http://bit.ly/2HsVAqB

Why expressive brows might have mattered in human evolution

Research to raise a few eyebrows: Why expressive brows might have mattered in human evolution

Highly mobile eyebrows that can be used to express a wide range of subtle emotions may have played a crucial role in human survival, new research from the University of York suggests.

Like the antlers on a stag, a pronounced brow ridge was a permanent signal of dominance and aggression in our early ancestors, which modern humans traded in for a smooth forehead with more visible, hairy eyebrows capable of a greater range of movement.

Mobile eyebrows gave us the communication skills to establish large, social networks; in particular to express more nuanced emotions such as recognition and sympathy, allowing for greater understanding and cooperation between people.

The study contributes to a long-running academic debate about why other hominins, including our immediate ancestors, had gigantic brow ridges while anatomically modern humans evolved flatter foreheads.

Senior author of the paper, Paul O'Higgins, Professor of Anatomy at the University of York, said: "Looking at other animals can offer interesting clues as to what the function of a prominent brow ridge may have been. In mandrills, dominant males have brightly coloured swellings on either side of their muzzles to display their status. The growth of these lumps is triggered by hormonal factors and the bones underlying them are pitted with microscopic craters - a feature that can also be seen in the brow bones of archaic hominins."

"Sexually dimorphic display and social signalling is a convincing explanation for the jutting brows of our ancestors. Their conversion to a more vertical brow in modern humans allowed for the display of friendlier emotions which helped form social bonds between individuals".

Using 3D engineering software, the researchers looked at the iconic brow ridge of a fossilised skull, known as Kabwe 1, held in the collections of the National History Museum.

It belonged to a species of archaic hominin - Homo heidelbergensis, who lived between 600,000 and 200,000 years ago.

The researchers discounted two theories commonly put forward to explain protruding brow ridges: that they were needed to fill the space where the flat brain cases and eye sockets of archaic hominins met, and that the ridge acted to stabilise their skulls from the force of chewing.

Professor O'Higgins said: "We used modelling software to shave back Kabwe's huge brow ridge and found that the heavy brow offered no spatial advantage as it could be greatly reduced without causing a problem. Then we simulated the forces of biting on different teeth and found that very little strain was placed on the brow ridge. When we took the ridge away there was no effect on the rest of the face when biting.

"Since the shape of the brow ridge is not driven by spatial and mechanical requirements alone, and other explanations for brow ridges such as keeping sweat or hair out of eyes have already been discounted, we suggest a plausible contributing explanation can be found in social communication."

According to the researchers, our communicative foreheads started off as a side-effect of our faces getting gradually smaller over the past 100,000 years. This process has become particularly rapid in last 20,000 years and more recently, as we switched from being hunter gatherers to agriculturalists - a lifestyle that meant less variety in both diet and physical effort.

Co-author of the paper, Dr Penny Spikins from the Department of Archaeology at the University of York, said: "Modern humans are the last surviving hominin. While our sister species the Neanderthals were dying out, we were rapidly colonising the globe and surviving in extreme environments. This had a lot to do with our ability to create large social networks - we know, for example, that prehistoric modern

humans avoided inbreeding and went to stay with friends in distant locations during hard times.

"Eyebrow movements allow us to express complex emotions as well as perceive the emotions of others. A rapid "eyebrow flash" is a cross-cultural sign of recognition and openness to social interaction and pulling our eyebrows up at the middle is an expression of sympathy. Tiny movements of the eyebrows are also a key component to identifying trustworthiness and deception. On the flip side it has been shown that people who have had botox which limits eyebrow movement are less able to empathise and identify with the emotions of others.

"Eyebrows are the missing part of the puzzle of how modern humans managed to get on so much better with each other than other now-extinct hominins."

Supraorbital morphology and social dynamics in human evolution is published in Nature Ecology and Evolution.

http://bit.ly/2qmq0cW

Payments to doctors linked to prescription practices for two cancer types

Physicians receiving payment from pharmaceutical companies for expenses more likely to prescribe those companies' drugs

CHAPEL HILL -- Physicians who received payment from pharmaceutical companies for meals, talks and travel were more likely to prescribe those companies' drugs for two cancer types, a University of North Carolina Lineberger Comprehensive Cancer Center-led study has found. The study was published Monday in the *Journal of the American Medical Association Internal Medicine*. The preliminary findings were presented last year at the American Society of Clinical Oncology's Annual Meeting.

"The main takeaway is that oncologists who received money from a pharmaceutical company were more likely to choose that company's drug the following year," said Aaron Mitchell, MD, a fellow in the UNC School of Medicine Division of Hematology & Oncology, and the study's lead author.

For the study, researchers analyzed prescriptions for Medicare patients with two cancers where there are multiple treatment options: metastatic renal cell cancer (kidney cancer), and chronic myeloid leukemia, a blood cancer.

The researchers used publicly available data from 2013 to 2014 that was reported through Open Payments, a provision of the federal Patient Protection and Affordable Care Act that required U.S. drug and device manufacturers to disclose transfers of financial value greater than $10 to physicians and teaching hospitals.

Compared to physicians who didn't receive any payments, those who received general payments for meals and lodging from a drug manufacturer had higher odds of prescribing that company's particular drug for metastatic renal cell carcinoma and for chromic myeloid leukemia. For metastatic renal cell cancer, physicians who received any general payment in 2013 had twice the odds of prescribing that company's drug, and for chronic myeloid leukemia physicians who received any general payment had 29 percent higher odds of prescribing that company's drug.

The researchers did not find a consistent relationship for physicians who received payments from pharmaceutical companies solely for research.

An analysis of the data by individual drug type found a statistically significant decrease in the use of the leukemia treatment imatinib when physicians received payments. The same manufacturer made both imatinib and another treatment, nilotinib, Mitchell said. Since imatinib was about to lose its patent protection, the authors interpreted this finding to mean that payments from this company have been oriented towards "switching" physicians from the older drug imatinib to the newer drug nilotinib.

The researchers said the "proof-of-principle" study was meant to investigate whether there was an association between industry

payments and prescriptions for cancer care, but researchers caution that it does not show a cause-and-effect relationship.

The study was supported by a National Research Service Award Post-Doctoral Traineeship from the Agency for Healthcare Research and Quality with the Cecil G. Sheps Center for Health Services Research at the University of North Carolina at Chapel Hill, and the American Cancer Society.

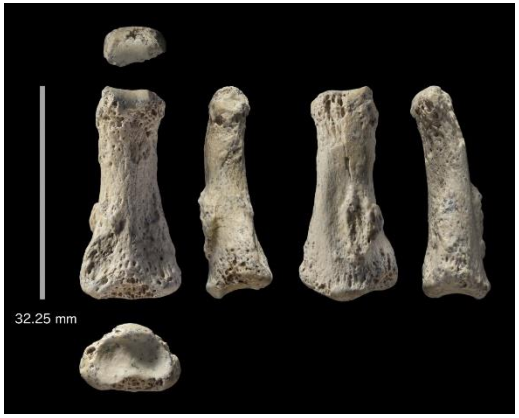
In addition to Aaron Mitchell, other authors include Aaron N. Winn, MPP, formerly a PhD candidate in the Department of Health Policy and Management at UNC Gillings School and now an Assistant Professor at University of Wisconsin, and Stacie Dusetzina, PhD, formerly of UNC Lineberger and now of the Vanderbilt University School of Medicine.

http://bit.ly/2EDBPj6

First human migration out of Africa more geographically widespread than previously thought

The first Homo sapiens fossil discovery from Saudi Arabia dates to 90,000 years ago during a time when the region's deserts were replaced by grasslands

A project led by the Max Planck Institute for the Science of Human History has discovered a fossilized finger bone of an early modern human in the Nefud Desert of Saudi Arabia, dating to approximately 90,000 years ago. The discovery, described in *Nature Ecology and Evolution*, is the oldest directly dated *Homo sapiens* fossil outside of Africa and the Levant and indicates that early dispersals into Eurasia were more expansive than previously thought.



Fossil finger bone of Homo sapiens from the Al Wusta site, Saudi Arabia. **Ian Cartwright**

Researchers conducting archaeological fieldwork in the Nefud Desert of Saudi Arabia have discovered a fossilized finger bone of an early member of our species, *Homo sapiens*. The discovery is the oldest directly dated *Homo sapiens* fossil outside of Africa and the immediately adjacent Levant, and indicates that early dispersals into Eurasia were more expansive than previously thought. Prior to this discovery, it was thought that early dispersals into Eurasia were unsuccessful and remained restricted to the Mediterranean forests of the Levant, on the doorstep of Africa. The finding from the Al Wusta site shows that there were both multiple dispersals out of Africa, and these spread further than previously known.

Oldest directly dated *Homo sapiens* fossil outside of Africa and the Levant

The results, published in Nature Ecology and Evolution, detail the discovery made at the site of Al Wusta, an ancient fresh-water lake located in what is now the hyper-arid Nefud Desert. Numerous animal fossils, including those of hippopotamus and tiny fresh water snails were found at Al Wusta, as well as abundant stone tools made by humans. Among these finds was a well preserved and small fossil, just 3.2 cm long, which was immediately recognized as a human finger bone. The bone was scanned in three dimensions and its shape compared to various other finger bones, both of recent *Homo sapiens* individuals and bones from other species of primates and other forms of early humans, such as Neanderthals. The results conclusively showed that the finger bone, the first ancient human fossil found in Arabia, belonged to our own species. Using a technique called uranium series dating, a laser was used to make microscopic holes in the fossil and measure the ratio between tiny traces of radioactive elements. These ratios revealed that the fossil was 88,000 years old. Other dates obtained from associated animals fossils and sediments converged to a date of approximately 90,000 years ago. Further environmental analyses also revealed the site to have been a freshwater lake in an ancient grassland environment far removed from today's deserts.

Lead author Dr. Huw Groucutt, of the University of Oxford and the Max Planck Institute for the Science of Human History, states, "This discovery for the first time conclusively shows that early members of our species colonized an expansive region of southwest Asia and were not just restricted to the Levant. The ability of these early people to

widely colonize this region casts doubt on long held views that early dispersals out of Africa were localized and unsuccessful."

Modern deserts of the Arabian Peninsula were once lush grasslands that humans were able to colonize

Project Lead, Professor Michael Petraglia of the Max Planck Institute for the Science of Human History adds, "The Arabian Peninsula has long been considered to be far from the main stage of human evolution. This discovery firmly puts Arabia on the map as a key region for understanding our origins and expansion to the rest of the world. As fieldwork carries on, we continue to make remarkable discoveries in Saudi Arabia."

The international consortium of researchers involved in this project is headed by the Max Planck Institute for the Science of Human History, in partnership with the Saudi Commission for Tourism and National Heritage. Additional partners include the Saudi Geological Survey, King Saud University, the University of Oxford and other key institutions in the United Kingdom and Australia.

http://bit.ly/2qnE1Gs

How tumors caused by STD quickly regress in dogs

The canine transmissible venereal tumor is a contagious cancer that has spread by mating among dogs worldwide.

One unique feature of this cancer is that, for unclear reasons, it regresses spontaneously or a few weeks after a single treatment of radiotherapy or chemotherapy. A study published April 9 in the journal *Cancer Cell* shines a light on this mystery, revealing a key role for the immune system in triggering fast cancer rejection in chemotherapy-treated dogs. Because the canine transmissible venereal tumor shares many similarities with various human cancers, the findings could point to more effective therapeutic strategies.

"We found that activation of the innate immune system and production of certain molecules called chemokines by the host tissue around the tumor is critical to attract immune cells within the tumor and trigger a chain reaction that leads to the rejection of the cancer and its elimination," says senior author Professor Ariberto Fassati of UCL (University College London). "We hope that this study will encourage the clinical testing of combined approaches to improve immunological therapies against cancer, in animals and humans alike."

First described in the 1800s, the canine transmissible venereal tumor rapidly grows into a cauliflower-like mass on genitalia, and it is naturally transmitted between dogs by coitus, biting, or licking tumor-affected areas. It is one of three known clonally transmissible cancers in nature, along with Tasmanian devil facial disease and leukemias in soft-shell clams. Because it originated from a single common ancestor, the canine transmissible venereal tumor consists of genetically identical cells in all affected dogs, making it easier to identify key factors driving cancer regression. Yet few labs have investigated this topic, leaving it unclear how cancer rejection occurs.

To answer this question, Fassati and his collaborators collected biopsies from canine transmissible venereal tumors in eight dogs before treatment as well as 6 days and 14 days after receiving a chemotherapy drug called vincristine. The researchers performed systematic genome-wide analyses to compare gene activity in tumors that fully regressed with those that did not regress.

They discovered that regression occurs in sequential steps. First, vincristine treatment led to a strong inflammatory response and the proliferation of host skin cells, which may represent an attempt by the tissue surrounding tumors to contain or replace the malignant tissue. "We were expecting that most changes leading to regression of this dog tumor would occur in the cancer cells," Fassati says. "Instead, we realized that the host cells were more important."

This early stage of regression was also characterized by an increase in the production of a chemokine called CCL5--a signaling protein that attracted cancer-fighting immune cells to the tumor. Ultimately, this process resulted in immune rejection of the tumor and repair of tissue damage.

"There are two key messages of our study," Fassati says. "First, we should not focus on the cancer cells only but also understand the importance of normal tissue around the cancer in promoting rejection. Second, we must be able to induce the production of large amounts of certain chemokines to attract loads of immune cells to the tumor site."

In the end, this research could have implications for human cancers, such as skin cancer, bone cancer, and certain blood cancers. For his own part, Fassati plans to investigate whether it's possible to stimulate chemokines that attract immune cells to tumors in human cancers. "However, it may take some time before these approaches are tested in the clinic," he says. "So the general audience should not take away the message that we have found the magic wand to make cancer disappear."

Despite these limitations, this research could help guide ongoing and future clinical investigations. "There might be ways to improve the efficacy of immunological therapies against cancer by combining different approaches, such as releasing the breaks of the immune system through checkpoint inhibitors and inducing host cells surrounding the tumor to attract the unleashed immune cells to the tumor site," Fassati says. "Indeed, there are already ongoing trials that combine low-dose radiotherapy or chemotherapy with immunological therapies, precisely to stimulate a strong inflammatory response in the tumor."

This study was funded by a grant from the UCL Cancer Center Development Fund and the Biotechnology and Biological Sciences Research Council. Additional support was received by the Wellcome Trust and the UK Medical Research Council.

*Cancer Cell, Frampton et al.: "*Molecular Signatures of Regression of the Canine Transmissible Venereal Tumor*"* *http://www.cell.com/cancer-cell/fulltext/S1535-6108(18)30071-0*

https://bbc.in/2JDm8ft

Tasmanian devil cancers targeted by human drugs

Cancers threatening to decimate the Tasmanian devil population could be halted by using drugs developed for human cancers, researchers have found.

Two transmissible cancers affect the endangered carnivorous marsupial found in the wild only in Tasmania.

Tumours usually spread when the animals bite each others' faces during fights.

However, Cambridge University scientists found drugs targeting receptors in humans could stop cancer in devils under laboratory conditions.

Two transmissible strains of the disease, which cause disfiguring facial tumours, have spread among the marsupials and led to a significant decline in populations in their namesake Australian island state.

Image copyright University of Cambridge Image caption Co-author of the study, Maximilian Stammnitz, examining a Tasmanian devil

One strain, which was first noted in one animal in 1996, has spread throughout the "Tassie devil" population, while a second - first documented in 2014 - is confined to the south east of the island.

However, while both strains are biologically different, visibly they are similar and are thought to be passed between devils through the transfer of living cancer cells when they bite each other.

"When fighting, Tasmanian devils often bite their opponent's face, which may predispose these animals to the emergence of this particular type of cancer via tissue injury," said Maximilian Stammnitz, co-author of the Cambridge University study into the disease.

"As biting occurs on the face, this would simultaneously provide a route of cell transmission."

The researchers, led by Dr Elizabeth Murchison, from the Department of Veterinary Medicine at the university, found molecules known as receptor tyrosine kinases (RTKs) played an important role in sustaining the growth and survival of both the cancers.

However, drugs targeting RTKs - developed for human cancer - were found to efficiently stop the growth of devil cancer cells in a lab setting.

"This study gives us optimism that anti-cancer drugs that are already in use in humans may offer a chance to assist with conservation efforts for this iconic animal," Dr Murchison said.

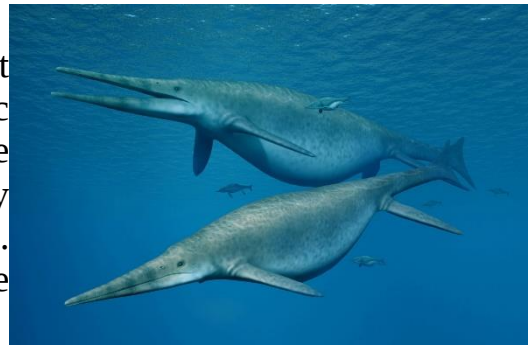
The results of the study have been published in the journal Cancer Cell.

http://bit.ly/2v3zSNr

UK giant ichthyosaur is one of the largest animals ever

The 205 million-year-old jaw bone of a prehistoric reptile belongs to 'one of the largest animals ever' say a group of international palaeontologists.

The new discovery has also solved a 150 year old mystery of supposed 'dinosaur bones' from the UK.



The bone belongs to a giant ichthyosaur, a type of prehistoric aquatic reptile, and experts estimate the length of this specimen's body would have been up to 26 metres. Approaching the size of a blue whale.

Fossil collector and co-author of the study, Paul de la Salle, found the bone on the beach at Lilstock, Somerset in May 2016. He later returned to the site and found even more pieces that together measured about one metre in length.

Paul said "Initially, the bone just looked like a piece of rock but, after recognising a groove and bone structure, I thought it might be part of a jaw from an ichthyosaur and immediately contacted ichthyosaur experts Dean Lomax (University of Manchester) and Prof. Judy Massare (SUNY College at Brockport, NY, USA) who expressed interest in studying the specimen. I also contacted Dr Ramues Gallois, a geologist who visited the site and determined the age of the specimen stratigraphically.

Lomax and Massare identified the specimen as an incomplete bone (called a surangular) from the lower jaw of a giant ichthyosaur. The bone would have made up only a portion of the entire skull. They compared it with several ichthyosaurs and visited the Royal Tyrrell Museum of Palaeontology in Alberta, Canada, and examined the largest ichthyosaur known, the shastasaurid *Shonisaurus sikanniensis*, which is 21 m long. They found similarities between the new specimen and S. sikanniensis which suggest the Lilstock specimen belongs to a giant shastasaurid-like ichthyosaur.

"As the specimen is represented only by a large piece of jaw, it is difficult to provide a size estimate, but by using a simple scaling factor and comparing the same bone in S. sikanniensis, the Lilstock specimen is about 25% larger. Other comparisons suggest the Lilstock ichthyosaur was at least 20-25 m. Of course, such estimates are not entirely realistic because of differences between species. Nonetheless, simple scaling is commonly used to estimate size, especially when comparative material is scarce." Added Lomax.

In 1850, a large bone was described from the Late Triassic (208 million-years-old) of Aust Cliff, Gloucestershire, UK. Four other similarly incomplete bones were also found and described. Two of them are now missing and presumed destroyed. They have been identified as the limb bones of several dinosaurs (stegosaurs and sauropods), indeterminate dinosaurs and other reptiles.

However, with the discovery of the Lilstock specimen, this new study refutes previous identifications and also the most recent assertion that the Aust bones represent an early experiment of dinosaur-like gigantism in terrestrial reptiles. They are, in fact, jaw fragments of giant, previously unrecognised ichthyosaurs.

Dean added: "One of the Aust bones might also be an ichthyosaur surangular. If it is, by comparison with the Lilstock specimen, it might represent a much larger animal. To verify these findings, we need a complete giant Triassic ichthyosaur from the UK - a lot easier said than done!"

The new study is open access and has been published today in the scientific journal, *PLOS ONE*.

Notes to editors

Dean is an internationally recognised multi-award-winning palaeontologist, science communicator and author. He has travelled the globe and worked on many fascinating projects from excavating dinosaurs in the American West, to describing

new species of extinct marine reptiles and winning a gold medal for excellence in science.

A visiting scientist at The University of Manchester, Dean is passionate about communicating palaeontology with the public and regularly appears on television, including as series advisor and recurring on-screen expert presenter for ITV's Dinosaur Britain. He has written two books, numerous scientific papers, and many popular articles. Dean is also the patron of the UK Association of Fossil Hunters (UKAFH). More here: http://www.deanrlomax.co.uk.

Please reference the article as: Lomax, D. R., De la Salle, P., Massare, J. A. and Gallois, R. 2018. A giant Late Triassic ichthyosaur from the UK and a reinterpretation of the Aust Cliff 'dinosaurian' bones. PLOS ONE, *http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0194742.*

http://bit.ly/2v3w4Mo

Man enters chilli-eating contest. Chilli wins

Medical journal reveals the folly of doing battle with little red fruits.

Andrew Masterson reports.

As readers who have had the dubious pleasure of watching combative cooking-themed television shows such as *Man v. Food* already know, sometimes the simple act of eating can take on an unpleasant aspect of machismo and challenge.

Eating enormous hamburgers or entire turduckens might be favourite pursuits for large gentlemen with loud voices and even louder shirts, but true food warriors know that the ultimate contest between humans and comestibles involves eating simple, uncooked, untreated chillies.

Some people like to do this sort of thing in private – testing their powers of endurance for reasons only they know – while for others competing against fellow hot-pepper fanatics is the name of the game. In both scenarios, however, there is only one paradigm: the hotter, the better.

And, of course, it's all good, clean fun until someone gets hurt – which is precisely the point at which the *British Medical Journal* gets involved.

In the latest edition of the journal's *Case Reports*, four New York-based emergency doctors, led by Satish Kumar Boddhula, report on a man who experienced crippling "thunderclap headaches" after attempting to eat a 'Carolina Reaper', billed as the hottest chilli in the world.

Chillies are measured on the Scoville Scale, in increments known as scoville heat units, or SHUs. The scale is named after a pharmaceutical researcher, Wilbur Scoville, who worked for Parke Davis and died in 1942.

Effectively, the Scoville Scale reflects the concentration of capsaicin, a neuropeptide-releasing agent found in all members of the pepper family. A capsicum, the baseline pepper, has one SHU. A bird's eye chilli – small and hot enough for most spice-lovers – contains up to 225,000. The Carolina Reaper contains 1,569,300.

The 34-year-old man who presented to Boddhula and his colleagues at the Bassett Medical Centre in New York presumably knew that. It was, indeed, probably the reason he chose to tackle the fruit at a chilli-eating contest in the first place.

By the time he arrived at the emergency department, two days of sheer misery had elapsed since his display of culinary masochism. Immediately after eating the chilli, the case study notes reveal, he started dry-heaving.

The description continues: "He then developed intense neck and occipital head pain." After that he experienced multiple thunderclap headaches: brief bouts of excruciating pain that sent him scurrying to the hospital.

Once there, he was tested for a variety of neurological conditions, including aneurism, but everything came back clear. A computed tomography (CT) scan, however, revealed that several of the arteries leading to his brain were constricted.

Boddhula and colleagues diagnosed a condition known as reversible cerebral vasoconstriction syndrome (RCVS). As the name implies, the artery restrictions gradually eased and the headaches disappeared.

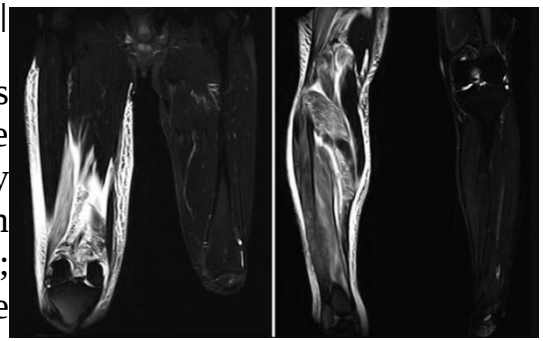
After five weeks, the man was found to be symptom-free. It is unknown whether he plans a return match with the chilli from hell.

http://bit.ly/2HurnO8

Deadly Pressure: Why These Two Men's Muscles 'Blew Up' From the Inside

Acute compartment syndrome doesn't sound especially dramatic, but its consequences can be gruesome and potentially lethal

By Mindy Weisberger, Senior Writer | April 9, 2018 02:07pm ET



The medical condition known as acute compartment syndrome (ACS) doesn't sound especially dramatic, but its consequences can be gruesome and potentially lethal; it causes swift and extreme muscle swelling that can require slicing through the skin and muscle wall to relieve the pressure.

Two MRI images show fluid-swollen tissue in a patient's leg. The injured leg, seen on the left in both images, displays swelling in the upper (R) and lower (L) part of the limb. **Takeda S, et al./BMJ Case Reports/CC BY 4.0**

The condition is usually associated with a highly traumatic injury, but for two people in Japan, doctors traced ACS to an unlikely source — bites from a venomous snake, according to a new report of the two cases. The two cases happened eight years apart — in 2008 and 2016 — and the people didn't know each other, according to the report, published April 1 in the journal BMJ Case Reports. In both instances, the patients had massively swollen extremities, and were separately diagnosed with ACS, but neither showed signs of severe trauma.

After treating them, doctors concluded that in both cases, the extraordinary localized swelling was a reaction to a bite from a type of viper known as the mamushi, which is native to Japan and other parts of Asia.

Under pressure

ACS is an exceptionally painful condition affecting groupings of muscles, blood vessels and nerves in the arms and legs that are known as compartments, which are bound together by a robust membrane called the fascia, according to the American Academy of Orthopaedic Surgeons (AAOS).

During ACS, pressure swiftly builds up inside the muscle compartment, blocking the flow of blood to and from the damaged site, said Dr. Sanjit Konda, an assistant professor of orthopedic surgery at NYU Langone Health in New York City.

"The pressure becomes so great in the compartment that the muscle and all of the other tissue is not getting any nutrients, and is going to start dying," said Konda, who was not involved in the case report. In urgent ACS cases, irreversible muscle damage can occur within 4 to 12 hours, and so surgeons must relieve the loss of circulation and prevent tissue death with a technique known as fasciotomy, a procedure that slices through the fascia, according to the case report authors.

Surgeons performed a fasciotomy on a patient's arm to prevent tissue death from the extreme pressure. **Takeda S, et al./BMJ Case Reports/CC BY 4.0**

Typically, ACS is caused by a severe, high-impact injury — "usually a crush injury," such as a car or motorcycle accident, or a trauma involving heavy machinery, Konda told Live Science. However, ACS can also develop from a minor trauma in people who are on blood-thinning medication, or it can emerge following the injection of a foreign material into the arm or leg, such as snake venom, he explained.

Two mysterious cases

In one of the cases described in the report, a 38-year-old man was hospitalized in 2016 with a dramatic swelling from his forearm to his shoulder. In the earlier case, from 2008, the report described a 42-year-old man who developed swelling throughout his right leg and foot. In both instances, the painful swelling was so severe that the surgeons had

to make cuts to the limbs, to relieve the pressure and prevent permanent muscle damage.

Neither patient had recently experienced a severe trauma that could explain his ACS, which puzzled the doctors. But they noted that the patients could also have been having a reaction to the venom of a snake or an insect. The time of year and locations where the injuries occurred, along with the rapid emergence of the swelling, suggested to the doctors that a type of snake in the viper family commonly known as the mamushi (*Gloydius blomhoffii*) was the culprit.

The mamushi is widespread in Japan, Korea and parts of China and Russia, according to a reptile database maintained by the Zoological Museum at the University of Hamburg in Germany. They hide under grasses and leaves and can be tough to spot, as they measure less than 24 inches (60 centimeters) in length. And their bites, delivered with delicate fangs that measure about 0.2 inches (5 millimeters) long, initially cause only minor pain and leave marks that are often too small to see, according to the case report.

A toxic attack

However, mamushi venom is powerful, and is so renowned that it was included in an ancient Japanese samurai scroll of deadly battle tactics. The powdered venom, when mixed with other ingredients and blown into an enemy's face, was said to be capable of rendering them unconscious, though it "has not been fully tested," according to the text.

After a bite, toxins in the venom could have made their way into a capillary and ruptured it, causing a leak that would have led to a buildup of extreme pressure, the study authors reported.

Venomous bites can also lead to ACS because they can trigger significant inflammation around the area where the venom was injected, and chemicals in the venom may hinder blood clotting, "which can cause you to bleed more," Konda said.

Although the study authors concluded that mamushi bites were the most plausible explanation for the patients' ACS, the "diagnosis could not be established owing to the lack of bite marks and clinical history of bite," and so they administered no antivenom, they wrote in the report.

Luckily, the swift actions of the medical teams in the study enabled both ACS patients to recover. The man with the swollen arm was discharged after 32 days, with normal function of his arm and hand restored. And though the patient with the swollen leg left the hospital with his injured limb paralyzed, he fully regained use of the leg after two years, the study authors reported.

http://bit.ly/2EFZqzU

Antibiotics do work on viruses

Common wisdom is overturned as researchers show anti-bacterial drugs can also knock viruses for six.

Paul Biegler reports.

Everybody knows antibiotics don't work on viruses, right? Not, it turns out, if you're a female mouse with a nasty case of genital herpes, in which case a well-timed dose of antibiotic might be just the thing, according to new research published in the journal *Nature Microbiology*.

The researchers, led by Akiko Iwasaki from the Department of Immunobiology at Yale University in New Haven, US, infected mice with the herpes simplex virus – no trifling matter in rodents. The virus migrates from the vagina to the spinal cord resulting in hind limb paralysis, hair loss and, in some cases, death.

However, mice that were pre-treated with the antibiotic neomycin, used in humans to treat ear and skin infection and to sterilise the bowel before gut surgery, were largely spared this fate. They displayed, write the authors, "little to no disease pathology".

How could antibiotics, which the received wisdom says are only effective against bacteria, possibly kill viruses?

Neomycin, it seems, is able to hack into the body's virus-slaying mechanism by recruiting dendritic cells, key regulators of the immune system. The result is a bumping up, by as much as two-to-fivefold, of

the expression of genes stimulated by the immune protein interferon, which produce a range of virus-killing substances.

And the good news isn't limited to herpes.

A shot of neomycin up the nose was able to ward off influenza A in 40% of mice, also by boosting those interferon-stimulated genes, this time in the lung. On top of that, the researchers found that kasugamycin, an antibiotic belonging to the same class as neomycin, shut down replication of the devastating mosquito-borne virus known as zika, linked to stunted head and brain growth in babies of women infected during pregnancy.

The study included a very important check. The team made sure their antibiotics weren't simply knocking out some of the legions of bacteria camped throughout the body, especially in the gut, collectively called the microbiome.

It is increasingly understood that our own special mix of gut microbes has serious clout in how well the immune system handles disease. A study published in *Science* in early 2018, for example, showed that people whose gut bacteria were depleted by antibiotics did worse on treatment for lung and kidney cancers, an effect related to impaired immunity.

Iwasaki's team repeated their experiment in "germ-free" mice, which have no such bugs growing in or on them. The antiviral effects held all the same, showing they occur independent of whatever bacteria happen to be in residence at the time.

If you find yourself with the sniffles or an unpleasant itch, however, don't expect to be racing off to the doctor for antibiotics any time soon. Note that most results were in mice treated *before* the infection began, although there was some success treating herpes in mice given the antibiotics four hours after infection.

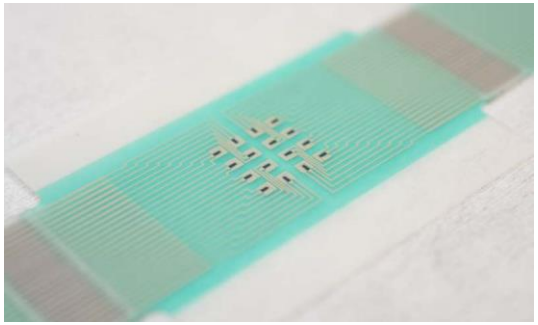
Nonetheless, isolating the mechanism by which an antibiotic might treat viruses is a big step and could, write the authors, "be useful for the future design of novel broad-acting antivirals".

http://bit.ly/2EGqJtP

Non-invasive, adhesive patch promises measurement of glucose levels through skin without finger-prick blood test

Bloodless revolution in diabetes monitoring

Scientists have created a non-invasive, adhesive patch, which promises the measurement of glucose levels through the skin without a finger-prick blood test, potentially removing the need for millions of diabetics to frequently carry out the painful and unpopular tests.



The sensor array is designed to draw fluid across a single hair follicle.
University of Bath

The patch does not pierce the skin, instead it draws glucose out from fluid between cells across hair follicles, which are individually accessed via an array of miniature sensors using a small electric current. The glucose collects in tiny reservoirs and is measured. Readings can be taken every 10 to 15 minutes over several hours.

Crucially, because of the design of the array of sensors and reservoirs, the patch does not require calibration with a blood sample—meaning that finger prick blood tests are unnecessary.

Having established proof of the concept behind the device in a study published in Nature Nanotechnology, the research team from the University of Bath hopes that it can eventually become a low-cost, wearable sensor that sends regular, clinically relevant glucose measurements to the wearer's phone or smartwatch wirelessly, alerting them when they may need to take action.

An important advantage of this device over others is that each miniature sensor of the array can operate on a small area over an individual hair follicle - this significantly reduces inter- and intra-skin variability in

glucose extraction and increases the accuracy of the measurements taken such that calibration via a blood sample is not required.

The project is a multidisciplinary collaboration between scientists from the Departments of Physics, Pharmacy & Pharmacology, and Chemistry at the University of Bath.

Professor Richard Guy, from the Department of Pharmacy & Pharmacology, said: "A non-invasive - that is, needle-less - method to monitor blood sugar has proven a difficult goal to attain. The closest that has been achieved has required either at least a single-point calibration with a classic 'finger-stick', or the implantation of a pre-calibrated sensor via a single needle insertion. The monitor developed at Bath promises a truly calibration-free approach, an essential contribution in the fight to combat the ever-increasing global incidence of diabetes."

Dr Adelina Ilie, from the Department of Physics, said: "The specific architecture of our array permits calibration-free operation, and it has the further benefit of allowing realisation with a variety of materials in combination. We utilised graphene as one of the components as it brings important advantages: specifically, it is strong, conductive, flexible, and potentially low-cost and environmentally friendly. In addition, our design can be implemented using high-throughput fabrication techniques like screen printing, which we hope will ultimately support a disposable, widely affordable device."

Bloodless revolution in diabetes monitoring

The patch can be attached to the wrist to measure blood glucose without piercing the skin. Credit: University of Bath

In this study the team tested the patch on both pig skin, where they showed it could accurately track glucose levels across the range seen in diabetic human patients, and on healthy human volunteers, where again the patch was able to track blood sugar variations throughout the day.

The next steps include further refinement of the design of the patch to optimise the number of sensors in the array, to demonstrate full functionality over a 24-hour wear period, and to undertake a number of key clinical trials.

Diabetes is a serious public health problem which is increasing. The World Health Organization predicts the world-wide incidence of diabetes to rise from 171M in 2000 to 366M in 2030. In the UK, just under six per cent of adults have diabetes and the NHS spends around 10% of its budget on diabetes monitoring and treatments. Up to 50% of adults with diabetes are undiagnosed.

An effective, non-invasive way of monitoring blood glucose could both help diabetics, as well as those at risk of developing diabetes, make the right choices to either manage the disease well or reduce their risk of developing the condition.

More information: Non-invasive, transdermal, path-selective and specific glucose monitoring via a graphene-based platform, Nature Nanotechnology (2018).
nature.com/articles/doi:10.1038/s41565-018-0112-4

https://bbc.in/2GTh5d8

More than half your body is not human

More than half of your body is not human, say scientists.

By James Gallagher Presenter, The Second Genome, BBC Radio 4

Human cells make up only 43% of the body's total cell count. The rest are microscopic colonists. Understanding this hidden half of ourselves - our microbiome - is rapidly transforming understanding of diseases from allergy to Parkinson's.

The field is even asking questions of what it means to be "human" and is leading to new innovative treatments as a result. "They are essential to your health," says Prof Ruth Ley, the director of the department of microbiome science at the Max Planck Institute, "your body isn't just you".

No matter how well you wash, nearly every nook and cranny of your body is covered in microscopic creatures. This includes bacteria, viruses, fungi and archaea (organisms originally misclassified as bacteria). The greatest concentration of this microscopic life is in the dark murky depths of our oxygen-deprived bowels.

Prof Rob Knight, from University of California San Diego, told the BBC: "You're more microbe than you are human." Originally it was thought our cells were outnumbered 10 to one. "That's been refined much closer to one-to-one, so the current estimate is you're about 43% human if you're counting up all the cells," he says. But genetically we're even more outgunned.

The human genome - the full set of genetic instructions for a human being - is made up of 20,000 instructions called genes.

But add all the genes in our microbiome together and the figure comes out between two and 20 million microbial genes.

Prof Sarkis Mazmanian, a microbiologist from Caltech, argues: "We don't have just one genome, the genes of our microbiome present essentially a second genome which augment the activity of our own.

"What makes us human is, in my opinion, the combination of our own DNA, plus the DNA of our gut microbes."

It would be naive to think we carry around so much microbial material without it interacting or having any effect on our bodies at all.

Science is rapidly uncovering the role the microbiome plays in digestion, regulating the immune system, protecting against disease and manufacturing vital vitamins.

Prof Knight said: "We're finding ways that these tiny creatures totally transform our health in ways we never imagined until recently."

It is a new way of thinking about the microbial world. To date, our relationship with microbes has largely been one of warfare.

Microbial battleground

Antibiotics and vaccines have been the weapons unleashed against the likes of smallpox, Mycobacterium tuberculosis or MRSA.

That's been a good thing and has saved large numbers of lives.

But some researchers are concerned that our assault on the bad guys has done untold damage to our "good bacteria".

Prof Ley told me: "We have over the past 50 years done a terrific job of eliminating infectious disease. "But we have seen an enormous and terrifying increase in autoimmune disease and in allergy. "Where work on the microbiome comes in is seeing how changes in the microbiome, that happened as a result of the success we've had fighting pathogens, have now contributed to a whole new set of diseases that we have to deal with."

The microbiome is also being linked to diseases including inflammatory bowel disease, Parkinson's, whether cancer drugs work and even depression and autism.

Obesity is another example. Family history and lifestyle choices clearly play a role, but what about your gut microbes? This is where it might get confusing. A diet of burgers and chocolate will affect both your risk of obesity and the type of microbes that grow in your digestive tract.

So how do you know if it is a bad mix of bacteria metabolising your food in such a way, that contributes to obesity?

Prof Knight has performed experiments on mice that were born in the most sanitised world imaginable. Their entire existence is completely free of microbes.

He says: "We were able to show that if you take lean and obese humans and take their faeces and transplant the bacteria into mice you can make the mouse thinner or fatter depending on whose microbiome it got."

Topping up obese with lean bacteria also helped the mice lose weight.

"This is pretty amazing right, but the question now is will this be translatable to humans" This is the big hope for the field, that microbes could be a new form of medicine. It is known as using "bugs as drugs".

Goldmine of information

I met Dr Trevor Lawley at the Wellcome Trust Sanger Institute, where he is trying to grow the whole microbiome from healthy patients and those who are ill. "In a diseased state there could be bugs missing, for example, the concept is to reintroduce those."

Dr Lawley says there's growing evidence that repairing someone's microbiome "can actually lead to remission" in diseases such as ulcerative colitis, a type of inflammatory bowel disease.

And he added: "I think for a lot of diseases we study it's going to be defined mixtures of bugs, maybe 10 or 15 that are going into a patient."

Microbial medicine is in its early stages, but some researchers think that monitoring our microbiome will soon become a daily event that provides a brown goldmine of information about our health.

Prof Knight said: "It's incredible to think each teaspoon of your stool contains more data in the DNA of those microbes than it would take literally a tonne of DVDs to store.

"At the moment every time you're taking one of those data dumps as it were, you're just flushing that information away. "Part of our vision is, in the not too distant future, where as soon as you flush it'll do some kind of instant read-out and tells you are you going in a good direction or a bad direction. "That I think is going to be really transformative."

http://bit.ly/2HvBrXa

New biological research framework for Alzheimer's seeks to spur discovery

NIA, Alzheimer's Association convene effort to update disease definition, speed testing

Joe Balintfy | 301-496-1752 | nianews3@mail.nih.gov

The research community now has a new framework toward developing a biologically-based definition of Alzheimer's disease. This proposed "biological construct" is based on measurable changes in the brain and is expected to facilitate better understanding of the disease process and the sequence of events that lead to cognitive impairment and dementia. With this construct, researchers can study Alzheimer's, from its earliest biological underpinnings to outward signs of memory loss and other clinical symptoms, which could result in a more precise and faster approach to testing drug and other interventions.

The National Institute on Aging (NIA), part of the National Institutes of Health, and the Alzheimer's Association (AA) convened the effort, which as the "NIA-AA Research Framework: Towards a Biological Definition of Alzheimer's Disease," appears in the April 10, 2018 edition of *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*. Drafts were presented at several scientific meetings and offered online, where the committee developing the framework gathered comments and ideas which informed the final published document. The framework, as it undergoes testing and as new knowledge becomes available, will be updated in the future.

The framework will apply to clinical trials and can be used for observational and natural history studies as well, its authors noted. They envision that this common language approach will unify how different stages of the disease are measured so that studies can be easily compared and presented more clearly to the medical field and public.

"In the context of continuing evolution of Alzheimer's research and technologies, the proposed research framework is a logical next step to help the scientific community advance in the fight against Alzheimer's," said NIA Director Richard J. Hodes, M.D. "The more accurately we can characterize the specific disease process pathologically defined as Alzheimer's disease, the better our chances of intervening at any point in this continuum, from preventing Alzheimer's to delaying progression,"

Evolution in thinking

This framework reflects the latest thinking in how Alzheimer's disease begins perhaps decades before outward signs of memory loss and decline may appear in an individual. In 2011, NIA-AA began to recognize this with the creation of separate sets of diagnostic guidelines that incorporated recognition of a preclinical stage of Alzheimer's and the need to develop interventions as early in the process as possible. The research framework offered today builds from the 2011 idea of three stages—pre-clinical, mild cognitive impairment and dementia—to a biomarker-based disease continuum.

The NIA-AA research framework authors, which included 20 academic, advocacy, government and industry experts, noted that the distinction between clinical symptoms and measurable changes in the brain has blurred. The new research framework focuses on biomarkers grouped into different pathologic processes of Alzheimer's which can be measured in living people with imaging technology and analysis of

cerebral spinal fluid samples. It also incorporates measures of severity using biomarkers and a grading system for cognitive impairment.

"We have to focus on biological or physical targets to zero in on potential treatments for Alzheimer's," explained Eliezer Masliah, M.D., director of the Division of Neuroscience at the NIA. "By shifting the discussion to neuropathologic changes detected in biomarkers to define Alzheimer's, as we look at symptoms and the range of influences on development of Alzheimer's, I think we have a better shot at finding therapies, and sooner."

In an accompanying editorial, Masliah and NIA colleagues, including Dr. Hodes, highlighted both the promise and limitations of the biological approach. They noted that better operational definitions of Alzheimer's are needed to help better understand its natural history and heterogeneity, including prevalence of mimicking conditions. They also emphasized that the research framework needs to be extensively tested in diverse populations and with more sensitive biomarkers.

Batching and matching biomarkers

The NIA-AA research framework proposes three general groups of biomarkers—beta-amyloid, tau and neurodegeneration or neuronal injury—and leaves room for other and future biomarkers. Beta-amyloid is a naturally occurring protein that clumps to form plaques in the brain. Tau, another protein, accumulates abnormally forming neurofibrillary tangles which block communication between neurons. Neurodegeneration or neuronal injury may result from many causes, such as aging or trauma, and not necessarily Alzheimer's disease.

Researchers can use measures from a study participant and identify beta-amyloid (A), tau (T) or neurodegeneration or neuronal injury (N) to characterize that person's combination of biomarkers in one of eight profiles. For example, if a person has a positive beta-amyloid (A+) biomarker but no tau (T-), he or she would be categorized as having "Alzheimer's pathologic change." Only those with both A and T biomarkers would be considered to have Alzheimer's disease, along a continuum. The N biomarker group provides important pathologic staging information about factors often associated with Alzheimer's development or worsening of symptoms.

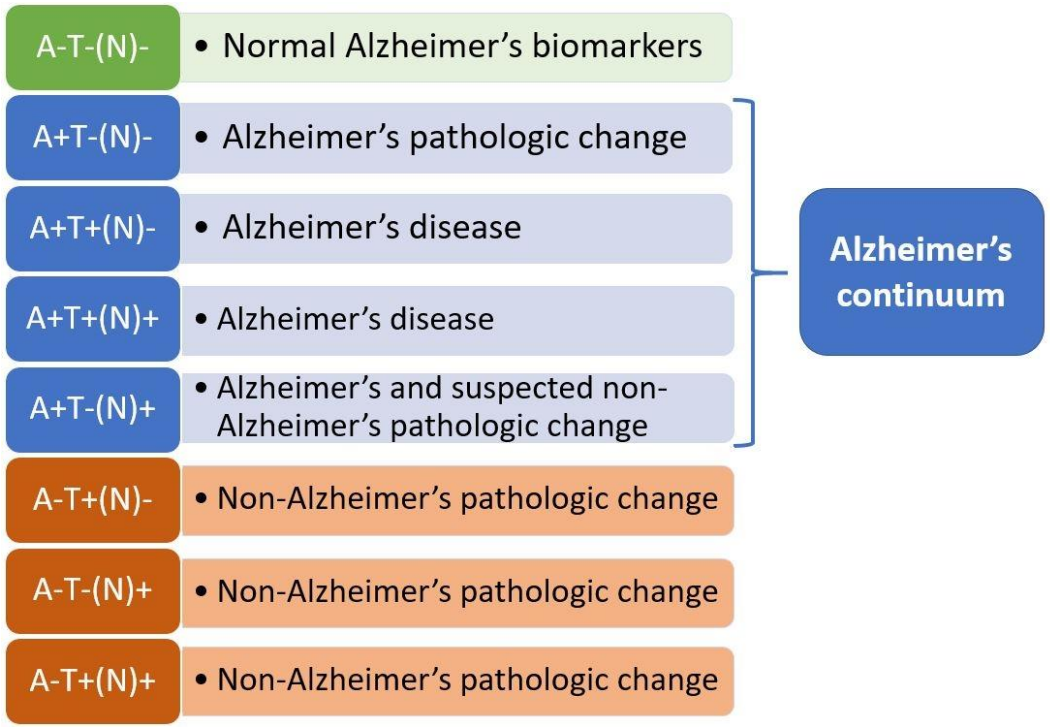


Table shows column of the eight biomarker profiles (left) and corresponding categories (right) outlined in the framework that could be used to group research participants. The biomarker profiles can be sorted into three broader categories: Normal Alzheimer's biomarkers, Alzheimer's continuum and non-Alzheimer's pathologic change.

Framework for certain research only

The authors emphasized that the NIA-AA research framework is neither a diagnostic criteria nor guideline for clinicians. It is intended for research purposes, requiring further testing before it could be considered for general clinical practice, they noted.

They also stressed that the biological approach to Alzheimer's is not meant to supplant other measures, such as neuropsychological tests, to study important aspects of the disease such as its cognitive outcomes. In some cases, the article pointed out, biomarkers may not be available

or requiring them would be counterproductive for particular types of research.

The authors acknowledge that the research framework may seem complex, but stress that it is flexible and may be employed to answer many research questions, such as how cognitive outcomes differ among various biomarker profiles, and what the influence of age is on those relationships.

In its commentary the NIA leadership developed a table to help explain how the proposed framework might be used and where it might not apply:

The research framework is…	The research framework is NOT…
A testable hypothesis	***A requirement for NIH grant submission***
An approach that facilitates standardized research reporting	***A statement about Alzheimer's pathogenesis or etiology***
A common language and a reference point for researchers for longitudinal studies and clinical trials	***An NIA policy, guideline or criterion for papers or grants***
A welcome for other approaches	***A disease definition for standard medical use***
A welcome for other indicators of Alzheimer's and comorbidities	***A fixed notion of Alzheimer's***

Jack CR et al. NIA-AA Research Framework: Towards a Biological Definition of Alzheimer's Disease. Alzheimers Dement. *2018 Apr 10. doi: 10.1016/j.jalz.2018.02.018*

Silverberg N et al. NIA commentary on the NIA-AA research framework: Towards a biological definition of Alzheimer's disease. Alzheimers Dement. *2018 Apr 10. doi: 10.1016/j.jalz.2018.03.004*

http://bit.ly/2qqWeD0

Weight loss is an important predictor of cancer

Unintended weight loss is the second highest risk factor for some forms of cancer, concludes the first robust research analysis to examine the association

Unintended weight loss is the second highest risk factor for some forms of cancer, concludes the first robust research analysis to examine the association.

A team led by the Universities of Oxford and Exeter conducted the first systematic review and meta-analysis to examine all available evidence on the association between weight loss and cancer in primary care. Their study, funded by the National Institute for Health Research and published in the *British Journal of General Practice*, found that unintended weight loss is the second highest risk factor for colorectal, lung, pancreatic and renal cancers.

The research analysed the findings of 25 studies, incorporating data from more than 11.5 million patients in total, found that weight loss was linked with 10 types of cancer. The analysis found that unintended weight loss in people over 60 exceeded the 3% risk threshold for urgent investigation in NICE guidelines. In females over 60, the average risk across all sites involved was estimated to be up to 6.7%, and in males up to 14.2%.

Lead author Dr Brian Nicholson, of the University of Oxford, said: "Streamlined services that allow GPs to investigate non-specific symptoms like weight loss are vitally important and urgently needed if we are to catch cancer earlier and save lives. Our research indicates that coordinated investigation across multiple body sites could help to speed up cancer diagnosis in patients with weight loss. We now need to continue our research to understand the most appropriate combination of tests and to give guidance on how much weight loss GPs and patients should worry about."

Professor Willie Hamilton, of the University of Exeter, was co-author on the study. He said: "We've always known that unplanned weight loss may represent cancer. This study pulls together all the published evidence and demonstrates beyond doubt that it is important in efforts to save lives from cancer. It is particularly timely with this week's announcement of 'one-stop' shops for cancer diagnosis. These units pull together all the necessary tests under one roof - making the investigation of weight loss much more speedy and convenient for the patient."

The paper, 'Weight loss as a predictor of cancer in primary care: a systematic review and meta-analysis', is published in British Journal of General Practice. *Authors are Brian D Nicholson, William Hamilton, Jack O'Sullivan, Paul Aveyard and FD Richard Hobbs.*

http://bit.ly/2qpiLju

Research suggests alternative treatment for beta blocker intolerant heart attack patients

Beta blockers cannot be tolerated by many patients who are at higher risk for developing cardiovascular disease

Beta blockers have become a prescription drug staple for recovering heart attack patients. However, these blood pressure-reducing medications cannot be tolerated by many patients who are at higher risk for developing cardiovascular disease, including those with chronic obstructive pulmonary disease (COPD) and asthma, the elderly, and diabetics. As seen in the March 26 issue of Thyroid, researchers at New York Institute of Technology College of Osteopathic Medicine (NYITCOM) now pose a new treatment for patients with beta blocker intolerance: thyroid hormone therapy.

Formally known as "beta-adrenergic blocking agents," beta blockers came to prominence in the 1960s, when deaths from myocardial infarction (MI), the clinical term for heart attack, were very common. The drugs work by blocking the neurotransmitters norepinephrine and epinephrine, also known as adrenaline, from binding to receptors in the heart. Consequently, when the effects of the neurotransmitters are impeded, heart rate and blood pressure are lowered, allowing the heart to beat with less force and more easily deliver circulation to the body.

During MI, increased adrenaline raises pressure in the arteries and increases heart rate to compensate for the sudden loss of contractile tissue. Unfortunately, this places added stress on surviving myocardium, the heart's muscular tissue. Muscular damage to the heart sustained during infarction may cause the organ to be less effective in pumping blood to the rest of the body, a condition that can eventually lead to heart failure and death.

Since beta blockers are known to improve chance of survival, patients unable to tolerate beta blockers may then be at greater risk for heart failure than those able to withstand the drugs. However, the NYITCOM researchers suggest that the thyroid hormone triiodothyronine (T3), which controls many aspects of cardiovascular function and is also a powerful regulator of beta receptor function, may offer an alternative therapy.

"While beta blockers have been viewed as the gold standard in MI treatment for years, a significant population at risk for heart failure is unable to tolerate these drugs. If given beta blockers, these patients' conditions can, in fact, worsen -- heart rate may fall too low and heart function could deteriorate," said Martin Gerdes, Ph.D., chair, Biomedical Sciences, NYITCOM, and senior investigator in the study. "Preclinical studies have shown thyroid hormone treatment to be a safe and effective method for managing cardiovascular disorders, and may offer a better option for these patients."

To investigate this option, Gerdes' team, which included experts from China's top cardiovascular center, FuWai Heart Hospital, compared the effectiveness of T3 and metoprolol, a commonly prescribed beta blocker, in female laboratory rats. Immediately following MI, the rats were provided either a low dose of T3 or the beta blocker in their drinking water for a total of eight weeks. At the end of that period, thyroid hormone proved to be as good, if not better, than metoprolol at improving heart function and reversing expression of detrimental genes linked to heart failure, providing all the benefits of the beta blocker plus some additional benefits unique to thyroid hormones, such as improved expression of genes related to better contraction and relaxation of the heart.

"Both treatments provide comparable results and similar long-term benefits, including improved function in the left ventricle, an area often damaged during heart attack, as well as reduced infarction size and improved vessel function," said Gerdes, who has studied the cardiovascular benefits and effects of thyroid hormone treatment for more than a decade. "Overall, these results suggest that T3 is capable

of providing a safe alternative for beta blocker intolerant patients following MI."

The researchers will continue studying the effectiveness of thyroid hormone after MI and encourage clinical researchers to consider examining low dose T3 treatment of MI patients who cannot tolerate beta blockers.

http://bit.ly/2JJjzZq

Japan team maps 'semi-infinite' rare earth reserves

"Rare earths" are found in several high tech products including mobile phones

Japanese researchers have mapped vast reserves of rare earth elements in deep-sea mud, enough to feed global demand on a "semi-infinite basis," according to a fresh study.

The deposit, found within Japan's exclusive economic waters, contains more than 16 million tons of the elements needed to build high-tech products from mobile phones to electric vehicles, according to the study, released Tuesday in the journal *Scientific Reports*.

The team, comprised of several universities, businesses and government institutions, surveyed the western Pacific Ocean near Minamitorishima Island, Japan.

In a sample area of the mineral-rich region, the team's survey estimated 1.2 million tons of "rare earth oxide" deposited there, said the study, conducted jointly by Yutaro Takaya, researcher with Waseda University and Yasuhiro Kato of the University of Tokyo, among others.

The finding extrapolates that a 2,500-square kilometre region off the southern Japanese island should contain 16 million tons of the valuable elements, and "has the potential to supply these metals on a semi-infinite basis to the world," the study said.

The area reserves offer "great potential as ore deposits for some of the most critically important elements in modern society," it said.

The report said there were hundreds of years of reserves of most of the rare earths in the area surveyed.

The team has also developed an efficient method to separate valuable elements from others in the mud.

The world relies heavily on China for rare earths, with Beijing producing most of the elements currently available on the market.

But Beijing has severely restricted exports of these products at times of diplomatic tension.

In 2010, for example, Japanese manufacturers faced serious supply shortages as China limited the valuable exports.

That came after Japan arrested the captain of a Chinese trawler that was involved in a run-in with Japanese coastguards near the disputed Senkaku Islands, claimed by China as the Diaoyus.

The Japanese study stressed the importance of the efforts to develop efficient and economic methods to collect the deep-sea mud.

"The enormous resource amount and the effectiveness of the mineral processing are strong indicators that this new (rare-earth rich mud) resource could be exploited in the near future," the study said.

More information: *Yutaro Takaya et al. The tremendous potential of deep-sea mud as a source of rare-earth elements, Scientific Reports (2018). DOI: 10.1038/s41598-018-23948-5*

http://bit.ly/2HjdPHz

Drones will soon decide who to kill

Algorithms will soon be able to decide who to target.

Peter Lee

The US Army recently announced that it is developing the first drones that can spot and target vehicles and people using artificial intelligence (AI). This is a big step forward. Whereas current military drones are still controlled by people, this new technology will decide who to kill with almost no human involvement.

Once complete, these drones will represent the ultimate militarisation of AI and trigger vast legal and ethical implications for wider society. There is a chance that warfare will move from fighting to extermination, losing any semblance of humanity in the process. At the same time, it could widen the sphere of warfare so that the companies, engineers and scientists building AI become valid military targets.

Existing lethal military drones like the MQ-9 Reaper are carefully controlled and piloted via satellite. If a pilot drops a bomb or fires a missile, a human sensor operator actively guides it onto the chosen target using a laser.

Ultimately, the crew has the final ethical, legal and operational responsibility for killing designated human targets. As one Reaper operator states: "I am very much of the mindset that I would allow an insurgent, however important a target, to get away rather than take a risky shot that might kill civilians."

Even with these drone killings, human emotions, judgements and ethics have always remained at the centre of war. The existence of mental trauma and post-traumatic stress disorder (PTSD) among drone operators shows the psychological impact of remote killing.

And this actually points to one possible military and ethical argument by Ronald Arkin, in support of autonomous killing drones. Perhaps if these drones drop the bombs, psychological problems among crew members can be avoided. The weakness in this argument is that you don't have to be responsible for killing to be traumatised by it. Intelligence specialists and other military personnel regularly analyse graphic footage from drone strikes. Research shows that it is possible to suffer psychological harm by frequently viewing images of extreme violence.

When I interviewed over 100 Reaper crew members for an upcoming book, every person I spoke to who conducted lethal drone strikes believed that, ultimately, it should be a human who pulls the final trigger. Take out the human and you also take out the humanity of the decision to kill.

Grave consequences

The prospect of totally autonomous drones would radically alter the complex processes and decisions behind military killings. But legal and ethical responsibility does not somehow just disappear if you remove human oversight. Instead, responsibility will increasingly fall on other people, including artificial intelligence scientists.

The legal implications of these developments are already becoming evident. Under current international humanitarian law, "dual-use" facilities – those which develop products for both civilian and military application – can be attacked in the right circumstances. For example, in the 1999 Kosovo War, the Pancevo oil refinery was attacked because it could fuel Yugoslav tanks as well as fuel civilian cars.

With an autonomous drone weapon system, certain lines of computer code would almost certainly be classed as dual-use. Companies like Google, its employees or its systems, could become liable to attack from an enemy state. For example, if Google's Project Maven image recognition AI software is incorporated into an American military autonomous drone, Google could find itself implicated in the drone "killing" business, as might every other civilian contributor to such lethal autonomous systems.

Ethically, there are even darker issues still. The whole point of the self-learning algorithms – programs that independently learn from whatever data they can collect – that technology uses is that they become better at whatever task they are given. If a lethal autonomous drone is to get better at its job through self-learning, someone will need to decide on an acceptable stage of development – how much it still has to learn – at which it can be deployed. In militarised machine learning, that means political, military and industry leaders will have to specify how many civilian deaths will count as acceptable as the technology is refined.

Recent experiences of autonomous AI in society should serve as a warning. Uber and Tesla's fatal experiments with self-driving cars suggest it is pretty much guaranteed that there will be unintended autonomous drone deaths as computer bugs are ironed out.

If machines are left to decide who dies, especially on a grand scale, then what we are witnessing is extermination. Any government or military that unleashed such forces would violate whatever values it claimed to be defending. In comparison, a drone pilot wrestling with a "kill or no kill" decision becomes the last vestige of humanity in the often inhuman business of war.

This article was amended to clarify that Uber and Tesla have both undertaken fatal experiments with self-driving cars, rather than Uber experimenting with a Tesla car as originally stated.

Disclosure statement

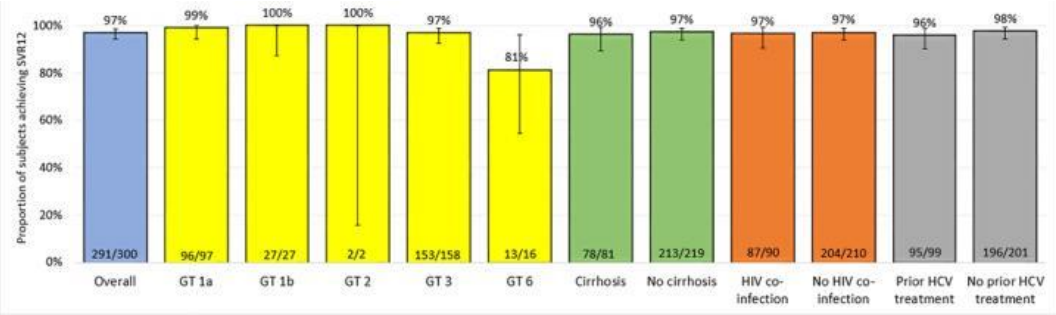
Peter Lee does not work for, consult, own shares in or receive funding from any company or organisation that would benefit from this article, and has disclosed no relevant affiliations beyond their academic appointment.

http://bit.ly/2Hqod0b

New affordable hepatitis C combination treatment shows 97 percent cure rate

Results support a public health approach to hepatitis C

PARIS - An affordable hepatitis C combination treatment including the new drug candidate ravidasvir has been shown to be safe and effective, with extremely high cure rates for patients, including hard-to-treat cases, according to interim results from the Phase II/III STORM-C-1 trial presented by the non-profit research and development organisation Drugs for Neglected Diseases *initiative* (DND*i*) at the International Liver Conference in Paris.



STORM-C-1 : SVR12 rates overall and per pre-defined sub groups-Intend to treat analysis* DND*i

"The results indicate that the sofosbuvir/ravidasvir combination is comparable to the very best hepatitis C therapies available today but it is priced affordably and could allow an alternative option in countries excluded from pharmaceutical company access programs," said Bernard Pécoul Executive Director, DND*i*.

The trial using medicines produced by Egyptian drug manufacturer Pharco Pharmaceuticals was run by DNDi and co-sponsored by the Malaysian Ministry of Health, in ten sites in Malaysia and Thailand. Agreements signed in 2016 and 2017 enabling the trials and patient scale-up in Malaysia set out a target price of US$300 for a 12-week treatment, an almost 100% drop from existing treatment prices in Malaysia.

"As hepatitis C has become a major public health concern in Malaysia, it is crucial to increase access to treatment for the benefit of the nation," said Datuk Dr Noor Hisham Abdullah Director General of Health, Ministry of Health, Malaysia. In September 2017, the government of Malaysia issued a "government-use" license on sofosbuvir patents to allow 400,000 people living with hepatitis C in Malaysia to access generic HCV regimens in public hospitals.

DND*i* conducted the STORM-C-1 open label trial to assess the efficacy, safety, tolerance and pharmacokinetics of the drug candidate ravidasvir combined with sofosbuvir. 301 chronically infected adults were treated with the ravidasvir/sofosbuvir combination for 12 weeks for patients without cirrhosis of the liver, and for 24 weeks for those with compensated cirrhosis. In accordance with international standards defining cure for HCV treatments, 12 weeks after treatment completion, 97% of those enrolled were cured (95% CI: 94.4-98.6). Cure rates were very high even for the hardest-to-treat patients: people with liver cirrhosis (96% cured), people living with HIV using their usual treatment (97%), people infected with genotype 3 (97%) including those with cirrhosis (96%), and people who had been exposed to previous HCV treatments (96%). Importantly, patients combining several of these risk factors were cured, and no unexpected safety signals were detected.

"From a treatment provider perspective, this is very exciting as we have been waiting for a simple, affordable, robust treatment tolerated by all patients groups, including those whose treatment outcomes are currently poorer, like patients under antiretroviral therapy," said Pierre Mendiharat, Deputy Operations Director for Médecins Sans Frontières / Doctors Without Borders (MSF). "This will be crucial to expand treatment to the most vulnerable categories of patients in developing

countries. "MSF and DNDi are working together to increase access to care and treatment for HCV patients in key low- and middle-income countries, through the STORM-C project financed by MSF's Transformational Investment Capacity (TIC) initiative.

Over 71 million people live with hepatitis C worldwide, a disease which causes 400,000 deaths a year. Although highly effective treatments have existed for a number of years, less than three million people are on treatment, with more people infected every year than are put on treatment. The World Health Organization aims for 80% of people diagnosed with HCV to be put on treatment by 2030.

Ravidasvir is an oral NS5A inhibitor licensed to DNDi by Presidio Pharmaceuticals. Most people enrolled in the DNDi trial in Malaysia and Thailand had genotype 1 (42% of participants) or genotype 3 (53%), thereby confirming the combination's effectiveness for those two additional genotypes. Further trials are planned to document the efficacy and safety of the combination in patients infected with the other HCV genotypes and in particularly vulnerable groups, to enable a public health approach to the treatment of hepatitis C.

"Pharco is proud to enable a public health approach to hepatitis C treatment by providing affordable treatments. We look forward to future collaboration in additional clinical trials to confirm the safety and efficacy of ravidasvir," said Dr. Sherine Helmy, CEO, Pharco.

Poster reference: Isabelle Andrieux-Meyer, Tan Soek Siam,Nicolas Salvadori, François Simon, Tim R. Cressey, Hajiah Rosaida Hi Mohd Said, Muhammad Radzi Abu Hassan, Haniza Omar, Hoi-Poh Tee, Chan Wah Kheong, Goh Khean Lee, Sharifah Faridah Syed Omar, Adeeba Kamarulzaman, Suresh Kumar, Satawat Thongsawat, Kanawee Thetket, Anchalee Avihingsanon, Suparat Khemnark, Sombat Thanprasertsuk, Jean-Michel Piedagnel, Sasikala Siva, Nur Asimah, Nelson Da Silva, Jennifer Brenner, Bernard Pecoul, Marc Lallemant, Shahnaz Murad. Safety and efficacy of ravidasvir plus sofosbuvir 12 weeks in non-cirrhotic and 24 weeks in cirrhotic patients with hepatitis C virus genotypes 1, 2, 3 and 6: the STORM-C-1 phase II/III trial. International Liver Congress, Paris, April 11-15 2018, France. Poster LBP-032.

https://bbc.in/2IW00f8

Chinese baby born four years after parents' death

The fertilised eggs had been frozen for years

A baby has been born in China to a surrogate mother four years after his parents died in a car crash, Chinese media reported. The couple, who died in 2013, had frozen several embryos hoping to have a child through IVF. After the accident, their parents fought a protracted legal battle to be allowed to use the embryos.

The boy was born in December to a surrogate from Laos and The Beijing News first reported the case this week. The newspaper explained how the lack of precedent for a case of this kind had forced the deceased couple's parents through a legal minefield before the surrogacy could proceed.

No precedent

At the time of the accident, the embryos were stored safely in a Nanjing hospital, frozen at minus 196 degrees in a liquid nitrogen tank. A court battle gave the four grandparents-to-be the right over the fertilised eggs. There was no precedent as to whether they could inherit their children's frozen embryos, according to reports.

They were eventually granted the embryos, but it wasn't long until the next problem occurred. The embryos could only be taken from the Nanjing hospital if there was proof that another hospital would store them. But given the legal uncertainty around untransplanted embryos, it was hard to find another medical institution in China willing to get involved. And with surrogacy illegal in China, the only realistic option was to look beyond the country's borders.

Proving paternity and nationality

Eventually, the future grandparents worked with a surrogacy agency and decided on Laos, where commercial surrogacy was legal.

As no airline was willing to accept a thermos-sized bottle of liquid nitrogen, the precious cargo had to be transported by car.

In Laos, the embryo was implanted into the womb of the surrogate mother and in December 2017 the boy was born.

Citizenship of the child, named Tiantian, was another problem though and so he was born not in Laos but in China - with the surrogate travelling there on a simple tourist visa.

With no parents left to prove paternity, all four grandparents had to give blood and take DNA tests to establish that the baby was indeed their grandson and that both parents had been Chinese nationals.

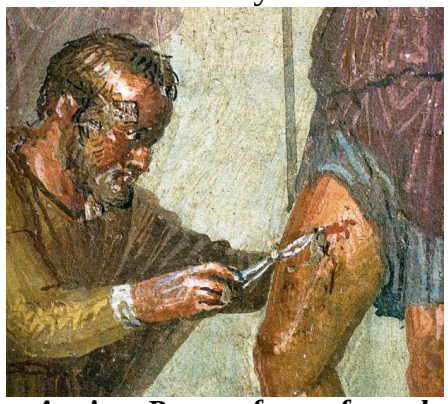
http://bit.ly/2H1F9GO

Medicine in Antiquity: From ancient temples to Roman logistics

A showdown with religious dogmas, an early scientific approach, and diligent use of plants were some of the ingredients of ancient medicine. Welcome aboard a historic journey to Greek temples, body fluids, and Roman hygiene.

We usually regard the Greek doctor Hippocrates as the father of the Western medicine. His greatest achievement was to separate healing from religion and apply natural science methods – an early medical science that was in use centuries before the Christian era.

In contrast, the Romans looked down on physicians, but they were good with logistics and hygiene. Their drinking water supply was legendary: Miles of watercourses brought fresh water from the mountains to the cities, which were kept separate from the waste water.



The doctor Japyx heals Aeneas' wounded leg. Ancient Roman fresco from the "House of Sirico" in Pompeii, Italy, mid 1st century. On display at the Museo Archeologico Nazionale (Naples). **(Photo: Wikimedia Commons)**

It is not unthinkable that this was more important for survival than medical treatments.

But how did the Ancients perceive disease? And how were they treated? We dive into this history, on a journey that includes Greek temples, human body fluids, and Roman hygiene.

Illness was a religious matter

In ancient Greece, treating disease was a religious concern that stretched right to the top.

The god of healing was Apollon, the son of Zeus. Apollon handed much of the medical work over to his son, Asclepius, the god of medicine. He in turn delegated the work to his five daughters and three sons, of which Hygieia stood for cleanliness and is the name sake for the field of hygiene.

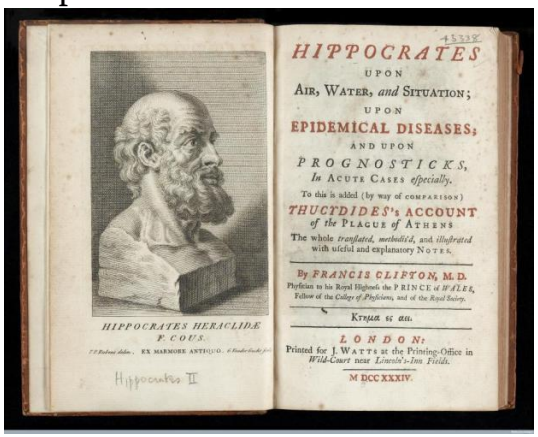
Doctors were organised in family guilds, and work was passed down from father to son. The patients came to Asclepius temples to be cured using a mixture of medical art and religious spells.

This connection between the medical profession and the temples lasted from about 600 to 300 BCE.

Hippocrates took medicine out of the temples

The biggest contribution that Hippocrates (about 460-375 BCE) made was in moving medicine out of the temples. He concluded that sickness was not the wrath of the gods, but instead, it was due to natural causes.

Even though he lacked evidence to support this – there was a pronounced taboo against dissection of humans in Ancient Greece – he followed a science-based approach to his studies of medical science and disease.



Engraving of a bust of Hippocrates and the title sheet in an English translation of his main work. **(Illustration by Peter Paul Rubens after Gerard van der Gucht. J. Watts, London 1734. Wellcome Collection, London, L0041093)**

According to Hippocrates, the patient underwent a critical phase, meaning the time when either the disease or the patient could win. However, the disease could still take revenge in the form of a relapse, and then the patient had to wait for a new crisis. Treatment was mostly confined to bed rest in order to strengthen the patient during this struggle.

In time, the four humours of Hippocratic medicine (blood, yellow bile, black bile, and mucus) became associated with the four elements (air, fire, earth, and water) corresponding to the two contradictory conditions: Dryness-humidity and heat-cold.

The Greek-Roman doctor Galen (119-199 CE) further developed humoral pathology and combined it with the natural perception of bodily fluids, natural elements, and Aristotle's (384-322 BCE) view of nature. Illness could, therefore, be attributed to an imbalance between these four humours.

Humours also determined our mood

Personalities could now be characterised by the surplus of the different bodily humours – a remarkable link between psyche and the body. Air was paired with blood (*Lat. sanguis*), which was thought to be produced in the liver. An overproduction of blood made you sanguine: Happy and optimistic.

Fire was associated with yellow bile (*Gr. chole*). This was thought (almost correctly) to be produced in the gall bladder, and overproduction gave the person a choleric temper: Upbeat and angry.

The gloomy mindset and depression of melancholic types, was due to an excess of black bile (*Gr. melan chole*), which allegedly came from the spleen and was linked to the earth.

The brain was ascribed to produce mucus (*Gr. phlegma*), and a surplus produced a phlegmatic (sluggish) temperament.

The four humours in Hippocratic medicine with the associated organs combined with Empedocles' four elements, the seasons, and the two coupled contrasting conditions. **(Illustration: Ole Sonne)**

The excess of a harmful fluid should be removed by suitable means, via a vomitive, laxative, or diuretic. A surplus of blood was removed by bleeding, which over the years has killed significantly more patients than the few who benefited from this treatment.

Wounds were cleaned with wine

Surgery consisted predominantly of repairing battlefield or sports injuries. Actual interventions were rare and limited to hernia, removal of bladder stones, and burning of haemorrhoids.

Many of the doctrines of surgery were quite reasonable: Wounds should only be cleaned with wine since the water was contaminated; clean cuts should be kept dry so that they can heal; all blood should be emptied from the wound, and wounds with broken tissue should be cleansed of pus and ample drainage provided to avoid infection.

Bleeding was stopped by cold wrapping, compression, or burning.

Hippocrates writes: "What is not healed with medicine, is healed with the knife; what the knife does not heal, is healed with the cautery, and what the cautery does not heal must be considered incurable."

Orthopaedic surgery involved more reasoned treatments. Patients with fractures were stretched to relieve the fracture site and promote setting, and to prevent a shortening of the fractured bone, which caused the patient to limp.

Sporting activities offered plenty of opportunities to put dislocated joints back into place. Dislocated shoulders were fixed by pushing the heel into the armpit of the lying patient while pulling and turning his arm – a procedure that has not changed over the past 2,300 years.

Herbs and plants were popular drugs

Medications used included mandrake, hemlock, henbane, and other plants belonging to the Solanaceae (nightshade) as narcotics. Mandrake was used to treat seizures, depression, and malaria.

Cauteries and a braizer. These items were used at the Royal Frederik's Hospital in Copenhagen until a couple of hundred years ago. Stenomuseet cat.no. 76071. **(Photo: Ole Sonne)**

Other treatments included apices such as chamomile, wormwood, cumin, anise, and rosemary.

We know this from the first written sources from the first century CE and from seeds excavated from the remains of temples.

Hippocrates's methods influenced the following 2,300 years of medicine, thanks to Galen of Pergamon, who cemented the concept of humoral pathology. This 'spell' was not broken until Rudolf Virchow in 1858 put forward his ground-breaking work of the biological understanding of the onset of disease.

The Greeks of Alexandria

Alexander III of Macedonia (Alexander the Great, 356-323 BCE) is reported to have said "I die with the help of too many doctors." But before that, he founded Alexandria and made the city the centre of science – a position that was established with the construction of the Library in Alexandria at the end of the third century BCE.

It was here that Herophilus of Chalcedon (330-260 BCE) came up with the theory that the brain controlled the rest of the body. He distinguished between the functions of the brain and the cerebellum, and connected the nervous system with movement and sensation.

He also described the flow of blood from the heart into the arteries, and even invented the water clock in order to achieve reproducible pulse measurements.

Galen and Hippocrates together even though Galen was born 500 years after the death of Hippocrates. Fresco from the twelth century, Anagni, Italy. **(Photo: Nina Aldin Thune, Wikimedia Commons)**

The Romans looked down on doctors

The Romans had a diametrically opposed relationship with doctors.

Roman education included a detailed knowledge with the philosophers, and as medical science was based on philosophy, self-care was a natural progression. The Romans' medical insights were therefore in-line with folk medicine. Cato the Elder (234-149 BCE) said to his son: "I forbid you any communion with doctors!"

But if the Romans had inferior medical insights, they were supreme in terms of logistics and hygiene. Aqueducts brought clean water from the mountains into towns via an extensive network, where sewage and drinking water were strictly separated. This preventative effort may have saved more people than the treatments of the Greek doctors.

Galen's theories undisputed until the seventeenth century

Galen studied medicine for four years in Pergamon, followed by studies in Smyrna, Corinth and Alexandria. In 157 CE he became a doctor at the gladiator school in Pergamon and was later appointed physician-in-ordinary for emperor Marcus Aurelius.

He was very self-assertive: "The one who wants to be famous only needs to get into what I've explored throughout my life."

His ideas, which were based on animal dissections and matched the perceptions of the church, were undisputed until around 1550 CE.

Galen divided diseases into three categories, which were conditional upon:

1. Physiological causes that we cannot influence: Innate or outward conditions (gender, age, temperament, climate, and seasons).

2. Controllable conditions (food, drink, exercise, and bathing).

3. Causes that contradict physiological conditions (pain, mental causes, and all processes that can cause disease).

The treatment was almost Hippocratic, discharged by vomiting, coughing, stools, urination, sweating, or bleeding.

https://bbc.in/2GY9Bph

Why some cancers are 'born to be bad'

A groundbreaking study has uncovered why some patients' cancers are more deadly than others, despite appearing identical.

By James Gallagher Health and science correspondent, BBC News

Francis Crick Institute scientists developed a way of analysing a cancer's history to predict its future. The study on kidney cancer patients showed some tumours were "born to be bad" while others never became aggressive and may not need treating.

Cancer Research UK says the study could help patients get the best care.

"We don't really have tools to differentiate between those that need treatment and those that can be observed," said researcher and cancer doctor Samra Turajlic. One cancer could kill quickly while a patient with a seemingly identical cancer could live for decades after treatment. It means uncertainty for both the patient and the doctor.

Kidney cancer

It is most common in people in their 60s and 70s. Symptoms include:

- ***Blood in your pee***
- ***Persistent pain in the lower back or side***
- ***Sometimes a lump or swelling in your side***

The work, published in three papers in the journal Cell, analysed kidney cancers in 100 patients. The team at the Crick performed a sophisticated feat of genetics to work out the cancer's history.

It works like a paternity or ancestry test on steroids.

As cancers grow and evolve, they become more mutated and, eventually, different parts of the tumour start to mutate in different ways. Researchers take dozens of samples from different parts of the same tumour and then work out how closely related they are.

It allows scientists to piece together the evolutionary history of the whole tumour. "That also tells us where the tumour might be heading as well," said Dr Turajlic.

Chance to change care

The researchers were able to classify kidney cancer into one of three broad categories:

- ***Born to be bad***
- ***Benign***
- ***Intermediate***

The "born to be bad" tumours had rapid and extensive mutations and would grow so quickly they are likely to have spread round the body before they are even detected. Surgery to remove the original tumour may delay the use of drugs that can slow the disease.

The benign tumours are at the complete opposite and are likely to grow so slowly they may never be a problem to patients and could just be monitored.

Michael Malley, 72, from London, took part in the trial at the Royal Marsden Hospital after being diagnosed with kidney cancer.

He said: "Clearly studies like these are really important for understanding how kidney cancer evolves over time, and I hope this one day leads to better treatments for patients like me."

There is still the challenge of figuring out how best to tailor treatments to each tumour type, and even how to perform such tests in a hospital rather than a research lab. The tools used in this study are being investigated in other cancers, including lung cancer.

Dr Turajlic says: "We've no doubt they will be applicable to other types of cancer." The studies also revealed that the earliest mutations that lead to kidney cancer were happening up to half a century before the cancer was detected.

Sir Harpal Kumar, the chief executive of Cancer Research UK, said the study was "groundbreaking". He added: "For years we've grappled with the fact that patients with seemingly very similar diagnoses nevertheless have very different outcomes. "We're learning from the history of these tumours to better predict the future.

"This is profoundly important because hopefully we can predict the path a cancer will take for each individual patient and that will drive us towards more personalised treatment."

https://go.nature.com/2GY9dTJ

East Asia braces for surge in deadly tick-borne virus

Rapid rise in number of infections concerns researchers.

David Cyranoski

Infectious-disease experts in East Asia are preparing for this year’s wave of a lethal tick-borne virus. The virus causes a disease called severe fever with thrombocytopenia syndrome (SFTS), which has affected a rapidly growing number of people since it emerged nearly a decade ago.

Scientists in the region say they are worried by the rising incidence of the disease, and by signs that the virus can spread more easily than previously thought. In March, Japan launched the first clinical trial of

a drug to treat the disease, and some researchers say that governments should devote more resources to raising awareness and studying the virus.

"It is our responsibility to come up with an effective treatment," says Masayuki Saijo, a virologist at the National Institute of Infectious Diseases in Tokyo, who helped to launch the trial.

An emerging virus in East Asia gets transmitted to people by the tick Haemaphysalis longicornis. **Aukid/iStock/Getty**

Cases of SFTS were first reported in China in 2009[1] . Researchers identified the virus responsible in blood samples from a cluster of people who shared a combination of symptoms that included high fever, gastrointestinal problems, low white blood cell count and low platelet count (thrombocytopenia).

The virus killed 30% of those infected in China that year[1]. It was even more lethal when the first cases appeared in Japan and South Korea in 2013. More than one-third of those infected in Japan and nearly half of those infected in South Korea died that year.

And the number of cases in each country has risen sharply. In 2013, there were 36 reported cases in South Korea, but by 2017 the number had jumped to 270. In 2010, China reported 71 cases; in 2016, there were around 2,600. Japan experienced a 50% increase between 2016 and 2017.

Improved prognosis

All three countries implemented measures aimed at educating local physicians and citizens in endemic areas about the risks of tick bites. Those infected now fare much better. In China, only around 3% of people infected died in 2016, and in Japan the number fell to 8%. In South Korea, the figure dropped from 47% in 2013 to 20% in 2017. Scientists credit the reduced fatality to earlier recognition and better general treatment — although no cure exists — and to the likelihood that wider surveillance has led them to recognize mild as well as severe cases.

The SFTS virus is not expected to evolve into a rapidly transmitted disease like Ebola. And those infected are generally limited to people, such as farmers or hunters, who come into contact with the animals that carry *Haemaphysalis longicornis*, the tick that harbours the virus.

But many say that the virus's toll and potential threat have been under appreciated. Those infected have a better prognosis, but the virus still kills a higher percentage than any other infectious disease in South Korea, says Keun-Hwa Lee, a microbiologist at Jeju National University in South Korea. And the higher number of infections means that the disease claims more than 100 lives globally each year.

Many animals, including goats, cattle, sheep and deer, expose humans to the ticks, and are often infected without showing symptoms. Current efforts that focus on known endemic areas could fail, says Bao Chang-jun, a biostatistician at Jiangsu Provincial Center for Disease Control and Prevention in Nanjing. The course of the epidemic "may change with human activities and climate change," say Bao. "It's necessary to conduct research on potential risk areas."

Two reports from Japanese health officials last year caused particular alarm. One stated that a woman had likely been fatally infected through a cat bite, and the other that a man had been infected by his dog. "To the warnings of previous years, we have to add the risk of touching sick domestic animals," says Kazunori Oishi, director of the Infectious Disease Surveillance Center in Tokyo.

Clinical trial

Last month, Japan began a clinical trial of an influenza drug, favipiravir, that was used to treat Ebola during the 2014 outbreak in West Africa. The drug is effective on viruses with a certain molecular structure that Ebola and SFTS share, says Saijo.

Although the number of cases has risen sharply, scientists can't say whether the increase is due to heightened surveillance and awareness, a real growth in the number of ticks and the animals that carry them, or

an increase in risk as humans encroach on areas where the disease is endemic. Shigeru Morikawa, director of the department of veterinary science at the National Institute of Infectious Diseases, says that some researchers suspect the number of ticks has increased because fewer people hunt wild animals in Japan now, and this has allowed deer and boar populations to surge.

Researchers say they have many questions about the virus and how it spreads, but they are concerned that the chances to study the disease will go up soon, as warm weather returns and people flock to the outdoors, where they come in contact with the ticks. “There will be more cases,” says Hideki Hasegawa, a pathologist at the National Institute of Infectious Diseases. “The season is just beginning.”

doi: 10.1038/d41586-018-04486-6

http://bit.ly/2H2cf9u

Japan faces record low eel catch, renewing stock fears

Japan is on track for a record low catch of baby eels this year, renewing fears about declining stocks of the endangered fish, a favoured summer delicacy for Japanese.

April 13, 2018 by Miwa Suzuki

At the end of March, Japan had 8.8 tons of baby "Anguilla japonica" eels in culture ponds, including imports from China, Taiwan and South Korea, according to a preliminary tally by the fisheries agency. That is a plunge from more than 18 tons logged at the same time in the last two years. The tally refers to baby eels caught in Japan, as well as those caught elsewhere in Asia and imported by Japan.

Eel is a delicacy enjoyed all over Japan

The fish are usually caught in the wild and sold to farmers who raise them until they are big enough for culinary use. The fishing season that began in December will end in late April, and Japan's volume is on track to fall below the record-low season-end figure of 12.6 tons it hit in 2013.

Eels, known as unagi in Japan, are a prized summer delicacy and demand for the fish is high across Asia.

In addition to overfishing, experts say river dams, pollution and the draining of wetlands, as well as oceanic changes and parasites may be playing a role in declining stocks.

'Further depletion'

Japan's fisheries agency strongly rejected the suggestion that overfishing was endangering stocks. "Annual catches are largely swayed by how ocean currents move... 'The haul halved' does not mean the stock resource halved," agency official Tatsuya Nakaoku told AFP.

Environmentalists have regularly sounded the alarm on the status of Anguilla japonica eels, with the fish on the International Union for Conservation of Nature's "endangered" list. "We fear further depletion in the stock," said Hiromi Shiraishi at Traffic, a non-governmental group focused on the trade of wild animals. "In addition, a bigger problem is that we think the current resource control method cannot respond sufficiently to the decreasing stock," she told AFP.

She noted that the cap on eels in Japanese farming ponds is fixed at 21.7 tons, unlike that for tuna, whose quota decreases with signs of stock depletion.

Eels spawn near the Mariana Islands in the Pacific and the babies travel thousands of kilometres towards East Asia in ocean currents.

Their spawning process remains a mystery, and efforts to breed them in captivity for commercial purposes have been unsuccessful. Baby eels are cultivated in ponds. The peak unagi season for Japan is summertime. Many Japanese believe the eels, served barbecued and basted in a thick sauce of sake, soy sauce and sugar, provide much-needed stamina during the energy-sapping heat and humidity of the summer.

Prices for the dish have been on the rise in recent years, and this season's low catch will only push costs up further, said Takashi Moriyama, chief of the Japan Eel Importers Association. Even with imports of adult or cooked eels to boost supply, "prices will rise inevitably," he told AFP.

http://bit.ly/2H2BqSf

Bad News, Night Owls: You Might Have a Higher Risk of Dying Early

Researchers found a 10 percent higher risk of early death in late night sleepers, but aren't sure why

By Kristen Knutson and Malcolm von Schantz

Do you wake up bright eyed and bushy-tailed, greeting the sunrise with cheer and vigor? Or are you up late into the night and dread the sound of your alarm clock? We call this inherent tendency to prefer certain times of day your "chronotype" (chrono means time). And it may be more than a scheduling issue. It has consequences for your health, well-being and mortality.

Being a night owl has been associated with a range of health problems. For example, night owls have higher rates of obesity, high blood pressure and cardiovascular disease. Night owls are also more likely to have unhealthy behaviors, such as smoking, alcohol and drug use, and physical inactivity.

We study the health effects of being a night owl. In our recent study published in Chronobiology International, we found even worse news for the owls of the world: a higher risk of early death.

Our bodies have their own internal time-keeping system, or clock. This clock would keep running even if a person were removed from the world and hidden away in a dark cave (which some dedicated researchers did to themselves years ago!). We believe these internal clocks play an important role in health by anticipating the time of day and preparing the body accordingly.

For example, as humans, we typically sleep at night, and our bodies start preparing for our habitual bedtime even before we try to fall asleep. Similarly, we eat during the day, so our body is prepared to process the food and nutrients efficiently during the daytime.

Our chronotype is also related to our biological clock. Morning larks' biological clocks are set earlier. Their habitual bedtimes and wake times occur earlier in the day. Night owls have internal clocks set for later times. But are there any problems related to being a lark or owl, other than scheduling difficulties? Research suggests that there are; night owls tend to have worse health.

And, in our new study, we compared risk of dying between night owls and morning larks. In this study, death certificates were collected for an average of 6.5 years after the initial study visit to identify those who died. We found that night owls had a 10 percent increased risk of death over this six-and-a-half year period compared to larks. We also found that owls are more likely to have a variety of health problems compared to larks, particularly psychiatric disorders like depression, diabetes and neurological disorders.

The switch to daylight saving time in the U.S. (or summer in the U.K.) only makes things more difficult for night owls. There are higher rates of heart attacks following the switch to daylight savings, and we have to wonder if more night owls are at risk.

We researchers do not fully understand why we see more health problems in night owls. It could be that being awake at night offers greater opportunity to consume alcohol and drugs. For some, being awake when everyone else is sleeping may lead to feelings of loneliness and increased risk of depression. It could also be related to our biological clocks.

As explained above, an important function of internal biological clocks is to anticipate when certain things, like sunrise, sleep and eating, will occur. Ideally, our behavior will match both our internal clock and our environment. What happens when it doesn't? We suspect that "misalignment" between the timing of our internal clock and the timing of our behaviors could be detrimental over the long run.

A night owl trying to live in a morning lark world will struggle. Their job may require early hours, or their friends may want to have an early dinner, but they themselves prefer later times for waking, eating, socializing and sleep. This mismatch could lead to health problems in the long run.

It is true that someone's "chronotype" is (approximately) half determined by their genes, but it is not entirely preordained. Many experts believe that there are behavioral strategies that may help an individual who prefers evening. For example, gradually advancing your bedtime – going to bed a little earlier each night – may help to move someone out of the "night owl zone."

A gradual advance is important because if you try to go to bed two to three hours earlier tonight, it won't work, and you may give up. Once you achieve an earlier bedtime, maintain a regular schedule. Avoid shifting to later nights on weekends or free days because then you'll be drifting back into night owl habits. Also, avoiding light at night will help, and this includes not staring into smartphones or tablets before bed.

On a broader scale, flexibility in work hours would help to improve the health of night owls. Night owls who can schedule their day to match their chronotype may be better off.

It is important to make night owls aware about the risks associated with their chronotype and to provide them with this guidance on how to cope. We researchers need to identify which strategies will work best at alleviating the health risks and to understand exactly why they are at increased risk of these health problems in the first place.

http://bit.ly/2qzMFSq

Too Much Sitting May Shrink the Part of Your Brain Tied to Memory

It may be time to ditch the desk chair: A new study links sitting too much each day with memory problems in middle-age and older adults.

By Samantha Mathewson, Live Science Contributor

Researchers from the University of California, Los Angeles (UCLA) found that long stretches of sedentary behavior — like spending all day in your desk chair — were linked to changes in a part of the adult brain that's critical for memory.

Earlier research has linked sedentary behavior to an increased risk of heart disease, diabetes and premature death in middle-age and older adults. The new study, published yesterday (April 12) in the journal PLOS One, builds on this, focusing on inactivity's impacts on the brain, according to a statement from the researchers.

Specifically, the new study linked sedentary behavior to thinning of the medial temporal lobe, a brain region involved in the formation of new memories, the researchers said in the statement. Brain thinning can be a precursor to cognitive decline and dementia in middle-age and older adults, the researchers added.

The study included 35 people between the ages of 45 and 75. Researchers asked the participants about their physical activity levels and the average number of hours per day they'd spent sitting over the previous week.

Then, the researchers scanned the participants' brains. Using a high-resolution MRI scan, the scientists got a detailed look at the medial temporal lobe of each participant and identified relationships among this region's thickness, the participants' physical activity levels and their sitting behavior, according to the study.

The results showed that sitting for extended periods of time was closely associated with thinning in the medial temporal lobe, regardless of one's physical activity level. In other words, the study suggests that "sedentary behavior is a significant predictor of thinning of the [medial temporal lobe] and that physical activity, even at high levels, is insufficient to offset the harmful effects of sitting for extended periods," the researchers said in the statement.

The participants reported that they spent from 3 to 7 hours, on average, sitting per day. With every hour of sitting each day, there was an observed decrease in brain thickness, according to the study.

And although the study found no significant correlations between physical activity levels and thickness of the medial temporal lobe, the researchers said in the statement that "reducing sedentary behavior may

be a possible target for interventions designed to improve brain health in people at risk for Alzheimer's disease."

The researchers noted that the study didn't prove that sitting led to thinner brain structures, but instead found an association between sitting for long periods of time and thinning structures.

In addition, thefindings are preliminary, and although the studyfocused on hours spent sitting, it did not take into consideration whether participants took breaks during long stretches of sedentary behavior. This, researchers said, could be a limitation of their results.

Going forward, the researchers said they plan to survey people that sit for longer periods of time each day, in order to determine if sitting causes the observed thinning. They would also like to explore the role gender, weight and race play in the effect on brain health to sitting, according to the statement.

http://bit.ly/2vfJLrA

Fecal microbiota transplantation produces sustained improvements in cognitive and clinical outcomes

Single treatment of FMT produces sustained clinical and cognitive improvements

Paris, France: A single treatment using an optimized, targeted form of faecal microbiota transplantation (FMT) produces sustained clinical and cognitive improvements, according to the results of a long-term follow-up of patients with liver cirrhosis and hepatic encephalopathy (HE) who had participated in a short-term study. The original, randomized, open label study, which enrolled 20 outpatient men with cirrhosis and recurrent HE receiving standard-of-care (SOC) treatment, had previously reported that a single FMT enema after antibiotic pretreatment improved cognitive function at Day 20 and reduced HE episodes and hospitalizations over the following 5 months compared with SOC.[1] The long-term outcomes of this study, which were presented today at The International Liver Congress™ 2018 in Paris, France, demonstrated sustained and statistically significant reductions in the number of HE episodes and hospitalizations as well as improvements in cognitive function over 1 year in the men who received FMT compared with the control group.

Liver cirrhosis is a leading cause of morbidity and mortality, with complications such as HE resulting in recurrent emergency hospitalizations, irreversible brain injury, and a poor prognosis.[2-5] There is some evidence that HE patients have a reduced relative abundance of certain beneficial gut microbiota (e.g. Lachnospiraceae and Ruminococcaceae) and an enrichment of potentially pathogenic Enterobacteriaceae - a microbial profile that has been linked to cognitive impairment and systemic inflammation in cirrhotic patients with HE.[1] Faecal microbiota transplants have been used successfully to correct dysbiotic conditions such as recurrent Clostridium difficile and ulcerative colitis,[6-8] and a preliminary report suggested that FMT may be promising in the management of HE.[9]

'In conducting the original study, we primarily wanted to evaluate whether FMT was safe in patients with recurrent HE compared with SOC alone', explained Dr Jasmohan Bajaj from Virginia Commonwealth University and McGuire VA Medical Center in Richmond, USA, and lead author of the study. 'We identified a single stool donor from a universal donor bank who had the highest relative abundance of Lachnospiraceae and Ruminococcaceae, and FMT enemas were prepared using a single stool specimen provided by this donor'.

The long-term analysis of this study followed all participants from the original 5-month study[1] who were still alive and without liver transplant for an additional 6 months, assessing both cognitive and clinical outcomes. At 1 year after randomization, one participant in the FMT arm and three in the SOC arm had died or undergone liver transplant. Amongst the remaining participants, a median of 1.5 (IQR 0.75-2.75) HE episodes and 3.0 (IQR 0.75-5.75) hospitalizations were reported during the subsequent 6 months of the study in the SOC arm compared with 0 (range 0-1.0) and 0 (range 0-1.5) in the FMT arm ($p<0.05$ and $p<0.02$, respectively). The FMT arm also demonstrated sustained and

significant improvements in cognitive function at 1 year compared with both baseline and SOC.

'Although this was a small randomized trial, we believe it confirms that FMT from a rationally selected donor was safe and associated with substantial long-term improvements in both clinical and cognitive outcomes in patients with cirrhosis and recurrent HE', said Dr Bajaj. 'These findings now need to be confirmed in a larger patient population'.

'Hepatic encephalopathy is a debilitating condition and a major burden to patients and caregivers, and new therapies are urgently needed', said Prof. Annalisa Berzigotti from the University of Bern, Switzerland, and EASL Governing Board Member. 'This study provides an important piece of evidence. The encouraging long-term results of FMT in HE strongly support the need for a larger, multicentre study of this intervention'.

References

14. Bajaj JS, et al. Fecal microbiota transplant from a rational stool donor improves hepatic encephalopathy: a randomized clinical trial. Hepatology. *2017;66(6):1727-38.*

15. American Association for the Study of Liver Diseases; European Association for the Study of the Liver. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases. J Hepatol. 2014;61(3):642-59.

16. Bajaj JS, et al. Persistence of cognitive impairment after resolution of overt hepatic encephalopathy. Gastroenterology. *2010;138(7):2332-40.*

17. Stepanova M, et al. In-hospital mortality and economic burden associated with hepatic encephalopathy in the United States from 2005 to 2009. Clin Gastroenterol Hepatol. *2012;10(9):1034-41.e1.*

18. Ellul MA, et al. Hepatic encephalopathy due to liver cirrhosis. BMJ. *2015;351:h4187.*

19. van Nood E, et al. Duodenal infusion of donor feces for recurrent Clostridium difficile. N Engl J Med. *2013;368(5):407-15.*

20. Moayyedi P, et al. Fecal microbiota transplantation induces remission in patients with active ulcerative colitis in a randomized controlled trial. Gastroenterology. *2015;149(1):102-109.e6.*

21. Kelly CR, et al. Effect of fecal microbiota transplantation on recurrence in multiply recurrent clostridium difficile infection: a randomized trial. Ann Intern Med. 2016;165(9):609-16.

22. Kao D, et al. Fecal microbiota transplantation in the management of hepatic encephalopathy. Hepatology. *2016;63(1):339-40.*

https://theatln.tc/2EN27zM

All of the World's Yeast Probably Originated in China

Baker's yeast, brewer's yeast, yeast that lives in infected toenails—they all descended from a common ancestor.

When scientists in France set out to sequence 1,000 yeast genomes, they looked at strains from all the places you might expect: beer, bread, wine. But also: sewage, termite mounds, tree bark, the infected nail of a 4-year-old Australian girl, oil-contaminated asphalt, fermenting acorn meal in North Korea, horse dung, fruit flies, human blood, seawater, a rotting banana. For five years, two geneticists—Gianni Liti, from the Université Côte d'Azur, and Joseph Schacherer, from the Université de Strasbourg—asked for samples of *Saccharomyces cerevisiae* from nearly everyone they met, whether doctors in French Guiana collecting human feces or Mexican tequila makers.

"It's easy to get a thousand wine strains," says Schacherer, "But that's not how we wanted to proceed." They wanted little-known wild strains of yeast that live all over the world in a great variety of environments. And they wanted these samples to see if they could confirm their suspicions about the historical origin of yeast. The results of their analysis, published in *Nature*, suggest that yeast came from, of all places, China.

The most telling clue is that yeast in and around China has the most genetic diversity of anywhere in the world. Liti had already suspected this, having worked with Chinese researchers who collected yeast from remote primeval forests. But the massive sequencing confirmed just how unique yeast in East Asia are: There are more differences between yeast strains from Taiwan and Hainan—both tropical islands off the coast of China—than there are between strains in the United States and Europe, separated by the entire Atlantic Ocean.

The out-of-China hypothesis for yeast is not so different from the out-of-Africa hypothesis for humans. Among *Homo sapiens*, Africa has the most genetic diversity of anywhere on Earth. All humans elsewhere descend from populations that came out of Africa; all yeast elsewhere

descend from strains that came out of East Asia. Once wild yeast strains made it out of Asia, humans likely domesticated them several times to make the yeasty foods that we know: beer, bread, wine.

How yeast strains are different from each other turned out to be surprising, too. A standard way to measure difference is to take the same gene in two separate yeast strains and compare how many letters have changed—like typos that have accumulated over time. But Liti and Schacherer found that the number of times a particular gene is repeated in the genome—a phenomenon known as copy-number variation—actually accounts for more of the differences between, say, strains used to brew tasty lagers and strains that live on insects in the wild. In other words, it's not just the sequence of the gene that matters, but the number of copies the yeast has.

This could be true in other species as well, says Ed Louis, a yeast geneticist at the University of Leicester—possibly even in humans. But copy-number variation is not as easy to study in humans, whose genomes are more than 200 times the size of yeasts'. So studies looking for genes that factor into heart disease, for instance, usually spot-check the genome for single-letter changes. The yeast results suggest that maybe human geneticists should take a closer look at copy-number variation, too.

Applying insights from tiny, single-celled yeast to big, multicellular humans is not so far-fetched. We share a lot of the same cellular machinery—in many cases, you can replace a yeast gene with its human version and the yeast goes on functioning just fine. Because yeast strains reproduce quickly and grow easily in the lab, scientists long have used it to study genetics.

Leonid Kruglyak, a geneticist at UCLA, calls the new study a "treasure trove of information." He's already planning experiments based on some of its data. Kevin Verstrepen, a geneticist at KU Leuven who has sequenced many strains of domesticated yeast used in beer, is also enthusiastic: "Everybody in the yeast community is quite excited," he says.

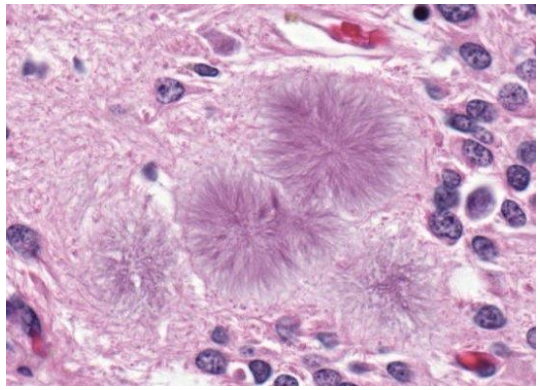
And if you're wondering if wild yeast can indeed be used to brew beer, the answer is yes. Yeast is yeast. It turns sugars into alcohol. But don't expect great results. "We've done quite a few of them," says Verstrepen. "Let's say the beers are funky."

http://bit.ly/2GZR3VQ

Prions Are Forever

The lethal proteins are in the Hard-to-Kill Hall of Fame--and may be more common than we realize

By Jennifer Frazer on April 9, 2018



Tribble-like amyloid plaques of variant Creutzfeldt-Jakob Disease acquired from eating prion-infected beef. **Sherif Zaki; MD; PhD and Wun-Ju Shieh; MD; PhD; MPH *CDC***

The 55-year-old Dutch woman's brain just didn't seem to be working right. Her memory and concentration were slipping. She began suffering headaches and hearing and seeing things that weren't there. She had trouble speaking, then became mute. She developed signs of Parkinson's Disease.

Within 27 months of her symptoms appearing, she was dead. But Parkinson's Disease was not what had killed her.

Scientists were curious about what had. Instead of freezing her brain, they immersed it in the chemical preservative formaldehyde – which cross-links the amino acids in proteins, "fixing" them -- for three long days. They sliced it thinly and placed the pieces in paraffin.

After examining the tissue under the microscope and forming an opinion, they filed the slides away, and they sat for several years at room temperature.

A second set of scientists acquired the slides and extracted some of the preserved, dried tissue. They diluted it and injected the solution into mice.

To their surprise, four of eight mice so injected developed signs of the woman's disease, despite a brutal processing regimen that should have been sufficient to kill just about any pathogen.

This most recent example – published just this February -- of credibility-straining biochemical endurance caught my eye a few weeks ago. It underscores the awesome power of prions.

Infectious Proteins

A prion is an illness-inducing misfolded protein. Depending on how it is misfolded, the prion may also be infectious, and they often are.

Oddly enough, all known prion diseases but one are caused by changes to a *single* mammalian protein, the somewhat confusingly-named "prion protein". This protein, in its healthy, properly-folded state, is, if not trivial, relatively unimportant. Its complete loss is certainly not catastrophic.

Yet in a highly unfortunate accident of nature, this protein stirs up an extraordinary amount of trouble when broken. When mutated or misfolded in one of 34 known ways, it becomes a prion proper. When a prion bumps into a normal prion protein, the prion protein's shape metamorphoses to the diseased form. Like a zombie, now it, too, can create more prions.

This, at least, is the prion hypothesis as promulgated by biologist Stanley Prusiner, who won the Nobel Prize in Medicine in 1997 for the idea. The ensuing chain reaction drives a relentless conversion of normal prion proteins into prions.

In many prion diseases, the shape of the prion also drives them to polymerize into fibers called amyloid (erroneously and confusingly named after starches in the 19th century because early tests had trouble distinguishing them, but having nothing to do with starches in reality).

Amyloid fibers accumulate outside cells, where they may punch holes in brain tissue that cause a swiss-cheese-like situation (which certainly happens with or without their help). Or they may be toxic in some other way that generates the neural degeneration and brain atrophy seen in prion diseases.

In the case of variant Creutzfeldt-Jakob disease (seen at the top of this post), the fibrils of the amyloid plaques radiate from a central point, giving them the appearance of tribbles.

Prion protein, for reasons again unknown, has a remarkably similar structure among mammals, which provides prions it a passport to interspecies mischief.

Famous prion diseases include mad cow disease (a.k.a. bovine spongiform encephalopathy, contracted when cattle were given feed laced with sheep that had died of the prion disease scrapie; note that cattle are vegetarians); kuru (infamously contracted by people who ritually consuming the brains of dead relatives in Papua New Guinea), and variant Creutzfeldt-Jakob Disease (acquired by people who ate Mad-Cow-infected beef).

Prion diseases are universally dreaded because they are uniformly lethal. Once symptoms appear, they cause a relatively swift full-system shut down that may include, in addition to the symptoms the Dutch woman experienced, uncontrolled drooling, uncoordinated movement, and convulsions. It is not a nice way to go, and you will go.

The Stainless Steel Vector

Avoiding this awful, if improbable, fate is something you unfortunately have little control over.

Prion diseases are most commonly acquired by inheriting a faulty prion protein gene from a parent, consuming prion-contaminated food, or receiving prion-contaminated donor tissues or organs.

But there is a final disturbing transmission possibility, one that stems from prions' mind-boggling powers of endurance.

Those powers are considerable. According to one account, prions resist digestion by protein-cleaving enzymes, may remain infectious for years when fixed by drying or chemicals, can survive 200°C heat for 1-2 hours, and become glued to stainless steel within minutes. Oh, and they're also resistant to ionizing radiation.

Why *are* prions so hard to kill (if kill is even the right word for an evil protein meme)?

No one knows for sure. One expert hypothesized that because our decontamination methods have always targeted DNA and RNA – molecules possessed by all actual living creatures -- they are by design not as effective on proteins.

The structure of prions themselves may also lend them supernatural survival powers. Just 3% of a prion protein is composed of beta-sheets, a common fold. But 43% of a prion is so folded.

Such a substantial percentage makes the protein highly resistant to degradation, the reasoning goes. The herding of prions into chain-linked amyloid fiber may also protect them from assault.

Whatever the cause, prions are, to put it mildly, good survivors. And that may be why neurosurgical equipment can remain infectious even after it undergoes standard sterilization.

At least 2 cases of prion disease were contracted by people whose implanted depth electrodes had been previously used on a patient with Creutzfeldt-Jakob but were “inadequately” cleaned with benzene and disinfected with 70% alcohol and formaldehyde and sat unused for 2 years prior to implantation. And at least nine other cases of spontaneous Creutzfeldt-Jakob seem likely to have been contracted from inadequately sterilized medical equipment.

What is actually required to remove prions from medical equipment could best be described as destructive at best and draconian at worst and usually involves large quantities of sodium hydroxide or bleach (which is very hard on stainless steel), heat, and pressure, but even these measures are not 100% certain to get the job done. The World Health Organization recommends disposing of any suspected contaminated equipment entirely.

Standard sterilization routines *have* improved since most of the suspected surgical transmission cases occurred. And it should be heartily emphasized that the number of strongly suspected or confirmed cases of surgical prion transmission is tiny.

But because the incubation period of prion diseases can be decades, patients with prion diseases don’t always know they are ill when operated on, and hospitals still don’t routinely use the extreme sterilization protocols recommended for prions, risk remains. Many people have been so exposed over the years, a worrying occurrence *Scientific American* editor Phil Yam wrote about just a few years ago.

Are Prions More Common Than We Realize?

The enduring infectious power of prions is unsettling all on its own, but some scientists are beginning to suspect something far scarier.

Aggregates of prions form amyloids. But amyloids also form from proteins called amyloid-beta, tau, and alpha-synuclein.

You may recognize these names. The accumulation of these proteins in amyloids -- as plaques, tangles, and Lewy bodies -- are signature indications, and perhaps causes, of Alzheimer’s and Parkinson’s diseases.

These amyloids, like prions, stick to surgical instruments “like glue” and survive standard sterilization procedures. They, too, are distressingly hard to "kill".

The only thing that keeps such amyloids from being considered prions is infectivity. But recently, at least one team of scientists found circumstantial, controversial -- and stomach-churning -- evidence that amyloids from patients with these diseases may be infective. What if *Alzheimer’s* could be transmitted on surgical equipment? Prion diseases are rare. Alzheimer's and Parkinson's are not.

Given the horrifying implications, and in spite of the expense and effort, I think it's time for surgeons to start taking this possibility very seriously. If there's one thing prions have shown me, it's that you should *never* underestimate the capabilities of the most badass protein polymers on the planet.

Reference

Race, Brent, Katie Williams, Andrew G. Hughson, Casper Jansen, Piero Parchi, Annemieke JM Rozemuller, and Bruce Chesebro. "Familial human prion diseases associated with prion protein mutations Y226X and G131V are transmissible to transgenic mice expressing human prion protein." Acta neuropathologica communications 6, no. 1 (2018): 13.

http://bit.ly/2HqFQwX

We've found the cells norovirus targets—we just don't know what they do

Targeting a small population of cells seems to be enough for some big effects.

Diana Gitig - 4/14/2018, 11:30 PM

Norovirus inflames the stomach and/or intestines and causes pain, nausea, vomiting, and diarrhea. It is super contagious and kills tens of thousands of people each year. But until now, we did not even know which cells it targets to create all this havoc. A recent study by a public-private consortium working in universities and Genetech has just discovered the elusive cell type (in mice): they're called tuft cells, and they reside in the ilium and colon.

Obviously, norovirus attacks intestinal epithelial cells, the specialized cells that line tubes within the body. But last year, the same group reported that noroviruses would infect only a rare subset of them and not most of their neighbors. But the researchers could not discern what made these select cells so special.

They knew that norovirus used a particular receptor to infect cells and that this receptor is both necessary and sufficient for infection. Oddly, the receptor is an immunoregulator thought to be expressed by blood-forming cells, specifically immune progenitor cells in the bone marrow. These could make their way to the intestines once they mature. But mice that got bone marrow transplants that lacked this receptor were still susceptible to norovirus infection, so that's clearly not the case.

Instead, it now turns out that these isolated intestinal cells infected by norovirus express this very immune receptor, which had never been seen in epithelial cells before. They turned out to be tuft cells, named for the long tuft they sport, which extend into the intestine like truffula trees from *The Lorax*. Aside from their tuft, these cells are known for making IL-25, a cytokine that coordinates the immune response to tapeworms and other parasites.

IL-25 stimulates the growth of the tuft cells that produce it, which explains the observation that infection with parasites augments norovirus infection. The parasite induces IL-25 production, which expands the population of tuft cells, which in turn expands the available opportunities for norovirus infection.

Work done in 2015, also in mice, showed that treatment with broad spectrum antibiotics that ablate intestinal bacteria will prevent norovirus infection. This led the researchers who performed it to reasonably conclude that the microbiome is required for norovirus infection. But in the new study, sterile, germ-free mice were infected just fine. This turned out to be because the antibiotics also diminished the numbers of tuft cells in the colon; only they, and not commensal bacteria, are required for norovirus infection.

Since norovirus infection can elicit inflammatory-bowel-disease-like symptoms and it acts through tuft cells, the authors wonder if maybe tuft cells are responsible for inflammatory bowel disease. It's also possible that other viruses infect tuft cells. To understand further, we'll have to figure out why harming these cells can produce such a dramatic and potentially fatal collection of symptoms.

Science, *2018. DOI: 10.1126/science.aar3799 (About DOIs).*