http://bit.ly/2SioEOG

Bats' unique immune systems make them stealthy reservoirs for viruses

Bats have been at the center of many major viral outbreaks because they can carry viruses without showing symptoms

Marnie Willman

In 2001, Nipah virus emerged in India, causing an estimated 66 cases and 45 deaths after people unknowingly drank contaminated raw date palm sap. In 2002, SARS (a coronavirus termed Severe Acute Respiratory Syndrome) arose in Asia, resulting in 8,000 infections and almost 800 deaths globally. And from 2014-2016, the Ebola virus outbreak shocked the world, sickening over 28,000 people and killing over 11,000 across Africa.

Coronaviruses (a family of closely related respiratory viruses) have now made headlines again, in the form of 2019-nCoV, the new coronavirus that emerged in Wuhan, China. As of February 2, there have been 14,564 cases and 305 deaths from 2019-nCoV, with cases confirmed in 25 countries. All of these alarming outbreaks have one intriguing factor in common: bats.

We have known for quite some time that bats were the primary source of the both SARS epidemic and the Nipah virus. The Ebola virus also originates in fruit bats, which can infect other forest animals who then pass the virus to humans. And evidence strongly suggests that bats have played this same role – which scientists term the "reservoir species" – in the coronavirus outbreak. There are over 1,300 known species of bats, making them the second largest group of mammals on Earth. But their strange immune systems that make them the reservoir species for so many viruses are what make them truly special.

Humans aren't constantly exercising; we jog, or work out for a bit, but then we stop**.** As a result, unless we are very sick, our body temperature stays around 36.4 degrees Celsius. If we do have a fever, that stimulates an inflammatory response, and our immune system quickly kicks into action, eliminating the foreign pathogen from our bodies.

However, bats *are* constantly exercising: they fly, which increases body temperature and metabolic rate. This led scientists to come up with an initial theory as to why bats have a strange immune system, known as the "Flight as Fever" hypothesis. Because bats' bodies are often put into what, for humans, is an "fever" state, they may be more resistant to viral damage, allowing them to become symptom-less carriers of viral disease.

In a recent review, virologist Arinjay Banjeree and colleagues summarized the immunological differences between bats and humans to uncover why these animals make such effective viral reservoirs.

The first difference they noted was interferon levels. Interferons (IFNs) are an immune substance animals secrete to eliminate viruses. Humans have them, and so do bats. When grown in labs, analysis showed that bat cell lines produce higher levels of type I IFNs than human cell lines. Type I IFN is responsible for a variety of anti-viral jobs including limiting viral replication, killing infected cells, and activating other immune cells. Though wild bats have been shown to carry high IFN levels as well, the link between bat cell line behavior in the lab and bat's natural immune system needs more work.

There's more strangeness, on top of their high interferon levels and flight-induced fevers. A study on Big Brown Bats revealed that bats have lower levels of inflammatory cytokines in their blood than we do. Inflammatory cytokines are substances in our bodies that race to the site of an infection, bringing immune cells with them, which helps to quench it locally before it can spread. This allows infected bats to keep spreading diseases to other animals without becoming victims themselves.

Environmental stressors – such as drought or extreme temperatures – can increase the rate at which bats pass diseases to humans. Not only does stress in general tend to reduce animals' immune functions, but stressors such as shortages of food or water can force bats to migrate, spreading disease further.

In fact, a recent "spillover" (the passing of a virus from a reservoir species into a new host) of Hendra virus from fruit bats in Australia correlated with a food shortage for local bats due to a climate shift. Because the bats were under nutritional stress, they were more infectious, which coincided with their moving into new territories in search of food. This created a perfect storm of new hosts and infectious reservoirs, resulting in an outbreak of Hendra among horses.

Attempts to study bat immune cells in the lab haven't made much progress. Many bats do not develop the symptoms of the viral diseases they carry, and when they do, attempts to culture their cells in the lab have been unsuccessful (essentially, the cells cannot survive in a laboratory environment, and they die). In 2018, a Gammaherpesvirus was isolated from Big Brown Bats and maintained in tissue culture, representing a huge leap forward in bat-virology research. However, progress has been slow and restricted to just a few cells types from a few species of bats.

With the great diversity in bat species, their unique immune adaptations that support asymptomatic carriage of viral diseases, and the fact that bats are in close contact with humans around the world, it is no great surprise that bat-borne diseases have followed humans throughout history.

From Ebola to herpes, bats represent a reservoir for a number of devastating diseases and viral outbreaks due to these animals is likely to continue increasing. With so much left to learn and discover about these little creatures, it's no wonder they remain at the forefront of human health headlines.

http://bit.ly/2HjUbd0

Cervical cancer elimination possible within two decades in the US

Scaling up cervical cancer screening coverage in the U.S. to 90% could expedite elimination of the disease and avert more than 1,000 additional cases per year

Boston, MA--Scaling up cervical cancer screening coverage in the U.S. to 90% could expedite elimination of the disease and avert more than 1,000 additional cases per year, according to a new study led by researchers from Harvard T.H. Chan School of Public Health. Their modeling study found that this would be the most effective way to speed up elimination, compared to current levels of screening and human papillomavirus (HPV) vaccination.

"Although HPV vaccination will be a major contributor to reducing cervical cancer over time, we found that in the immediate term, screening continues to play a critical role in reducing the burden of cervical cancer in U.S.," said Emily Burger, a research scientist in the Center for Health Decision Science at Harvard Chan School who co-led the study.

The study will be published online in *The Lancet Public Health* on February 10.

In 2018, the World Health Organization (WHO) issued a global call to eliminate cervical cancer as a public health problem, setting a disease target of four or fewer cases per 100,000 women. With vaccination against HPV, the virus known to cause cervical cancer, and early detection through screening, cervical cancer is one of the most preventable and treatable forms of cancer.

In the U.S., the HPV vaccine is recommended routinely for both girls and boys ages 11-12 years and up to age 26 years for catch-up vaccination. For the study, using current vaccine coverage rates and trends, the researchers estimated that 75% of girls would be

vaccinated by age 26 and 62% of boys would be vaccinated by age 21.

Cervical cancer screening using Pap testing is recommended every three years for women ages 21-65 years, yet there is a large proportion of women who do not adhere to guidelines, either screening too much or too little; an estimated 14% of women are never screened.

This study is the first known comparative modeling analysis to project a timeframe for cervical cancer elimination in the U.S. The researchers used two independent disease modeling platforms (one from Harvard Chan School and one from Cancer Council New South Wales, Australia) to compare nine different HPV vaccination and cervical cancer screening interventions with a "status quo" scenario reflecting current screening and vaccination practices. They evaluated the potential for each scenario to achieve a threshold for cervical cancer elimination of four cases per 100,000 women, as well as a more ambitious threshold of one case per 100,000 women, over time.

They found that under the status quo scenario, cervical cancer elimination could be achieved by the years 2038-2046. Scaling up screening coverage to 90% expedited the timing of elimination by 10-13 years and averted an average of 1,400-2,088 additional cases per year. Increasing HPV vaccination coverage to 90% of girls and vaccinating adults of both sexes aged 26-45 years had almost no impact on elimination timing and minimal impacts on incidence.

This analysis is an extension of two studies published last week (see links below) evaluating the potential for and timing of cervical cancer elimination, as well as the mortality impacts of scaling up HPV vaccination, cervical cancer screening, and cancer treatment services in 78 low-income and lower-middle income countries. Those analyses, published in The Lancet, were co-led by three modeling groups comprising the WHO Cervical Cancer Elimination Modeling Consortium (CCEMC), which includes the authors of the current study.

"Across all three analyses, we were able to project the vast number of cervical cancer cases and deaths averted globally by ensuring high uptake of both prevention and treatment services for cervical cancer," said co-lead author Megan Smith, program manager at the Cancer Council New South Wales in Australia.

"Together with the WHO elimination initiative, we hope this analysis will galvanize public health efforts to improve access to both primary and secondary cervical cancer prevention in the U.S.," said senior author Jane Kim, professor of health decision science at Harvard Chan School.

Harvard Chan School's Stephen Sy was also a co-author.

This study was funded by U.S. National Cancer Institute grant (U01CA199334). Emily Burger receives salary support from the Norwegian Cancer Society (#198073), and Megan Smith receives salary support from the National Health and Medical Research Council, Australia (APP1159491) and Cancer Institute NSW (ECF181561).

"Cervical Cancer Elimination in the United States: A CISNET Model-based Analysis," Emily A. Burger, Megan A. Smith, James Killen, Stephen Sy, Kate Simms, Karen Canfell, Jane J. Kim, Lancet Public Health, online February 4, 2020.

http://bit.ly/3bqgonk

Common medication may lower risk of 'broken heart' during bereavement

Daily doses of a beta blocker and aspirin successfully reduced spikes in blood pressure and heart rate, as well as demonstrating some positive change in blood clotting tendency

The increased risk of heart attack or "a broken heart" in early bereavement could be reduced by using common medication in a novel way, according to a world-first study led by the University of Sydney and funded by Heart Research Australia.

Lead Investigator Professor Geoffrey Tofler said while most people gradually adjust to the loss of a loved one, there is an increase in heart attack and death among bereaved people, particularly those grieving a spouse or child.

"The increased risk of heart attack can last up to six months. It is highest in the first days following bereavement and remains at four times the risk between seven days to one month after the loss."

The study, published in the *American Heart Journal*, is the first randomised controlled clinical trial to show it is possible to reduce several cardiac risk factors during this time, without adversely affecting the grieving process.

"Bereavement following the death of a loved one is one of the most stressful experiences to which almost every human is exposed," said Professor Tofler, Professor of Preventative Cardiology at the University of Sydney's Faculty of Medicine and Health, and Senior Staff Cardiologist at Royal North Shore Hospital.

"Our study is the first clinical trial to examine how the cardiac risk factors could be mitigated during early bereavement."

About the study

The research team from the University of Sydney, Royal North Shore Hospital and the Kolling Institute enrolled 85 spouses or parents in the study within two weeks of losing their family member. Forty-two participants received low daily doses of a beta blocker and aspirin for six weeks, while 43 were given placebos. Heart rate and blood pressure were carefully monitored, and blood tests assessed blood clotting changes.

"The main finding was that the active medication, used in a low dose once a day, successfully reduced spikes in blood pressure and heart rate, as well as demonstrating some positive change in blood clotting tendency," said Professor Tofler.

The investigators also carefully monitored the grief reaction of participants. "We were reassured that the medication had no adverse effect on the psychological responses, and indeed lessened symptoms of anxiety and depression," said Professor Tofler.

"Encouragingly, and to our surprise, reduced levels of anxiety and blood pressure persisted even after stopping the six weeks of daily beta blocker and aspirin."

Co-investigator Associate Professor Tom Buckley said the study builds on the team's novel work in this area with their earlier studies among the first to identify the physiological correlates of bereavement.

"While beta blockers and aspirin have been commonly used long term to reduce cardiovascular risk, they have not previously been used in this way as a short-term preventative therapy during bereavement," said Associate Professor Buckley of the University of Sydney Susan Wakil School of Nursing and Midwifery.

Implications and next steps

The authors acknowledge that larger long-term studies are needed to identify who would benefit most however the findings provide encouragement for health care professionals to consider this preventative strategy among individuals that they consider to be at high risk associated with early bereavement.

"Our finding on the potentially protective benefit of this treatment is also a good reminder for clinicians to consider the well-being of the bereaved," said Associate Professor Buckley.

"Future studies are needed to assess if these medications could be used for other short periods of severe emotional stress such as after natural disasters or mass bereavement where currently there are no guidelines to inform clinicians."

Co-investigator Dr. Holly Prigerson, Co-Director of the Center for Research on End-of-Life Care at Weill Cornell Medicine in New York, said, "This is an important study because it shows ways to improve the physical and mental health of at-risk bereaved people. It is a preventive intervention that is potentially practice-changing, using inexpensive, commonly available medicines."

People experiencing cardiac symptoms should discuss their condition with a health care professional before taking medication as incorrect use could be harmful.

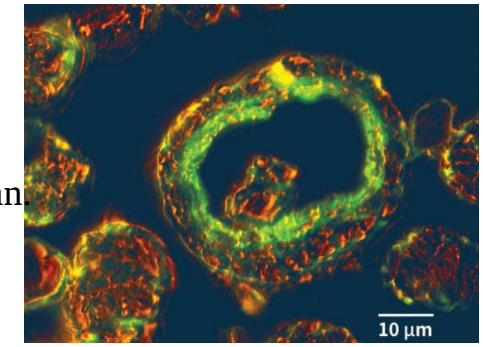
Declaration: The study was funded by Heart Research Australia. The study protocol was approved by the Institutional Review Board of Northern Sydney Health Ethics Committee, Australia. The authors declare no competing interests.

http://bit.ly/2vp4r0I

Strange Grains in 'Flammable Ice' Contain Microbes

An international team of researchers has found bacterial communities within microscopic spheroidal aggregates of dolomite, oil and water found in sheets of frozen methane and ice, known as 'flammable ice,' in Joetsu Basin, Japan Sea.

"We're melting hydrate to study methane gas when we noticed an unusual powder consisting of microscopic spheroids with mysterious dark cores," said Dr. Glen T. Snyder, a researcher at the Meiji University Global Front, Japan. "We then set about collecting a group of like-minded scientists to investigate further."



Epifluorescence imagery of a tiny grain within methane hydrate showing internal presence of microbial DNA. **Image credit: Snyder *et al*, doi: 10.1038/s41598-020-58723-y.**

Using innovative analytical techniques, Dr. Snyder and colleagues were able to show that oil was being degraded in the microenvironments within 'flammable ice.'

"In combination with the other evidence collected by my colleagues, my results showed that even under near-freezing temperatures, at extremely high pressures, with only heavy oil and saltwater for food-sources, life was flourishing and leaving its mark," said Dr. Stephen Bowden, a researcher at the University of Aberdeen.

The methane in 'flammable ice' is known to form as microbes degrade organic matter on the seafloor.

"But what we never expected to find was microbes continuing to grow and produce these spheroids, all of the time while isolated in tiny cold dark pockets of saltwater and oil," Dr. Snyder continued said.

"It certainly gives a positive spin to cold dark places, and opens up a tantalising clue as to the existence of life on other planets."

"It certainly changes how I think about things," Dr. Bowden said.

"Providing they have ice and a little heat, all those frigid cold planets at the edge of every planetary system could host tiny microhabitats with microbes building their own 'death stars' and making their own tiny little atmospheres and ecosystems, just as we discovered here."

The team's paper was published in the journal *Scientific Reports*.

G.T. Snyder et al. *2020. Evidence in the Japan Sea of microdolomite mineralization within gas hydrate microbiomes.* Sci Rep *10, 1876; doi: 10.1038/s41598-020-58723-y*

http://bit.ly/38p1V9r

Japan's silence on HPV vaccinations will lead to 11,000 cancer deaths, study says

Decision will likely result in almost 11,000 deaths from cervical cancer if it is not reversed

A decision by the government to stop recommending adolescent girls receive an HPV vaccination will likely result in almost 11,000 deaths from cervical cancer if it is not reversed, according to a study in a prestigious medical journal.

The HPV vaccine has been a political lightning rod in Japan, where claims of side effects prompted the government to halt active recommendation of the shots in June 2013.

A study published in The Lancet Public Health on Monday said that policy would lead to more than 24,600 cervical cancer cases that could have been prevented.

Using Japanese population and medical data and forecasted cervical cancer incidence, the study found that, if nothing changes, there would be 10,800 preventable deaths from cervical cancer over the next 50 years. “If the government were to resume promoting the HPV vaccine in Japan, our study shows that we could avoid most of this loss of life,” said study co-author Sharon Hanley, a professor at Hokkaido University.

The government could not immediately be reached for comment on the Lancet report. Kei Tamura, deputy director of the health ministry’s immunization office, said in an interview in December that “there is a sort of inner conflict in that we are not aggressively, proactively recommending it, but I do think it’s better to take it.”

HPV, which stands for the human papilloma virus, causes genital warts in both sexes and cervical cancer in women. Each year, about 10,000 Japanese women are newly diagnosed with the cancer, while 3,000 die from it.

Uptake was swift when the vaccine was introduced in Japan in 2009, with immunization reaching about 70 percent in adolescent girls. However, the vaccination rate has since slid to below 1 percent after the health ministry suspended its active recommendation following reports of side effects including muscle pain, sleep disorders, and light and sound sensitivity.

Girls age 12 to 16 can still get free HPV vaccines under the national health care system if they ask for it. Everyone else must pay out of pocket.

In November, ruling party legislator Junko Mihara, a cervical cancer survivor, said lawmakers would hold talks on the vaccine this summer. Tokyo Gov. Yuriko Koike and eight other regional leaders signed a letter supporting HPV vaccination.

The health ministry said in December it was working on improving leaflets on the vaccine, but had no time table for a return to regular immunization.

https://go.nature.com/2uyR1PT

As coronavirus spreads, the time to think about the next epidemic is now

World leaders and international donors must strengthen the most vulnerable nations’ health-care systems.

As the 2019 novel coronavirus continues its deadly rampage, the World Health Organization (WHO) is rightly drawing attention to the risks the virus poses to the poorest and most vulnerable nations — particularly in Africa.

As *Nature* went to press, more than 43,000 infections and more than 1,000 deaths had been confirmed. Soon, thousands of China’s citizens will be returning to their jobs on the African continent after an extended new-year holiday. If the virus also reaches Africa, it could spread rapidly and undetected because health systems in many regions are too fragile and underfunded to cope.

Philanthropist Bill Gates (left) has pledged $100 million for coronavirus-response efforts. Tedros Adhanom Ghebreyesus (right), director-general of the World Health Organization, is calling for urgent support to bolster weak health systems. **Credit: Mustafa Yalcin/Anadolu Agency/Getty**

As a result, the WHO has scrambled to equip 14 countries — including the Democratic Republic of the Congo, Ethiopia and Nigeria — with diagnostics, expertise and equipment to detect and contain the virus. The agency has also appealed for US$675 million to assist vulnerable countries — an amount that it estimates will last only until the end of April.

And yet, as donors start to provide emergency aid — the Bill & Melinda Gates Foundation was among the first with a $100-million pledge — it’s hard to avoid the feeling of déjà vu. Infectious-

disease outbreaks are often accompanied by such pledges to improve disease surveillance, and by promises to provide funds for drug and vaccine development. What is less forthcoming is sustainable funding for clinics providing community-level general medicine, and for medical and nursing education, as well as investments to sustain hospitals with supplies, electricity and running water.

These are all steps that would help countries to combat infectious diseases and improve overall public health — as WHO director-general Tedros Adhanom Ghebreyesus urged in a statement at the end of last month. Seven of the nations that the WHO will be helping scarcely have one nurse per 1,000 people, according to the most recent statistics from the World Bank. And more than 50% of the continent's 1.2 billion inhabitants lack access to essential primary care.

To be fair, a shift in outlook has already begun. In 2016, the World Bank and the Global Fund to Fight AIDS, Tuberculosis and Malaria committed $24 billion over three to five years for universal health care in Africa. And over the past year, Rwanda's president, Paul Kagame, has been leading an African Union task force with the explicit aim of achieving measurable universal health coverage in all of its 55 member states, partly by committing to spending 5% of gross domestic product on health care. This is an ambitious aim, and it needs to be. "Governments should surely be willing and able to increase domestic investment in healthcare," Kagame said as the project got under way.

A temporary surge of assistance aimed at infectious-disease surveillance — as is happening now — might suffice in places where health systems are reasonably robust. But for the poorest countries with the weakest systems, even the best projects will struggle once these grants come to an end, as the case of Ebola shows all too well.

After the world's biggest Ebola outbreak ended in 2016, donors, including the US government and the World Bank, put more than $100 million into initiatives to strengthen health and disease-surveillance systems in the three countries that were worst hit — Liberia, Sierra Leone and Guinea.

But many of these initiatives are ending and health care is showing signs of erosion. Since last summer, protests have been erupting in Liberia as the economy and the national health system have crumbled. Major hospitals are reported to lack life-saving drugs, and health workers and lab technicians say they have not been paid for months. Patients have been turned away from clinics empty-handed, meaning that someone infected with coronavirus might not bother going to a clinic — or, if they did, could be sent back home. This problem isn't specific to Liberia.

In many of the poorest countries, staff in national health systems barely earn a living.

International donors have sound reasons for not providing long-term funding for certain facets of basic public health — such as salaries for government employees.

Arguably, one of their biggest fears is that in doing so they would become too deeply involved in the workings of national government departments, which are often complicated organizations to navigate. Another worry is that donors could be perceived as telling sovereign governments what to do. Instead, many international donors reduce their direct involvement with a nation's public sector by funnelling their assistance through large, non-governmental institutions such as charitable aid agencies. But when this happens, national health systems remain weak.

Clearly, finding solutions to these problems will not be easy, but avoidance is no longer an acceptable option — especially now that the African Union and the WHO are taking steps to prioritize universal health coverage. Donors must consider how their

initiatives can help to strengthen national health systems in the long term. For example, they could ensure that the health workers being trained to handle patients suspected of having coronavirus are still employed at hospitals five years later. This might not seem like a priority in the middle of an emergency, but it will pay off handsomely down the line.

The march of the coronavirus reminds us yet again that world leaders and philanthropic donors pay attention to epidemics only when an infection is on their doorsteps. They must recognize that the time to think about the next epidemic is now.

Nature ***578****, 191 (2020) doi: 10.1038/d41586-020-00379-9*

http://bit.ly/2UQ9C4j

Foot-and-mouth-disease virus could help target the deadliest cancer

The foot-and-mouth-disease virus is helping scientists to tackle a common cancer with the worst survival rate - pancreatic cancer.

Researchers at Queen Mary University of London have identified a peptide, or protein fragment, taken from the foot-and-mouth-disease virus that targets another protein, called AvB6 (alpha-v-beta-6). This protein is found at high levels on the surface of the majority of pancreatic cancer cells.

Working jointly with Spirogen (now part of AstraZeneca) and ADC Therapeutics, the team have used the peptide to carry a highly potent drug, called tesirine, to the pancreatic cancer cells. When mice with pancreatic cancer tumours were treated with the drug and peptide combination, the tumours were completely killed.

The study, published in *Theranostics*, was funded by the UK medical research charity Pancreatic Cancer Research Fund.

Lead researcher Professor John Marshall, from the Cancer Research UK Barts Centre, explains: "Foot-and-mouth-disease virus uses AvB6 as a route to infect cattle, as the virus binds to this protein on a cow's tongue. By testing pieces of the protein in the virus that attaches to AvB6, we've developed a route to deliver a drug specifically to pancreatic cancers. Our previous research had shown that 84 per cent of pancreatic cancer patients have high levels of AvB6 on their cancers."

The team performed tests of the peptide/tesirine combination in both cells in the laboratory and in mice. They used genetically identical human cancer cells, some that had AvB6 on their surface and some that had no AvB6. Both types of cells were exposed to the peptide and drug combination. The cells with AvB6 were most affected, while the AvB6 negative cells needed much higher doses of the drug for the cells to be killed.

The tests in mice gave the most impressive results. Mice that had AvB6-positive tumours were given a tiny dose of the peptide-drug combination three times a week, and this stopped the tumours growing completely. But when the dose was increased and given just twice a week, all tumours in mice that were AvB6 positive were completely killed.

"These very exciting results, that are the result of many years of laboratory testing, offer a completely new way of treating pancreatic cancer." says Professor Marshall. "One advantage of targeting AvB6 is that it is very specific to the cancer, because most normal human tissues have little or none of this protein. So we're hopeful that, if we can develop this into an effective treatment for pancreatic cancer, it would have limited side effects."

The team now plan to further test the peptide and drug combination in more complex mice models, to determine if it can also impact on pancreatic cancer metastases, before moving to clinical trials.

Dr Emily Farthing, senior research information manager at Cancer Research UK said: "Although we have made great progress in treating many types of cancer, survival remains stubbornly low for people with pancreatic cancer and there is an urgent need for more effective treatments. This early-stage research has developed a

promising new drug that reduces the growth of pancreatic tumours in the lab. And with further research to see if it's safe and effective for patients, we hope that this could one day offer new hope for people with this disease."

http://bit.ly/2OOC2I8

Water pipe technology kills microorganisms with localised electric field

Scientists in the US have developed a device that kills pathogens using an electric field. The tubular system can fit inside water distributions systems to deliver safe drinking water.

By Polly Wilson

Drinking water typically goes through two disinfection phases. The first occurs at a treatment plant. The second combats pathogen regrowth and takes place in the pipe distribution system. Chlorination is a common part of this disinfection process.

It is cheap, efficient and residual chlorine acts as a secondary treatment. It also has challenges to do with transport, storage and carcinogenic byproducts. Alternative disinfection techniques include membrane filtration, ozonation and UV.

However, high costs, bromate byproducts and microbial regrowth in pipelines are the respective drawbacks of those alternatives. The ideal solution combines continuous disinfection with minimal maintenance, low power requirements and low costs.

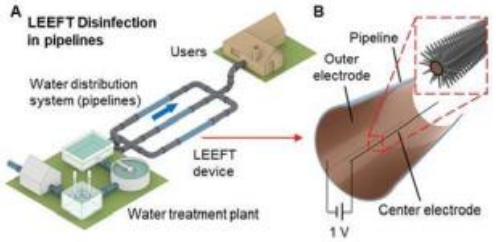
Xing Xie and his team at the Georgia Institute of Technology have devised another disinfection system, which uses locally enhanced electric field treatment to kill pathogens.

Central to the system are electrodes comprised of vertically aligned copper oxide nanowires coated with a protective polydomamine layer. Commercially available aluminium or copper tubing can serve as outer electrodes, making this tubular coaxial configuration scalable and compatible with current pipes.

The system creates a strong localised electric field around the nanowire tips – known as the lightening rod effect. Electrophoresis drives cells towards the centre of the device where irreversible electroporation kills them.

Bulk water only encounters the background electric field. The system only consumes $1.4Jl^{-1}$ at an applied voltage of 1V, a power level that flowing water can generate in situ.

Sudipta Roy, head of the chemical and process engineering department at the University of Strathclyde, UK, calls it an 'interesting and innovative design for water remediation using nanoscale electrochemistry.'



The device inactivates pathogens by irreversible electroporation from an enhanced electric field near the tips of the nanowires **Source: © Xing Xie/Georgia Institute of Technology**

'In a real-world scenario, segments of pipelines can be replaced with the locally enhanced electric field device every certain distance to provide consecutive antimicrobial power,' comments Xie.

He does concede that 'pipeline replacement is a big project and cannot be done at once.' Their first target would be existing pipelines that have exceeded their service life and are at risk of breaking.

Installing the technology on a large-scale would require the electrodes to be strong enough to endure high water flow and pressure.

It's also possible that debris in water may shield bacteria from inactivation at the electrode tips. Xie plans further investigations into these issues.

References *J Zhou* et al, Environ. Sci.: Nano, *2020*, *DOI: **10.1039/c9en00875f***

https://wb.md/3bC93B5

Tramadol Linked to Increased Hip Fracture Risk in Older Adults

Older patients treated with the pain medication tramadol show significant increases in the risk of hip fracture compared with those using codeine or commonly used nonsteroidal anti-inflammatory drugs (NSAIDs), new research shows.

Nancy Melville

"Considering the significant impact of hip fracture on morbidity, mortality, and healthcare cost, our results point to the need to consider tramadol's associated risk of fracture in clinical practice and treatment guidelines," first author Jie Wei, PhD, an associate professor of epidemiology at Xiangya Hospital, Central South University, China, told *Medscape Medical News*.

In commenting on the research, Shailendra Singh, MD, noted that the "article clearly reinforces [prior] knowledge…that opiates are associated with an increased risk of falls and fractures."

The American Geriatric Society BEERS criteria for inappropriate drugs for the elderly, for instance, lists tramadol and opiates as drugs to avoid in patients with increased risk of falls and fractures, added Singh, who is rheumatology medical director of the White River Medical Center in Batesville, Arkansas, and was not involved with the current study.

Increased Risk of Hip Fracture With Tramadol Even Compared With Codeine

The new study, published this month in the *Journal of Bone and Mineral Research*, involved data on 146,956 patients in the United Kingdom who were age 50 years and older and enrolled in The Health Improvement Network (THIN).

The patients had initiated treatment with tramadol between 2000 and 2017 for noncancer-related pain, and had no history of hip fracture, cancer, or opioid use disorder.

In the propensity-matching analysis, those initiating tramadol were matched 1:1 with well-balanced characteristics to patients identified as initiating codeine during the same period (146,956 in each group).

Equal-numbered groups were also matched between tramadol and naproxen (115,109 in each group) or ibuprofen (107,438 per group), both NSAIDs, or celecoxib (43,130 per group) or etoricoxib (27,689 per group), which are both cyclooxygenase-2 inhibitors.

Participants in the matched groups had a mean age of 65 and 56.9% were women.

For the primary outcome of the incidence of hip fracture over 1 year, the risk was higher for tramadol compared with codeine (hazard ratio [HR], 1.28), with 518 cases of hip fracture (3.7 per 1000 person-years) in the tramadol cohort and 401 (2.9 per 1000 person-years) in the codeine cohort. Likewise, the risk was higher with tramadol compared with naproxen (HR, 1.69), ibuprofen (HR, 1.65), celecoxib (HR, 1.85), and etoricoxib (HR, 1.96).

A sensitivity analysis restricted to individuals aged 60 or older showed no major differences in the associations for all of the drug groups.

"The sensitivity analyses had similar results, indicating that the observed associations were robust and raising a concern on the potential risk of hip fracture among initiators of tramadol use," the authors say.

The increased risk compared with the initiation of codeine is particularly notable, as codeine is regarded as a weak opioid and often used in a similar context as tramadol, Wei noted.

"The risk of incident hip fracture among tramadol initiators was not only higher than that among NSAIDs initiators, but also higher than that among codeine initiators, suggesting that the confounding by indication may not substantially account for an increased risk of hip fracture for tramadol," she observed.

She added that "this was further supported by the evidence that risk factor profiles between initial prescription of tramadol and that of codeine were similar even before propensity-matching, except a few (for instance BMI was higher among tramadol than codeine prescriptions)."

"Nevertheless, as in all observational studies, we can't rule out the impact of potential residual confounders when comparing the risk of hip fracture between initial prescription of tramadol and other pain-relief medications," Wei stressed.

Tramadol Seen as Beneficial NSAID Alternative for Pain

Tramadol is seen as a valuable analgesic alternative to NSAIDs, with perceived lower cardiovascular and gastrointestinal effects while providing a reduced risk of addiction and respiratory depression compared with traditional opioids, the authors note.

Guidelines of professional organizations recommend tramadol for pain under various conditions, including the most recent guidelines of the American College of Rheumatology (ACR), which conditionally recommend tramadol for the treatment of knee or hip osteoarthritis, "including when patients may have contraindications to NSAIDs, find other therapies ineffective, or have no available surgical options."

Use of the drug has been on the rise worldwide in recent decades, with one survey showing a 22.8% increase in tramadol prescriptions in the US from 2012 to 2015.

The authors note that important limitations of the study include the fact that the THIN database does not include measures on two potentially important confounders — bone density and frailty.

Singh said it's unknown whether propensity score matching can adjust for important factors, such as the severity of disease: "(For instance), people with severe osteoporosis are at a higher risk of fracture, compared to moderate…the lower the T-score, the higher the risk of fracture."

Link Between Increased Risk of Falls and Tramadol? Don't Prescribe It First-Line

As reported by *Medscape Medical News*, Wei and her colleagues showed an association between tramadol use and a higher risk of all-cause mortality among patients in the THIN network in a study published last year. The specific mechanisms linking tramadol use to an increased risk of mortality remain unclear, however.

And that study, which — as opposed to the current one — was limited to patients with osteoarthritis pain, showed the increased mortality risk did not extend to those treated with codeine.

Although the mechanisms that may explain the increased risk of fracture are not known, Wei and colleagues note previous research suggesting an effect of tramadol in activating mu-opioid receptors while suppressing central serotonin and norepinephrine reuptake, which can be linked to the risk of seizures, dizziness, and/or delirium — all of which could increase the risk of fall.

"In fact, several studies have reported that tramadol use was indeed associated with a higher risk of fall, which is a critical risk factor for fracture," they note. "All these studies appear to suggest that relation of tramadol to the risk of hip fracture may be, at least partly, through its effect on fall," they surmise.

"In this population-based cohort study, the initiation of tramadol was associated with a higher risk of hip fracture than initiation of codeine and commonly used NSAIDs, suggesting a need to revisit several guidelines on tramadol use in clinical practice."

Singh agrees. While underscoring that further studies are needed to determine the mechanism of action in the increased hip fracture risk, he concluded that "opiates of any kind, including tramadol, should not be used as a first line drug for pain management in any setting."

The study was supported by the National Institutes of Health, the National Natural Science Foundation of China, and the Postdoctoral Science Foundation of Central South University. The authors and Singh have disclosed no relevant financial relationships.

Journal of Bone and Mineral Research. Published February 5, 2020. Abstract

http://bit.ly/2SHITEG

Shingles vaccine may also reduce stroke risk

A new study found that Zoster Vaccine Live may prevent some older adults from having a stroke

DALLAS -- Shingles, a viral infection caused by the chickenpox virus, is linked to an increased risk of stroke. A new study found that Zoster Vaccine Live, one type of shingles vaccination, may prevent some older adults from having a stroke, according to preliminary research to be presented at the American Stroke Association's International Stroke Conference 2020 - Feb. 19-21 in Los Angeles, a world premier meeting for researchers and clinicians dedicated to the science of stroke and brain health.

More than 99% of people aged 40 or older in the United States carry the dormant chickenpox virus, also known as the varicella-zoster virus. Shingles is a reactivation of the chicken pox virus and typically occurs after age 50. The risk of developing shingles, a painful condition that causes skin blisters and can have serious complications, increases with age and other health conditions.

"One in three people who have had chickenpox develop shingles in their lifetime," said Quanhe Yang, Ph.D., lead study author and senior scientist at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. "The Zoster Vaccine Live helps to prevent shingles and reduces the risk for shingles by about 51%. But its effect declines with increased age, about 64% in people 60-69 years, about 41% for ages 70-79 years and about 18% in those 80 years or older."

To help determine if the shingles vaccine reduces the risk of stroke, Yang and colleagues reviewed the Medicare health records of more than one million Medicare fee-for-service beneficiaries age 66 or older who had no history of stroke and who were vaccinated with the Zoster Vaccine Live between 2008 and 2014, and followed them for an average of almost four years. That group was matched with the same number of Medicare fee-for-service beneficiaries who did not receive the shingles vaccine with the same four-year follow-up. To examine the effect of the vaccine on risk of stroke, researchers controlled for age, gender, race, medications and co-existing health conditions.

Researchers found:

- ***Receiving the shingles vaccine lowered the risk of stroke by about 16%, lowered the risk of ischemic (clot-caused) stroke by about 18% and lowered the risk of hemorrhagic (bleeding) stroke by about 12%;***
- ***The vaccine's protection was strongest among people ages 66 to 79 years; and***
- ***Among those under the age of 80 years, the shingles vaccine reduced the risk of stroke by nearly 20% and in those older than 80, reduced the risk by about 10%.***

"The reason for increased risk of stroke after a shingles infection may be due to inflammation caused by the virus," according to Yang.

"Approximately one million people in the United States get shingles each year, yet there is a vaccine to help prevent it," said Yang. "Our study results may encourage people ages 50 and older to follow the recommendation and get vaccinated against shingles. You are reducing the risk of shingles, and at the same time you may be reducing your risk of stroke."

This study was conducted when the only shingles vaccine was Zoster Vaccine Live (available since 2006). The newest shingles vaccine, Adjuvanted, Non-Live Recombinant Shingles Vaccine (available since 2017), confers even greater protection and is now the preferred vaccine recommended by the CDC's Advisory Committee on Immunization Practices. Two doses of Adjuvanted, Non-Live Recombinant Shingles Vaccine is more than 90% effective at preventing shingles and is recommended for adults age 50 and older.

Future studies are needed to confirm the link between Zoster Vaccine Live and stroke and to determine any association between Adjuvanted, Non-Live Recombinant Shingles Vaccine and risk for stroke.

American Stroke Association International Stroke Conference - Poster Presentation TP493 Co-authors are Anping Chang, M.S.; Xin Tong, M.P.H.; and Robert Merritt, M.A. Author disclosures are available in the abstract.

The U.S. Centers for Disease Control and Prevention funded this study.

https://go.nature.com/31QfrAs

A teenager's body clock can ring in school success

When lessons start at 7:45 a.m., morning-loving students do better than those who naturally wake up later.

Whether they're early birds or not, teenagers could get healthy amounts of sleep and improve their academic performance by attending school in the evening, according to a study of Argentinian adolescents.

Around the world, secondary school tends to start very early in the morning. But the biological clock ticking away inside many adolescent brains doesn't align with school schedules, resulting in sleep loss and other problems.

María Juliana Leone at the National Council of Scientific and Technical Research in Buenos Aires and her colleagues collected sleep data from teenagers at a local secondary school at which students were randomly assigned to start classes at 7:45 a.m., 12:40 p.m. or 5:20 p.m. The researchers placed students on a continuum from early-rising 'larks' to later-rising 'owls', according to their preferred waking time.

Analysis of students who started school in the morning showed that, compared with larks, owls had overall lower grades that worsened as they advanced through school. Almost no students on the morning schedule got adequate sleep, leading researchers to suggest that a progressive delay of school start times throughout adolescence could benefit all. *Nature Hum. Behav.* (2020)

http://bit.ly/2vstpwd

Gene associated with autism also controls growth of the embryonic brain

UCLA-led research uncovers new details about the Foxp1 gene, which also is involved in timing of neuron production

A UCLA-led study reveals a new role for a gene that's associated with autism spectrum disorder, intellectual disability and language impairment.

The gene, Foxp1, has previously been studied for its function in the neurons of the developing brain. But the new study reveals that it's also important in a group of brain stem cells -- the precursors to mature neurons.

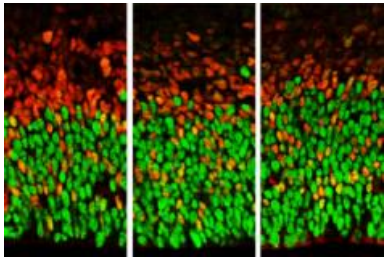


Image showing brain cells with lower levels of Foxp1 function (at left) and higher levels (right). Apical radial glia are stained in green and secondary progenitors and neurons stained in red. **UCLA Broad Stem Cell Research Center/Cell Reports**

"This discovery really broadens the scope of where we think Foxp1 is important," said Bennett Novitch, a member of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA and the senior author of the paper. "And this gives us an expanded way of thinking about how its mutation affects patients."

Mutations in Foxp1 were first identified in patients with autism and language impairments more than a decade ago. During embryonic development, the protein plays a broad role in controlling the activity of many other genes related to blood, lung, heart, brain and spinal cord development. To study how Foxp1 mutations might cause autism, researchers have typically analyzed its role in the brain's neurons.

"Almost all of the attention has been placed on the expression of Foxp1 in neurons that are already formed," said Novitch, a UCLA professor of neurobiology who holds the Ethel Scheibel Chair in Neuroscience.

In the new study published in Cell Reports, he and his colleagues monitored levels of Foxp1 in the brains of developing mouse embryos. They found that, in normally developing animals, the gene was active far earlier than previous studies have indicated -- during the period when neural stem cells known as apical radial glia were just beginning to expand in numbers and generate a subset of brain cells found deep within the developing brain.

When mice lacked Foxp1, however, there were fewer apical radial glia at early stages of brain development, as well as fewer of the deep brain cells they normally produce. When levels of Foxp1 were above normal, the researchers observed more apical radial glia and an excess of those deep brain cells that appear early in development. In addition, continued high levels of Foxp1 at later stages of embryonic development led to unusual patterns of apical radial glia production of deep-layer neurons even after the mice were born.

"What we saw was that both too much and too little Foxp1 affects the ability of neural stem cells to replicate and form certain neurons in a specific sequence in mice," Novitch said. "And this fits with the structural and behavioral abnormalities that have been seen in human patients."

Some people, he explained, have mutations in the Foxp1 gene that blunt the activity of the Foxp1 protein, while others have mutations that change the protein's structure or make it hyperactive.

The team also found intriguing hints that Foxp1 might be important for a property specific to the developing human brain. The researchers also examined human brain tissue and discovered that Foxp1 is present not only in apical radial glia, as was seen in mice, but also in a second group of neural stem cells called basal radial glia.

Basal radial glia are abundant in the developing human brain, but absent or sparse in the brains of many other animals, including mice. However, when Novitch's team elevated Foxp1 function in the brains of mice, cells resembling basal radial glia were formed. Scientists have hypothesized that basal radial glia also are connected to the size of the human brain cortex: Their presence in large quantities in the human brain may help explain why it is disproportionately larger than those of other animals.

Novitch said that although the new research does not have any immediate implications for the treatment of autism or other diseases associated with Foxp1 mutations, it does help researchers understand the underlying causes of those disorders.

In future research, Novitch and his colleagues are planning to study what genes Foxp1 regulates in apical radial glia and basal radial glia, and what roles those genes play in the developing brain.

The study's first author is Caroline Alayne Pearson, a UCLA assistant project scientist. Other authors are from the University of Texas at Austin, the University of Alabama at Birmingham and the University of Puerto Rico.

The study was funded by the National Institutes of Health, the California Institute for Regenerative Medicine, the Cancer Prevention and Research Institute of Texas, the University of Texas at Austin's Marie Betzner Morrow Centennial Endowment and the UCLA Broad Stem Cell Research Center's Research Award Program, including support from the Binder Foundation.

http://bit.ly/37nhpcB

Human language most likely evolved gradually

Hypotheses for the origin of human language

One of the most controversial hypotheses for the origin of human language faculty is the evolutionary conjecture that language arose instantaneously in humans through a single gene mutation. `

Two recent publications by researchers at the University of Barcelona (UB), led by Cedric Boeckx, ICREA Research professor from the Section of General Linguistics and member of the Institute

of Complex Systems of the UB (UBICS), question this hypothesis, advocated among others by linguist Noam Chomsky, and suggest that it is more likely that language evolved gradually.

Merge, the cognitive operation key to human language

For decades, several scholars such as Chomsky have proposed that modern humans are genetically equipped with a unique cognitive capacity that specifically allows us to implement computations over hierarchically structured symbolic representations. This capacity is enabled by a formally simple cognitive operation known as Merge, which is the basis of our ability to represent complex grammars in a way that other species cannot. "Merge is claimed to be sufficient to yield grammatical structure. Put it simple, Merge takes two linguistic units (say, words) and combines them into a set that can then be combined further with other linguistic units, effectively creating unbounded linguistic expressions. These, in turn, are claimed to form the basis for our cognitive creativity and flexibility, setting us aside from other species," said Cedric Boeckx.

"The strongest version of this hypothesis --Cedric Boeckx continued -- suggests that the biological foundation of our modern language capacity is a single genetic mutation, a macromutation, that emerged instantaneously in a single hominin individual who is an ancestor of all modern humans, and spread through the population."

Modeling the single gene mutation hypothesis

In the first paper, published in Scientific Reports -with participation of Cedric Boeckx and researchers from the Free University of Brussels (Belgium) and the Max Plank Institute of Psycholinguistics (Netherlands), they examine this hypothesis by modeling the evolutionary dynamics of such a scenario, taking into account different parameters such as how long ago this mutation would have happened and the population size at the time. "We examine the dynamics of a single, critical, mutation spreading rapidly through a population in a given time window, combining this theoretical proposal with contemporary genetic and demographic findings", said Cedric Boeckx.

In this case, researchers have applied a variety of techniques from theoretical biology to the question of how to quantify the probability of a complex trait like language evolving in a single step, in many small steps, or in a limited number of intermediate steps, within a specific time window and population size.

Researchers concluded that, instead of a single mutation with an extremely large fitness advantage, the most likely scenario is one where higher number of mutations, each with moderate fitness advantages, accumulate. "A scenario in which the genetic bases of our linguistic ability evolved through a gradual accumulation of smaller biological changes. This scenario can be articulated in many different ways, for instance as syntax evolving from phonological form, from rapid manual actions or from much simple pragmatic sequencing of words", said Boeckx.

Challenging the logic of the hypothesis

In the other study, published in *PLoS Biology*, UB graduate student Pedro Tiago Martins and Cedric Boeckx question this evolutionary hypothesis from a different angle: by going over its logic. Defendants of the single hypothesis claim that Merge, being such a simple operation had to be the result of a single genetic mutation that endowed one individual with the necessary biological equipment for language. In addition, because Merge is either fully present or fully absent --in other words, there cannot be such a thing as half-Merge--, the human language faculty had to emerge suddenly, as the result of this single mutation.

"From the formal properties of Merge, it is not possible to derive of number of evolutionary steps that led to the emergence of Merge. The computational simplicity of Merge does not correlate in any meaningful way to biological simplicity, and that once different

levels of organization are taken into account there is no way to derive such simplistic evolutionary scenarios for any complex trait.",said Pedro Tiago Martins. The study highlights that even if a trait, such as the Merge operation, does not manifest itself in intermediate steps, its evolution may very well be gradual.

Researchers explained that the evolution of something as complex as human language deserves integration of results and insights from different corners of the research landscape, namely the fields of neurobiology, genetics, cognitive science, comparative biology, archaeology, psychology, and linguistics. "This is hard because it requires compatible levels of granularity between all fields involved, but it is the only way of achieving meaningful understanding," said Pedro Tiago Martins.

Together, these studies suggest that evolutionary reasoning does not warrant a scenario of sudden emergence of human language by means of a single mutation, and that it is more likely instead that language evolved gradually.

http://bit.ly/2HzmLqZ

Gut feelings: Gut bacteria are linked to our personality

Both gut microbiome composition and diversity were related to differences in personality

Dr Katerina Johnson, who conducted her PhD in the University's Department of Experimental Psychology, was researching the science of that 'gut feeling' - the relationship between the bacteria living in the gut (the gut microbiome) and behavioural traits. In a large human study she found that both gut microbiome composition and diversity were related to differences in personality, including sociability and neuroticism.

She said: "There has been growing research linking the gut microbiome to the brain and behaviour, known as the microbiome-gut-brain axis. Most research has been conducted in animals, whilst studies in humans have focused on the role of the gut microbiome in neuropsychiatric conditions. In contrast, my key interest was to look in the general population to see how variation in the types of bacteria living in the gut may be related to personality."

Previous studies have linked the gut microbiome to autism (a condition characterised by impaired social behaviour). Dr Johnson's study found that numerous types of bacteria that had been associated with autism in previous research were also related to differences in sociability in the general population. Katerina explained: "This suggests that the gut microbiome may contribute not only to the extreme behavioural traits seen in autism but also to variation in social behaviour in the general population. However, since this is a cross-sectional study, future research may benefit from directly investigating the potential effect these bacteria may have on behaviour, which may help inform the development of new therapies for autism and depression."

Another interesting finding related to social behaviour was that people with larger social networks tended to have a more diverse gut microbiome, which is often associated with better gut health and general health. Katerina commented: "This is the first study to find a link between sociability and microbiome diversity in humans and follows on from similar findings in primates which have shown that social interactions can promote gut microbiome diversity. This result suggests the same may also be true in human populations." Conversely, the study found that people with higher stress or anxiety had a lower microbiome diversity.

Various other key and novel findings were also reported in this study. Most notably, adults who had been formula-fed as children had a less diverse microbiome in adulthood. Katerina commented: "This is the first time this has been investigated in adults and the results suggest that infant nutrition may have long-term consequences for gut health." Diversity was also positively related to international travel, perhaps due to exposure to novel microbes

and different diets. More adventurous eaters had a more diverse gut microbiome whilst those on a dairy-free diet had lower diversity. Furthermore, diversity was greater in people with a diet high in natural sources of probiotics (e.g. fermented cheese, sauerkraut, kimchi) and prebiotics (e.g. banana, legumes, whole grains, asparagus, onion, leek), but notably not when taken in supplement form.

"Our modern-day living may provide a perfect storm for dysbiosis of the gut. We lead stressful lives with fewer social interactions and less time spent with nature, our diets are typically deficient in fibre, we inhabit oversanitized environments and are dependent on antibiotic treatments. All these factors can influence the gut microbiome and so may be affecting our behaviour and psychological well-being in currently unknown ways."

http://bit.ly/31TvNrX

Newly Discovered Older Cousin of T. Rex Is So Badass It's Been Named After Death Itself

Scientists said Monday they had discovered a new species of dinosaur closely related to* Tyrannosaurus rex *that strode the plain of North America some 80 million years ago.

Thanatotheristes degrootorum – Greek for "Reaper of Death" – is thought to be the oldest member of the *T. rex* family yet discovered in northern North America, and would have grown to around eight metres (26 feet) in length.

(Julius Csotonyi/The University of Calgary and Royal Tyrrell Museum/AFP)

"We chose a name that embodies what this tyrannosaur was as the only known large apex predator of its time in Canada, the reaper of death," Darla Zelenitsky, assistant professor of Dinosaur Palaeobiology at Canada's University of Calgary.

http://bit.ly/2OUfaai

NASA Just Updated Earth's Most Iconic Portrait, And We Are as Lonely as Ever

On 14 February 1990, the Voyager 1 space probe shut down its cameras for the rest of eternity. A mere half hour before that, it recorded one final image.

Signe Dean

Humanity now knows that picture as the Pale Blue Dot. Suspended in a beam of sunlight, Earth is a mere speck of blue set against the black nothingness of space. Never before had we seen our home world quite like this - so vulnerable and alone.

***Carl Sagan unveils the Pale Blue Dot in 1990.* (The Planetary Society/Vimeo)**

Thirty years after the original release, NASA's Jet Propulsion Laboratory (JPL) has published a new version of this iconic portrait of Earth, and it's as breathtaking as ever.

Yep. That tiny speck you can barely see, that's Earth. As legendary astronomer Carl Sagan once put it, "every human being who ever was, lived out their lives" on that tiny dust mote.

Using modern software, JPL's engineer Kevin M. Gill has processed the original data captured by Voyager 1 Narrow-Angle Camera in three spectral filters, re-balancing the colour channels and revealing more detail in the rays of sunlight scattered by the camera optics.

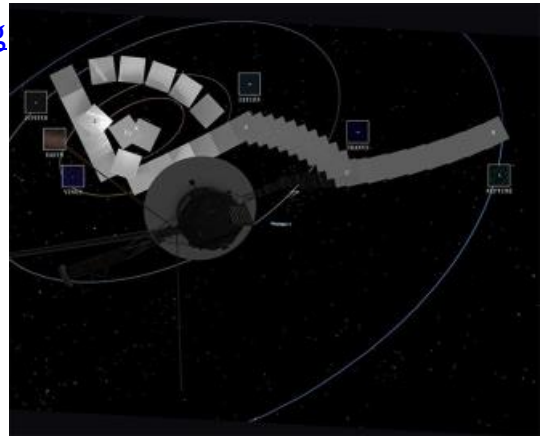
***Enlarged version of the new Pale Blue Dot release.* (NASA/JPL-Caltech)**

Earth is still barely larger than a crumb in this new release; the space probe was already so far from us when the image was captured, our planet occupied just 0.12 of a pixel.

The Pale Blue Dot forms a part of the 'family portrait' Voyager 1 took of our Solar System - an endeavour that wasn't originally intended as part of the Voyager mission, but came to life thanks to a bright idea from Sagan, who saw the opportunity to capture our world floating in the great cosmic ocean.

"Our planet is a lonely speck in the great enveloping cosmic dark. In our obscurity, in all this vastness, there is no hint that help will come from elsewhere to save us from ourselves," he wrote in his 1994 book *Pale Blue Dot*.

For years, the Voyager 1 mosaic of our Solar System has been on display at JPL's Theodore von Kármán Auditorium. According to NASA, the photo of Earth keeps needing to be replaced - visitors can't help but want to touch it.



We can only hope that the renewed release of the Pale Blue Dot will inspire generations to come. It might be decades old, but its meaning is as important as ever.

'Family portrait' mosaic of Voyager 1 Solar System images. **(NASA/JPL-Caltech)**

"There is perhaps no better demonstration of the folly of human conceits than this distant image of our tiny world," wrote Sagan.

"To me, it underscores our responsibility to deal more kindly with one another, and to preserve and cherish the pale blue dot, the only home we've ever known."

http://bit.ly/2uE8AOv

Can bilingualism protect the brain even with early stages of dementia?

Researchers find bilingualism provides the brain with greater cognitive reserve, delaying onset of symptoms

TORONTO - A study by York University psychology researchers provides new evidence that bilingualism can delay symptoms of dementia.

Alzheimer's disease is the most common form of dementia, making up 60 to 70 per cent of dementia cases.

Of all activities with neuroplastic benefits, language use is the most sustained, consuming the largest proportion of time within a day. It also activates regions across the entire brain.

Ellen Bialystok, Distinguished Research Professor in York's Department of Psychology, Faculty of Health, and her team tested the theory that bilingualism can increase cognitive reserve and thus delay the age of onset of Alzheimer's disease symptoms in elderly patients.

Their study is believed to be the first to investigate conversion times from mild cognitive impairment to Alzheimer's disease in monolingual and bilingual patients.

Although bilingualism delays the onset of symptoms, Bialystok says, once diagnosed, the decline to full-blown Alzheimer's disease is much faster in bilingual people than in monolingual people because the disease is actually more severe.

"Imagine sandbags holding back the floodgates of a river. At some point the river is going to win," says Bialystok. "The cognitive reserve is holding back the flood and at the point that they were when they were diagnosed with mild cognitive impairment they already had substantial pathology but there was no evidence of it because they were able to function because of the cognitive reserve.

When they can no longer do this, the floodgates get completely washed out, so they crash faster."

In the five-year study, researchers followed 158 patients who had been diagnosed with mild cognitive impairment. For the study, they classified bilingual people as having high cognitive reserve and monolingual people as having low cognitive reserve.

Patients were matched on age, education, and cognitive level at the time of diagnosis of mild cognitive impairment. The researchers followed their six-month interval appointments at a hospital memory clinic to see the point at which diagnoses changed from mild cognitive impairment to Alzheimer's disease.

The conversion time for bilinguals, 1.8 years after initial diagnosis, was significantly faster than it was for monolinguals, who took 2.6 years to convert to Alzheimer's disease.

This difference suggests that bilingual patients had more neuropathology at the time they were diagnosed with mild cognitive impairment than the monolinguals, even though they presented with the same level of cognitive function.

These results contribute to the growing body of evidence showing that bilinguals are more resilient in dealing with neurodegeneration than monolinguals. They operate at a higher level of functioning because of the cognitive reserve, which means that many of these individuals will be independent longer, Bialystok says.

This study adds new evidence by showing that the decline is more rapid once a clinical threshold has been crossed, presumably because there is more disease already in the brain.

"Given that there is no effective treatment for Alzheimer's or dementia, the very best you can hope for is keeping these people functioning so that they live independently so that they don't lose connection with family and friends. That's huge."

The study is published in *Alzheimer Disease and Associated Disorders* today.

http://bit.ly/37yDZyV

New potential cause of Minamata mercury poisoning identified

Minamata disease possibly caused by a previously unstudied form of mercury discharged directly from a chemical factory

SASKATOON - One of the world's most horrific environmental disasters--the 1950 and 60s mercury poisoning in Minamata, Japan--may have been caused by a previously unstudied form of mercury discharged directly from a chemical factory, research by the University of Saskatchewan (USask) has found.

"By using state-of-the-art techniques to re-investigate a historic animal brain tissue sample, our research helps to shed new light on this tragic mass poisoning," said USask professor Ingrid Pickering, Canada Research Chair in Molecular Environmental Science. "Mercury persists for a long time in nature and travels long distances. Our research helps with understanding how mercury acts in the environment and how it affects people."

The study examining which mercury species could be responsible for the Minamata poisoning was published Feb. 12th in the journal *Environmental Science & Technology*. It is expected to prompt a wider re-assessment of the species of mercury responsible for not only the Minamata tragedy but perhaps also of other organic mercury poisoning incidents, such as in Grassy Narrows, Ontario.

Mercury-containing industrial waste from the Chisso Corporation's chemical factory continued to be dumped in Minamata Bay up to 1968. Thousands of people who ingested the mercury by eating local fish and shellfish died, and many more displayed symptoms of mercury poisoning including convulsions and paralysis.

"Something that was unknown at that time was that unborn children would also suffer the devastating effects of mercury poisoning, with many being born with severe neurological conditions," said USask PhD toxicology student Ashley James, the first author of the paper.

"A mother may be essentially unaffected by the poisoning because the mercury within her body was absorbed by the unborn child."

The Minamata poisoning has been considered a textbook example of how inorganic mercury turns into organic mercury, and how a toxic substance propagates up the food chain to humans. For decades, it has been assumed that micro-organisms in the muds and sediments of Minamata Bay had converted the toxic inorganic mercury from the factory wastewater into a much more lethal organic form called methyl mercury, which targets the brain and other nervous tissue. This compound was thought to spread to humans from eating contaminated seafood.

Recent studies have suggested that methyl mercury itself may have been discharged directly from the Minamata plant.

But USask research--involving 60-year-old Minamata feline tissue samples--has found these assumptions may be misplaced.

Using a new type of spectroscopy and sophisticated computational methods, the USask researchers have found that the cat brain tissue contained predominantly organic mercury, contradicting previous findings and assumptions. The team's computer modelling was also able to predict which kinds of mercury waste compounds the chemical plant would be likely to produce.

"The most probable neurotoxic chemical form of mercury discharged from the factory was neither methyl mercury nor inorganic mercury," said Graham George, Canada Research Chair in X-ray Absorption Spectroscopy and an expert in spectroscopy of toxic heavy elements at USask's Toxicology Centre and geological sciences department. "We think that it was caused by an entirely different type of organic mercury discharged directly from the Chisso factory at Minamata in an already deadly chemical form."

The cat brain samples from the USask study come from an experiment conducted by the Chisso company doctor in 1959 to determine the causes of the sickness, which was not at first connected to the industrial dumping. The doctor fed cats the industrial waste and they soon showed symptoms similar to the sick villagers. While the doctor was ordered to stop his experiments, he kept samples of brain tissue from one of the cats.

The USask team has found that the ***likely culprit of the poisoning is alpha-mercuri-acetaldehyde***, a mercury waste product from aldehyde production not previously identified.

"It was this species that very likely contaminated Minamata Bay and subsequently gave rise to the tragedy of Minamata disease. We think that this was the dominant mercury species in the acetaldehyde plant waste. More work is needed to explore the molecular toxicology of these compounds, to understand the ways they could be toxic to humans, animals and the environment," said George.

The 12-member research team included researchers from USask, Stanford Synchrotron Radiation Lightsource at the SLAC National Accelerator Laboratory, Japanese National Institute for Minamata Disease, and the environmental medicine department of the University of Rochester. While USask is home to the Canadian Light Source synchrotron, there are only two synchrotrons in the world set up with the specialized equipment needed for the advanced work that the team does with these precious samples--one in Grenoble, France and the other at Stanford.

The USask research was funded by the Natural Sciences and Engineering Research Council, the Canadian Institutes of Health Research, and the Canada Foundation for Innovation.

The new findings coincide with renewed public interest in the tragedy due to the much-anticipated premiere on Feb. 21st at the Berlin International Film Festival of a new movie "*Minamata*" which stars Johnny Depp as photojournalist W. Eugene Smith whose work publicized the devastating effects of the mercury poisoning.

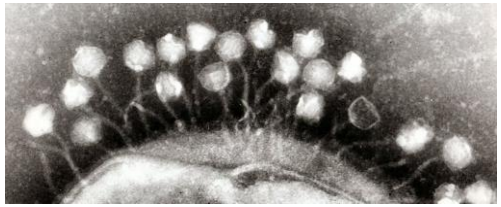
http://bit.ly/2UUkGOc

Scientists Discover Giant Viruses With Features Only Seen Before in Living Cells

Entire new groups of giant phages discovered and 351 gene sequences pieced together.

Tessa Koumoundouros

Sifting through a soup of genes sampled from many environments, including human saliva, animal poop, lakes, hospitals, soils and more, researchers have found hundreds of giant viruses - some with abilities only seen before in cellular life.



(Graham Beards/Wikipedia/CC BY-SA 3.0)

The international team, led by scientists from University of California, Berkeley, has discovered entire new groups of giant phages (viruses that infect bacteria) and pieced together 351 gene sequences.

Within these they found genes that code for unexpected things, including bits of the cellular machinery that reads and executes DNA instructions to build proteins, also known as translation.

"They have an unusual number of components of the translation machinery that you do not find on a typical virus," microbiologists Basem Al-Shayeb and Jill Banfield from UC Berkeley told ScienceAlert. The translation process takes place in molecular structures known as ribosomes, and the researchers actually found genes that code for some of their components - ribosomal proteins.

"Typically, what separates life from non-life is to have ribosomes and the ability to do translation; that is one of the major defining features that separates viruses and bacteria, non-life and life," said microbial ecologist Rohan Sachdeva from UC Berkeley. "Some large phages have a lot of this translational machinery, so they are blurring the line a bit."

The team also found sequences for CRISPR systems, which also happens to be the 'immune system' bacteria use against viruses, the very same system we humans have co-opted for our own gene manipulation purposes.

The newly discovered viruses all have genomes more than 200,000 base pairs long, whereas the average known phage size is more along the lines of 52,000 base pairs.

Some phage genomes identified by the team were true whoppers; the researchers have named one group Whopperphage, and designated the other nine new groups after the word "big" in the different languages of the contributing authors.

"The genomes of these phages are at least four times the size of a typical phage, and the largest is 15 times larger - 735,000 bases of DNA," Al-Shayeb and Banfield said. These larger phages are thought to infect Bacteroidetes, a group of bacteria widely dispersed in our environment, from soil to our intestines.

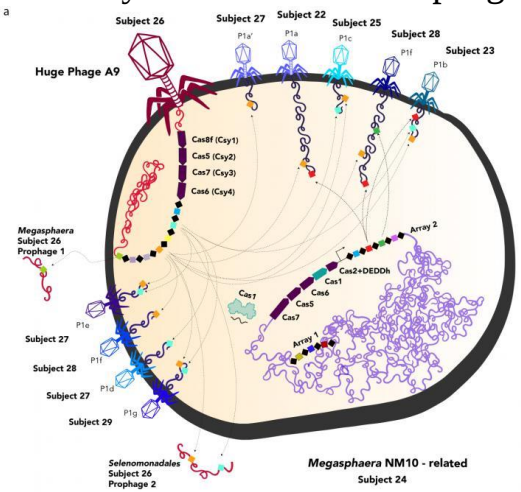
The genomes of these hefty phages are large enough to rival those of small bacteria, but the amoeba-infecting pandoraviruses still hold the title of the largest viral genome at 2.5 million base pairs.

"Large phages have been found before, but they were spot findings," Sachdeva told the Innovative Genomics Institute. "What we found in this paper is they are essentially ubiquitous. We find them everywhere." Like other phages, these chonkers inject their DNA into their bacterial host, hijacking the victim's gene replication equipment to make copies of themselves.

The researchers suspect that while this is happening, the giants also use some of their additional genes to derail early stages of translation inside the bacteria, and divert protein production to suit their own needs. Such control of protein creation has also been observed in animal viruses.

Al-Shayeb explained that giant phages use their CRISPR system for phage-on-phage warfare, by specifically targeting competing viruses that try to infect the same host bacterium. A study from last year shows how some phages use this system to thwart anti-phage measures their host bacteria may deploy.

"The sense we have looking at these large genomes is that phages have acquired a lot of different genes and pathways - some of which we can predict, some of which we can't for really taking control of bacterial hosts' function during infection," Banfield told the Innovative Genomics Institute.



A huge phage (Subject 26) infecting a bacterium and manipulating its response to other phages. **(Jill Banfield Lab/UC Berkeley)**

As we learn more about the links between our physical and mental health and the microbes we share our bodies and environments with, it is clear that what affects them can also profoundly impact us.

"Phages are also known to transfer genes for bacterial toxins and antibiotic resistance between bacteria, which contribute to disease," Al-Shayeb said. "Since we have both harmful and useful bacteria living on us and within us, understanding what kinds of phages coexist with them in humans and animals and how they affect those environments is of great value."

The researchers suggest that the interesting CRISPR systems some of these phages possess may have the potential to help us control our own microbiomes, by altering the function of bacteria or eliminating the troublesome ones.

They now hope to grow some of these whopper phages in the lab, to learn more about these phage-associated CRISPR systems and "discover their roles and test for value in genome editing", according to Al-Shayeb and Banfield.

Biochemist Christoph Weigel, who was not associated with the study, suggested on Twitter that the paper provides "strong support" for considering viruses living "virocells".

"These huge phages bridge the gap between non-living bacteriophages, on the one hand, and bacteria and Archaea," explained Banfield. "There definitely seem to be successful strategies of existence that are hybrids between what we think of as traditional viruses and traditional living organisms."

Whatever else this huge addition to our knowledge of viral biodiversity brings, it's already sparking further discussion on what it means to be alive. This study was published in *Nature*.

http://bit.ly/2Hn5T6u

10,000 steps a day: Not a magical formula for preventing weight gain

Even far eclipsing 10K steps didn't prevent weight gain for college freshmen studied

For years now, 10,000 steps a day has become the gold standard for people trying to improve their health -- and recent research shows some benefits can come from even just 7,500 steps. But if you're trying to prevent weight gain, a new Brigham Young University study suggests no number of steps alone will do the trick.

Researchers from BYU's Exercise Science Department, along with colleagues from the Nutrition, Dietetics & Food Science Department, studied 120 freshmen over their first six months of college as they participated in a step-counting experiment. Participants walked either 10,000, 12,500 or 15,000 steps a day, six days a week for 24 weeks, while researchers tracked their caloric intake and weight.

The goal of the study was to evaluate if progressively exceeding the recommended step count of 10,000 steps per day (in 25% increments) would minimize weight and fat gain in college freshmen students. In the end, it didn't matter if the students walked more than even 15,000 steps; they still gained weight. Students in the study gained on average about 1.5 kg (roughly 3.5 lbs.) over the study period; a 1 to 4 kg average weight gain is commonly observed during the first academic year of college, according to previous studies.

"Exercise alone is not always the most effective way to lose weight," said lead author Bruce Bailey, professor of exercise science at BYU. "If you track steps, it might have a benefit in increasing physical activity, but our study showed it won't translate into maintaining weight or preventing weight gain."

Study subjects wore pedometers 24 hours a day for the six-week study window. On average, students walked approximately 9,600 steps per day prior to the study. By the end of the study, the participants in the 10,000-step group averaged 11,066 steps, those in the 12,500-step group averaged 13,638 steps and those in the 15,000-step group averaged 14,557 steps a day.

Although weight was not affected by the increased steps, there was a positive impact on physical activity patterns, which "may have other emotional and health benefits," study authors said. One positive, if not unsurprising, outcome of the study was that sedentary time was drastically reduced in both the 12,500- and 15,000-step groups. In the 15,000-step group, sedentary time decreased by as much as 77 minutes a day.

"The biggest benefit of step recommendations is getting people out of a sedentary lifestyle," Bailey. "Even though it won't prevent weight gain on its own, more steps is always better for you."

BYU professors James LeCheminant and Larry Tucker were also authors on the study, which published in the Journal of Obesity. BYU students Ciera Bartholomew, Caleb Summerhays, Landon Deru, Sharla Compton and Joseph Hicks were also authors.

http://bit.ly/2UU7yZp

Effectiveness of travel bans -- readily used during infectious disease outbreaks -- mostly unknown, study finds

Very little research into the effectiveness of travel bans exists.

Because of the quick and deadly outbreak in late December of a novel coronavirus in Wuhan, China, now known as COVID-19 - infecting tens of thousands and killing hundreds within weeks, while spreading to at least 24 other countries - many governments, including the United States, have banned or significantly restricted travel to and from China.

And while travel bans are frequently used to stop the spread of an emerging infectious disease, a new University of Washington and Johns Hopkins University study of published research found that the effectiveness of travel bans is mostly unknown.

However, said lead author Nicole Errett, a lecturer in the UW Department of Environmental & Occupational Health Sciences in the School of Public Health, that's largely due to the fact that very little research into the effectiveness of travel bans exists.

"Some of the evidence suggests that a travel ban may delay the arrival of an infectious disease in a country by days or weeks.

However, there is very little evidence to suggest that a travel ban eliminates the risk of the disease crossing borders in the long term," said Errett, co-director of the ColLABorative on Extreme Event Resilience, a research lab focused on addressing real-world issues relevant to community resilience.

The researchers combed through thousands of published articles in an effort to identify those that directly addressed travel bans used to reduce the geographic impact of the Ebola virus, SARS (Severe Acute Respiratory Syndrome), MERS (Middle East Respiratory Syndrome) and the Zika virus.

They did not include studies of influenza viruses, for which travel bans have already been shown to be ineffective in the long term.

In the end, the researchers were able to identify just six studies that fit their criteria.

Those six were based on models or simulations, not data from actual bans after they were implemented, to assess the effectiveness of travel bans in controlling outbreaks.

Consequently, to improve research in this area, the study authors recommend that research questions, partnerships and study protocols be established ahead of the next outbreak so empirical data can be collected and assessed quickly.

"Travel bans are one of several legal options that governments have drawn on to mitigate a pandemic," said co-author Lainie Rutkow, a professor of health policy and management at Johns Hopkins Bloomberg School of Public Health.

"As coronavirus spreads, our study raises the importance of understanding the effectiveness of legal and policy responses intended to protect and promote the public's health."

"When assessing the need for, and validity of, a travel ban, given the limited evidence, it's important to ask if it is the least restrictive measure that still protects the public's health, and even if it is, we should be asking that question repeatedly, and often," said co-author Lauren Sauer, an assistant professor of emergency medicine at Johns Hopkins University's School of Medicine and director of operations with the university's Office of Critical Event Preparedness and Response.

Consequently, the authors write, additional research is "urgently needed" to inform policy decisions, especially in light of the tremendous social, economic and political impacts of their implementation.

https://wb.md/31XmRBT

Physician on Boosting Sex With Foods: Keep an Open Mind

If your Valentine's Day plans include something a little more interactive than settling in with a meta-analysis and a highlighter, Niket Sonpal, MD, suggests you might want to make a grocery run for a few key items.

Marcia Frellick

Topping the list? Oysters, chocolate, avocados, pistachios, bananas, chai tea, and red wine. Others say don't waste your time searching the grocery aisles for aphrodisiacs. Or at least not if your V-Day best practices need to be strictly evidence-based.

The debate has been historically touchy, but there is wide agreement that the foods won't work on their own.

Sonpal, a gastroenterologist and an adjunct assistant professor at Touro College of Osteopathic Medicine in New York City, does suggest nine foods, though — from asparagus to chili martinis — that might help jump start the process.

Blood Flow at the Heart of the Matter

"There are specific chemicals in these foods, ranging from zinc to nitric-oxide releasers to caffeine. All of these have something in them that will change blood flow. Blood flow starts to move to places where love happens," Sonpal told *Medscape Medical News.*

Other foods, he says, are considered arousing because of their appearance. Think bananas. Think oysters.

Sonpal points out that bananas also contain bromelain, which has been shown to be positively associated with testosterone and erectile dysfunction (ED). The vitamin B in bananas can elevate energy levels, he said.

Oysters contain a hefty amount of amino acids, which, along with their look and texture, earned them a spot on his list.

"These amino acids down the line in the chemical process build a lot of our hormones and things like serotonin," Sonpal said.

Pistachios are on the list, he explained, because they contain protein and flavonoids that can help stimulate blood flow. He pointed to a small study that also suggests a positive effect on ED.

Avocados, which Sonpal said have a seductive reputation dating to the ancient Aztecs of being known as "the testicle fruit," are full of vitamins B6, B9, and folic acid, "which provide your body with energy and even help to increase testosterone production."

Chocolate has long appeared on such lists, and this one is no exception. Sonpal noted that chocolate contains tryptophan, a building block for serotonin, methylxanthines, and phenylethylamine, a stimulant related to amphetamine, which is released in the brain when people fall in love. "There are also the tastes, the aromas," he said. "We are programmed to think of chocolate with Valentine's and Valentine's with sex."

Sonpal emphasized that these foods won't have an effect by themselves. "These are all adjunctive to things normally used to drive sex life," he said. "If people have ED, these foods aren't going to fix it. They should be used in conjunction with other things.

"At the end of the day," Sonpal said, "you'll be treating your patients with evidenced-based treatments, but what's to say a little chai tea or a couple of pistachios aren't going to help?"

Yes, But…

Chocolate is probably the item on Sonpal's list that has the most scientific connection to boosting libido, says Kate Thomas, PhD, director of clinical services at the Sex and Gender Clinic of Johns Hopkins in Baltimore, Maryland. "It's been universally touted in many different cultures as an aphrodisiac," she said. And she agreed chocolate's components can be physically tied to feelings of being in love. "The potential could be there for chocolate to be utilized," Thomas told *Medscape Medical News*.

However, "We have yet to figure out what sorts of foods or chemicals are going to provide aphrodesia across the board," she said. Human sexuality is very complex, Thomas noted, and has many components, including status of the relationship, mood, and how a person feels physically that day.

For example, "Giving men Viagra will increase their erection but doesn't necessarily make them feel more sexual," she noted.

Laura Berman, LCSW, PhD, assistant clinical professor of obstetrics and gynecology and psychiatry at Feinberg School of Medicine, in Chicago, Illinois, agreed that although there is some evidence to support the idea that some ingredients in these foods are associated with sexual function, there is no solid cause-and-effect evidence. Additionally, it is unlikely even with ingredients known to increase arousal that a person would eat an amount large enough to have an effect, she told *Medscape Medical News*.

"While there is a small foundation [Sonpal] is extrapolating from, there are no real studies that demonstrate that eating these foods will arouse you and/or increase your desire except, perhaps, suggestively and psychologically from their appearance as an aphrodisiac," Berman said.

She isn't saying not to try the foods for a special night.

"If you want to create a sexy meal and you want to be suggestive, and maybe want to take advantage of the placebo effect, it can't hurt, but I wouldn't count on it to guarantee some action," Berman said.

A Word From the FDA

So what does the US Food and Drug Administration (FDA) think about aphrodisiac claims?

The answer is decidedly unsexy: "Any product that bears labeling claims that it will arouse or increase sexual desire, or that it will improve sexual performance, is an aphrodisiac drug product. Anise, cantharides, don qual, estrogens, fennel, ginseng, golden seal, gotu kola, Korean ginseng, licorice, mandrake, methyltestosterone,

minerals, nux vomica, Pega Palo, sarsaparilla, strychnine, testosterone, vitamins, yohimbine, yohimbine hydrochloride, and yohimbinum have been present as ingredients in such drug products."

But, the statement continues: "There is a lack of adequate data to establish general recognition of the safety and effectiveness of any of these ingredients, or any other ingredient, for OTC use as an aphrodisiac."

Sonpal, Thomas, and Berman have disclosed no relevant financial relationships.

https://bbc.in/39FOylc

Human brain parts left over from surgery boosts research

US researchers are developing a better understanding of the human brain by studying tissue left over from surgery.

They say that their research is more likely to lead to new treatments than studies based on mouse and rat models. Dr Ed Lein, who leads the initiative at the Allen Institute has set up a scheme with local doctors to study left over tissue just hours after surgery.

Researchers at the Allen Institute are developing a deeper understanding of how our brains work by studying tissue left over from surgery **Allen Institute**

He gave details at the American Association for the Advancement of Science meeting in Seattle.

"It is a little bit crazy that we have such a huge field where we are trying to solve brain diseases and there is very little understanding of the human brain itself," said Dr Lein.

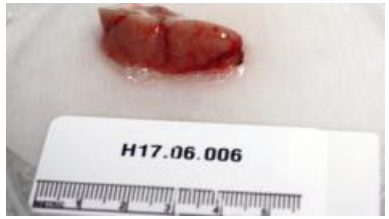
"The field as a whole is largely assuming that the human brain is similar to those of animal models without ever testing that view.

"But the mouse brain is a thousand times smaller, and any time people look, they find significant differences."

Dr Lein and his colleagues at the Allen Institute in Seattle set up the scheme with local neurosurgeons to study brain tissue just hours after surgery - with the consent of the patient. It functions as if it is still inside the brain for up to 48 hours after it has been removed.

So Dr Lein and his colleagues have to drop everything and often have to work through the night once they hear that brain tissue has become available.

"What we are finding is that there are many more types of cells in the human brain than in animal models. Their electrical properties and their anatomy can be significantly different between mouse and human," he said.



A small piece of brain just after surgery continues to function as if it is still in the body for 24 hours **Allen Institute**

And it is for this reason that efforts to come up with treatments for brain diseases, such as Alzheimer's and Parkinson's have been "relatively fruitless", according to Dr Lein. He says that patients, undergoing invasive brain surgery for disorders such as epilepsy, have been enthusiastic about signing up to the scheme.

But Dr Lein's comments have gone down badly with some UK geneticists who do much of their work with mice and rats.

Prof Robin Lovell-Badge, a medical researcher at the Crick Institute in London, said: "Of course, the brains of mice and humans are quite different, in size, shape, and complexity.

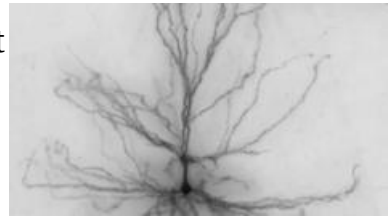
"And they connect to bodies that are also very different. I don't think I know any mouse neuroscientist who would pretend otherwise. Indeed, his claims that they do are ridiculous."

"Studies can be carried out on live animals that would be very difficult to do otherwise. We can control variables, such as genetics, age, nutrition, etc, in way that is simply not possible in humans."

The UK Medical Research Council (MRC) is to close its mouse mammalian genetics centre in Harwell in Oxfordshire. A senior genetics researcher, who did not wish to be named, told BBC News that the decision was influenced in part by views of the sort expressed by Dr Lein.

"There is a movement to downgrade the importance of mouse and other model organisms and (animal) studies in general, with the naïve belief that human genetics will solve it all, reflected in the comments of Ed Lein.

"But mechanism is key, and to explore and validate hypotheses you need a manipulable whole organism. "It will be important to resist the push against animal studies and I think across the majority of our community this is indeed strongly resisted, and is of considerable concern."



One of the billions of brain cells in the human brain. The researchers have found significant differences between these cells and those of mice **Allen Institute**

Prof Lovell-Badge also questioned how useful Dr Lein's approach was likely to be in the long run. "Is a maximum of 48 hours in culture going to be sufficient? What about connections the particular piece of brain will have to other parts of the central nervous system that might well influence how it functions? What about the absence of systemic influences, such as from the such as from the immune system, the gut and gut microbiota."

Prof Elizabeth Fisher, a researcher at UCL studying the genetic basis of brain diseases, said studying the mouse brain had given scientists "many insights into what it means to be human in health and disease, and new treatments. "While gaining access to living human brain tissue will undoubtedly help research, samples will always be limited, especially from people with very rare disorders."

Responding to the comments, Dr Lein said: "I want to be clear that brain research in animal models is essential to provide experimentally testable systems to perform mechanistic studies, which is a fundamental limitation to human brain studies.

"In this sense the studies we are doing on human brain are highly complementary and allow a critical evaluation of potential models for studying brain function and disease. All models have limitations, and we believe this will illuminate a path to new and better models and treatments for brain diseases and disorders.'

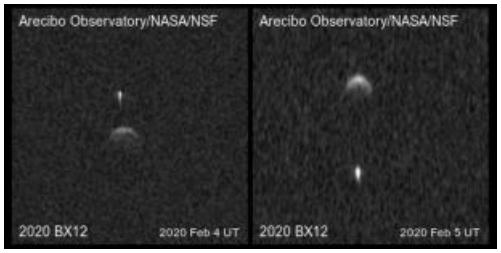
http://bit.ly/2UWQeD4

Scientists just watched a newfound asteroid zoom by Earth. Then they saw its moon.

New observations show that a newly discovered space rock is actually two separate asteroids.

By Meghan Bartels - Space.com Senior Writer

One of Earth's premier instruments for studying nearby asteroids is back to work after being rattled by earthquakes, and its first new observations show that a newly discovered space rock is actually two separate asteroids.



Radar images show the binary asteroid 2020 BX12, which scientists discovered this year. **Arecibo Observatory/NASA/NSF**

The instrument is the planetary radar system at the Arecibo Observatory in Puerto Rico. The observatory was closed for most of January, after a series of earthquakes hit the island beginning on Dec. 28, 2019. The observatory reopened on Jan. 29. Meanwhile, on Jan. 27, scientists using a telescope on Mauna Loa in Hawaii spotted an asteroid that astronomers hadn't seen before. The team dubbed the newfound space rock 2020 BX12 based on a formula recognizing its discovery date.

Because of the size of 2020 BX12 and the way its orbit approaches that of Earth, it is designated a potentially hazardous asteroid. However, the space rock has already come as close to Earth as it will during this pass (2.7 million miles or 4.3 million kilometers); astronomers have calculated the asteroid's close approaches with Earth for the next century, and all will be at a greater distance than this one was.

The asteroid's flyby wasn't a threat to life on Earth, but it was an opportunity for scientists who were hoping to learn more about space rocks.

On Feb. 4 and 5, the radar station at Arecibo set its sights on 2020 BX12. Based on the observations, the scientists discovered that 2020 BX12 is a binary asteroid, with a smaller rock orbiting the larger rock. About 15% of larger asteroids turn out, on closer inspection, to be binary, according to NASA.

The larger rock is likely at least 540 feet (165 meters) across, and the smaller one is about 230 feet (70 m) wide, according to the observations gathered by Arecibo. When the instrument observed the two space rocks on Feb. 5, they appeared to be separated by about 1,200 feet (360 m).

Scientists couldn't gather enough data to be sure, but they suspect that the two rocks might complete an orbit of each other in 45 to 50 hours and that the smaller rock may be brighter than, and tidally locked with, its companion, meaning the same side always faces the larger object.

Existential dread is a key motivator for asteroid discoveries, and planetary defense experts hope that, by surveying nearby space rocks, they will identify a threat with enough time for us to protect ourselves.

But asteroids are also scientifically interesting, since they represent rubble from the formation of the solar system.

http://bit.ly/2Hu9Whu

Here's why the WHO says a coronavirus vaccine is 18 months away

Let's explore why, even with global efforts, it might take this long.

Rob Grenfell, Trevor Drew

The World Health Organisation said this week it may be 18 months before a vaccine against the coronavirus is publicly available. Let's explore why, even with global efforts, it might take this long.

China shared publicly the full RNA sequence of the virus – now known as SARS-CoV-2 rather than COVID-19, which refers to the disease itself – in the first half of January. This kickstarted efforts to develop vaccines around the world, including at the University of Queensland and institutions in the US and Europe.

By late January, the virus was successfully grown outside China for the first time, by Melbourne's Doherty Institute, a critically important step. For the first time, researchers in other countries had access to a live sample of the virus.

Using this sample, researchers at CSIRO's high-containment facility (the Australian Animal Health Laboratory) in Geelong, could begin to understand the characteristics of the virus, another crucial step in the global effort towards developing a vaccine.

Vaccines have historically taken two to five years to develop. But with a global effort, and learning from past efforts to develop coronavirus vaccines, researchers could potentially develop a vaccine in a much shorter time.

Here's why we need to work together

No single institution has the capacity or facilities to develop a vaccine by itself. There are also more stages to the process than many people appreciate.

First, we must understand the virus's characteristics and behaviour in the host (humans). To do this, we must first develop an animal model.

Next, we must demonstrate that potential vaccines are safe and can trigger the right parts of the body's immunity, without causing damage. Then we can begin pre-clinical animal testing of potential vaccines, using the animal model.

Vaccines that successfully pass pre-clinical testing can then be used by other institutions with the capacity to run human trials.

Where these will be conducted, and by whom, has yet to be decided. Generally, it is ideal to test such vaccines in the setting of the current outbreak.

Finally, if a vaccine is found to be safe and effective, it will need to pass the necessary regulatory approvals. And a cost-effective way of making the vaccine will also need to be in place before the final vaccine is ready for delivery. Each of these steps in the vaccine development pipeline faces potential challenges.

Here are some of the challenges we face

The international Coalition for Epidemic Preparedness Innovations has engaged our team in those first two steps: determining the characteristics of the current virus, then pre-clinical testing of potential vaccines.

While Melbourne's Doherty Institute and others have been instrumental in isolating the novel coronavirus, the next step for us is growing large amounts of it so our scientists have enough to work with. This involves culturing the virus in the lab (encouraging it to grow) under especially secure and sterile conditions.

The next challenge we face is developing and validating the right biological model for the virus. This will be an animal model that gives us clues to how the coronavirus might behave in humans.

Our previous work with SARS (severe acute respiratory syndrome) has given us a good foundation to build on.

SARS is another member of the coronavirus family that spread during 2002-03. Our scientists developed a biological model for SARS, using ferrets, in work to identify the original host of the virus: bats.

SARS and the new SARS-CoV-2 share about 80-90% of their genetic code. So our experience with SARS means we are optimistic our existing ferret model can be used as a starting point for work on the novel coronavirus.

We will also explore other biological models to provide more robust data and as a contingency.

What good will a vaccine be if the virus mutates?

There's also the strong possibility that SARS-CoV-2 will continue to mutate. Being an animal virus, it has already likely mutated as it adapted – first to another animal, and then jumping from an animal to humans. Initially this was without transmission among people, but now it has taken the significant step of sustained human-to-human transmission.

As the virus continues to infect people, it is going through something of a stabilisation, which is part of the mutation process. This mutation process may even vary in different parts of the world, for various reasons.

This includes population density, which influences the number of people infected and how many opportunities the virus has to mutate.

Prior exposure to other coronaviruses may also influence the population's susceptibility to infection, which may result in variant strains emerging, much like seasonal influenza. Therefore, it's crucial we continue to work with one of the latest versions of the virus to give a vaccine the greatest chance of being effective.

All this work needs to be done under stringent quality and safety conditions, to ensure it meets global legislative requirements, and to ensure staff and the wider community are safe.

Other challenges ahead

Another challenge is manufacturing proteins from the virus needed to develop potential vaccines. These proteins are specially designed

to elicit an immune response when administered, allowing a person's immune system to protect against future infection. Fortunately, recent advances in understanding viral proteins, their structure and functions, has allowed this work to progress around the world at considerable speed.

Developing a vaccine is a huge task and not something that can happen overnight. But if things go to plan, it will be much faster than we've seen before.

So many lessons were learned during the SARS outbreak. And the knowledge the global scientific community gained from trying to develop a vaccine against SARS has given us a head-start on developing one for this virus.

http://bit.ly/2OYY6zV

These Are The Early Symptoms of The New Coronavirus, According to The Latest Research

A recent study of nearly 140 hospitalised patients in Wuhan, China, has identified a pattern of symptoms associated with the new coronavirus, now officially known as COVID-19.

Aria Bendix, Business Insider

The most common symptom is fever, according to the researchers at Zhongnan Hospital of Wuhan University. They observed fevers in 99 percent of the patients in their study.

Other common symptoms include fatigue and a dry cough, which appeared in more than half of the patients studied. About a third also experienced muscle pain and difficulty breathing, though it took about five days (on average) for a patient to have difficulty breathing after first showing symptoms.

Other symptoms associated with common colds – such as a headache or sore throat – were seen in only a small number of cases.

The coronavirus outbreak likely originated at a seafood market in Wuhan in December. It has since spread to 25 countries outside China, though most of the cases remain concentrated on the Chinese mainland. So far, more than 1,100 people have died and more than 45,000 have been infected by the virus.

Learning more about the virus' symptoms could help physicians identify severe cases before a person becomes critically ill. It could also help scientists better understand how the virus spreads.

"We don't know yet the arc of how infectious someone is over the course of their infection," Lauren Meyers, an epidemiologist at the University of Texas at Austin, told Business Insider.

"We don't know if people are infectious before they have symptoms, and we are not sure how infectious they are even while they have symptoms."

Patients could spread the virus before they're hospitalised

The new study found that the virus is most likely to affect older men with preexisting health problems. More than 54 percent of the patients in the study were men, and the median age of patients was 56.

On average, it took about 10 days for patients with severe cases to be admitted to the ICU from the time their symptoms began, the researchers found. But it's possible that these patients contracted the virus long before they developed a fever.

Meyers guessed that a typical infected person is probably contagious without showing symptoms for five or more days. In total, health experts have estimated a person with COVID-19 can be contagious for between one and 14 days; one group of Chinese scientists recently suggested that people could be contagious for up to 24 days.

But according to the new study, it is taking about seven days for patients who are already showing symptoms in Wuhan to be admitted to a hospital there.

The authors didn't say why that's the case, but Reuters reported last week that hospitals in Wuhan have turned away some patients with milder symptoms.

Other infected people may choose not to admit themselves right away, since there's no cure for the virus – doctors just provide supportive care such as fluids or steroids.

Whatever the reason, that delay could help the virus spread.

"Assuming that people are not hospitalised, not isolated for the first week of their symptomatic period, then that certainly is a key opportunity for onward transmission," Meyers said.

But she added: "It's not clear necessarily how mobile those people would have even been in that week. If they're really feeling lousy and they have a fever and they're already having issues with breathing, they may not be moving around."

Early symptoms could also include diarrhoea

The new study also found that patients who ended up in the ICU had more abdominal pain and appetite loss than patients with milder coronavirus cases.

The researchers noted some early, "atypical" symptoms as well: They found that 14 patients developed diarrhoea and nausea one to two days before their fever or difficulty breathing set in.

This might suggest another way the virus is spreading. According to the study, one patient with abdominal symptoms was sent to the surgical department, since the symptoms didn't align with typical coronavirus cases.

That person went on to infect at least four other hospitalised patients – all of whom showed "atypical abdominal symptoms" as well – and at least 10 healthcare workers.

"If true, then this confirms that some patients are likely to be far more infectious than others, and this poses further difficulties in managing their cases," Michael Head, a senior global health research fellow at the University of Southampton, said in a statement.

Of the nearly 140 patients in the Zhongnan Hospital study, nearly 30 percent were healthcare workers.

Scientists still think the coronavirus is mostly transmitted through respiratory droplets such as saliva and mucus when a person coughs or sneezes.

But Meyers said diarrhoea could be a possible route of transmission, too. A January study from researchers in Beijing and Shanghai identified the coronavirus in stool samples from patients with diarrhoea and nausea. Meyers pointed to one "gruesome anecdote" from the SARS outbreak in 2003, when a patient with severe diarrhoea infected hundreds of residents in his apartment complex in Hong Kong. The virus is believed to have spread through pipes, entering people's bathrooms via floor drains.

"It's too early to say how significant of a contribution diarrhoea would be to future transmission of this novel coronavirus," Meyers said. "With SARS, diarrhoea was not a super common symptom, but it certainly occurred in a fraction of SARS patients."

Health authorities recently evacuated more than 100 people from a building in Hong Kong after two residents 10 floors apart tested positive for COVID-19. They're now investigating whether the virus can spread through sewage systems.

http://bit.ly/3bH0ncK

How did dinosaur parents know when their kids had a fever?

Prehistoric egg shells provide clues to dinosaurs' evolution from cold- to warm-blooded creatures

From the time that dinosaur fossils were first discovered, these creatures have fascinated scientists and laypeople alike. In the academic world, their remains provide important clues into the prehistoric world; in popular culture, dinosaurs have inspired blockbuster hits, such as Jurassic Park and King Kong.

Now, a research team headed by Professor Hagit Affek at the Hebrew University of Jerusalem's Institute of Earth Sciences has unlocked a mystery that has stymied researchers for decades: How

did dinosaurs regulate their body temperatures? Were they warm-blooded or cold-blooded?

Affek's study, published today in Science Advances, relies on a novel method to measure historical temperatures. Called clumped isotope geochemistry, this method analyzes chemical bonds among heavy isotopes in calcium carbonate minerals--the main ingredient in egg shells. This allows scientists to calculate both the temperature at which the minerals formed and the body temperature of the mother that laid the egg.

Affek and her team applied this method to fossilized eggs from three distinct dinosaur species along the evolutionary path from reptile to bird and found that their body temperature ranged from 35-40 degrees Celsius. However, this bit of information still did not answer the question as to whether dinosaurs were endothermic or exothermic, meaning, did they generate their own body heat or get warm from the sun and their environment?

"The global climate during the dinosaur era was significantly warmer than it is today. For this reason, measuring only the body temperatures of dinosaurs who lived near the equator wouldn't tell us whether they were endo- or exothermic because their body temperature may simply have been a cold-blooded response to the hot climates they lived in," shared Affek.

To address this issue, her team focused on dinosaurs that lived in high latitudes like Alberta, Canada--far enough north to ensure that their warm body temperatures were the result of an internal, metabolic warming process rather than merely reflecting the climate around them.

To verify their hypothesis, Affek and her team needed to determine the environmental temperature in Alberta back when dinosaurs lived. They accomplished this by applying their isotope method to mollusk shells that lived in Alberta alongside the dinosaurs. Since mollusks are cold-blooded creatures, they reflect the ambient climate of the time. The mollusks' body temperature measured 26°C and showed that the dinosaurs living in Alberta were endothermic; otherwise, they could not have maintained a body temperature of 35-40°C.

As dinosaurs evolved, they moved from lizard-like (cold-blooded) characteristics to avian (warm-blooded) ones. "We believe that this transformation happened very early on in dinosaurs' evolution since the Mayasaura eggs--a lizard-like dinosaur species that we tested--were already able to self-regulate their body temperature, just like their warm-blooded, bird-like cousins, the Torrdons," explained Affek.

The fact that both of these species, located at opposite ends of the dinosaur evolutionary tree, had body temperatures higher than those of their environment means that both had the ability to warm themselves.

Either way, Mother of Dragons, if your baby is showing a fever of 41 degrees, it's time to call the doctor.

http://bit.ly/323oRc2

Monkeys Wake From Anaesthetic When Brain Region Linked to Consciousness Is Stimulated

Recent experiment that stimulated the brains of anaesthetised macaques, provides a clearer idea of just which neurological structures might be primarily responsible

Mike Mcrae

Later today I'll lose consciousness for a few hours to rest and repair. There's a good chance you will, too. Yet as ubiquitous as sleep is, we know very little about which parts of the brain are fundamental to staying awake.

Thanks to a recent experiment that stimulated the brains of anaesthetised macaques, we have a clearer idea of just which neurological structures might be primarily responsible for switching us on each day.

The results not only help us to better understand the processes behind anaesthesia; for those trapped in vegetative or comatose states by illness or injury it could mean a pathway out again.

While we can use brain-scanning technologies to watch how different parts of the brain activate as a subject falls unconscious, it's a lot harder to work out how any single area produces a specific response, let alone which are the most crucial.

Studies on sleeping and comatose patients have given researchers a sound idea of the kinds of structures involved, from the brain stem to the prefrontal cortex. Needless to say, many different parts of our nervous system determine our state of awareness.

Researchers from the University of Wisconsin in the US and the Israel Institute of Technology noticed one tiny piece of tissue deep inside our forebrain – the central lateral thalamus – had a rather prominent role in directing our neurological affairs.

Based on its connectivity, it seemed to be pivotal in influencing how signals were passed from the higher-order 'thinking' sections such as the cortex to deeper structures such as the thalamus and back again – areas known to be integral to consciousness.

Researchers often focus on different parts of the brain in relative isolation to work out how relevant they might be to any given task.

In this case, the team were interested in the precise way this tiny piece of brain tissue communicated with other areas during different states of activity, requiring a more holistic approach.

"We decided to go beyond the classical approach of recording from one area at a time," says neuroscientist Yuri Saalmann from the University of Wisconsin. "We recorded from multiple areas at the same time to see how the entire network behaves."

To get past the hurdles of using human subjects for such a task, the researchers used the macaque as their model, imaging the animals' brain structures before inserting specially tailored electrodes.

These electrodes were then used to monitor activity while the monkeys were awake, asleep, and under the effects of a strong anaesthetic.

The variations in electrical activity confirmed suspicions that the central lateral thalamus played a role in maintaining consciousness, at least in macaques. But it's one thing to find activity, and another to prove that a part of the brain is responsible for causing it.

To do this, the team used their remarkably fine electrodes to stimulate the small patch of neurons with incredible precision, tickling them into action while the macaques were knocked out with a good dose of ketamine.

"We found that when we stimulated this tiny little brain area, we could wake the animals up and reinstate all the neural activity that you'd normally see in the cortex during wakefulness," says Saalmann.

"They acted just as they would if they were awake."

Incredibly, once the stimulation stopped, the macaques drifted right back off to sleep within seconds. It was like the central lateral thalamus acted like a consciousness switch, directing mental traffic when active to give rise to awareness, and reinstating unconsciousness when it was quiet.

None of this helps much with the big questions around what consciousness is on a more philosophical level, and of course drawing conclusions about our own species based on non-human models is also problematic. But this is one more piece of evidence we can use to fine-tune a physical model of how a brain like ours switches between different states of function.

Given we're still unclear on how anaesthesia renders us oblivious – and, shockingly, even if it's always effective – it helps having precise knowledge of how the smallest bundles of nerves affect one another while we're slipping in and out of awareness.

As for people whose brains are permanently locked into a state of consciousness, having avenues for treatment would be a welcome product of studies like this one. Previous research has already provided strong evidence that stimulating the thalamus could help some comatose patients regain awareness.

In 2007, deep brain stimulation saw a patient who'd been minimally conscious for 6 years following a traumatic brain injury slowly regain movements and control over some body functions, including a small improvement in speech.

"There are many exciting implications for this work," says University of Wisconsin psychologist Michelle Redinbaugh.

"It's possible we may be able to use these kinds of deep-brain stimulating electrodes to bring people out of comas. Our findings may also be useful for developing new ways to monitor patients under clinical anaesthesia, to make sure they are safely unconscious." This research was published in *Neuron*.

https://wb.md/37vFe1W

'Different Flavors' of Gene Editing Moving Closer to Your Clinic

CRISPR editing has worked its way into the research world where it's been an engine of discovery and the clinical arena, where now there are clinical trials and testing.

Caron Jacobson, MD, MMSc; Catherine J. Wu, MD

This transcript has been edited for clarity.

Caron Jacobson, MD, MMSc: I'm Caron Jacobson, an assistant professor of medicine and the medical director of the Immune Effector Cell Therapy Program at the Dana-Farber Cancer Institute. Joining me today is Cathy Wu, a professor of medicine and the chief of the Division of Stem Cell Transplantation and Cellular Therapies at Dana-Farber.

Cathy, you chaired a session at the recent American Society of Hematology annual meeting that went into the breadth and depth of gene editing technology, thinking about the propelling of cellular therapies, and gene editing and genetic therapies for genetically inherited diseases. Can you give us some background about what gene editing is, how it's done, and what some of the methods are?

Catherine J. Wu, MD: From the very beginning, knowing that all of these diseases have at the basis some fundamental aberration in their DNA has always raised the question of whether we can correct it, and if so, how? Can we correct a condition, or can we replace something that should not be there?

Blood disorders in general, both malignant and nonmalignant, have been "model diseases" at some level because we've understood very well that alterations are mechanistically and fundamentally the reason why they are there.

Sickle cell anemia and alpha and beta thalassemia are examples. It has been super-exciting over the past decade to recognize that fundamental elements have the ability to track to specific regions in the DNA and guide the cutting or the replacement of certain nucleotide bases, making that correction or altering genes that might regulate expression of that region.

All of that technology now has come of age. We have these tools. One general category is CRISPR editing, and we've gone past proof of concept now to many different flavors of CRISPR editing that can happen both at the DNA level and the RNA level. It's worked its way into the research world where it's been an engine of discovery and the clinical arena, where now there are clinical trials and testing.

Jacobson: CRISPR, for example, was discovered in bacteria. It's a bacterial defense mechanism against other pathogens infecting the bacteria, which is amazing. So in trying to understand how bacteria evolve and protect themselves, we identified this new system that we can use in human cells.

Wu: It's a fascinating story about how some of the fundamental biology that we learned from plant biology has direct implications on how we can treat human disease.

Jacobson: It brings us back to things we learned in grade school biology. It all has implications for much bigger things later on.

Gene Editing Technologies

Jacobson: Let's talk about CRISPR and some of the other gene editing technologies. How are they being used in human therapeutic trials at this point?

Wu: Currently, studies are ongoing to address sickle cell disease. One approach is to change the expression of an element that controls expression of hemoglobin F. It's not correcting the sickle mutation, but rather altering the balance of hemoglobin so that the manifestations of sickle cell are not apparent anymore.

Jacobson: Is it a repeated therapy, then? Or are they targeting a stem cell in that case? How are they thinking about doing this in sickle cell?

Wu: I believe it's in the stem cells and then it's being engrafted. The other area is doing CRISPR editing in T cells for CAR T-cell therapy for treatment of cancer.

Jacobson: Most of the CAR T cells that we have seen in clinical development have been from the patient's own T cells. They don't have the risk of graft-versus-host disease because they are genetically similar or the same as the patient. But people are moving past that and wondering whether we can use healthy donor T cells.

But if we keep that T-cell receptor in, then those T cells can cause graft-versus-host disease. A number of companies are using different gene editing technologies to get out that T-cell receptor.

Wu: One of the challenges with CAR T cells is how to make the manufacture more streamlined so that we can address more patients. One direction is to create third-party T cells. And there, the editing is really helpful in trying to adjust that third-party T cell so that it can be used.

Jacobson: There are people using them to adjust autologous T cells as well because we're learning about different immunomodulatory genes that are affecting the efficacy of CAR T cells. People are using things like CRISPR to knock out genes to prevent T-cell exhaustion, for example.

Wu: Exactly. We're learning more and more about what ingredients are needed to be present for CAR T-cell therapy to work most effectively. That is at the level of the receptor itself. It's also at the level of modulatory molecules and at the level of expression of different features that can modulate the activity.

Jacobson: And even the trafficking, right? That may help us break into solid tumors, which is the sort of glass ceiling at this point. Different companies are sort of attached to different methods of gene editing, like TALEN, ARCUS, and CRISPR. Are any of the processes different in your mind?

Wu: It's a calculus, right? It depends on the payload size and the efficiency of delivery. It depends on what cell you are editing. All of those factors have to be taken into account, and there are pluses and minuses with each technology.

Gene Editing for Other Diseases

Jacobson: Is there a role for this in treating nonmalignant, noncancer, nonhematologic diseases? What are some of the ones that might be next on the horizon?

Wu: Diseases that are related to a mutation or alteration that perhaps also have some lineage-restricted expression are actually quite amendable. For example, one could think of cystic fibrosis or Huntington disease.

Those are all attractive opportunities in the future. We do need the first proof of concept. Again, the hemoglobinopathies have been a

great first step out the door, but we can expect much more in the future.

Jacobson: When thinking about something like cystic fibrosis or Huntington disease, is it the same kind of concept? These are diseases that, once embryonic development is complete, it's hard to intervene because some of the damage is done. Is there a way to intervene early enough?

Wu: Conceptually, yes. As in any of these diseases that affect younger patients, we have to learn more about the safety profile. A robust discussion is ongoing about whether off-target effects are there or not. It's still a young technology, especially in the realm of clinical trials, so we have to wait and learn.

Jacobson: It makes total sense. CRISPR made its way into the media when there were some reports of embryos being genetically altered using this technology and the concern for regulation. Any thoughts?

Wu: It's a brave new world. I think that was a very impulsive moment. We always have to keep the ramifications of these new technologies in mind.

Jacobson: And we have to think globally, right? Because what we can regulate in one country may not be the same as what is being regulated in another.

That was very informative. Is there anything else you want the audience to know about these gene editing technologies and their prominence?

Wu: It's exciting. Keep your ears and eyes open because it's a very optimistic time. We should be seeing lots of exciting developments in the time to come.

Caron Jacobson is an assistant professor of medicine and the medical director of the Immune Effector Cell Therapy Program at the Dana-Farber Cancer Institute.
Cathy Wu is a professor of medicine and chief of the Division of Stem Cell Transplantation and Cellular Therapies at Dana-Farber.

http://bit.ly/2UUKp8W

Flu season is getting weirder

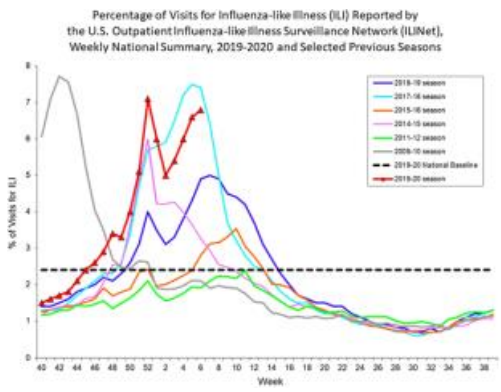
A second strain of flu is hitting the U.S mid-season.

By Rachael Rettner - Senior Writer 2 days ago

Coronavirus may be in the headlines, but it's still flu season, and a weird one at that — officials are seeing a new spike in flu activity as a second strain of flu hits on the heels of the first.

The 2019-2020 flu season already had an unusual start — in December and early January, the main strain of flu virus circulating was a type called influenza B, Live Science previously reported. Typically, influenza B does not cause as many cases as influenza A strains (H1N1 and H3N2) and tends to show up later in the flu season, not at the beginning. Indeed, the last time influenza B dominated flu activity in the U.S. was during the 1992-1993 flu season, according to the CDC.

But now, influenza A is making a comeback. In recent weeks, there has been a surge in activity of H1N1 in the U.S., according to data from the CDC. And that means even more people are going to the doctor for flu — the percentage of people visiting the doctor for flu-like illness increased from 6.6% of all visits last week to 6.8% of all visits this week, according to the CDC.



A graph comparing doctors' visits for flu during this season (red line, with arrows) with other recent seasons. An increase in H1N1 activity appears to be causing a second peak in flu season. **(Image credit: CDC)**

This type of "double-barreled" flu season is unusual, according to Healthline. Although something similar did happen last year, in which an initial wave of H1N1 activity was followed by a wave of

H3N2 activity. "We may well have, for the second year in a row — unprecedented — a double-barreled influenza season," Dr. William Schaffner, an infectious disease specialist at Vanderbilt University in Nashville, told WebMD.

So far this season, there have been an estimated 26 million illnesses, 250,000 hospitalizations and 14,000 deaths from flu, according to the CDC.

Although the number of hospitalizations are typical for this time of year, officials are seeing higher-than-typical hospitalization rates among children, Dr. Nancy Messonnier, director of the CDC's National Center for Immunization and Respiratory Diseases, said in a news conference today (Feb. 14).

As officials talk about the potential threat of coronavirus in the U.S., "I want to remind everyone of the very real threat of seasonal influenza," Messonnier said.

And with H1N1 activity increasing, it could mean flu season will drag out longer than usual, according to Healthline.

https://s.nikkei.com/38z1M3h

Common flu patients in Japan falls to 10-year low late-January

Authorities say coronavirus fears has improved personal hygiene, keeping disease at bay

Atsushi Teraoka and Yuko Nomura, Nikkei staff writers

TOKYO/NEW YORK -- Japan saw the lowest number of flu patients late-January in roughly 10 years, in part due to preventive measures against the Wuhan coronavirus that has spread throughout the world, authorities said.

The National Institute of Infectious Diseases said that 18 patients per clinic tested positive for common influenza at around 5,000 hospitals and clinics in Japan between Jan. 20 and Jan. 26. This was the lowest number since 6.46 were recorded in a week in 2010.

"The ministry started disclosing the coronavirus outbreak in China since the start of the year and telling people to take preventive measures, including washing hands and wearing surgical masks," said an official at the Ministry of Health, Labor and Welfare. "[The decline in the number of influenza patients] may be a reflection that personal hygiene has increased."

Japanese authorities have also been on high alert since early November when the number of flu patients per clinic exceeded one, a month earlier than usual. By late December, the number of patients hit a 10-year-high, the second-highest level reached in the month over the last 10 years.

There were fears then of an outbreak when children returned to school in January but between Dec. 30 and Jan. 5, the number of patients dropped 9.31 from the week before to 13.93, falling far below the warning level of 30.

Based on information provided by pharmacies, the overall number of flu patients in Japan is still declining. However, this is not the case for some prefectures in western Japan. As of late January, the number of flu patients per clinic was 33.83 in Kochi Prefecture and 30.56 in Miyazaki prefecture, breaching the dangerous level.

The picture in the U.S. is also bleaker.

According to data from Centers for Disease Control and Prevention, the number of patients infected with common flu increased by 4 million in just a week through Jan. 25. More than 19 million in America have fallen ill with the flu so far this winter, including 180,000 who were hospitalized. About 10,000 Americans have died, including 68 children.

The National Institute of Allergy and Infectious Diseases estimates that the 2019-2020 flu season will be one of the worst in decades. Some 45 million Americans came down with the flu and 61,000 people died in the 2017-2018 season. The flu season usually starts around October and lasts through May after peaking in February.

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

More than 80 clinical trials launch to test coronavirus treatments

As HIV drugs, stem cells and traditional Chinese medicines vie for a chance to prove their worth, the WHO attempts to bring order to the search.

Amy Maxmen

China has more than 80 running or pending clinical trials on potential treatments for COVID-19, the illness caused by a novel coronavirus that has thus far killed nearly 1,400 people and infected more than 48,000 across China.

New pharmaceutical drugs are listed beside thousand-year-old traditional therapies in a public registry of China's clinical trials, which is growing every day. There is no known cure, and doctors are eager to help those with the disease — but scientists caution that only carefully conducted trials will determine which measures work. Soumya Swaminathan, chief scientist at the World Health Organization, says that its teams have been taking stock of China's many trials, as well as drawing up a plan for a clinical trial protocol that could simultaneously be run by clinicians around the world. If China's trials, which include as many as 600 people each, are not designed with strict standards for study parameters, such as control groups, randomization and the measures of clinical outcomes, the efforts will be in vain. So the WHO is working with Chinese scientists to set standards from the start. For example, a person's stages of recovery or decline should be measured in the same way, regardless of the treatment being tested. "We can hopefully bring some sort of structure into the whole thing," Swaminathan explains.

The WHO's clinical-trial protocol is designed to be flexible and allow researchers around the world to pool their results over time. It will compare two or three therapies backed by scientific evidence, including an HIV-drug combination (lopinavir and ritonavir) and an experimental antiviral called remdesivir.

"Getting the clinical trials straight is a priority, since if we get information on what is working and not working, we can benefit patients now," Swaminathan says.

Best guesses

China has already begun trials on the drugs to be included in the WHO's master plan. The Chinese Clinical Trial Registry, a database of biomedical studies in China, lists these investigations among dozens of other controlled trials on existing therapies, experimental procedures and traditional medicines. These treatments have varying amounts of evidence backing their efficacy.

The two HIV drugs block enzymes that viruses need to replicate. In animal studies, they have reduced levels of the coronaviruses that cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)[1]. Remdesivir, a nucleotide analogue made by the biotechnology company Gilead in Foster City, California, has had some success against coronaviruses in animals, too[2]. In January, researchers reported that one person in the United States survived a COVID-19 infection after being treated with remdesivir[3]. During the first week of February, China launched two placebo-controlled trials on remdesivir, slated to include 760 people with COVID-19. The studies should be completed by the end of April, and remdesivir could be approved by Chinese authorities as early as May, says Shibo Jiang, a virologist at Fudan University in Shanghai. "But the epidemic might be gone by then," he says.

China has launched a few trials that test chloroquine, a malaria drug that killed off the new coronavirus (recently named SARS-CoV-2) in cell culture[4]. And researchers are studying whether steroids diminish inflammation in people with severe COVID-19, or cause harm. "It will be interesting to see these results," says Yazdan Yazdanpanah, an epidemiologist from France's national health

agency, INSERM, in Paris. Research clinicians around the world will need this information if the outbreak continues to spread, he adds.

Another study — a 300-person controlled trial — will test serum from COVID-19 survivors. The bare-bones strategy, based on the idea that the antibodies one person steadily builds up to fight a virus can rapidly help someone freshly infected to fight it off, has had modest success when used to treat other viruses in decades past[5].

Two stem-cell trials are also listed in China's registry. In one, a team at the First Affiliated Hospital of Zhejiang University will infuse 28 people with stem cells derived from menstrual blood, and compare results with those from people who did not receive the infusions. To date, there is minimal evidence indicating that stem cells clear coronavirus infections. Swaminathan says that the WHO cannot control what researchers do, but she says the WHO published guidance on the ethics of running trials amid outbreaks in 2016. And the organization will be posting a more accessible, brief report on the issue soon.

About 15 trials listed in China's registry expect to enroll a total of more than 2,000 people in studies on a variety of traditional Chinese medicines. One of the largest among them assesses shuanghuanglian, a Chinese herbal medicine that contains extracts from the dried fruit lianqiao (*Forsythiae Fructus*), which is purported to have been used for treating infections for more than 2,000 years. The trial has 400 participants, including a control group given standard care but not a placebo therapy.

The WHO is working with Chinese scientists to standardize the design of all the studies, including those on traditional medicines. Their efforts stem from a controversial move last year, in which the organization recognized traditional Chinese medicine in its compendium of diseases. Critics argued that the WHO's recognition amounted to endorsement, but Swaminathan disagrees. She says that the WHO's move helps the organization to codify medical terminology so that herbal remedies can be evaluated with the same rigour expected of pharmaceutical testing. "We want a scientific approach to testing traditional medicine," she says.

Moving forward

While these trials take off, researchers are searching for new drugs that would combat multiple coronaviruses, including those that haven't surfaced yet. A spike-shaped protein on the surface of the viruses underlying SARS, MERS and COVID-19 provides a tantalizing target. Already, Jiang and other research groups have found compounds and antibodies that glom onto that spike[6], which could prevent coronaviruses from invading human cells. But Emily Erbelding, a microbiologist at the US National Institutes of Health in Bethesda, Maryland, cautions that studies like these are at an early stage — and the compounds still need to be developed into drugs and tested in animals. To drive COVID-19 research, the NIH announced 'urgent award' grants in early February.

With many therapeutic possibilities and limited time, Jiang says the WHO should provide advice about which treatments to move forward, and which to ditch, as trials progress. And he hopes that research on better, broader therapies will be continued after the outbreak ends. "I worry this will be the same situation as during SARS," he says, "where the work starts, then stops."

doi: 10.1038/d41586-020-00444-3

References

1.Guangdi, L. & De Clercq, E. Nature Rev. Drug Discov. http://doi.org/10.1038/d41573-020-00016-0 (2020). Article Google Scholar

2.Sheahan, T. P. et al. Nature Commun. 11, 222 (2020). Article Google Scholar

3.Holshue, M. L. et al. New Engl. J. Med. http://doi.org/10.1056/NEJMoa2001191 (2020). Article Google Scholar

4.Wang, M. et al. Cell Res. https://doi.org/10.1038/s41422-020-0282-0 (2020). Article Google Scholar

5.Marano, G. et al. Blood Transfus. 14, 152–157 (2016). PubMed Article Google Scholar

6.Xia, S. et al. Science Advances 5, eaav4580 (2019). Google Scholar

http://bit.ly/31YAUaq

The verdict is in: Courtrooms seldom overrule bad science

Difficult for judges and juries to distinguish between solid research and so-called junk science

In television crime dramas, savvy lawyers are able to overcome improbable odds to win their cases by presenting seemingly iron-clad scientific evidence. In real-world courtrooms, however, the quality of scientific testimony can vary wildly, making it difficult for judges and juries to distinguish between solid research and so-called junk science.

This is true for all scientific disciplines, including psychological science, which plays an important role in assessing such critical pieces of testimony as eyewitness accounts, witness recall, and the psychological features of defendants and litigants.

A new, multiyear study published in Psychological Science in the Public Interest (PSPI), a journal of the Association for Psychological Science (APS), finds that only 40% of the psychological assessment tools used in courts have been favorably rated by experts. Even so, lawyers rarely challenge their conclusions, and when they do, only one third of those challenges are successful.

"Although courts are required to screen out junk science, legal challenges related to psychological-assessment evidence are rare," said Tess M.S. Neal of Arizona State University, one of the authors of the report. The other authors are Michael J. Saks of Arizona State University, Christopher Slobogin of Vanderbilt University Law School, David Faigman of the University of California Hastings School of Law, and Kurt F. Geisinger of the University of Nebraska-Lincoln.

"Although some psychological assessments used in court have strong scientific validity, many do not. Unfortunately, the courts do not appear to be calibrated to the strength of the psychological-assessment evidence," said Neal.

The new APS report examines more than 360 psychological assessment tools that have been used in legal cases, along with 372 legal cases from across all state and federal courts in the United States during the calendar years 2016, 2017, and 2018.

These findings are also presented at the 2020 American Association for the Advancement of Science (AAAS) meeting in Seattle.

Psychological scientists provide expert evidence in a variety of court proceedings, ranging from custody disputes to disability claims to criminal cases. In developing their expert evaluation of, for example, a defendant's competence to stand trial or a parent's fitness for child custody, they may use tools that measure personality, intelligence, mental health, social functioning, and other psychological features. A number of federal court decisions and rules give judges the latitude to gauge the admissibility of evidence, largely by evaluating its empirical validity and its acceptance within the scientific community.

For their review, Neal and her colleagues gathered results from 22 surveys of psychologists who serve as forensic experts in legal cases. They reviewed the 364 psychological assessment tools that the respondents reported having used in providing expert evidence. They found that nearly all of those tools have been subjected to scientific testing, but only about 67 percent are generally accepted by the psychological community at large. What's more, only 40% of the tools have generally favorable reviews in handbooks and other sources of information about psychological tests.

The scientists also found that legal challenges to the admission of assessment evidence are rare, occurring in only about 5% of cases they reviewed. And only a third of those challenges succeeded.

According to the report: "Attorneys rarely challenge psychological expert assessment evidence, and when they do, judges often fail to exercise the scrutiny required by law."

In an accompanying commentary, David DeMatteo, Sarah Fishel, and Aislinn Tansey, psychology and legal scholars at Drexel University, call for more research on whether trial court judges are functioning as effective gatekeepers for expert testimony. They point to studies indicating that many judges admit evidence from methodologically flawed studies and others that show attorneys and jurors lack the scientific literacy necessary to scrutinize scientific evidence. The Drexel scholars also called on forensic psychologists to ensure they use scientifically sound assessment tools when providing expert evaluations in legal settings.

http://bit.ly/2HtVBS7

A Common Cough Syrup Drug Just Passed Another Trial as Parkinson's Treatment

A drug used for 50 years as a cough medicine shows promise in treating Parkinson's disease.

Peter Dockrill

A drug first discovered over 50 years ago and long used as a medicine for coughs and respiratory illnesses appears to show promise in treating a very different kind of sickness: Parkinson's disease.

Ambroxol, an active ingredient in cough mixtures since the 1970s, has been investigated in recent years for its apparent potential to halt the progression of Parkinson's, and already this year, the drug has passed two important milestones that may bring us closer to a much-hoped-for treatment.

Last month, a multi-institutional team of researchers led by University College London (UCL) reported the results of a small Phase II clinical trial suggesting that ambroxol was safe and well-tolerated in human patients with Parkinson's disease, while hinting at possible neuroprotective effects that need to be examined further in subsequent trials.

Based on these outcomes, last week funding was announced to continue the next steps in evaluating ambroxol in a much larger cohort of people with Parkinson's, while also seeking to learn more about how individual patient genotypes may contribute to the disease.

"The ambroxol study is important because there are no treatments available for Parkinson's that slow, stop, or reverse [it]" says Simon Stott, deputy director of research at The Cure Parkinson's Trust, one of the bodies funding the research program.

"All of the current medications only deal with the symptoms of the condition – they do nothing to delay the progression of Parkinson's."

In the latest open-label trial, 17 patients with the disease were monitored while taking a daily dose of ambroxol over a six-month period.

In addition to checking that the therapy was safe at the dosage administered, the researchers also wanted to see whether ambroxol would cross the blood-brain barrier, and how the therapy might play out differently between patients either with or without particular mutations in a gene called GBA1 (the glucocerebrosidase gene).

Such GBA1 mutations are considered the most important genetic risk factor for Parkinson's, with the gene variant predisposing people to a greater risk of developing the disease at a younger age, and with a more rapid onset of symptoms.

Scientists think this happens because the mutation inhibits the natural release of glucocerebrosidase proteins (called GCase), which perform a clean-up process in the brain, preventing the harmful build-up of another kind of protein called alpha-synuclein,

viewed as a key culprit in the cognitive dysfunction we see in Parkinson's case.

"By increasing levels of GCase, ambroxol allows cells to remove waste, which would ideally keep cells healthier for longer and could slow down the progression of Parkinson's," says lead researcher and neurologist Tony Schapira from UCL.

Previous experiments with human cells and animal models suggests ambroxol can help increase GCase proteins while reducing alpha-synuclein levels, which is why the venerable cough syrup drug carries much hope as a potential treatment for Parkinson's disease.

We're not quite there yet, as the results from this new trial will need to be replicated in much larger tests, but the signs, the researchers say, are promising so far.

In the study, the experiment showed the drug successfully penetrated the blood-brain barrier, and increased GCase protein levels in participants' cerebrospinal fluid by about 35 percent, while being safe and well-tolerated by the patients taking the therapy, with no adverse effects reported.

The researchers did not find a difference between the responses of patients who do have the GBA1 mutation, and those who do not - another aspect of their results that will require further investigation.

Additionally, assessments of the patients' capacity for physical movement on the Movement Disorder Society Unified Parkinson Disease Rating Scale (MDS-UPDRS) saw the participants' movement scores slightly improve by a number of points on average, suggesting that the drug might have positive effects on motor control in Parkinson's disease patients.

That's a big 'might' though, as the researchers emphasise testing MDS-UPDRS scores was only one of many secondary outcomes in this small trial, which did not involve placebos being given to a control group.

Because of such limitations, the team says further testing is needed before drawing firmer conclusions about the effects of the drug on movement and other Parkinson's symptoms.

"However, the changes support the clinical impression that no substantial deleterious effect of ambroxol was observed among participants taking ambroxol, including any adverse effect on the motor features of their Parkinson's disease," the authors note.

The good news is ambroxol's next stage of evaluation – a double-blinded, placebo-controlled Phase III clinical trial, called PD-Frontline – is now accepting registrations for patients living in the UK, and this bigger, longer trial should tell us even more about the drug's viability as a potential treatment.

"This study provides us with the 'proof of concept' that we can raise levels of GCase in humans with ambroxol, and that the drug is safe and well tolerated in people with Parkinson's," says Stott.

"If further study shows ambroxol can improve the health and function of cells, it may result in slower disease progression for people with Parkinson's."

The findings are reported in *JAMA Neurology*, and you can find out more about the ambroxol trials here and here.