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Periodontal disease: Patent for new treatment method

New biodegradable rods promise to provide better treatment for periodontal disease.

Researchers from the Institute of Pharmacy at Martin Luther University Halle-Wittenberg (MLU) have re-combined an already approved active ingredient and filed for a patent for their invention together with two Fraunhofer Institutes from Halle. The innovation would spare patients from having many side effects. Their findings were published in the International Journal of Pharmaceutics.

Periodontal disease is widespread and usually caused by bacteria, which leads to an inflammation of the gums - the periodontitis. More than 50 % of adults in Germany develop periodontal disease in the course of their lives, mostly in old age. According to projections, more than ten million Germans have a severe form of the disease. "The body's barrier function is badly disrupted by the large wounds, allowing more substances and bacteria to enter the body," explains Professor Karsten Mäder, head of the Institute of Pharmacy at MLU. The inflammation affects the entire body and is often the cause of other diseases such as heart attacks or pneumonia. Therefore, mechanical cleaning procedures are often followed by antibiotics. These are usually administered in pill form, which puts a strain on the entire body. Common side effects are diarrhoea, abdominal pain and nausea as well as skin reactions such as redness and itching. The possible development of resistance to common antibiotics is also a major factor in this form of treatment.

Ideally, the antibiotic would only act locally in the mouth rather than throughout the entire body. Mäder's research group has therefore combined a proven antibiotic (minocycline) with an equally proven pharmaceutical excipient (magnesium stearate). "The complex is just as effective, but more stable. It slowly releases the antibiotic on the spot," explains Mäder. "In addition to the continuous and sustained release of the antibiotic, we needed to find an easy way of administering it." His research group found a practical solution to this problem by utilising pharma-grade polymers. The researchers were able to use these chemical substances to produce flexible, biodegradable rods containing the antibiotic. The small rods can be easily inserted into the gingival pocket. Since they are broken down by the body, they do not have to be removed after treatment. "The rods are much more effective in vitro than previous products on the market," says Martin Kirchberg, who is studying the topic as part of his doctoral thesis. Among other things, Kirchberg has optimised the composition of the polymers in order to achieve exactly the right balance between strength and flexibility and to make them long-lasting. Development is already so advanced that large-scale production would be possible.

The patent for the complex active ingredient and its formulation was applied for together with the Fraunhofer Institute for Cell Therapy and Immunology IZI and the Fraunhofer Institute for Microstructure of Materials and Systems IMWS, both in Halle, as well as with the Clinic for Dental Medicine at the University of Bern. Mäder and Kirchberg each have a 30 % stake in the invention, with the remaining 40 % shared by scientists from the Fraunhofer Institutes in Halle and the University of Bern. Rapid implementation in clinical studies is possible since all of the pharmaceutical-grade ingredients are already available on the market. The rods can also be produced using proven techniques so that they can be market ready in just a few years' time. The further development of the formulation and its subsequent market launch will be carried out by PerioTrap Pharmaceuticals GmbH, a start-up company founded by Fraunhofer IZI in Halle.

The project was financially supported by the State of Saxony-Anhalt with funds from the European Regional Development Fund

(ERDF) as part of the "Transfer and High-Performance Centre Chemical and Biosystems Technology"

http://bit.ly/2QZuWmc

Just how well could you design a baby?

Study questions whether IQ or height can be predicted at all.

By Paul Biegler

Not everyone wants to raise the lovechild of Albert Einstein and Arnold Schwarzenegger but, like it or not, designer babies are inching their way into the global marketplace.

This month it was reported that US start-up Genomic Predictions is offering genetic testing of IVF embryos that includes, among others, measures of intelligence and height.

The move reignites an ethical firestorm on predictive genetic testing. Philosophers such as Julian Savulescu, from the University of Oxford, have argued parents have a moral obligation to have the "best" possible child.

Contrarian views abound, however, including arguments that genetic enhancement stigmatises those who don't get it and is only available to people who can pay.

But a new study, published in the journal *Cell*, may render much of the kerfuffle moot. At least for now.

Led by Todd Lencz at the Feinstein Institutes of Medical Research in New York, US, the study used modelling and real-world outcomes to question whether IQ or height can be predicted at all.

The team took a hard look at genome wide association studies (GWAS) that link the genetic makeup of hundreds of thousands of people with their IQ and height. They wanted to get a handle on what gene patterns might predict the traits.

It's a many-headed beast because, unlike disorders such as cystic fibrosis that are caused by mutations in a single gene, intelligence and height are "polygenic" – determined by many genes.

Armed with software and algorithms sufficiently powerful to crunch the numbers, Lencz's team used the data to predict height and IQ in a bunch of "simulated embryos".

This did not require simulated sex. Rather the virtual offspring came from pairing up the genetic data of people, including some actual couples, who took part in other studies.

But a heads up for prospective parents wanting a ripped Nobel laureate – the results were underwhelming.

Simulated embryos selected to be the smartest and tallest were only around 2.5 IQ points and 2.5 centimetres above average.

And if you don't find mathematical embryos persuasive, the team checked their predictions in real people as well.

They had access to the genetic data and height stats of 28 unique families that had produced up to 20 kids apiece, with an average of 10.

Again, even if you wanted to create the mythical Übermensch, it seems you're up against it.

In only seven of those families – just a quarter – did the person predicted to be tallest turn out to be so. In five, the person genetically ordained to be its tower of power was actually shorter than average.

"The notion that you could accurately choose your child's height or select for a higher IQ, like in the movie *Gattaca*, has never been tested," says Lencz.

"Through our research, we can confidently say that trait predictions for embryos based on polygenic scores are not very accurate."

Why? Well, lots of reasons.

The base rate predictions from GWAS aren't watertight in the first place. In even the largest studies those "polygenic scores" only explain about 5% of the variation in intelligence and 25% of the variation in height.

Then the nature versus nurture effect kicks in.

Parents with genetically higher intelligence are likely to create more learning opportunities in the home: books for example. That muddies the water on how much the IQ results in those GWAS are genetic or environmental.

Another issue, write the authors, is that subtle genetic changes called SNPs (single nucleotide polymorphisms) used to predict traits, are themselves influenced by the environment.

And then there is the issue that gene findings derived in one ethnic group may not faithfully apply to others.

Having said all that, gene studies are getting ever more comprehensive, vacuuming in more data – including sequencing of the whole genome – from more people.

The authors' own modelling suggests, for example, that with access to data on 10 million folk, predictions could be refined to yield an expected IQ gain of around seven points.

But the aforementioned caveats still hold.

"There is much about these traits that is unpredictable," says Shai Carmi, co-lead author on the study from Israel's Hebrew University of Jerusalem.

"If someone selected an embryo that was predicted to have an IQ that was two points higher than the average, this is no guarantee it would actually result in that increase. There is a lot of variability that is not accounted for in the known gene variants."

Meanwhile, the debate on whether genetic enhancement is simply eugenics rebranded will roll on.

But this study raises a here-and-now pointy issue for the informed consent of parents wanting to access these tests, which have been called "23andMe on embryos" (after the home genetic testing kit).

Those parents may want to ask their test provider: "what traits can we really predict with genetic testing?"

And listen carefully to the answer.

http://bit.ly/2Dqdsr7

Smoker-survivor genes may have long ancestral history of fighting toxins

Longevity genes that helped humans survive airborne toxins may be the same making humans resilient to pollution today

Longevity genes that helped humans survive ancient airborne toxins may be the same genes that make humans resilient to pollution from fossil fuels and cigarette smoke today, according to a study published in the December 2019 issue of The Quarterly Review of Biology. In "The Exposome in Human Evolution: From Dust to Diesel," Ben Trumble (Arizona State University) and Caleb Finch (University of Southern California) examine the myriad toxins that humans have encountered through our evolutionary history and the immunity-related genes that have countered their harmful effects. "We hypothesize that adaptation to ancient pathogens and airborne toxins may, in some cases, be protecting us today from novel airborne pollutants such as cigarettes and diesel smoke," Trumble and Finch write. "Further inquiry into these unexplored domains of genetic processes may inform the future of human health and longevity during global warming."

Trumble and Finch's paper is a detailed examination of the human exposome - the interactions between human genes and the various environmental hazards we encountered through our evolutionary history. Each new environmental hazard posed a unique threat to humans and was addressed with various genes related to immunity. The authors focused in particular on genes of host defense and brain development during the evolution of the long human lifespan.

As human ancestors diverged from great apes, they encountered an array of new environmental hazards. First, as sub-Saharan Africa shifted from forest to savanna, humans breathed mineral dust and fecal aerosols from roaming herd animals and ingested pathogens from rotting meat. With the discovery of fire, humans were exposed

to toxins from smoke and the charred meat that they cooked. Later, as hunting and gathering gave way to an agricultural life, humans were exposed to new toxins from domesticated animals and limited sanitation in dense living quarters. Although an understanding of infectious disease and hygiene emerged, the industrial revolution ushered in the modern-day hazards airborne pollutants and cigarettes.

Trumble and Finch found that some genes appear to have provided benefits through long stretches of evolutionary time and in very different environments. The gene AHR appears to have made archaic humans more resistant to toxins in domestic cooking fires than their Neandertal counterparts. "AHR is important in detoxifying response to modern domestic smoke, including responses to cigarette smoke," they write. "We hypothesize that genetic adaptations to ancient airborne toxins may play important roles in ameliorating the effects of exposures today, including the survival of some elderly lifetime cigarette smokers."

Many other genes grew to lose their benefits over time, or, in the case of ApoE, became dependent on the environment in determining which version is the most beneficial. The ancestral version of ApoE was highly beneficial for survival in environments with high levels of infection. However, it also negatively impacts artery and brain aging, and is associated with shorter life spans. A newer version of the gene appears to have more beneficial effects, including lower cholesterol in meat-eating populations. The fact that the ancestral version of ApoE is still prevalent in the population is an important example of the human environment changing faster than our gene pools can keep up, Trumble and Finch write. It may regain its adaptive value, however, as global warming promotes the recurrence of global infections through the expansion of insect populations, such as malaria-carrying mosquitoes.

Understanding the extent of these historical gene-environment interactions is key to meeting future global health challenges. "Understanding the full breadth and history of the human exposome will inform the future of human health and longevity during the emerging ecological shifts from dust to diesel and beyond."

https://wb.md/34wKtxM

FDA Grants Psilocybin Second Breakthrough Therapy Designation for Resistant Depression

FDA grants Usona Institute breakthrough therapy designation for psilocybin for treatment of major depressive disorder

Megan Brooks

The US Food and Drug Administration (FDA) has granted the Usona Institute breakthrough therapy designation for psilocybin for the treatment of major depressive disorder (MDD).

This marks the second time the FDA has granted breakthrough designation for psilocybin, the psychoactive ingredient in "magic mushrooms."

In October 2018, Compass Pathways received the designation to test the safety and efficacy of psilocybin-assisted therapy for treatment-resistant depression, as reported by *Medscape Medical News*.

"The results from previous studies clearly demonstrate the remarkable potential for psilocybin as a treatment in MDD patients, which Usona is now seeking to confirm in its own clinical trials," Charles Raison, MD, Usona's director of clinical and translational research, said a news release.

The Usona Institute is a nonprofit medical research organization that conducts and supports preclinical and clinical research to further the understanding of the therapeutic effects of psilocybin and other consciousness-expanding medicines.

"What is truly groundbreaking is FDA's rightful acknowledgement that MDD, not just the much smaller treatment-resistant depression

population, represents an unmet medical need and that the available data suggest that psilocybin may offer a substantial clinical improvement over existing therapies," said Raison.

More than 17 million people in the United States suffer from MDD. Through the breakthrough therapy designation, psilocybin is recognized as possibly offering a clinically significant improvement over existing therapies.

The new status follows the recent launch of Usona's phase 2 clinical trial (PSIL201), which will recruit roughly 80 patients at seven study sites around the United States. The study will assess the safety and efficacy of a single dose of psilocybin in comparison with placebo in patients aged 21 to 65 years who have MDD.

Two of the study sites are currently recruiting patients; the others are expected to be active by the first quarter of 2020. Usona estimates that the trial will be completed by early 2021.

More information on the trial is available online.

http://bit.ly/2OsS22R

Healthy man dies after being licked by dog and getting rare infection, researchers found

A German man who was licked by his dog died after contracting a rare bacteria, German researchers said.

Joshua Bote

The 63-year-old, who was otherwise healthy, was hospitalized with fever, severe difficulty breathing, blood spots on his skin and pain in his legs, according to a paper published in the peer-reviewed European Journal of Case Reports in Internal Medicine.

“He had been touched and licked, but not bitten or injured, by his dog, his only pet, in previous weeks,” doctors from Red Cross Hospital in Bremen, Germany, noted in the report.

Over the next 30 hours, the report says, the man developed encephalopathy, brain damage and paralytic ileus, or paralysis of the intestine. He suffered cardiac arrest.

After 16 days of intensive treatment, the patient died.

The man’s death was caused by capnocytophaga canimorsus, a rare bacteria that naturally occurs in dog and cat mouths and is most commonly transmitted through dog bites.

Individuals with a weak immune system or a history of alcoholism or who have had their spleens removed are especially vulnerable to the infection, researchers said. The Centers for Disease Control and Prevention said the infection is more likely to take place in individuals older than 40.

A Wisconsin man's legs, hands and nose were amputated after he was licked by a dog in 2018. In 2016, a BMJ medical report found a greyhound owner who made a full recovery after two weeks of intensive care.

The doctors wrote that this man had trouble breathing. They advised physicians to ask about contact with pets if a patient comes to them with unusual symptoms.

Contributing: Ashley May, USA TODAY. Follow Joshua Bote on Twitter: @joshua_bote

http://bit.ly/37RuEnA

Over 1,000 Patients Possibly Exposed to HIV After Hospital's Sanitation Mistake

Surgical sterilization technician skipped a step in a multistep cleaning process for certain surgical instruments

By Yasemin Saplakoglu - Staff Writer

Over 1,000 patients at an Indiana hospital may have been exposed to HIV, hepatitis B and hepatitis C after an error in a sanitizing procedure, according to recent news reports.

Between April and September, one of the Goshen Hospital's seven surgical sterilization technicians skipped a step in a multistep cleaning process for certain surgical instruments, according to news reports and a statement from the hospital. Though those surgical instruments still went through other disinfection and sterilization procedures with a "wide margin of safety," it's not clear if the

instruments were completely sterile before they were used on people, the hospital statement said.

"Even though we believe the risk to be extremely low, out of an abundance of caution, we are offering patients free testing for these viruses," hospital representatives wrote in the statement. Officials from Goshen Hospital sent out notification letters and are offering free blood draws for the 1,182 patients who underwent surgery and who might have been exposed to these infectious diseases.

One of the patients, Linda Gierek, who underwent surgery at the hospital on June 24, filed a class-action lawsuit on Nov. 22 through attorney Walter J. Alvarez; the lawsuit lists several anonymous defendants with addresses at the hospital, according to The Goshen News.

Both hepatitis B and hepatitis C are liver infections caused by a virus that can be transmitted through blood, as can happen when people share needles. For some people, hepatitis B and C are short-term illnesses and symptoms resolve quickly, but for others, the illnesses become chronic and lead to more-serious health issues, according to the Centers for Disease Control and Prevention (CDC).

Symptoms of hepatitis B can include fever, fatigue and yellowing of the eyes, while symptoms of hepatitis C — if patients have any at all — are typically mild and resemble the flu; these can include sore muscles and tiredness.

HIV is a virus that can also be spread through blood and other bodily fluids and that slowly attacks the immune system, destroying the body's defenses such that it can't fight off disease, according to the CDC.

"As with any patient safety concern, we rigorously investigated all aspects around the incident," Dr. Daniel Nafziger, Goshen hospital chief medical officer, said in the statement. "We have put strict policies and additional safety measures in place to ensure it does not happen again."

http://bit.ly/2su8wPR

Polio Vaccination Causes More Infections than Wild Virus

In rare instances, the live virus in oral polio vaccines can mutate and become infectious, causing new outbreaks.

Jef Akst

Nigeria, Democratic Republic of Congo, Central African Republic, and Angola have experienced nine new cases of polio caused by the live virus in oral polio vaccines that has mutated into an infectious form, according to statistics released last week (November 20) by the World Health Organization. That brings the global total of these types of infections to 157 for the year, and it means that more children are paralyzed as a result of such vaccine-derived infections than illnesses caused by the wildtype virus, which has affected 107 people this year.

Other countries in Africa and Asia have also reported such vaccine-derived infections, which have the potential to spark new outbreaks. In Africa alone, there are currently a dozen vaccine-derived polio outbreaks, and another was declared in the Philippines last month—the country's first cases of the disease in more than 25 years, NPR reports.

To finally eliminate the world of polio, global leaders convened last week (November 19) at the Reaching the Last Mile (RLM) Forum in Abu Dhabi, pledging $2.6 billion to the effort. The main impediment is vaccination coverage in certain regions, particularly Afghanistan and Pakistan, the last two countries where polio remains to be eradicated.

While Western countries use an injectable solution of inactivated virus, an oral polio vaccine containing the live, attenuated virus is used for vaccination campaigns in Africa and Asia because it is relatively cheap to produce and easy to administer, requiring just two drops of medicine in the mouth. However, the risk is that the

attenuated live virus—in particular, type 2, which is at the root of all current vaccine-derived polio cases, the Associated Press reports—can mutate and become pathogenic. Fortunately, vaccination can protect against such vaccine-derived strains. “The solution is the same for all polio outbreaks: immunize every child several times with the oral vaccine to stop polio transmission, regardless of the origin of the virus,” the WHO states.

“It’s actually crazy because we’re vaccinating now against the vaccine in most parts of the world,” Vincent Racaniello, a virologist at Columbia University, tells NPR, “not against wild polio, which is confined to Pakistan and Afghanistan.”

Starting in April 2016, public health care workers around the world have made the transition from a trivalent vaccine with types 1, 2, and 3 to a bivalent version without type 2 to prevent such vaccine-derived cases.

http://bit.ly/2Y30tVJ

Using fungi to search for medical drugs

An enormous library of products derived from more than ten thousand fungi could help us find new drugs.

Researchers from the group of Jeroen den Hertog at the Hubrecht Institute, in collaboration with researchers from the Westerdijk Institute and Utrecht University, have set up this library and screened it for biologically active compounds. They tested the biological activity of these fungal products first using zebrafish embryos. The researchers chose to use zebrafish embryos, because it allows the analysis of effects on many cell types at the same time, in a working body, and because zebrafish are physiologically very similar to humans. They have already found various known compounds, among which the cholesterol lowering drug lovastatin. The library of fungal products offers ample opportunity to search for new drugs. The results of this research were published on the 26th of November in the scientific journal Scientific Reports.

Fungal products

We constantly need new therapeutic compounds in the clinic for various reasons, including our increasing age, with corresponding illnesses, and resistance to existing drugs. Fungi are an excellent, but underexplored source of these kinds of compounds, such as lovastatin, a compound produced by the fungus *Aspergillus terreus* and that is used as a cholesterol lowering drug. Jelmer Hoeksma, one of the researchers at the Hubrecht Institute, explains: "Every year new compounds produced by fungi are identified, but so far we have only investigated a very small subset of all existing fungi. This suggests that many more biologically active compounds remain to be discovered."

Ten thousand fungi

The collaboration with the Westerdijk Fungal Biodiversity Institute, home to the largest collection of live fungi in the world, enabled the researchers to set up a large library of filtrates derived from more than ten thousand different fungi. A filtrate contains all the products that the fungus excretes. To search for therapeutic compounds, the researchers investigated the effects of this large library of fungal products first on zebrafish embryos. The zebrafish embryos enabled the researchers to study effects on the whole body during development. Zebrafish are vertebrates that are physiologically very similar to humans and are often used to test drugs for a variety of disorders. Within a few days these embryos develop most of their organs, making biological activity of the fungal compounds readily detectable. In addition, comparison to known drugs may result in identification of new drugs and also point towards the underlying mechanisms of action of these compounds.

Pigmentation

The researchers found 1526 filtrates that contain biologically active compounds with an effect on zebrafish embryos, from which they selected 150 filtrates for further analysis. From these, they isolated

34 known compounds, including the cholesterol lowering drug lovastatin, which was produced by the fungus *Resinicium furfuraceum*. Until now it was unknown that this fungus produces lovastatin. In addition, the researchers found filtrates that affect pigmentation in zebrafish embryos. Other studies have shown that factors involved in pigmentation can also play a crucial role in the development of skin cancer. The researchers are currently isolating the active compounds that cause pigmentation defects in zebrafish embryos from the filtrates.

Tip of the iceberg

This study underlines the large variety of biologically active compounds that are produced by fungi and the importance of further investigating these compounds in the search for new drugs. Hoeksma: "The large library of fungal filtrates that we have set up can also be tested in many other systems, such as models for antibiotic resistance in bacteria and tumor development, making this study only the tip of the iceberg."

Publication

A new perspective on fungal metabolites: identification of bioactive compounds from fungi using zebrafish embryogenesis as read-out. Jelmer Hoeksma, Tim Misset, Christie Wever, Johan Kemmink, John Kruijtzer, Kees Versluis, Rob M.J. Liskamp, Geert Jan Boons, Albert J.R. Heck, Teun Boekhout en Jeroen den Hertog. Scientific Reports *2019.*

http://bit.ly/34z7AHR

We love coffee, tea, chocolate and soft drinks so much, caffeine is literally in our blood

Findings point to potential for contaminated blood transfusions, and suggest that blood used in research isn't necessarily pure

CORVALLIS, Ore. - Scientists at Oregon State University may have proven how much people love coffee, tea, chocolate, soda and energy drinks as they validated their new method for studying how different drugs interact in the body.

In conducting mass spectrometry research, Richard van Breemen and Luying Chen worked with various biomedical suppliers to purchase 18 batches of supposedly pure human blood serum pooled from multiple donors. Biomedical suppliers get their blood from blood banks, who pass along inventory that's nearing its expiration date.

All 18 batches tested positive for caffeine. Also, in many of the samples the researchers found traces of cough medicine and an anti-anxiety drug. The findings point to the potential for contaminated blood transfusions, and also suggest that blood used in research isn't necessarily pure.

"From a 'contamination' standpoint, caffeine is not a big worry for patients, though it may be a commentary on current society," said Chen, a Ph.D. student. "But the other drugs being in there could be an issue for patients, as well as posing a problem for those of us doing this type of research because it's hard to get clean blood samples."

The study was published in the Journal of Pharmaceutical and Biomedical Analysis.

In addition to caffeine, the research also involved testing pooled serum for alprazolam, an anti-anxiety medicine sold under the trade name Xanax; dextromethorphan, an over-the-counter cough suppressant; and tolbutamide, a medicine used to treat type 2 diabetes.

All of the pooled serum was free of tolbutamide, but eight samples contained dextromethorphan and 13 contained alprazolam - possibly meaning that if you ever need a blood transfusion, your odds of also receiving caffeine, cough medicine and an anti-anxiety drug are pretty good.

"The study leads you in that direction, though without doing a comprehensive survey of vendors and blood banks we can only speculate on how widespread the problem is," said van Breemen, the director of OSU's Linus Pauling Institute. "Another thing to consider is that we found drugs that we just happened to be looking

for in doing the drug interaction assay validation - how many others are in there too that we weren't looking for?"

The purpose of the study by Chen and van Breemen was to test a new method for evaluating the potential for interactions between botanical dietary supplements and drug metabolism.

The method involves rapid protein precipitation and ultra high pressure liquid chromatography and is being used to support clinical studies. In the clinical studies, participants take a drug cocktail along with a botanical supplement - hops, licorice or red clover - to see if the supplement causes any of the drugs to be metabolized differently than they otherwise would.

"Botanicals basically contain natural products with drug-like activities," van Breemen said. "Just as a drug may alter the drug-metabolizing enzymes, so can natural products. It can become a real problem when someone takes a botanical supplement and is also on prescription drugs - how do those two interact? It's not straightforward or necessarily predictable, thus the need for methods to look for these interactions. The odd thing in this case was finding all the tainted blood."

Two individual donors who agreed to abstain from caffeinated foods and beverages had to be enlisted so the research could be completed.

The National Institutes of Health's Office of Dietary Supplements and the NIH's National Center for Complementary and Integrative Health supported this research.

http://bit.ly/2DugeeU

Extra-terrestrial impacts may have triggered 'bursts' of plate tectonics

Transition to plate tectonics may in fact have been triggered by extra-terrestrial impacts

Boulder, Colo., USA: When -- and how -- Earth's surface evolved from a hot, primordial mush into a rocky planet continually resurfaced by plate tectonics remain some of the biggest unanswered questions in earth science research.

Now a new study, published in *Geology*, suggests this earthly transition may in fact have been triggered by extra-terrestrial impacts.

"We tend to think of the Earth as an isolated system, where only internal processes matter," says Craig O'Neill, director of Macquarie University's Planetary Research Centre. "Increasingly, though, we're seeing the effect of solar system dynamics on how the Earth behaves."

Modelling simulations and comparisons with lunar impact studies have revealed that following Earth's accretion about 4.6 billion years ago, Earth-shattering impacts continued to shape the planet for hundreds of millions of years.

Although these events appear to have tapered off over time, spherule beds -- distinctive layers of round particles condensed from rock vaporized during an extra-terrestrial impact -- found in South Africa and Australia suggest the Earth experienced a period of intense bombardment about 3.2 billion years ago, roughly the same time the first indications of plate tectonics appear in the rock record.

This coincidence caused O'Neill and co-authors Simone Marchi, William Bottke, and Roger Fu to wonder whether these circumstances could be related.

"Modelling studies of the earliest Earth suggest that very large impacts-- more than 300 km in diameter -- could generate a significant thermal anomaly in the mantle," says O'Neill. This appears to have altered the mantle's buoyancy enough to create upwellings that, according to O'Neill, "could directly drive tectonics."

But the sparse evidence found to date from the Archaean -- the period of time spanning 4.0 to 2.5 billion years ago -- suggests that

mostly smaller impacts less than 100 km in diameter occurred during this interval.

To determine whether these more modest collisions were still large and frequent enough to initiate global tectonics, the researchers used existing techniques to expand the Middle Archaean impact record and then developed numerical simulations to model the thermal effects of these impacts on Earth's mantle.

The results indicate that during the Middle Archaean, 100-kilometer-wide impacts (about 30 km wider than the much younger Chixculub crater) were capable of weakening Earth's rigid, outermost layer. This, says O'Neill, could have acted as a trigger for tectonic processes, especially if Earth's exterior was already "primed" for subduction.

"If the lithosphere were the same thickness everywhere, such impacts would have little effect," states O'Neill. But during the Middle Archean, he says, the planet had cooled enough for the mantle to thicken in some spots and thin in others.

The modelling showed that if an impact were to happen in an area where these differences existed, it would create a point of weakness in a system that already had a large contrast in buoyancy -- and ultimately trigger modern tectonic processes.

"Our work shows there is a physical link between impact history and tectonic response at around the time when plate tectonics was suggested to have started," says O'Neill.

"Processes that are fairly marginal today -- such as impacting, or, to a lesser extent, volcanism -- actively drove tectonic systems on the early Earth," he says. "By examining the implications of these processes, we can start exploring how the modern habitable Earth came to be."

FEATURED ARTICLE The role of impacts on Archaean tectonics *C. O'Neill* et al., *craig.oneill@mq.edu.au; URL: https://pubs.geoscienceworld.org/gsa/geology/article/doi/10.1130/G46533.1/575921/The-role-of-impacts-on-Archaean-tectonics*

https://go.nature.com/37Ox7iA

Tsunami sands reveal massive quakes in Japan's past

Great earthquakes have roiled a central region of Japan a number of times during the past two millennia.

The scars of centuries-old tsunamis suggest that large earthquakes shake central Japan's Tokai region more often, and affect a bigger geographical area, than scientists had suspected.

During the past four centuries, powerful earthquakes have occasionally hit Tokai and the neighbouring Nankai area simultaneously. To explore this history, a team led by Osamu Fujiwara at the Geological Survey of Japan in Tsukuba dug into layers of sediment along a coastal plain in Tokai. They found four layers of tsunami deposits, each created when a big earthquake generated a tsunami that rushed ashore and dumped a load of sand.

Two of the tsunami deposits came from known quakes in 1498 and 1096. But the scientists dated a third deposit to the year 887 and a fourth to the seventh century — pointing to quakes that are not documented in reliable historical records. Historical accounts do report that a quake was felt in Nankai in 887. This suggests that the event ruptured faults along a longer segment of the coast than previously recognized.

The discovery highlights the need for both Nankai and Tokai to prepare for the risk of future quakes.

Quat. Sci. Rev. (2019)

https://wb.md/2Owi9G7

Patients Benefit When Hospitalists Work Several Days in a Row

When hospitalists work several consecutive days, as opposed to working intermittent shifts, patient outcomes improve and costs decrease, new research suggests.

Marcia Frellick

Among 114,777 patient admissions studied, major outcomes, including 30-day mortality risk after discharge, readmission risk, and discharge to home improved with hospitalist continuity of care, report James S. Goodwin, MD, of the Department of Preventive Medicine and Community Health at the University of Texas Medical Branch at Galveston, and colleagues.

Findings were published online November 25 in *JAMA Internal Medicine*. The work was funded by the National Institute on Aging.

Table. Highest- vs Lowest-Continuity Cohort

Outcome	Adjusted Odds Ratio	95% CI
30-day mortality after discharge	0.88	0.81 - 0.95
Readmission	0.94	0.90 - 0.99
Discharge to home	1.08	1.03 - 1.13

Researchers also found that 30-day postdischarge costs were $223 lower per patient (95% CI, −$441 to −$7) for the highest-continuity cohort.

The results were consistent across a range of methods for defining continuity of hospitalist schedules and different ways of selecting the cohort, and after controlling for length of stay and diagnosis, among other factors.

The authors suggest the improvement in outcomes with continuity may be partly attributed to fewer handoffs with rotating providers and less chance that information could be lost between conversations and entries in the electronic health record. Trust in a provider is also key to patient care, they note.

"Patients and their families may be less comfortable soliciting and following the advice of a physician they are seeing for the first time, particularly if the issue is value-laden, such as end-of-life issues or discharge destination," the authors write.

In an audio interview with *JAMA Internal Medicine*, Goodwin said they worked to avoid selection bias by doing a conditional analysis of schedules across hospitals and within each hospital because they found such a wide range of scheduling models.

"None of the analyses suggested that hospitalists with discontinuous schedules took care of sicker patients, patients more likely to die, or patients more likely to be readmitted," he said.

The researchers assessed Medicare claims data for patients with a 3-day to 6-day length of stay from January 1, 2014, through November 30, 2016. The patients received all general medical care from hospitalists in 229 hospitals.

Goodwin explained in the *JAMA* interview that his team found schedules varied from 1 day a week to 10 days in a row.

"We found, for example, that 665 of 2334 (28%) Texas hospitalists had 0 working days in a year that were part of a 7-day or longer block of consecutive working days, whereas 591 of 2334 (25%) hospitalists had more than 54% of their working days as part of a 7-day or longer block," the authors explain.

Balancing Burnout With Better Outcomes

Goodwin said sometimes intermittent scheduling is designed to help physicians reduce burnout and the results from this study suggest that scheduling should take into consideration the balance between potential burnout and the potential for better outcomes with continuous care.

"What I hope this study does is start the discussion about the balance," Goodwin said.

The average age of people in the cohort was 79.9 (SD 8.3) years, and 61% were women. The lowest quartile for continuity of care included hospitalists who worked 0% to 30% of their total working days as part of a block of 7 days or more. The highest quartile of continuity included those who worked 67% to 100% of their total working days as part of a block of 7 consecutive days or more.

JAMA Intern Med. *Published online November 25, 2019.* Abstract

http://bit.ly/2P4n14B

Drug-Resistant Flu Can Emerge After Patients Take Antiviral

Roughly a quarter of 38 viral samples from people treated with Xofluza had mutations in their genomes that made the pathogens less susceptible to the drug.

Kerry Grens

An antiflu medication first approved in Japan in 2018 and given the green light later that year in the US may be fostering the emergence of drug-resistant strains of influenza. A study published yesterday (November 25) in *Nature Microbiology* finds that nearly one-fourth of patients who took baloxavir (Xofluza) harbored flu viruses with mutations in their genomes that made them less vulnerable to the drug. The mutations were not present before the treatment.

"In a worst case scenario, these mutations could render the drug entirely useless," Andrew Pekosz, a molecular biologist at Johns Hopkins who was not involved in the study, tells *Endpoints News*. "They haven't yet, and it's not clear why that's been the case."

In prior cell culture studies and clinical trials, scientists had observed mutant influenza sometimes occurring after Xofluza exposure. Each of the mutant viruses carried the same change, in a gene encoding a polymerase subunit. The variant weakened the drug's effect because Xofluza ordinarily disrupts the polymerase complex.

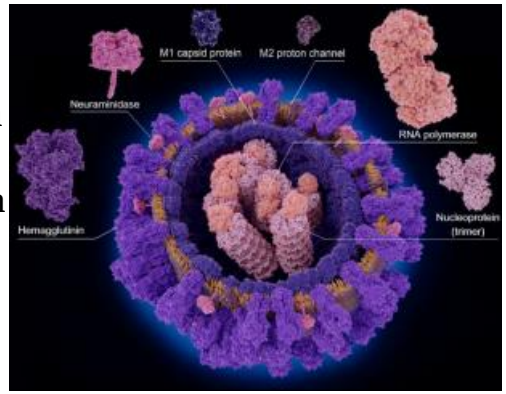

***Illustration of the influenza virus* © ISTOCK.COM, SELVANEGRA**

In this latest work, Yoshihiro Kawaoka of the University of Wisconsin–Madison and his colleagues collected viral samples from 38 patients with influenza infections before and after Xofluza treatment. Before the study participants took the drug, none of the viruses had the polymerase variant, but afterward, samples from nine patients had mutated.

To see if the treatment-associated variant made a difference to the drug's efficacy, the researchers conducted experiments in hamsters, ferrets, and cells, finding the mutant virus was pathogenic, transmissible, and more drug-resistant.

Kawaoka's team also sequenced the influenza virus from a boy before he took Xofluza and from his sister, who caught the flu a couple of days later. The genome was entirely the same between their samples, except for one mutation—in the gene for the polymerase subunit. "It tells you the virus acquired resistance during treatment and transmitted from brother to sister," Kawaoka says in a press release.

He adds that while this drug-resistant strain is a threat to those in close proximity to the person harboring it, it will not likely become a widespread problem. "The drug resistant virus does transmit but there are so many influenza viruses worldwide and only a small population will be treated with this drug," Kawaoka says in the press statement. "The vast majority remain drug sensitive."

http://bit.ly/37TA4hS

Discovering hidden plant medicines on your doorstep

Plants produce a vast array of bioactive compounds to guard themselves against pests and diseases

by Earlham Institute

EI is part of the global effort to sequence the DNA all of the known species of animals, plants and fungi on earth, known as the Earth BioGenome Project. Contributing to the UK arm Darwin Tree of Life Project, one aspect from EI is unearthing useful new medicines that are produced in plants by decoding their genomic data profile.

Plants produce a vast array of bioactive compounds to guard themselves against pests and diseases as well as to attract species like insects and microbes that help them grow. Some of these chemicals can help us too.

For example, a precursor of the well-known painkiller aspirin was originally found in willow bark, paclitaxel is a chemotherapy drug found in certain yew trees, and digoxin, found in foxgloves, is used to treat heart conditions.

Foxgloves and several species of willow trees are still common throughout the UK, but many other plant species are threatened by the rapid decline in hay meadows, which have largely been replaced by intensive grasslands since the second world war.

A team from EI and John Innes Centre led by Synthetic Biology Group Leader Nicola Patron aims to explore the chemical diversity of UK plants, identifying the genes that plants use to produce molecules that could provide benefits in health and industry.

The search will begin in the daisy family (Asteraceae) for which over 900 species have been recorded in the UK. Several of these were used in traditional medicine and, more recently, some of the molecules responsible for these healing properties have been identified.

The team will use biochemical techniques to identify the chemicals being made and sequence the genomes to discover the genes responsible for the production of these molecules. This will help us to understand how plants have evolved the ability to make such complex chemicals and could also enable the large-scale biomanufacturing of useful molecules in the future.

Dr. Nicola Patron, said: "Understanding how species evolve the ability to make new molecules is a major goal in evolutionary biology and it can also help us to identify and make new molecules for use in health and industry.

"By linking data about the chemicals being made and the genes being expressed, we will be able to identify unknown chemical diversity as well as the genes used for their biosynthesis."

Director of EI Prof Neil Hall, added: "This work is a great example of how sequencing genomes of wild species could lead to entirely new ways of harnessing nature for the public good. My hope is that in the next ten years we will have sequenced the vast majority of plant genomes, unlocking a treasure trove of pathways that make compounds which can be used in medicine and biotech."

This pilot project is funded as part of a £600k grant from the BBSRC for the Darwin Tree of Life Project.

http://bit.ly/34ySbYa

Go for lunch: Japanese yakitori chicken gets space thumbs-up

Chicken yakitori is one of the most popular fast foods in Japan

Japanese chicken yakitori kebabs, one of the country's most-loved fast foods, will soon be making an appearance in orbit after Japan's space agency cleared them for astronaut meals.

The charbroiled chicken meat on skewers and flavoured with a variety of sauces is hugely popular in Japan and abroad, and a canned version has just won certification as a "Japanese space food" for consumption on the International Space Station.

Yakitori joins 34 other Japanese items such as "onigiri" rice balls, ramen noodles, seaweed soup and cooked mackerel, as Japanese astronauts pine for a taste of home while in orbit.

They can pick what certified Japanese food to bring on their ISS missions, adding to base meals selected by NASA, a spokesman from the Japan Aerospace Exploration Agency (JAXA) explained on Wednesday.

The approved yakitori will come in two flavours—soy sauce and "yuzu kosho"—green pepper infused with the Japanese citrus fruit yuzu.

But while astronauts may want the full yakitori experience of chewing from a bamboo skewer, strict space rules will make this impossible.

"Eating from skewers in space would be good... but the policy is to leave as little waste as possible," the JAXA spokesman told AFP.

So the yakitori will be eaten from ring-pull cans with special velcro to keep it from floating away in the microgravity environment.

The approved yakitori cans are manufactured by Hotei Foods, based in Shizuoka, southwest of Tokyo. The company said they expect their cans will blast off when Japanese astronauts leave for the ISS next year.

They won JAXA approval after clearing a rigorous set of criteria such as guaranteeing the food would not degrade even after 18 months at room temperature.

https://go.nature.com/2Y5eORN

Ready-made cellular plugs heal skin wounds

The finding that a thin sheet of fibrous tissue under the skin contains a prefabricated, movable cellular sealant that can heal deep wounds might have implications for the treatment of scars and ulcers.

Mark C. Coles & Christopher D. Buckley

PDF version

Skin consists of an outer epidermal layer (the epidermis) and an inner dermal layer (the dermis). If you pinch your skin, you can lift it because these two cellular layers move freely above a membranous sheet called the fascia, which contains cells and extracellular-matrix material. This gelatinous tissue creates a frictionless interface between the skin and the more rigid structures beneath it, such as muscle and bone. However, it now seems that the fascia has roles beyond providing a non-stick surface. Writing in *Nature*, Correa-Gallegos *et al.*[1] report that the fascia contains a movable sealant that patches up deep injuries to enable rapid wound repair.

Read the paper: ***Fascia is a repository of mobile scar tissue***

The scar tissue of a healing skin wound contains fibroblast cells, which make and modify extracellular-matrix proteins. These fibroblasts can be identified by their expression of a protein called Engrailed-1, and are termed Engrailed-positive fibroblasts (EPFs). The idea that the fascia might be a repository of cellular components involved in wound healing and scar formation came from a previous study[2], which reported that EPFs reside not only in the skin, as expected, but also in the fascia.

To investigate wound healing in mice, Correa-Gallegos and colleagues grafted fascia that contained cells engineered to express green fluorescent protein onto skin cells expressing red fluorescent protein. The authors then wounded this dual-coloured 'fluorescent sandwich' and transplanted it into a healthy mouse. Comparison of the percentages of green and red cells revealed that 80% of cells in the healing wound came from the fascia. Furthermore, the vast majority of many cell types found in the healing injury originated from the fascia, including contractile fibroblasts (or myofibroblasts), blood-vessel cells, macrophages of the immune system and nerve cells.

To confirm that their observations were not due to any peculiarities of this artificial grafted structure, the authors injected a dye into the fascia of mice, and then gave the mice a deep wound that penetrated the animals' skin and fascia. The authors mapped the dye-labelled cells that populated the healing wound and the surrounding scar tissue. More than half of the cells in the healed wound were labelled with the dye, confirming that the fascia is a major source of scar-forming tissue after deep injury.

Deep wounds lead to scars that are larger and harder to heal than those arising from superficial wounds that do not penetrate the

fascia[3]. The authors used two-photon microscopy to analyse deep skin wounds in mice engineered[4] to express fluorescent proteins, which can be used to trace scar-forming EPFs. They found that a cellular plug in the fascia, consisting of extracellular matrix, macrophages, blood vessels and nerves, moved upwards into the damaged skin to form a scar.

This healing process did not require cell division, indicating that the plug was prefabricated. Importantly, the authors found that key proteins that have been reported to define the types of fibroblast found in scars[5] are expressed at higher levels on fascial than on dermal fibroblasts, consistent with a model in which fascial EPFs are a major source of fibroblasts in healing deep wounds (Fig. 1).

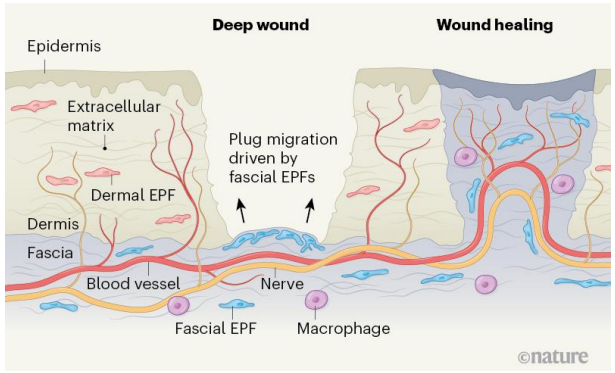

Figure 1 | ***The healing of deep skin wounds. The skin consists of an outer layer called the epidermis and an inner layer, the dermis. Superficial wounds no deeper than skin level can be repaired by cells called Engrailed-positive fibroblasts (EPFs) in the dermis, which make extracellular-matrix material. Working with mice, Correa-Gallegos et al.[1] investigated the healing of deep wounds that penetrated below the skin into a layer known as the fascia. The fascia contains EPFs, extracellular matrix, blood vessels, nerves and immune cells called macrophages. The authors report that a prefabricated plug of material from the fascia moves upwards, steered by fascial EPFs, to seal the wound.*** **(Image based on Fig. 6 of ref. 1.)**

Given that fibroblasts regulate the extracellular matrix, the authors used microscopy to visualize physical features of fibres of the protein collagen, which is a component of the extracellular matrix. Collagen in the fascia was more coiled and immature than were the stretched and interwoven collagen fibres in the dermis. Furthermore, when a fluorescent dye was used to tag collagen in an injured animal, this revealed that the extracellular matrix of the fascia moved upwards like a pliable gel into the damaged tissue, to plug and then repair the wound. By contrast, dermal collagen remained immobile.

The authors then tested whether EPFs from the fascia drive the movement of the prefabricated plug. They inserted non-adhesive membranes in mice to separate the fascia from the dermis, which resulted in delayed repair and non-healing wounds that remained open. Animals in which these membranes were not inserted did not show these effects. The removal of fascial EPFs by a genetic approach also resulted in the plug not entering wounds and in poor healing. These findings indicate that fascial EPFs do indeed steer the plug that seals deep wounds.

Although this study has potential relevance for human disease, most of the work was carried out in an artificial mouse model. Moreover, mice have a type of muscle called the panniculus carnosus, which lies between the fascia and the skin and is used to twitch the skin[6]. However, humans lack this twitching ability and have only a small remnant of this muscle. Therefore, the authors needed to determine whether scar formation occurs in a similar manner in humans and mice despite such differences.

The team analysed fascial fibroblasts in human skin and investigated a type of human raised scar called a keloid, which grows bigger than the original injury and can be profoundly itchy, inflamed and painful[7]. Many of the proteins that characterize the mouse fascia were also highly expressed in human fascia and keloid scars. This similarity suggests that the same processes are involved in wound healing and scar formation in both species. However, it is not yet clear whether these findings in mice reveal general principles that are relevant to human skin disease.

The authors' findings provide satisfying potential explanations for some unsolved clinical conundrums. Nerves, blood vessels and macrophages in the prefabricated plug are dragged into the mouse wound; if the same phenomenon occurs in humans, this could explain why keloids itch and are painful. Keloid formation is more common at sites of thicker fasciae (such as the chest, back and thighs) than at sites where the fascia is thinner (for example, the feet), which is consistent with a model in which the fascia drives keloid formation.

Could these discoveries about the skin shed light on other clinically relevant fibrotic diseases (conditions associated with the accumulation of extracellular matrix) that affect organs in which the fascia is not present, such as the lungs and liver? Perhaps the mechanisms uncovered in mice might have relevance for the processes underlying skin damage in the leg ulcers that can develop in people who have diabetes. In any case, it is clear that advances made in understanding the biology of the fascia might reveal new targets for treating scarring diseases of the skin.

doi: 10.1038/d41586-019-03602-4

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http://bit.ly/2L8fctu

New study shows a minimum dose of hydromethylthionine could slow cognitive decline

Even at the lowest dose the drug produced concentration-dependent effects on cognitive decline and brain atrophy

ABERDEEN, Scotland and Singapore - In a paper published in today's online issue of the Journal of Alzheimer's Disease (DOI 10.3233/JAD-190772), TauRx has reported unexpected results of a pharmacokinetic analysis of the relationship between treatment dose, blood levels and pharmacological activity of the drug hydromethylthionine on the brain in over 1,000 patients with mild-to-moderate Alzheimer's disease. These results showed that, even at the lowest dose of hydromethylthionine previously tested in two Phase 3 global clinical trials (8 mg/day), the drug produced concentration-dependent effects on cognitive decline and brain atrophy.

Hydromethylthionine, taken as a tablet, is the WHO-approved non-proprietary name for the compound previously referred to by TauRx as LMTM. This drug blocks abnormal aggregation of tau protein in the brain,2, 3 which is increasingly recognised as an important driver of clinical dementia.1 In Phase 3 global clinical trials conducted in almost 1,700 patients with mild-to-moderate Alzheimer's disease between 2012-2016, hydromethylthionine was tested at doses of 150-250 mg/day against a low dose of 8 mg/day, which was intended only as a control to mask the discolouration of urine that can sometimes occur with the drug. The study designs were based on the findings from an earlier trial that used a different variant of the drug. 6 Surprisingly, there was no difference between the high doses and the low dose of hydromethylthionine on any of the clinical outcomes in the trials. 4,5

To further explore these results, the researchers conducted a new pharmacokinetic population analysis using plasma concentration

data from 1,162 of the patients who participated in either of the two completed Phase 3 hydromethylthionine trials to measure how blood levels of the drug relate to its effects on the brain. Using a new assay, the researchers found that the effects of hydromethylthionine at the 8 mg/day dose were determined by the blood level, and that the majority of patients had high enough blood levels of the drug at this dose to produce meaningful reductions in cognitive decline and brain atrophy. They concluded that a slightly higher dose of hydromethylthionine of 16 mg/day would ensure that all patients would have the blood levels needed to maximise the drug's activity, since its effects plateau at higher concentrations and doses. The pharmacokinetic profile they found, typical of many drugs, now explains why the pharmacological effects of hydromethylthionine at the high doses tested in the trials were no better than those seen in patients with high blood levels at the 8 mg/day dose.

The analysis also showed that whilst hydromethylthionine has a similar concentration-response profile in patients taking the drug as an add-on therapy to the routinely used symptomatic treatments in Alzheimer's disease, the maximum effect in these patients was reduced by half. This finding supports the hypothesis that symptomatic drugs for this condition interfere with the disease-modifying treatment effects of hydromethylthionine. This hypothesis was initially proposed on the basis of the drug's Phase 3 trial results. 4,5

"Since we already have a substantial database supporting the safety and tolerability of hydromethylthionine in clinical trials of patients with mild-to-moderate Alzheimer's disease, the additional results of this analysis have given us the confidence to expand the scope of the new TauRx Lucidity clinical trial to confirm the potential efficacy of the hydromethylthionine 16 mg/day dose in these types of patients," said Prof. Claude Wischik, of Aberdeen University and executive chairman of TauRx Therapeutics Ltd.

He noted that hydromethylthionine is taken in a convenient oral form at home and does not require patients to attend clinics for intravenous infusions or injections, unlike various other Alzheimer's disease treatments currently being tested in clinical trials.

"In addition to the reduction in brain atrophy, we were surprised to see the large cognitive effects of treatment in the patient group with the higher blood levels of hydromethylthionine at the 8 mg daily dose," he added. "According to scores from the ADAS-cog scale, the effect was around 7.5 points, or three times that seen from current routine Alzheimer's treatments, and would be equivalent to an 85% reduction in cognitive decline over 65 weeks." The Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-Cog) is the standard cognitive scale used to measure neuropsychological changes in Alzheimer's disease clinical trials. A 4-point change is generally considered as indicating a clinically meaningful difference.

Professor George Perry, Editor-in-Chief of Journal of Alzheimer's Disease, commented: "The extensive data, experience, and now pharmacokinetics, highlight the potential of hydromethylthionine treatment as an important new avenue forward in Alzheimer's disease. The clinical benefit and reduction in brain atrophy greatly exceed those reported for other therapeutic routes."

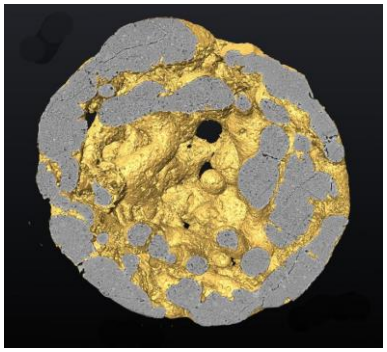
Professor Serge Gauthier, Director of the Alzheimer Disease Research Unit, McGill Center for Studies in Aging, commented: "The researchers are aiming to confirm what they have found so far in the placebo-controlled trial that is now ongoing. Hydromethylthionine is the best hope we have right now for a disease-modifying drug acting on the tau pathology associated with Alzheimer's disease."

http://bit.ly/2OEmLdr

Researchers say animal-like embryos preceded animal appearance

Study suggests animal-like embryological traits developed long before animals themselves

Animals evolved from single-celled ancestors before diversifying into 30-40 distinct anatomical designs. When and how animal ancestors made the transition from single-celled microbes to complex multicellular organisms is unclear. But a new scientific study suggests animal-like embryological traits developed long before animals themselves.



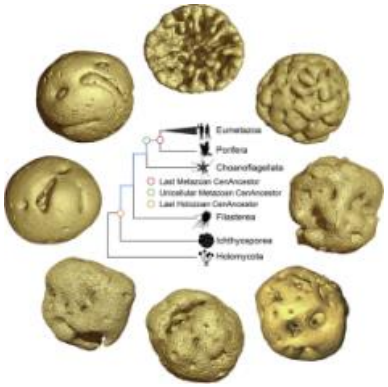
Three-dimensional reconstruction of a Caveasphaera specimen, showing cell structures. **NIGPAS**

The research - by an international research team led by scientists from the Nanjing Institute of Geology and Palaeontology of the Chinese Academy of Sciences (NIGPAS) and the University of Bristol - focused on ancient fossils of Caveasphaera, a multicellular organism found in 609-million-year-old rocks in South China's Guizhou Province that defies easy definition as animal or non-animal.

Using X-ray microscopy, the researchers analyzed the tiny fossils, which measure about a half-millimeter in diameter and were preserved down to their component cells. Various fossils displayed different stages of Caveasphaera development - from a single cell to a multicellular organism. "We were able to sort the fossils into growth stages, reconstructing the embryology of Caveasphaera," said Kelly Vargas from the University of Bristol.

YIN Zongjun of NIGPAS interpreted the discovery: "Our results show that Caveasphaera sorted its cells during embryo development in just the same way as living animals, including humans." YIN emphasized, however, there is "no evidence that these embryos developed into more complex organisms." Still, the discovery offers the earliest evidence of a key step in the evolution of animals - the capacity to develop distinct tissue layers and organs.

The verdict still seems to be out on whether Caveasphaera was itself an animal or just an important step in animal evolution, even as researchers search for more fossils. Co-author ZHU Maoyan of NIGPAS said, "Caveasphaera looks a lot like the embryos of some starfish and corals - we don't find the adult stages simply because they are harder to fossilize."



Proposed life cycle of Caveasphaera. **NIGPAS**

Whatever Caveasphaera turns out to be, its fossils tell us that animal-like embryonic development evolved long before the oldest definitive animals appeared in the fossil record.

This research was funded through the Biosphere Evolution, Transitions and Resilience (BETR) programme, which is co-funded by the UK's Natural Environment Research Council (NERC) and the Natural Science Foundation of China (NSFC).

https://nyti.ms/2OzUrJ7

This Is What It Looks Like When an Asteroid Gets Destroyed

At first astronomers thought they had spotted a comet, but it was really an asteroid in the belt between Mars and Jupiter being struck by another object.

By Robin George Andrews

The asteroid belt, hanging out between Mars and Jupiter, is not like the cluttered debris field in “The Empire Strikes Back.” It may contain millions of rocky and metal objects, but the distances separating them are vast, and collisions are rare.

That is what makes P/2016 G1 such an exciting object. Spotted zipping through the asteroid belt in early 2016, this object had a strange orbit and a tail of dust that resembled a comet. Through a careful analysis of telescopic imagery, scientists identified multiple showers of debris shooting up from its surface, the sort that could have only been produced by an impact.

What they had stumbled across was not a comet, but the immediate aftermath of an asteroid's assassination.

On or around March 6, 2016, an asteroid at least 1,300 feet in diameter was minding its own business when another space rock, weighing around 2.2 pounds and perhaps a foot long or so, slammed into the larger asteroid at roughly 11,000 miles per hour. That's about five times as fast as a bullet fired from a sniper rifle. The projectile was obliterated upon impact; the target then broke up in stages over the coming months before becoming impossible to see.

Without this collision, these two small objects would have remained forever anonymous. Instead scientists gained a serendipitous insight into the destructibility of asteroids, which could help defend Earth against future asteroid hazards. After all, "the best way to see how hard something is, is to break it," said Olivier Hainaut, an astronomer at the European Southern Observatory and lead author of the study published earlier this year in Astronomy & Astrophysics.

Astronomers first discovered P/2016 G1 with the Pan-Starrs1 telescope in Hawaii in April 2016. Backtracking through archived images, astronomers realized that it had first been visible the previous month as a centralized collection of rocky clumps: the fractured, rubbly remnants of the asteroid, surrounded by a fine dust cloud, most likely the immediate debris jettisoned by the impact.

Over the ensuing weeks, an expanding ring of debris could also be seen emerging from the object. Computer simulations revealed this to be the beginning of a cone of uplifted rubble, a signature feature of an impact event.

After the initial debris cloud was created, the cratering process lost energy and subsequent streams of debris were more slowly excavated from the asteroid's new scar. On Earth, this ring of debris would land around the crater. But on a tiny asteroid with little gravity, this debris ring simply flew into space, expanding as it went.

There is no clear date when the asteroid disappeared. Documenting the vanishing of P/2016 G1 was like tracking a drop of milk in your coffee, Dr. Hainaut said: Parts spread out and faded away individually. In any case, as of December 2018, the asteroid could no longer be seen.

While the asteroid may be gone, the collected data could be helpful in the future. With sufficient warning time, an asteroid heading toward Earth would ideally be deflected away by ramming a spacecraft into it at remarkable speeds. But an overzealous impact could break an asteroid into fragments that could still disastrously crash into Earth.

Knowing what types of impacts cause deflections and disruption is key to Earth's protection from errant asteroids. That makes the demise of P/2016 G1 a vital source of information, said Megan Bruck Syal, a planetary defense researcher at the Lawrence Livermore National Laboratory who was not involved with the study.

This spectacularly documented event may not be such a rarity for much longer. Increasingly comprehensive sky-scanning surveys, including the upcoming Large Synoptic Survey Telescope in Chile, will catch many more of these impacts on camera, giving planetary defense researchers more data to play with in cutting-edge simulations. "An asteroid cannot misbehave anymore" without us seeing it, Dr. Hainaut said.

http://bit.ly/2Y52fWl

Exercising Before Eating Burns More Fat: Study

Men had better fat-burning results when they had breakfast after cycling instead of beforehand.

Emily Makowski

Exercising before breakfast may have more health benefits than waiting until after the meal to get moving, according to a study published in the *Journal of Clinical Endocrinology & Metabolism* in October.

Researchers led by Javier Gonzalez, a physiologist at the University of Bath in England, conducted the study on a group of 30 overweight, sedentary men. One group drank a carbohydrate-laden vanilla shake for breakfast two hours before moderate cycling, while another group drank it after the same exercise. Both groups exercised three times per week. A third group was given the carb-rich drink but did not work out.

While riders in both cycling groups burned about the same number of calories each time they exercised, those in the group that worked out before drinking the shake burned about twice as many calories from fat per ride as the ones who had the shake beforehand. After the six-week study, members of the exercise-before-meal group also had improved insulin sensitivity, which lowers the risk of diabetes. People in both exercise groups had improved cardiorespiratory fitness compared to those who did not cycle, according to the study.

Exercising before breakfast may have burned more fat because fatty acids can fuel cells if glucose isn't available, such as after a time of fasting when blood sugar is low, according to *Runner's World*. While exercising before breakfast takes advantage of overnight fasting, similar results might be possible by abstaining from food at another time. "We believe that the key is the fasting period, rather than the time of day," Gonzalez tells *The New York Times*.

https://bbc.in/37UlV3S

Siberia: 18,000-year-old frozen 'dog' stumps scientists

Researchers are trying to determine whether an 18,000-year-old puppy found in Siberia is a dog or a wolf.

The canine - which was two months old when it died - has been remarkably preserved in the permafrost of the Russian region, with its fur, nose and teeth all intact.

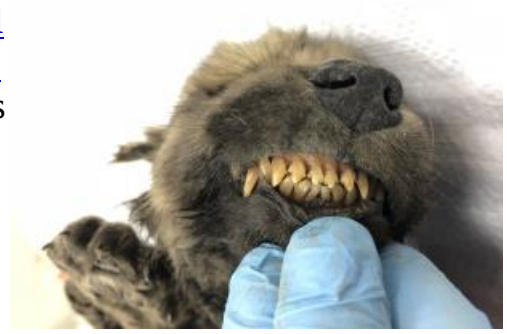
DNA sequencing has been unable to determine the species.

Scientists say that could mean the specimen represents an evolutionary link between wolves and modern dogs.

Researchers carefully cleaned the specimen to reveal it was still mostly covered in fur **Sergey Fedorov**

Radiocarbon dating was able to determine the age of the puppy when it died and how long it has been frozen. Genome analyses showed that it was male.

Researcher Dave Stanton at the Centre for Palaeogenetics in Sweden told CNN the DNA sequencing issue meant the animal could come from a population that is a common ancestor of both dogs and wolves.



"We have a lot of data from it already, and with that amount of data, you'd expect to tell if it was one or the other," he said.

Even the whiskers of the puppy were preserved **Sergey Fedorov**

Another researcher from the centre, Love Dalen, tweeted a question about whether the specimen is a wolf cub or "possibly the oldest dog ever found".

Scientists will continue with DNA sequencing and think the findings could reveal a lot about the evolution of dogs.

The puppy has been named "Dogor", which means "friend" in the Yakut language and is also the start of the question "dog or wolf?"

Modern dogs are believed to be descendants of wolves, but there is debate over when dogs were domesticated.

A study published in 2017 suggested domestication could have occurred 20,000 to 40,000 years ago.

http://bit.ly/33D7fmm

Home urine test for prostate cancer could revolutionize diagnosis

Simple urine test under development for prostate cancer detection can now use urine samples collected at home

A simple urine test under development for prostate cancer detection can now use urine samples collected at home - according to new research from University of East Anglia and the Norfolk and Norwich University Hospital.

Scientists pioneered the test which diagnoses aggressive prostate cancer and predicts whether patients will require treatment up to five years earlier than standard clinical methods.

Their latest study shows how the 'PUR' test (Prostate Urine Risk) could be performed on samples collected at home, so men don't have to come into the clinic to provide a urine sample - or have to undergo an uncomfortable rectal examination.

This is an important step forward, because the first urination of the day provides biomarker levels from the prostate that are much higher and more consistent.

And the research team hope that the introduction of the 'At-Home Collection Kit' could revolutionise diagnosis of the disease.

Lead researcher Dr Jeremy Clark, from UEA's Norwich Medical School, said: "Prostate cancer is the most common cancer in men in the UK. It usually develops slowly and the majority of cancers will not require treatment in a man's lifetime. However, doctors struggle to predict which tumours will become aggressive, making it hard to decide on treatment for many men.

"The most commonly used tests for prostate cancer include blood tests, a physical examination known as a digital rectal examination (DRE), an MRI scan or a biopsy.

"We developed the PUR test, which looks at gene expression in urine samples and provides vital information about whether a cancer is aggressive or 'low risk'.

"Because the prostate is constantly secreting, the collection of urine from men's first urination of the day means that the biomarker levels from the prostate are much higher and more consistent, so this is a great improvement.

"Being able to simply provide a urine sample at home and post a sample off for analysis could really revolutionise diagnosis.

"It means that men would not have to undergo a digital rectal examination, so it would be much less stressful and should result in a lot more patients being tested."

The research team provided 14 participants with an At Home Collection Kit, and instructions.

They then compared the results of their home urine samples, taken first thing in the morning, with samples collected after a digital rectal examination.

"We found that the urine samples taken at home showed the biomarkers for prostate cancer much more clearly than after a rectal examination. And feedback from the participants showed that the at home test was preferable.

"Using our At Home test could in future revolutionise how those on 'active surveillance' are monitored for disease progression, with

men only having to visit the clinic for a positive urine result. This is in contrast to the current situation where men are recalled to the clinic every six to 12 months for painful and expensive biopsies.

"Because the PUR test accurately predicts aggressive prostate cancer, and predicts whether patients will require treatment up to five years earlier than standard clinical methods - it means that a negative test could enable men to only be retested every two to three years, relieving stress to the patient and reducing hospital workload."

The Norfolk and Norwich University Hospital receives more than 800 referrals a year to investigate and treat potential prostate cancers.

Prostate cancer usually develops slowly and the majority of cancers will not require treatment in a man's lifetime.

Robert Mills, Consultant Surgeon in Urology at the Norfolk and Norwich University Hospital, said: "This is a very exciting development as this test gives us the possibility of differentiating those who do from those who do not have prostate cancer so avoiding putting a lot of men through unnecessary investigations.

"When we do diagnose prostate cancer, the urine test has the potential to differentiate those who need to have treatment from those who do not need treatment, which would be invaluable. These patients go on to an active surveillance programme following the diagnosis which may involve repeat biopsies and MRI scans which is quite intrusive. This urine test has the potential to tell us whether we needed to intervene with these patients."

The research team say that their findings could also help pioneer the development of home-collection tests for bladder or kidney cancer.

'Methodology for the At-Home Collection of Urine Samples for Prostate Cancer Detection' is published in the journal BioTechniques.

https://go.nature.com/2Y6LFoZ

Reptiles known as 'living rocks' show surprising cognitive powers

They might not be fast on their feet, but these massive reptiles have long memories.

Giant tortoises can learn and remember tasks, and master lessons much faster when trained in groups.

Tamar Gutnick and Michael Kuba at the Hebrew University in Jerusalem, Israel, and Anton Weissenbacher at Schönbrunn Zoo in Vienna trained Galapagos tortoises (*Chelonoides nigra)* and Aldabra tortoises (*Aldabrachelys gigantea*) to bite a ball of a particular colour — blue, green or yellow.

Experimenter Tamar Gutnick with George, a 90-year-old Aldabra tortoise who was schooled to follow a toy of a particular colour. **Michael Kuba**

When tested three months later, the tortoises recalled the task. The authors tested three of the tortoises again after nine years and found that all three responded to toys of the correct colour. The researchers also found that both species of tortoise could be conditioned with fewer training sessions if they were taught in groups than if learning occurred in isolation, hinting that tortoises learn from watching their peers.

Giant tortoises have generally been considered solitary. However, they often sleep and graze together, and the authors' results bolster the view that the creatures that have been called 'living rocks' might be more social than scientists thought.

Anim. Cogn. (2019)

http://bit.ly/2PehKYj

Public believe more than half of fake news about healthcare spread online, major study reveals

More than 60 percent of fake news read online about healthcare issues is considered credible

New research by leading health economists from Kingston University in London has revealed more than 60 percent of fake news read online about healthcare issues is considered credible—and trust in such claims increases if a story is seen multiple times.

With vaccine hesitancy named as one of the 10 biggest global threats by the World Health Organisation, discriminating between scientifically proven facts and fake news is becoming increasingly important in safeguarding public health.

Yet a major new piece of research by leading health economists from Kingston University has revealed more than 60 percent of fake news read online about healthcare issues is considered credible—and trust in such claims increases if a story is seen multiple times.

The study, by Professor Giampiero Favato and Dr. Andrea Marcellusi from Kingston Business School, also revealed web banners warning audiences about the potential inaccuracy of information were ineffective in limiting its circulation—with users just as likely to share content labelled as unverified.

"The belief in fake news stories about healthcare is understandable. Most people do not have specialist medical knowledge, so if claims are put in a way that sounds like they make sense, why would the public not believe them?" Professor Favato said.

"One of our most concerning findings is that prior exposure to stories increases credibility—repetition counts, so the more someone sees something, the more they believe it."

More than 1,900 people aged between 18 and 60 from a wide range of backgrounds were recruited to take part in the research, commissioned by the Italian Government's Ministry of Health. Participants were randomly assigned to two groups, then shown social media style posts about six real and six fake news stories and asked whether or not they would share them on Facebook. One group saw web banners warning about the credibility of the fake news posts, while the other did not. Later, participants were shown the same 12 stories again, along with 12 new ones, and asked to rate whether these were true or false.

Warnings about unverified information were shown to have no impact on study participants' behaviour in terms of believing or sharing information.

Even when a story was recognised as fake, the probability it would be shared was still higher than 50 percent, Professor Favato said. With fake healthcare news stories so readily becoming viral, media companies needed to do more to tackle the problem, he added.

"Media organisations publishing fake news stories have a responsibility to act. Facebook is planning to invest in teams of experts to look at the trustworthiness of the information being shared on its platform. If a story is not reliable, we recommend a publisher should have two choices—either delete the post or use the search algorithm to ensure scientifically inaccurate stories are relegated to appearing at the end of search results," Professor Favato said.

The economic value of fake news was fuelling the problem, he added. "As sensationalist stories generate high numbers of views and shares, most fake news is money-making in terms of advertising revenue. However we have to recognise the very high economic cost of the spread of inaccurate information. It threatens the implementation of public health policies, such as vaccination programmes, and increases the economic burden of preventable diseases on society," Professor Favato said.

http://bit.ly/37UAIeV

Japan's love of ramen tempered by mortality warning

Overindulging in ramen could prove deadly

Slurping down a steaming hot bowl of ramen is a great way to warm the soul on a cold winter's day but overindulging in the dish could prove deadly, a British medical paper has warned.

In a paper published on BioMed Central in September, three Japanese researchers from the Jichi Medical University School of Medicine in Tochigi Prefecture found a direct link between the prevalence of ramen restaurants and stroke mortality in certain parts of the country.

Following up on this issue, the Asahi Shimbun said that Tochigi, Akita, Aomori, Yamagata, Niigata and Kagoshima prefectures - all famed for their ramen offerings - were by far the worst offenders.

The newspaper also noted that households in these regions were also more likely to use more salt, which causes high blood pressure.

According to a survey conducted by the General Affairs Agency, Yamagata Prefecture consumes more salt than any other part of the country.

Although this report has the potential to affect Japan's love of ramen, social media was awash with comments from people who appeared more likely to go into denial than give up slurping down a bowl of noodles on a regular basis.

http://bit.ly/2YauWRR

Certain beers are 'very good for you' and improve gut health, according to a Dutch scientist

Strong Belgian beers like Hoegaarden, Westmalle Tripel, and Echt Kriekenbier, are rich in probiotic microbes that offer a range of health benefits.

Olivia Petter,

Certain beers could be considered "very healthy" thanks to the amount of gut-friendly bacteria they contain, according to scientists specializing in gut health. Professor Eric Claassen, who works at Amsterdam University, explained that strong Belgian beers, including Hoegaarden, Westmalle Tripel, and Echt Kriekenbier, are rich in probiotic microbes that offer a range of health benefits.

Presenting his research at an event held by probiotic drink maker Yakult, Claassen said that unlike most mainstream beers, which go through a single fermentation process, these beers are fermented twice.

The second fermentation not only creates a drier flavor and boosts the strength of the beer, but it also uses a different strain of yeast found in traditional pints. This strain of yeast produces acids that kill harmful bacteria in the gut that can make us ill. "You are getting a stronger beer that is very, very healthy," Claassen said.

While the professor stressed that the research does not mean it's okay to start guzzling pint after pint, it might mean that those who consume these beers in moderation could see major health benefits.

Hoegaarden is a strong Belgian beer which is rich in probiotic microbes.
Supawadee56 / Shutterstock

"We don't want to give people a license to drink more beer," he added. "Those of us who advocate good health know it's very difficult for people to stop at one.

"In high concentrations alcohol is bad for the gut but if you drink just one of these beers every day it would be very good for you."

The health benefits of probiotics are well-documented.

While they can be found in foods such as yogurt, kimchi, and kefir, they are most commonly taken in capsule form as food supplements and are thought to restore the natural balance of bacteria in the gut after periods of illness, when taking a course of antibiotics might've

irritated the stomach and intestines. The NHS claims that probiotics may also help reduce bloating and flatulence in IBS sufferers.

https://nyti.ms/2LaSd0U

How a Poisonous Mammal Evolved Its Venom

Solenodons are highly unusual, and very difficult to study.

By Veronique Greenwood

The Hispaniolan solenodon is a wondrously strange creature.

About the size of a guinea pig, it has a long, hairless snout, sharp little teeth and, to top it all off, venom-laced saliva. Highly endangered, it lives quietly in the forests of the Dominican Republic and Haiti, and scientists have been hard pressed to understand much about its habits and evolution.

But in a paper published Tuesday in the Proceedings of the National Academy of Sciences, a diverse group of researchers outline the intriguing conclusions they reached about how the solenodon got its dangerous spit, after they sequenced its genome and analyzed its venom.

The Hispaniolan solenodon, which is related to hedgehogs, moles and shrews. **Credit...Lucy Emery**

It was not easy finding solenodons to study, said Nicholas Casewell, a venom expert at the Liverpool School of Tropical Medicine in England and a co-author of the new paper. The team managed to track down two of the animals in the wild with venom they could sample. At the National Zoological Park in the Dominican Republic, they took blood for genome sequencing from another solenodon — one of a handful of captive specimens in the world. They compared the genome to those of related animals, like hedgehogs, moles and shrews, and identified substances present in the venom, including a set of enzymes called kallikreins.

Kallikreins mince up other proteins, including some involved in maintaining blood pressure. The researchers injected mice with solenodon venom and saw that indeed, while their pulse and breathing did not change, their blood pressure dropped precipitously as soon as the venom went in. This could render prey foggy-headed and easier for the solenodon to finish off, the researchers suggest.

Another venomous mammal among the solenodon's relatives, the northern short-tailed shrew, also has kallikreins in its venom.

"To us, it was a real surprise to find very similar proteins in the venom of the solenodon and shrews," Dr. Casewell said.

They asked whether venom might have existed in the common ancestor of moles, hedgehogs, shrews and solenodons. But if a common ancestor did have this trait, an improbably large fraction of its descendants would have had to mysteriously lose it for the modern family tree to make sense.

The researchers concluded that it is more likely that shrews and solenodons came up with the adaptation after they branched off from these other small mammals. They think the trait is likely to have evolved independently in each animal, as shrews and solenodons do not use the exact same kallikreins in their venom.

But the fact that there is an overlap in these enzymes in two different animals implies that mammals have a very limited palette of options to work with when it comes to ginning up a venom. Kallikreins are commonly present in mammal saliva, so modifying them little by little to get something more dangerous is a plausible route for venom's evolution.

The researchers wonder, however: Are solenodons still using their venom? The last 500 years have seen the extinction of many prey species, like lizards, birds and other vertebrates, on their home island. This ecological destruction has left behind mainly insects, which may not be affected by the venom.

Dr. Casewell and his colleagues hope that future observations of wild solenodons on the hunt may provide insight into whether its unusual venom is still useful to solenodons in their daily lives, or if it is a relic of a time, and an ecosystem, that no longer exists.

http://bit.ly/2RlgPYL

Facial deformity in royal dynasty was linked to inbreeding, scientists confirm

First study to indicate a direct relationship between inbreeding and facial morphology

King Charles II of Spain was the last in the Habsburg line and one of the most afflicted with the facial deformity. **Credit: Don Juan Carreño de Miranda**

The "Habsburg jaw", a facial condition of the Habsburg dynasty of Spanish and Austrian kings and their wives, can be attributed to inbreeding, according to new results published in the *Annals of Human Biology*.

The new study combined diagnosis of facial deformities using historical portraits with genetic analysis of the degree of relatedness to determine whether there was a direct link.

The researchers also investigated the genetic basis of the relationship.

Generations of intermarriage secured the family's influence across a European empire including Spain and Austria for more than 200 years but led to its demise when the final Habsburg monarch was unable to produce an heir. However, until now no studies have confirmed whether the distinct chin known as "Habsburg jaw" was a result of inbreeding.

"The Habsburg dynasty was one of the most influential in Europe, but became renowned for inbreeding, which was its eventual downfall. We show for the first time that there is a clear positive relationship between inbreeding and appearance of the Habsburg jaw," says lead researcher Professor Roman Vilas from the University of Santiago de Compostela.

The researchers recruited 10 maxillofacial surgeons to diagnose facial deformity in 66 portraits of 15 members of the Habsburg dynasty. Despite differences in artistic style, the portraits are characterised by a realistic approach to the human face. The surgeons were asked to diagnose 11 features of mandibular prognathism, otherwise known as "Habsburg jaw", as well as seven features of maxillary deficiency, the most recognisable of which are a prominent lower lip and an overhanging nasal tip.

The portraits, which can be viewed online, are preserved by some of the most important art museums in the world, including the Kunsthistorisches Museum in Vienna and the Prado Museum in Madrid.

The surgeons gave scores for the degree of mandibular prognathism and maxillary deficiency in each member of the Habsburg family. Mary of Burgundy, who married into the family in 1477, showed the least degree of both traits. Mandibular prognathism was most pronounced in Philip IV, King of Spain and Portugal from 1621 to 1640. Maxillary deficiency was diagnosed to the greatest degree in five members of the family: Maximilian I (regent from 1493), his daughter Margaret of Austria, his nephew Charles I of Spain, Charles' great-grandson Philip IV and the last in the Habsburg line, Charles II.

The study authors detected a correlation between the two conditions, suggesting that "Habsburg jaw" is in fact characterised by them both and that they share a common genetic basis. The extent of inbreeding was calculated from a large-scale family tree, including more than 6,000 individuals belonging to more than 20 generations. Analysis was carried out to determine if it was connected to the degree of facial deformity. The researchers detected a strong

relationship between the degree of inbreeding and the degree of mandibular prognathism. The relationship to maxillary deficiency was also positive, but it was only statistically significant in two of the seven features diagnosed.

The causes of the relationship between inbreeding and facial deformity remain unclear, but the authors suggest it's because the main effect of mating between relatives is an increase in the chances of offspring inheriting identical forms of a gene from both parents, known as genetic homozygosity. This reduces people's genetic fitness, so "Habsburg jaw" should be considered a recessive condition.

However, the authors note that the study involves only a small number of individuals so it's possible that the prevalence of Habsburg jaw is due to the chance appearance of traits, or genetic drift. They suggest this scenario is unlikely, but can't rule it out.

"While our study is based on historical figures, inbreeding is still common in some geographical regions and among some religious and ethnic groups, so it's important today to investigate the effects," says Vilas. "The Habsburg dynasty serves as a kind of human laboratory for researchers to do so, because the range of inbreeding is so high."

The article will be freely available once the embargo has lifted via the following link: *http://tandfonline.com/10.1080/03014460.2019.1687752*

http://bit.ly/35ZbnyN

Study identifies brain networks that play crucial role in suicide risk

More research into suicide needed 'urgently', say international team

An international team of researchers has identified key networks within the brain which they say interact to increase the risk that an individual will think about - or attempt - suicide. Writing today in *Molecular Psychiatry*, the researchers say that their review of existing literature highlights how little research has been done into one of the world's major killers, particularly among the most vulnerable groups.

The facts in relation to suicide are stark: 800,000 people die globally by suicide every year, the equivalent of one every 40 seconds. Suicide is the second leading cause of death globally among 15-29 year olds. More adolescents die by suicide than from cancer, heart disease, AIDS, birth defects, stroke, pneumonia, influenza, and chronic lung disease combined. As many as one in three adolescents think about ending their lives and one in three of these will attempt suicide.

"Imagine having a disease that we knew killed almost a million people a year, a quarter of them before the age of thirty, and yet we knew nothing about why some individuals are more vulnerable to this disease," said Dr Anne-Laura van Harmelen, co-first author from the University of Cambridge. "This is where we are with suicide. We know very little about what's happening in the brain, why there are sex differences, and what makes young people especially vulnerable to suicide."

A team of researchers, including Hilary Blumberg, MD, John and Hope Furth Professor of Psychiatric Neuroscience at Yale, carried out a review of two decades' worth of scientific literature relating to brain imaging studies of suicidal thoughts and behaviour. In total, they looked at 131 studies, which covered more than 12,000 individuals, looking at alterations in brain structure and function that might increase an individual's suicide risk.

Combining the results from all of the brain imaging studies available, the researchers looked for evidence of structural, functional, and molecular alterations in the brain that could increase risk of suicide. They identified two brain networks - and the connections between them - that appear to play an important role.

The first of these networks involves areas towards the front of the brain known as the medial and lateral ventral prefrontal cortex and their connections to other brain regions involved in emotion. Alterations in this network may lead to excessive negative thoughts and difficulties regulating emotions, stimulating thoughts of suicide. The second network involves regions known as the dorsal prefrontal cortex and inferior frontal gyrus system. Alterations in this network may influence suicide attempt, in part, due to its role in decision making, generating alternative solutions to problems, and controlling behaviour.

The researchers suggest that if both networks are altered in terms of their structure, function or biochemistry, this might lead to situations where an individual thinks negatively about the future and is unable to control their thoughts, which might lead to situations where an individual is at higher risk for suicide.

"The review provides evidence to support a very hopeful future in which we will find new and improved ways to reduce risk of suicide," said Professor Hilary Blumberg. "The brain circuitry differences found to converge across the many studies provide important targets for the generation of more effective suicide prevention strategies. "It is especially hopeful that scientists, such as my co-authors on this paper, are coming together in larger collaborative efforts that hold terrific promise."

The majority of studies so far have been cross-sectional, meaning that they take a 'snapshot' of the brain, rather than looking over a period of time, and so can only relate to suicidal thoughts or behaviours in the past. The researchers say there is an urgent need for more research that looks at whether their proposed model relates to future suicide attempts and at whether any therapies are able to change the structure or function of these brain networks and thereby perhaps reduce suicide risk.

The review highlighted the paucity of research into suicide, particularly into sex differences and among vulnerable groups. Despite suicidal thoughts often first occurring as early as during adolescence, the majority of studies focused on adults.

"The biggest predictor of death by suicide is previous suicide attempt, so it's essential that we can intervene as early as possible to reduce an individual's risk," said co-first author Dr Lianne Schmaal from the University of Melbourne. "For many individuals, this will be during adolescence. If we can work out a way to identify those young people at greatest risk, then we will have a chance to step in and help them at this important stage in their lives."

Even more striking, despite the fact that transgender individuals are at increased risk for suicide, just one individual in the 131 samples included for the review was identified to be transgender.

"There are very vulnerable groups who are clearly not being served by research for a number of reasons, including the need to prioritise treatment, and reduce stigma," said van Harmelen. "We urgently need to study these groups and find ways to help and support them."

In 2018, the researchers launched the HOPES (Help Overcome and Prevent the Emergence of Suicide) study, supported by the mental health research charity MQ. HOPES brings together data from around 4,000 young people across 15 different countries in order to develop a model to predict who is at risk of suicide. Over the course of the project, the team will analyse brain scans, information on young people's environment, psychological states and traits in relation to suicidal behaviour from young people from across the world, to identify specific, universal risk-factors.

The research was supported by the mental health charity MQ Brighter Futures Award Program, National Institutes of Health, Department of Veterans Affairs, NHMRC, Royal Society Dorothy Hodgkin Fellowship, American Foundation for Suicide Prevention, Brain and Behavior Foundation, Robert E. Leet and Clara M. Guthrie Patterson Trust, and For the Love of Travis Foundation.

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http://bit.ly/2qVTceu

Brush your teeth to protect the heart

Brushing teeth frequently is linked with lower risks of atrial fibrillation and heart failure

Sophia Antipolis: Brushing teeth frequently is linked with lower risks of atrial fibrillation and heart failure, according to a study published today in the *European Journal of Preventive Cardiology*, a journal of the European Society of Cardiology (ESC).1

Previous research suggests that poor oral hygiene leads to bacteria in the blood, causing inflammation in the body. Inflammation increases the risks of atrial fibrillation (irregular heartbeat) and heart failure (the heart's ability to pump blood or relax and fill with blood is impaired). This study examined the connection between oral hygiene and occurrence of these two conditions.

The retrospective cohort study enrolled 161,286 participants of the Korean National Health Insurance System aged 40 to 79 with no history of atrial fibrillation or heart failure. Participants underwent a routine medical examination between 2003 and 2004. Information was collected on height, weight, laboratory tests, illnesses, lifestyle, oral health, and oral hygiene behaviours.

During a median follow-up of 10.5 years, 4,911 (3.0%) participants developed atrial fibrillation and 7,971 (4.9%) developed heart failure.

Tooth brushing three or more times a day was associated with a 10% lower risk of atrial fibrillation and a 12% lower risk of heart failure during 10.5-year follow up. The findings were independent of a number of factors including age, sex, socioeconomic status, regular exercise, alcohol consumption, body mass index, and comorbidities such as hypertension.

While the study did not investigate mechanisms, one possibility is that frequent tooth brushing reduces bacteria in the subgingival biofilm (bacteria living in the pocket between the teeth and gums), thereby preventing translocation to the bloodstream.

Senior author Dr. Tae-Jin Song of Ewha Womans University, Seoul, Korea noted that the analysis was limited to one country and as an observational study does not prove causation. But he added: "We studied a large group over a long period, which adds strength to our findings."

An accompanying editorial states: "It is certainly too early to recommend tooth brushing for the prevention of atrial fibrillation and congestive heart failure". It adds: "While the role of inflammation in the occurrence of cardiovascular disease is becoming more and more evident, intervention studies are needed to define strategies of public health importance."2

Funding*: This project was supported by a grant (2018R1D1A1B07040959) from the Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Education.* ***Disclosures****: None.*

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https://bbc.in/2RcWKDx

How a wrong injection helped cause Samoa's measles epidemic

The number of people killed in Samoa's measles outbreak has reached 53, with almost 4,000 cases reported in total.

Health Ministry statistics show that 48 of the dead are children below the age of five. Although measles deaths worldwide have fallen sharply since the 1960s, the World Health Organization has warned of a comeback around the world since 2017. Samoa's low

vaccination rates are in part due to the deaths in 2018 of two children given a wrongly-mixed vaccine.

Measles is a highly contagious illness that causes coughing, rashes and fever. Although effective and safe vaccination is available, even some developed countries have seen a resurgence in recent years. The rise is - in part - due to some parents shunning vaccines for philosophical or religious reasons, or concerns, debunked by medical science, that vaccines are linked to autism.

How bad is the Samoa measles outbreak?

On Monday, the Pacific island nation said the overall number of cases stands at 3,728. The number of new cases recorded on Sunday and Monday alone was 198. The country, with a population of around 200,000, declared a state of emergency on 20 November.

Most public gatherings have been banned and schools and universities have been closed.

"The situation has a tremendous impact on everybody," Sheldon Yett, Unicef representative to the Pacific, told the BBC. "People are nervous, people are seeing the impact of this disease. Samoa is a very small country and everybody knows somebody who's been affected by this."

Since the emergency declaration last month, a mass vaccination campaign has got under way, with more than 58,000 people successfully vaccinated, the government said. The epidemic has also seen a surge in alternative medicines touted as cures. Some reports suggest vitamin products or alkalised water are being sold as treatment.

Why is Samoa hit so hard?

Vaccination rates - meaning the number of young children covered - recently dropped to a low of only 31% in Samoa, compared to 99% in nearby Nauru, Niue, and Cook Islands. In part, that low rate has been attributed to the deaths of two children.

In July 2018, two infants died in Samoa after receiving vaccinations against measles, mumps and rubella, raising local fears over the vaccine itself. But the deaths were later established to have been due to the nurses mixing the vaccine with an expired muscle relaxant, instead of water.

The two nurses pleaded guilty to manslaughter and were sentenced to five years in prison.

"We have to make clear that vaccines are perfectly safe," Mr Yett said. "These deaths were due to human error. But the fact that you had two children die on the same day in the same institution, obviously caused a great deal of distrust towards the health system and towards vaccinations. "It provided the perfect opening for people who wanted to spread misinformation and lies."

'Lies and misinformation'

Aid from the US, New Zealand and Australia is helping local health authorities in Samoa to drive the mass vaccination. But the key message from the current crisis, said Mr Yett, is that parents should vaccinate their children.

"People who are spreading lies and misinformation about vaccinations are killing children," he said. "The best way to keep children safe is to make sure they're immunised. Preventing vaccination and presenting false information kills children. That is clear - the evidence speaks for itself." Ideally, every country should have an immunisation level of above 90%, he said.

Samoa's fellow Pacific island nations Tonga and Fiji have also declared states of emergency to tackle their measles outbreaks.

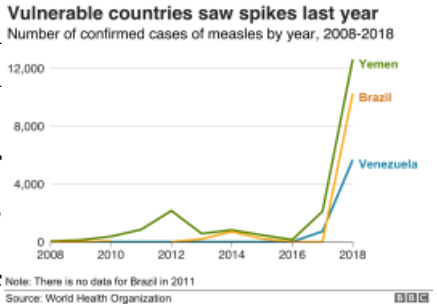
However, both countries have far higher vaccination rates and have so far not reported any deaths.

The global surge

Worldwide, the number of cases quadrupled in the first three months of 2019 compared with the same time last year, according to the World Health Organization (WHO).

Before the introduction of a vaccine in 1963, "major epidemics occurred approximately every 2-3 years and measles caused an estimated 2.6 million deaths each year", according to the WHO.

Numbers of measles cases were steadily declining worldwide until three years ago, when the illness saw a resurgence.



Earlier this year, the WHO said four European countries, including the UK, were no longer seen as measles-free.

It is estimated that a global total of 110,000 people die from measles each year.