and not directly related to real-world tasks. "It's not clear if we have a killer application, but it's very interesting that you can get improvements."

Journal reference: arxiv.org/abs/1608.01683

http://bit.ly/2b8yHNH

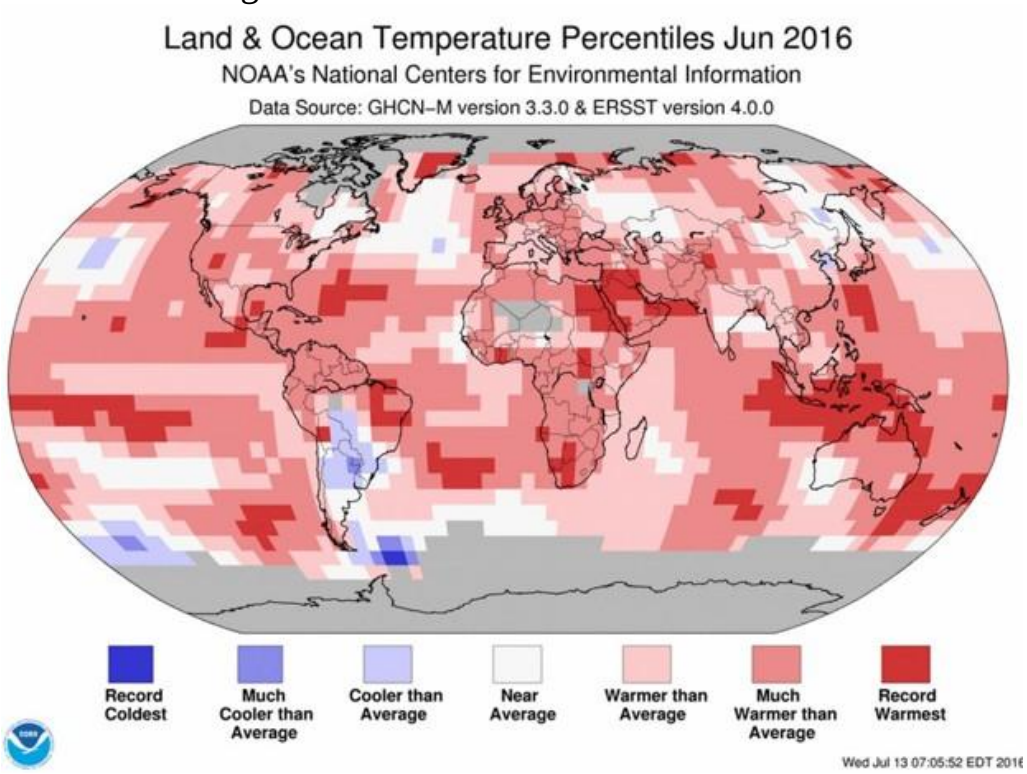
The Earth Has Endured 14 Straight Months of Record-Breaking Heat

Such an extreme warming spell has never occurred in nearly 140 years of observations.

John Metcalfe

The lower part of South America, the Beijing region, and a little patch of far-east Russia: These were the landmasses that experienced abnormally cool temperatures in June.

The vast majority of the Earth's surface, however, was either warmer than usual or scalding with record-breaking heat, according to NOAA's latest global analysis. At 1.6 degrees above the 20th-century average of roughly 60 degrees, it was the warmest June in modern history and the 14th consecutive month of unprecedented hotness. That's the longest streak of record-busting temperatures in observations dating back to 1880.



NOAA/NCDC

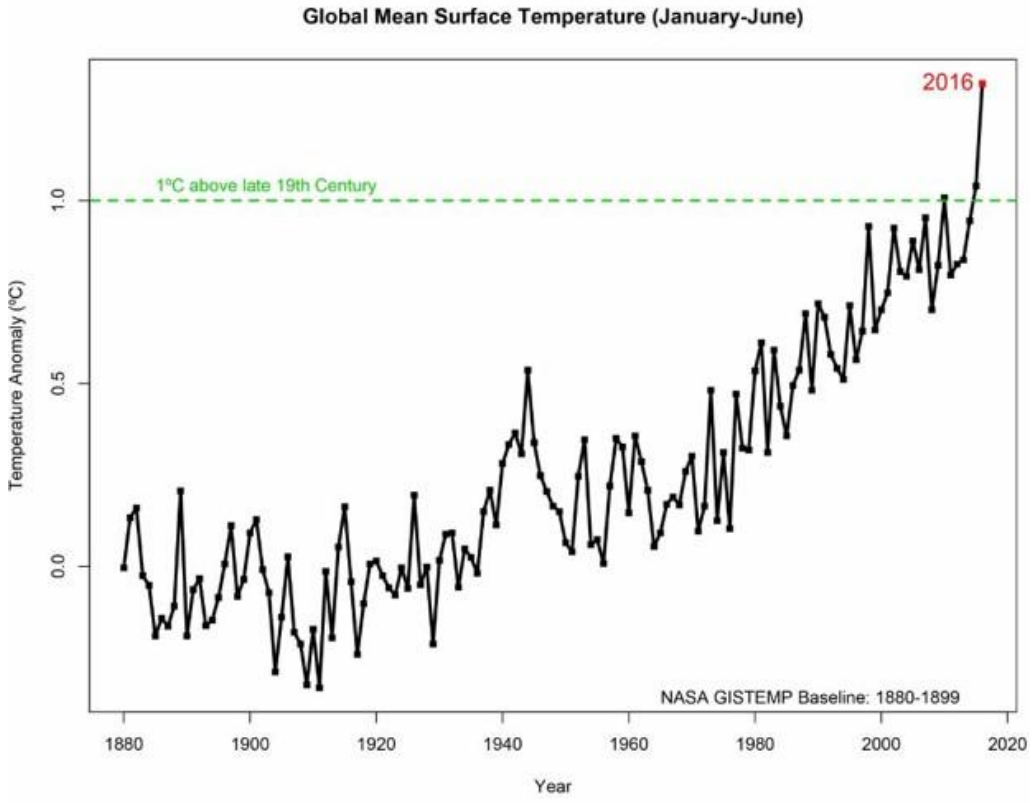
As has become common, worrying signs of accelerated warming and breakdown continue to pop up in the Arctic. The average sea-ice extent in the region was the most piddling ever recorded for the month of June—100,000 square miles smaller than the previous record-low extent in 2010.

Here's more from NASA on last month's dismal hot spell, which the agency says is a result of "rising concentrations of heat-trapping carbon dioxide and other greenhouse gases in the atmosphere":

Five of the first six months of 2016 also set records for the smallest respective monthly Arctic sea ice extent since consistent satellite records began in 1979, according to analyses developed by scientists

at NASA's Goddard Space Flight Center, in Greenbelt, Maryland. The one exception, March, recorded the second smallest extent for that month….

The extent of Arctic sea ice at the peak of the summer melt season now typically covers 40 percent less area than it did in the late 1970s and early 1980s. Arctic sea ice extent in September, the seasonal low point in the annual cycle, has been declining at a rate of 13.4 percent per decade.



NASA