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Zika Virus Test Is 'Weeks, Not Years' Away, W.H.O. Says

Weeks, not years from developing a test for the Zika virus, but large-scale clinical trials for a potential vaccine are at least 18 months away

By SEWELL CHAN Donald G. McNeil Jr.

LONDON — Scientists are "weeks, not years" from developing a test for the fast-spreading Zika virus, but large-scale clinical trials for a potential vaccine are at least 18 months away, the World Health Organization announced on Friday.

The W.H.O. declared Zika a global public health emergency on Feb. 1, only the fourth time it had raised such an alert. The Zika virus — a mosquito-transmitted infection related to dengue, yellow fever and West Nile virus — has spread through Latin America. It was first detected in Brazil in May, and as many as four million people worldwide could be infected by year's end, the health organization has said.

The main public health concern is a suspected link between the virus and two neurological disorders: microcephaly, which is associated with unusually small heads and, often, brain damage in infants; and Guillain-Barré syndrome, in which a person's immune system attacks part of the nervous system, leaving some almost completely paralyzed for weeks.

Scientists are close to confirming those links, Dr. Marie-Paule Kieny, the W.H.O. assistant director general for health systems and innovation, said at a news conference in Geneva.

There is no reliable test yet for Zika. Ten companies are poised to provide tests that try either to use a molecular technique to detect the virus's presence in blood or to confirm Zika infection by measuring the levels of antibodies in a patient who has been exposed to the virus. Another 10 companies are trying to develop tests using similar approaches.

"It is important to point out, however, that none of these tests have been independently validated and none have regulatory approval," Dr. Kieny said. She added, however, that "we are talking weeks, not years," for the first commercial and independently validated tests to become available.

There is no vaccine for Zika, although a race to develop one is underway. Dr. Kieny pointed to two particularly promising efforts: one by the National Institute of Allergy and Infectious Diseases, in Bethesda, Md., and the other by Bharat Biotech, a pharmaceutical company in Hyderabad, India. "In spite of this encouraging landscape, vaccines are at least 18 months away from large-scale trials," she said.

Most people who contract the Zika virus experience symptoms like fever, rash, joint pain and red eyes, and there is no lasting harm.

But the risk of birth defects is so serious that El Salvador advised women to avoid becoming pregnant until 2018. The Centers for Disease Control and Prevention has urged pregnant women to postpone traveling to more than 20 countries in Latin America and the Caribbean, as well as Puerto Rico, until the public health emergency is brought under control.

The W.H.O. on Friday advised pregnant women to consider delaying travel to any areas where the Zika virus is being transmitted. At the same time, the agency said it was "not recommending any travel or trade restrictions related to Zika virus disease."

Its advice now brings it in line with public health authorities in the United States, England, Canada and other major industrialized nations who have suggested that pregnant women avoid areas where the mosquito-borne virus is circulating.

Acknowledging that there are at least two cases where sexual transmission of the virus was suspected, the W.H.O. also advised women and their partners who have visited Zika-infested areas to practice safe sex "including the correct and consistent use of condoms."

Although the virus was discovered in the Zika forest of Uganda in 1947, it did not come to prominence outside Africa and Asia until 2007, after an outbreak in the South Pacific.

Dr. Kieny acknowledged that "relatively poor knowledge of the Zika virus" had hampered the response to the outbreak in Latin America.

Recently, she said, scientists reported the case of a European woman who became pregnant while living in Brazil and who had an abortion when it was clear the child would have microcephaly. Tests confirmed the presence of the Zika virus in the fetus's brain. "Can you treat a fetus in the womb, in the mother, and try to eliminate the virus?" Dr. Kieny asked. "At which stage can you do it? These are all questions that are not resolved at the moment."

Dr. Kieny noted that even the relationship between the Zika virus and microcephaly was not yet clear. In Colombia, scientists are monitoring a group of pregnant women who have the virus.

"In a few weeks or months, we will find out how many of these women deliver a child with microcephaly," she said.

On Friday, Thomas Bach, the president of the International Olympic Committee, said no countries had announced plans to pull out of the Summer Games in Rio de Janeiro over concerns about the virus.

Mr. Bach, speaking before the opening ceremony of the Winter Youth Olympics in Lillehammer, Norway, said on Friday that he had "full confidence" in the steps taken by the Brazilian government and global health organizations.

"We are taking the situation very seriously," he added.

http://www.eurekalert.org/pub_releases/2016-02/uop-nsh021216.php

New study highlights effectiveness of a herpesvirus CMV-based vaccine against Ebola

This study represents a crucial step in the translation of herpesvirus-based Ebola virus vaccines into humans and other great apes

As the latest in a series of studies, researchers at Plymouth University, National Institutes of Health and University of California, Riverside, have shown the ability of a vaccine vector based on a common herpesvirus called cytomegalovirus (CMV) expressing Ebola virus glycoprotein (GP), to provide protection against Ebola virus in the experimental rhesus macaque, non-human primate (NHP) model. Demonstration of protection in the NHP model is regarded as a critical step before translation of Ebola virus vaccines into humans and other great apes.

The study is published today, Monday 15th February, in the online journal from Nature publishing, *Scientific Reports*.

In addition to establishing the potential for CMV-based vaccines against Ebola virus, these results are exciting from the potential insight they give into the mechanism of protection. Herpesvirus-based vaccines can theoretically be made to produce their targeted protein (in this case, Ebola virus GP) at different times following vaccination. The current CMV vaccine was designed to make the Ebola virus GP at later times. This resulted in the surprising production of high levels of antibodies against Ebola virus with no detectable Ebola-specific T cells. This immunological shift towards antibodies has never been seen before for such primate herpesvirus-based vaccines, where responses are always associated with large T cell responses and poor to no antibodies.

"This finding was complete serendipity," says Dr Michael Jarvis who is leading the project at Plymouth University. "Although we will definitely need to explore this finding further, it suggests that we may be able to bias immunity towards either antibodies or T cells based on the time of target antigen production. This is exciting not just for Ebola, but for vaccination against other infectious as well as non-infectious diseases".

A largely untold story is the devastating effect Ebola virus is having on wild great ape populations in Africa. Although the present study administered the vaccine by direct inoculation, a CMV-based vaccine that can spread from animal to animal may be one approach to protect such inaccessible wild animal populations that are not amenable to vaccination by conventional approaches. The current study is a step forward, not only for conventional Ebola virus vaccines for use in humans, but also in the development of such 'self-disseminating vaccines' to target Ebola in great apes, and other emerging infectious diseases in their wild animal host before they fully establish themselves in humans.

Link to paper - http://www.nature.com/articles/srep21674 DOI: 10.1038/srep21674

http://www.eurekalert.org/pub_releases/2016-02/tjnj-ppi021116.php

Proton pump inhibitors may be associated with increased risk of dementia

Proton pump inhibitors, may be associated with increased risk of dementia

The use of proton pump inhibitors, the popular medications used to treat gastroesophageal reflux and peptic ulcers, may be associated with an increased risk of dementia in a study using data from a large German health insurer, according to an article published online by JAMA Neurology.

The use of proton pump inhibitors (PPIs) has increased among older patients and PPIs are among the most frequently used classes of drugs.

Britta Haenisch, Ph.D., of the German Center for Neurodegenerative Diseases, Bonn, Germany, and coauthors examined the association between the use of PPIs and the risk of dementia using data from 2004 to 2011 on inpatient and outpatient diagnoses and drug prescriptions.

Regular PPI use was at least one PPI prescription in each quarter of an 18-month interval.

The study population included 218,493 individuals 75 or older before 144,814 individuals were excluded, leaving 73,679 individuals included in the final analysis.

The authors identified 29,510 patients who developed dementia during the study period.

Regular users of PPIs (2,950 patients, mostly female and average age nearly 84) had a 44 percent increased risk of dementia compared with those (70,729 patients, mostly female and average age 83) not receiving PPI medication, according to the results.

Limitations to the study include the authors only being able to integrate some other risk factors for dementia into the analysis from the data.

"The present study can only provide a statistical association between PPI use and risk of dementia. The possible underlying causal biological mechanism has to be explored in future studies. To evaluate and establish direct cause and effect relationships between PPI use and incident dementia in the elderly, randomized, prospective clinical trials are needed," the study concludes.

JAMA Neurol. Published online Feb. 15, 2016. doi:10.1001/jamaneurol.2015.4791. Available pre-embargo to the media at http://media.jamanetwork.com.

Editor's Note: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Editorial: Do Proton Pump Inhibitors Increase the Risk of Dementia

"Gomm et al have provided an important and interesting challenge to evaluate the possible association of the use of PPIs and the risk of dementia. This is a very important issue given the very high prevalence of pharmacological drugs' long-term use in elderly populations that have a very high risk of dementia," writes Lewis H. Kuller, M.D., Dr.PH., of the University of Pittsburgh, in a related editorial.

JAMA Neurol. Published online Feb. 15, 2016. doi:10.1001/jamaneurol.2015.4931. Available pre-embargo to the media at http://media.jamanetwork.com.

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Sweet discovery in leafy greens holds key to gut health

Critical discovery about how bacteria feed on a sugar molecule found in leafy green vegetables could explain how 'good' bacteria protect our gut

A critical discovery about how bacteria feed on an unusual sugar molecule found in leafy green vegetables could hold the key to explaining how 'good' bacteria protect our gut and promote health.

The finding suggests that leafy greens are essential for feeding good gut bacteria, limiting the ability of bad bacteria to colonise the gut by shutting them out of the prime 'real estate'.

Researchers from Melbourne and the UK identified a previously unknown enzyme used by bacteria, fungi and other organisms to feed on the unusual but abundant sugar sulfoquinovose - SQ for short - found in green vegetables. Each year, leafy green vegetables - such as spinach - produce the sugar on an enormous scale globally, comparable to the world's total annual iron ore production.

The research, published today in the journal Nature Chemical Biology, was led by Dr Ethan Goddard-Borger from the Walter and Eliza Hall Institute, Professor Spencer Williams from the Bio21 Institute and University of Melbourne, and Professor Gideon Davies from the University of York, UK.

Dr Goddard-Borger said the discovery could be exploited to cultivate the growth of 'good' gut bacteria. "Every time we eat leafy green vegetables we consume significant amounts of SQ sugars, which are used as an energy source by good gut bacteria," he said.

"Bacteria in the gut, such as crucial protective strains of E. coli, use SQ as a source of energy. E. coli provides a protective barrier that prevents growth and colonisation by bad bacteria, because the good bugs are taking up all the habitable real estate," Dr Goddard-Borger said.

"E. coli is a key bacterial coloniser needed by our gut. We speculate that consumption of this specific molecule within leafy greens will prove to be an important factor in improving and maintaining healthy gut bacteria and good digestive health."

Professor Williams said the team had revealed how bacteria extract the sugar from plants in order to fuel their growth. "We discovered the enzyme YihQ, which is used by bacteria to absorb and metabolise these sulfur-containing sugars as food," he said.

"Sulfur is critical for building proteins, the essential components of all living organisms. SQ is the only sugar molecule which contains sulfur, and 'digestion' of the molecule by bacteria releases sulfur into the environment, where it re-enters the global 'sulfur cycle' to be reused by other organisms."

Professor Williams said that the pathway was unusual, but abundant in biological organisms. "This work answers a 50-year mystery that has surrounded how sulfur - an element essential for life on Earth - was used and recycled by living organisms," he said. "What is remarkable is that the YihQ enzyme was hiding in plain sight and is produced by the humble bacterium E. coli, present in nearly every biologist's laboratory."

The discovery also provides crucial insights that may one day be exploited to develop an entirely new class of antibiotics, Dr Goddard-Borger said. "New antimicrobial strategies are desperately needed as more and more bacteria acquire resistance to existing classes of antibiotics."

"We think it will be possible to use these widespread enzymes to enable highly specific delivery of antibiotics to harmful forms of E. coli and other pathogens, such as Salmonella, responsible for food poisoning, while leaving the good gut bacteria untouched."

The research was supported by the National Health and Medical Research Council, Australian Research Council, Ramaciotti Foundation, veski, the Victorian Government Operational Infrastructure Support Program, UK Biotechnology and Biological Sciences Research Council and the European Research Council.

http://www.eurekalert.org/pub_releases/2016-02/uu-sdn021216.php

Scientists discover new microbes that thrive deep in the earth

They live several kilometers under the surface of the earth, need no light or oxygen and can only be seen in a microscope.

By sequencing genomes of a newly discovered group of microbes, the Hadesarchaea, an international team of researchers have found out how these microorganisms make a living in the deep subsurface biosphere of our planet.

Microorganisms that live below the surface of the earth remain one of the last great areas of exploration. Organisms that live there have not been grow in the laboratory and therefore their lifestyles are unknown. An international team led by microbiologists Brett Baker, Assistant Professor at The University of Texas and

Thijs Ettema, senior lecturer at Uppsala University, along with scientists from UNC Chapel Hill and the University of Bremen, have discovered how microorganisms, first discovered in a South African gold mine at a depth of two miles, are able to make a living in the absence of oxygen and light. The study is published in Nature Microbiology.

Baker and Ettema found these microbes in vastly different aquatic and terrestrial environments; the deep mud of a temperate estuary in North Carolina and underneath hot springs at Yellowstone National Park.

- This new class of microbes are specialized for survival beneath the surface, so we called them "Hadesarchaea", after the ancient Greek god of the underworld, says Brett Baker, lead author of the study.

As its name suggests, the Hadesarchaea belong to a relatively unknown group of microorganisms, the archaea. Like bacteria, archaea are single-celled and microscopically small, but from an evolutionary perspective, they differ more from each other than a human does from a tree.

Archaea were discovered only some 40 years ago, by the acclaimed American biologist Carl Woese. To date, archaea remain poorly studied in comparison to bacteria and more complex life forms, such as animals and plants.

- The discovery of the Hadesarchaea will help us increase our understanding of the biology and lifestyle of archaea that thrive in the deep biosphere, says Thijs Ettema.

In order to understand these elusive organisms, Baker and Ettema sequenced the genomes of several Hadesarchaea. They were able to determine how these microbes should be classified and what physiologies they use to survive under these extreme conditions. Hadesarchaea have the ability to live in areas devoid of oxygen and the scientists suggest that they are able to survive there by using carbon monoxide to gain energy. Interestingly, the chemical pathways the Hadesarchaea cells use to metabolize carbon monoxide are unique to what has been seen before.

“Before this essentially nothing was known about the Hadesarchaea's ecological role and what makes them so prominent throughout the world. The new discovery expands our knowledge of how these organisms may have adapted to the extreme conditions of the deep biosphere,” says Jimmy Saw, researcher at Uppsala University and co-author of the paper.

The discovery is published in the new journal, Nature Microbiology, released by Nature Publishing Group.

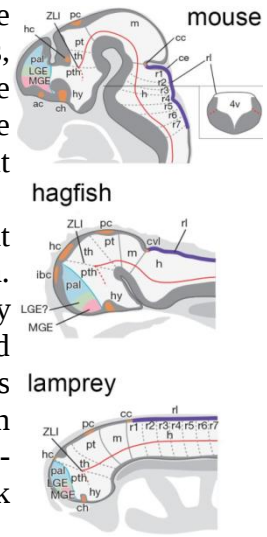
Baker et al (2016) Genomic inference of the metabolism of cosmopolitan subsurface Archaea, Hadesarchaea, Nature Microbiology, DOI: 10.1038/NMICROBIOL.2016.2

http://www.eurekalert.org/pub_releases/2016-02/r-jfb021416.php

Jawless fish brains more similar to ours than previously thought

Complex divisions in the vertebrate brain first appeared before the evolution of jaws, more than 500 million years ago

Researchers at the RIKEN Evolutionary Morphology laboratory and other institutions in Japan have shown that complex divisions in the vertebrate brain first appeared before the evolution of jaws, more than 500 million years ago. Published in Nature, the study shows that two elements of brain genoarchitecture thought to be unique to jawed vertebrates are actually present in two jawless fish--the hagfish and lamprey.



Most living vertebrate species have jaws, a development thought to have occurred sometime in the Paleozoic era. Jawed vertebrates--including humans--share many developmental characteristics that have remained unchanged for millennia. The brain's basic developmental plan was thought by many scientists to have reached completion in jawed vertebrates because the brains of lampreys and hagfish--the only jawless fish that remain alive today--seem to lack two key domains.

Schematic Drawings of Embryonic Mouse, Hagfish, and Lamprey Brains

(top) The embryonic gnathostome brain based on a mouse embryo (day 12.5). Inset shows a transverse section at the level of the hindbrain showing the position of the rhombic lip. (middle and bottom) Embryonic hagfish and lamprey brains (stages 53 and 26, respectively) as revealed by the present study. rl, rhombic lip; MGE, medial ganglionic eminence. **RIKEN**

Recent evidence brought this into question, and as the only lab in the world able to study hagfish embryos, the RIKEN team led by Shigeru Kuratani was in a unique position to use techniques derived from developmental biology to tackle this critical issue.

The vertebrate brain develops from a neural tube that is divided into sections. The development of each section is very specific, and is controlled by the expression of particular genes at very precise times and locations. These gene-expression patterns--or the genoarchitecture--are highly conserved in jawed vertebrates. Lampreys--a type of jawless fish--appear to lack two brain regions common to jawed vertebrates--the cerebellum and a region called the medial ganglionic eminence, or MGE, from which the pallidum and cortical interneurons originate.

In jawed vertebrates, the MGE develops from a forward section of the neural tube that expresses Nkx2.1 and Hedgehog genes, and the cerebellum develops from a

region called the rhombic lip that expresses Pax6. In hagfish, the team found a region in the correct location that expresses both Nkx2.1 and a Hedgehog gene that was identified for the first time in this study. This indicated that the hagfish brain does indeed have an MGE region. Similarly, although hagfish do not have a true cerebellum, the team was able to identify a clear rhombic lip region that expresses Pax6.

At this point, the team was confident that the brains of both hagfish and jawed vertebrates contain similar developmental patterning.

"The problem was that lampreys had not yet been shown to have a similar patterning," explains Kuratani. "The shared pattern of brain development between hagfish and jawed vertebrates raised the possibility that the apparently primitive brain of the lamprey is simply a lamprey-unique characteristic."

Additionally, without an answer to the lamprey question, these shared patterns could be interpreted as changes that independently occurred in each lineage--jawed and jawless--after they split from each other.

To address the issue, the team reinvestigated the lamprey, and discovered several new Nkx2.1 genes expressed in the correct location, but did not find any Hedgehog expression, indicating that the lamprey MGE is slightly different from that found in jawed vertebrates. Then the team looked at lamprey larvae and found a rhombic-lip like region that expresses Pax6B, albeit slightly differently than in hagfish or jawed vertebrates.

"We found that jawed-vertebrate patterning was more similar to the hagfish than to lampreys," says Kuratani, "and the evidence indicates that this is likely due to secondary evolutionary changes in lamprey evolution, rather than changes unique to jawed vertebrates."

"With these new findings from hagfish and lampreys, we have shown that both of the extant jawless-fish species have a rhombic lip and an MGE --the sources of the cerebellum, pallidum, and GABAergic interneurons in jawed vertebrates. This firmly places the development of these genoarchitectural patterns back to a common ancestor shared by jawless and jawed vertebrates."

http://bit.ly/218BoDU

Take exams early in the morning to get a higher score

It's so unfair! Here's a good excuse for people who have done badly in an afternoon exam – the later in the day you sit a test, the lower your score is likely to be.

By Sam Wong

Hans Henrik Sievertsen from the Danish National Centre for Social Research in Copenhagen and his team have looked at 2 million standardised test scores from Danish children aged between 8 and 15. Starting from 8 am, for every hour later that a test was taken, scores declined by an amount equivalent to the effect of missing 10 days of school. Children who were performing worse at school seemed most affected by the time they sat the exam. The team thinks the difference is down to cognitive fatigue. If a test was taken just after a 20 or 30 minute break, scores improved by as much as if the children had taken it 2 hours earlier.

How children's mental resources get recharged is unclear. "I'm very interested in what's going on in these breaks," says Sievertsen. "Is it because they have something to eat, or fresh air? If we know that, we can maybe speculate why some children are more affected than others."

Time is against you

Sievertsen doesn't advocate changing school schedules. Instead, he suggests that tests should always be taken at the same time in different schools, possibly after a break. "Another solution would be to calculate ways to adjust test scores according to test time and whether you had a break," he says.

In the US, some national tests used to select college applications start at 8 am. But school isn't all about exams. Many studies have found that teenagers tend to benefit from a school day that starts later, and some countries are debating whether school days should start later to suit teenagers' body clocks.

"The medical sleep researchers who have been specifically studying teenagers around the world have found that teens tend to become more alert as the day progresses," says Kyla Wahlstrom, at the University of Minnesota in Minneapolis. However, this latest study didn't detect any differences at different ages.

The hour of the day doesn't just influence the performance of children. Judges are much more likely to offer a favourable ruling at the start of the day or just after lunch, and doctors are more likely to prescribe antibiotics for respiratory infections as the day wears on.

Journal reference: PNAS, DOI: 10.1073/pnas.1516947113

http://nyti.ms/1U7OwqO

A New Culprit in Lyme Disease

Mosquitoes may be receiving all the attention amid the Zika virus epidemic, but they are hardly the only disease vectors to worry about.

By KAREN WEINTRAUB FEB. 15, 2016

Researchers at the Mayo Clinic in Rochester, Minn., have discovered a new species of tick-borne bacteria that causes Lyme disease.

The new species, provisionally named Borrelia mayonii, after the clinic, has been found only in the upper Midwest but may be present elsewhere. Six patients with the infection were identified by the researchers. The patients had symptoms similar to, but not precisely the same as, those caused by Borrelia burgdorferi, until now the only species known to cause Lyme disease in North America.

Lyme disease was diagnosed in the patients with available tests**.** But available diagnostic screens may be missing others infected with the newly discovered bacteria, the scientists acknowledged.

Dr. Bobbi Pritt, the medical director of the microbiology laboratory at the Mayo Clinic, where the new strain was first detected, recommended that patients with exposure to ticks in Minnesota and Wisconsin receive antibody and polymerase chain reaction testing to detect B. mayonii if they are concerned about Lyme infection but do not have the telltale bull's-eye rash.

Because the symptoms vary slightly from those normally seen in B. burgdorferi infection, doctors may not even think to test for Lyme disease, she said.

Only one of the six patients had the bull's-eye rash that is Lyme's signature, present in 70 percent to 80 percent of reported cases. Three patients had a rash that was more spread out, Dr. Pritt said.

The new strain apparently adds nausea and vomiting to the list of typical Lyme symptoms, which include fever, headache and neck pain. B. mayonii patients also had a higher-than-expected concentration of bacteria in their blood.

Fortunately, the antibiotic treatment normally used to treat Lyme disease appears to be effective against B. mayonii, Dr. Pritt said.

In the summer of 2013, a technician in Dr. Pritt's lab noticed some unusual results from a genetic screen of a patient's bacterial infection. The test suggested Lyme disease, but a closer analysis found a new species of bacteria causing the condition.

It is not yet clear where B. mayonii came from, Dr. Pritt said, though it does not seem to have recently diverged from B. burgdorferi. It may be that the species has always been present, but was picked up only with better detection tools, or that the new bacteria are increasing for some reason. "We hope to be able to answer that with more studies," Dr. Pritt said.

In Europe, Lyme disease is caused by multiple pathogenic species of Borrelia, said Per-Eric Lindgren, a professor of medical microbiology at Linkoping University in Sweden.

Borrelia mayonii in a laboratory dish. **Mayo Foundation for Medical Education and Research**

While scientists were already aware that there were several possible causes of Lyme disease, the discovery of the first Borrelia species in more than a decade is "really exciting and interesting," said Dr. Lindgren, who wrote a commentary accompanying the report in The Lancet Infectious Diseases.

Although the six patients at the Mayo Clinic received the diagnoses with typical tests, he said, "normally you're only able to detect what you are looking for." Other cases are probably being missed, Dr. Lindgren added: "It's very likely you could make the diagnostic tools better."

Field studies in Minnesota have shown that one-third to one-half of adult ticks, and one in five young ticks, called nymphs, carry B. burgdorferi, the previously known bacteria. Only 1 percent to 4 percent carry B. mayonii, said Dave Neitzel, the supervisor of the vector-borne disease unit at the Minnesota Department of Health.

"This is just another great reason to protect yourself against ticks," he said.

To protect against tick-borne illnesses, people should wear repellents and check their skin for black specks after spending time outdoors, particularly in wooded areas and during the late spring and early summer months when nymphs are present. The nymphs are smaller than the adults and easier to miss on the skin, Mr. Neitzel said. If a tick is removed within the first 24 to 48 hours, it is unlikely to cause disease. "The sooner you get that tick off of your body, the better," he said. "You don't have to get too many ticks on you before you find one that's infected with something."

Dr. Pritt said she was now far more cautious outdoors.

"If you've ever looked at an idyllic picture of a beautiful meadow with flowers — I look at it and think about all the ticks in there," she said.

http://www.bbc.com/news/health-35581454

Doctors 3D-print 'living' body parts

Custom-made, living body parts have been 3D-printed in a significant advance for regenerative medicine, say scientists.

By James Gallagher Health editor, BBC News website

The sections of bone, muscle and cartilage all functioned normally when implanted into animals. The breakthrough, published in Nature Biotechnology, raises the hope of using living tissues to repair the body. Experts described the technology, developed in the US, as a "goose that really does lay golden eggs".

The idea of placing individual human cells in a precise pattern to replace a damaged jaw, missing ear or scarred heart muscle holds much promise.

But the field has been limited by the huge challenge of keeping the cells alive - they become starved of oxygen and nutrients in tissues thicker than 0.2 millimetres.

Sponge

The team at Wake Forest Baptist Medical Centre developed a new technique that 3D-prints a tissue riddled with micro-channels, rather like a sponge, to allow nutrients to penetrate the tissue.

The Integrated Tissue and Organ Printing System - or Itop - combines a bio-degradeable plastic which gives the structure and a water-based gel which contains the cells and encourages them to grow.

When the structures were implanted into animals, the plastic broke down as it was replaced by a natural, structural "matrix" of proteins produced by the cells.

Meanwhile, blood vessels and nerves grew into the implants.

Prof Anthony Atala, the lead researcher, said tissues could now be printed on a human scale.

While the implants have the same strength as human tissues, the researchers are now waiting to see how durable they are.

But Prof Atala said 3D printing was opening new doors for medicine.

He told the BBC News website: "Let's say a patient presented with an injury to their jaw bone and there's a segment missing.

"We'd bring the patient in, do the imaging and then we would take the imaging data and transfer it through our software to drive the printer to create a piece of jawbone that would fit precisely in the patient."

Similar techniques in which the biodegradable scaffolding is built first and then soaked in cells are already being used in patients.

Women were given lab-grown vaginas at the Wake Forest centre two years ago, but the range of treatments is again limited by keeping the cells alive.

Prof Atala added: "In this study we printed a wide range of tissue strengths - from muscles as a soft tissue to cartilage and bone as a hard tissue showing a whole range of tissue strengths is possible.

"The hope is to continue work on these technologies to target other humans tissues as well."And ultimately they aim to print directly into a patient.

'Golden goose'

Prof Martin Birchall, a surgeon at University College London, said the results were "striking".

He told the BBC: "The prospect of printing human tissues and organs for implantation has been a real one for some time, but I confess I did not expect to see such rapid progress.

"They have managed to create what appears to be the goose that really does lay golden eggs!"

He cautioned there was still more research to be done before the printer could be used in patients.

But he concluded: "Given the scale of this breakthrough, progress in other fields, the resources available to the researchers at Wake Forest and the imperatives for human health, I think it will be less than a decade before surgeons like me are trialling customised printed organs and tissues. I can't wait!"

http://www.eurekalert.org/pub_releases/2016-02/jhm-mpa021516.php

Mind-controlled prosthetic arm moves individual 'fingers'

Physicians and biomedical engineers from Johns Hopkins report what they believe is the first successful effort to wiggle fingers individually and independently of each other using a mind-controlled artificial "arm" to control the movement.

The proof-of-concept feat, described online this week in the *Journal of Neural Engineering*, represents a potential advance in technologies to restore refined hand function to those who have lost arms to injury or disease, the researchers say.

The young man on whom the experiment was performed was not missing an arm or hand, but he was outfitted with a device that essentially took advantage of a brain-mapping procedure to bypass control of his own arm and hand.

"We believe this is the first time a person using a mind-controlled prosthesis has immediately performed individual digit movements without extensive training," says senior author Nathan Crone, M.D., professor of neurology at the Johns Hopkins University School of Medicine. "This technology goes beyond available prostheses, in which the artificial digits, or fingers, moved as a single unit to make a grabbing motion, like one used to grip a tennis ball."

For the experiment, the research team recruited a young man with epilepsy already scheduled to undergo brain mapping at The Johns Hopkins Hospital's Epilepsy Monitoring Unit to pinpoint the origin of his seizures.

While brain recordings were made using electrodes surgically implanted for clinical reasons, the signals also control a modular prosthetic limb developed by the Johns Hopkins University Applied Physics Laboratory.

Prior to connecting the prosthesis, the researchers mapped and tracked the specific parts of the subject's brain responsible for moving each finger, then programmed the prosthesis to move the corresponding finger.

First, the patient's neurosurgeon placed an array of 128 electrode sensors -- all on a single rectangular sheet of film the size of a credit card -- on the part of the man's brain that normally controls hand and arm movements. Each sensor measured a circle of brain tissue 1 millimeter in diameter.

The computer program the Johns Hopkins team developed had the man move individual fingers on command and recorded which parts of the brain the "lit up" when each sensor detected an electric signal.

In addition to collecting data on the parts of brain involved in motor movement, the researchers measured electrical brain activity involved in tactile sensation. To do this, the subject was outfitted with a glove with small, vibrating buzzers in the fingertips, which went off individually in each finger. The researchers measured the resulting electrical activity in the brain for each finger connection.

After the motor and sensory data were collected, the researchers programmed the prosthetic arm to move corresponding fingers based on which part of the brain was active. The researchers turned on the prosthetic arm, which was wired to the patient through the brain electrodes, and asked the subject to "think" about individually moving thumb, index, middle, ring and pinkie fingers. The electrical activity generated in the brain moved the fingers.

"The electrodes used to measure brain activity in this study gave us better resolution of a large region of cortex than anything we've used before and allowed for more precise spatial mapping in the brain," says Guy Hotson, graduate student and lead author of the study. "This precision is what allowed us to separate the control of individual fingers."

Initially, the mind-controlled limb had an accuracy of 76 percent. Once the researchers coupled the ring and pinkie fingers together, the accuracy increased to 88 percent.

"The part of the brain that controls the pinkie and ring fingers overlaps, and most people move the two fingers together," says Crone. "It makes sense that coupling these two fingers improved the accuracy."

The researchers note there was no pre-training required for the subject to gain this level of control, and the entire experiment took less than two hours.

Crone cautions that application of this technology to those actually missing limbs is still some years off and will be costly, requiring extensive mapping and computer programming. According to the Amputee Coalition, over 100,000 people living in the U.S. have amputated hands or arms, and most could potentially benefit from such technology.

Additional authors on the study include David McMullen, Matthew Fifer, William Anderson and Nitish Thakor of Johns Hopkins Medicine and Matthew Johannes, Kapil Katyal, Matthew Para, Robert Armiger and Brock Wester of the Johns Hopkins Applied Physics Laboratory.

This study was funded by the National Institute of Neurological Disorders and Stroke (grant number 1R01NS088606-01).

http://bit.ly/1Qr8irm

These Glass Discs Can Store Data for Billions of Years

"Five-dimensional" data discs could be the future of information storage)

By Danny Lewis smithsonian.com February 18, 2016

For all of humanity's achievements, one of the most important is how we communicate and pass down knowledge. From clay tablets to hard drives, long-term data storage ensures the flow of information from generation to generation. Now, a new data format could preserve that information for a virtually unlimited amount of time by encoding it into glass discs about the size of a coin.

The idea for this method, known as "five-dimensional storage," has floated around for a few years since scientists at the United Kingdom's University of Southampton first demonstrated it in a 2013 paper. Back then, they were only able to code a single 300 kilobyte text file into a glass disc. Three years later, the same scientists say that they believe they have refined the technique to the point where they can code about 360 terabytes of data onto a single disc.

What's more, at room temperature the discs have a nearly unlimited lifespan. At high temperatures, 374 degrees Fahrenheit to be exact, the disc's creators estimate the lifespan to be 13.8 billion years—about as long as the universe has existed, Doug Bolton writes for *The Independent*.

"We can encode anything," Aabid Patel, a postgraduate student who worked on the project tells James Vincent for *The Verge*. "We're not limited to anything—just give us the file and we can print it [onto a disc]."

Here's how it works: using a femtosecond laser, the scientists engrave the data into the glass disc's structure. By firing intense laser pulses a quadrillionth of a second long, the information is carved into a series of miniscule dots. When the disc is read later, a laser interprets the information based off of the three-dimensional position of the dot in the disc, as well as its size and orientation—hence the name five-dimensional storage.

In some ways, it's similar to how data is encoded onto CDs, except in this case the information is stored directly in the disc's structure instead of on its surface, Vincent writes. That's why five-dimensional data discs can store information much more densely than on CDs. Glass is also much stronger and more chemically stable than the polycarbonate plastic most CDs and DVDs are made of, which is why the scientists believe they could potentially last for such a long time.

"It is thrilling to think that we have created the technology to preserve documents and information and store it in space for future generations," researcher Peter Kazansky said in a statement. "This technology can secure the last evidence of our civilization: all we've learnt will not be forgotten."

As a demonstration, Kazansky and his colleagues have encoded several major works onto glass discs, including the United Nations' Universal Declaration of Human Rights, the Magna Carta, the King James Bible and Isaac Newton's Opticks, Jamie Condliffe reports for *Gizmodo*.

But while the researchers are optimistic about the possibilities for five-dimensional storage, the average person won't be replacing their hard drives for glass discs any time soon. Not only is it hard to get consumers to switch over to a new data format, but femtosecond lasers are expensive and delicate tools that probably won't become common outside of the lab for a while. On the other hand, developing a device to read the discs wouldn't be too hard, which might make the

discs more useful for institutions like libraries and museums, David Nield writes for *ScienceAlert*.

"Who knows what's going to happen thousands of years down the line, no one can predict that," Patel tells Vincent. "But what we can guarantee is that we have the ability to store the culture, language, and essence of the human race in a simple piece of glass. For future civilizations—or whatever else is out there."

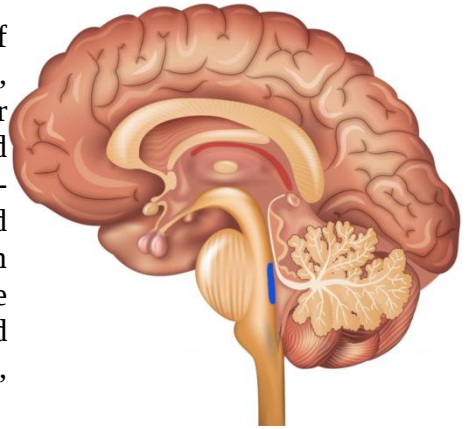
http://www.eurekalert.org/pub_releases/2016-02/uosc-rhb021216.php

Researchers highlight brain region as 'ground zero' of Alzheimer's disease

Essential for maintaining cognitive function as a person ages, the tiny locus coeruleus region of the brain is vulnerable to toxins and infection

A critical but vulnerable region in the brain appears to be the first place affected by late onset Alzheimer's disease and may be more important for maintaining cognitive function in later life than previously appreciated, according to a new review of the scientific literature.

The locus coeruleus is a small, bluish part of the brainstem that releases norepinephrine, the neurotransmitter responsible for regulating heart rate, attention, memory, and cognition. Its cells, or neurons, send branch-like axons throughout much of the brain and help regulate blood vessel activity. Its high interconnectedness may make it more susceptible to the effects of toxins and infections compared to other brain regions, said lead author Mara Mather.



Blue indicates the location of the locus coeruleus region in the brainstem. **Brain illustration: shutterstock.com/Tefi**

Mather, Professor of Gerontology and Psychology at the University of Southern California Leonard Davis School of Gerontology, added that the locus coeruleus is the first brain region to show tau pathology -- the slow-spreading tangles of protein that can later become telltale signs of Alzheimer's disease. Though not everyone will get Alzheimer's, autopsy results indicate that most people have some initial indications of tau pathology in the locus coeruleus by early adulthood, she added.

The norepinephrine released from the locus coeruleus may contribute to preventing Alzheimer's symptoms. Studies conducted with rats and mice have shown that norepinephrine helps protect neurons from factors that kill the cells and accelerate Alzheimer's disease, such as inflammation and excessive stimulation from other neurotransmitters.

Norepinephrine is released when someone is engaged in or mentally challenged by an activity, whether it's solving problems in the workplace, completing a word puzzle, or playing a difficult piece of music.

"Education and engaging careers produce late-life 'cognitive reserve,' or effective brain performance, despite encroaching pathology," Mather said. "Activation of the locus coeruleus-norepinephrine system by novelty and mental challenge throughout one's life may contribute to cognitive reserve."

"The Locus Coeruleus: Essential for Maintaining Cognitive Function and the Aging Brain" appears in Trends in Cognitive Sciences on Feb. 16, 2016 and was funded by National Institutes of Health grant RO1AG025340. The study was co-authored by Professor Emeritus Carolyn W. Harley of the Memorial University of Newfoundland.

http://www.eurekalert.org/pub_releases/2016-02/twi-wss021116.php

Wistar scientists show how cancerous cells evade a potent targeted therapy

Significant antitumor activity was shown in cancers when this therapy was combined with an enzyme

PHILADELPHIA -- Imagine developing a drug designed to inhibit a protein that helps cancer cells proliferate and survive only to find that the drug does not perform very well in the clinic. This was the dilemma faced by scientists researching inhibitors of signal transducer and activator of transcription (STAT3), a protein that controls transcription by the STAT3 gene. When STAT3 was knocked out in a mouse model, researchers observed increased T-cell immune responses, suggesting a valuable therapeutic target. However, targeting STAT3 in tumors has had only limited success to date.

Now, researchers at The Wistar Institute have discovered how STAT3 behaves in immature myeloid cells known as myeloid-derived suppressor cells (MDSCs), and they believe they have found the basis for a much more effective method of using STAT3 inhibitors to stop cancer progression in its tracks. The findings were published in the journal *Immunity*.

In healthy individuals, MDSCs regulate immune responses and tissue repair, and the population of these cells rapidly expands during inflammation, infection and cancer. However, when these myeloid cells migrate to tumor sites, they can differentiate to tumor associated macrophages (TAMs), which can in turn stimulate the formation of blood vessels in tumors and promote enhanced tumor cell invasion and motility. Previous studies showed that STAT3 plays a major role in the expansion of MDSCs, so the researchers decided to study if there was a link between STAT3 and MDSC differentiation.

"Studies pointed to STAT3 being an important target in the development of cancer," said Dmitry I. Gabrilovich, M.D., Ph.D., the Christopher M. Davis Professor and Professor and Program Leader in the Translational Tumor Immunology Program at The Wistar Institute and lead author of the study. "Clinically speaking, we do not observe the robust results that we would expect. The purpose of this study was to discover why this is happening and figure out a way to make these therapies as effective as our research would suggest."

Gabrilovich and colleagues analyzed blood samples from patients with cancer to determine the level of activity. Even though STAT3 activity drives the expansion of MDSCs and is involved in immune responses mediated by the cells, they found that high levels of STAT3 activity actually prevent the differentiation of MDSCs to macrophages. Low levels of STAT3 inside tumors are what cause this activity, but the levels are low enough that STAT3 inhibitors cannot effectively target STAT3.

What causes the lower levels of STAT3 activity in tumor MDSC that help drive their differentiation to TAMs? The answer lies in the tumor microenvironment. Hypoxia, or a lack of oxygen, is a phenomenon in tumors that occurs when they outgrow their blood supply. When hypoxia occurs, the activity of CD45 - a protein found in myeloid and lymphoid cells - increases. This increase in CD45 activity is what lowers the levels of STAT3, allowing for the differentiation of MDSCs to TAMs.

Finally, the researchers wanted to see whether targeting CD45 would help STAT3 inhibitors become more effective. In a sarcoma that was shown to be resistant to STAT3 inhibitors, the team used a combination of an experimental STAT3 inhibitor called JSI-124 (cucurbitacin I) and sialidase, an enzyme that disrupts CD45 activity. When either JSI-124 or sialidase were used alone, they either did not have any effect tumor growth or enhanced tumor progression, respectively. When the pair was used together, the result was substantial antitumor activity.

"Our results suggest that sialidase could sensitize myeloid cells in tumors to previously ineffective STAT3 inhibitors," said Vinit Kumar, Ph.D., staff scientist in the Gabrilovich laboratory at The Wistar Institute and first author of the study. "We confirmed that STAT3 is indeed a great potential target for cancer immunotherapies as long as we account for the other factors affecting the tumor microenvironment."

This work was supported by the National Institutes of Health grants CA177646 and CA100062, the animal and flow cytometry facilities at The Wistar Institute, and in part by a Wistar/Penn SPORE grant P50-CA174523.

Co-authors of this study from The Wistar Institute include Thomas Condamine, Sridevi Mony, and Dario C. Altieri. Other co-authors include: Pingyan Cheng and Judith C. McCaffrey from H. Lee Moffitt Cancer Center in Tampa, Fla.; Lucia R. Languino from Thomas Jefferson University in Philadelphia; Neil Hockstein, Michael Guarino, Gregory Masters, Emily Penman, and Fred Denstman from the Helen F. Graham Cancer Center and Research Institute of the Christiana Care Health System in Newark, De.; Xiaowei Xu from the University of Pennsylvania in Philadelphia; and Hong Du and Cong Yan from Indiana University School of Medicine in Indianapolis.

Additionally, the researchers would like to thank the team at Helen F. Graham Cancer Center of Christiana Care Health System for their support in organizing the clinical part of this study.

http://www.eurekalert.org/pub_releases/2016-02/p-dic021516.php

Decline in Chinese HFMD epidemic projected under new vaccination scheme

Vaccination with newly available monovalent hand, foot, and mouth disease vaccines will decrease HFMD incidence in China

Broad vaccination with newly available monovalent hand, foot, and mouth disease (HFMD) vaccines will decrease HFMD incidence in China, according to predictions from an epidemiologic model published this week in *PLOS Medicine*. The study, conducted by Saki Takahashi and Bryan T. Grenfell at Princeton University, New Jersey, USA, Hongjie Yu at the Chinese Center for Disease Control and Prevention, Beijing, China, and colleagues, further suggests that serotype replacement (spread of viruses that differ from those in a vaccine, replacing viruses to which the vaccine confers immunity) will not significantly deplete the benefits of a HFMD vaccination campaign.

China reported 9 million cases of HFMD between 2008 and 2013. In clinical trials, inactivated monovalent vaccines against enterovirus serotype EV-A71-associated HFMD were highly efficacious against infection with EV-A71 but did not cross-protect against serotype CV-A16-associated HFMD. To estimate the effects of broad vaccination, Takahashi and colleagues used HFMD incidence data collected in 31 Chinese provinces between 2009 and 2013 to develop a two-serotype time series susceptible-infected-recovered epidemic model. According to model outcomes, cross-protection following infection with EV-A71 or CV-A16 lasts 6.77 weeks on average (95% confidence interval: 2.50, 10.03), resulting in cross-serotype protection. Based on this and the estimated basic reproduction number (which represents the average number of people who will become infected by each individual infected person) for both serotypes (26.63 for EV-A71 (interquartile range [IQR]: 23.14, 30.40) and 27.13 for CV-A16 (IQR: 23.15, 31.34)), Takahashi and colleagues predicted that EV-A71 vaccination will decrease EV-A71-associated HFMD incidence and leave CV-A16 incidence relatively unchanged, and that coverage above 96% will achieve population-level immunity.

The accuracy of these findings depends on the assumptions included in the model and the quality of the data. However, the modeling is conservative and tested within the study for its ability to replicate observed epidemic cycles. The authors state, "a mass EV-A71 vaccination program of infants and young children should provide significant benefits in terms of a reduction in overall HFMD burden."

Funding:

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Competing Interests:

The views expressed in this study are solely the responsibility of the authors and do not necessarily represent the official views of the National Institute of General Medical Sciences, the National Institutes of Health, or the Chinese Center for Disease Control and Prevention. BJC has received research funding from MedImmune Inc. and Sanofi Pasteur, and consults for Crucell NV. MedImmune Inc, Sanofi Pasteur, and Crucell NV do not market HFMD vaccines. The other authors have declared that no competing interests exist.

Citation:

Takahashi S, Liao Q, Van Boeckel TP, Xing W, Sun J, Hsiao VY, et al. (2016) Hand, Foot, and Mouth Disease in China: Modeling Epidemic Dynamics of Enterovirus Serotypes and Implications for Vaccination. PLoS Med 13(2): e1001958.doi:10.1371/journal.pmed.1001958

http://www.eurekalert.org/pub_releases/2016-02/wsu-cig021616.php

Compound in green tea found to block rheumatoid arthritis

Findings confirmed in animal model

Researchers at Washington State University in Spokane have identified a potential new approach to combating the joint pain, inflammation and tissue damage caused by rheumatoid arthritis. Their discovery is featured on the cover of *Arthritis and Rheumatology*, a journal of the American College of Rheumatology, in print Tuesday, Feb 16.

Rheumatoid arthritis is a debilitating autoimmune disorder that mostly affects the small joints of the hands and feet. It causes painful swelling that progresses into cartilage damage, bone erosion and joint deformity. "Existing drugs for rheumatoid arthritis are expensive, immunosuppressive and sometimes unsuitable for long-term use," said Salah-uddin Ahmed, the lead WSU researcher on the project.

His team evaluated a phytochemical called epigallocatechin-3-gallate (EGCG), which is a molecule with anti-inflammatory properties found in green tea. Their study suggests that EGCG has high potential as a treatment for rheumatoid arthritis because of how effectively the molecule blocks the effects of the disease without blocking other cellular functions.

"This study has opened the field of research into using EGCG for targeting TAK1 - an important signaling protein - through which proinflammatory cytokines transmit their signals to cause inflammation and tissue destruction in rheumatoid arthritis," said Ahmed.

The researchers confirmed their findings in a pre-clinical animal model of human rheumatoid arthritis, where they observed that ankle swelling in animals given EGCG in a 10-day treatment plan was markedly reduced. Ahmed has focused his research on studies related to rheumatoid arthritis for the last 15 years.

The WSU team, which includes researchers Anil Singh and Sadiq Umar, has been studying rheumatoid arthritis and other inflammatory diseases at the WSU College of Pharmacy in Spokane since 2014. They joined with researchers from the National Institute of Pharmaceutical Education and Research in Hajipur, India, for this project.

http://www.eurekalert.org/pub_releases/2016-02/fos--owp021616.php

Oxygen was present in the atmosphere much earlier than previously assumed

Indications that small levels of atmospheric oxygen developed already 3.8 billion years ago

LIFE ON EARTH - Reconstructing the emergence and evolution of life on our planet is tightly linked to the questions as to when and to what extent Earth's atmosphere became oxygenated. New geological studies based on data from Western Greenland indicate that small levels of atmospheric oxygen developed already 3.8 billion years ago, some 0.7-0.8 billion years earlier than previously thought.

Today, most researchers agree that the oxygenation of Earth's atmosphere happened in two major steps: the first during the so-called Great Oxidation Event about 2.5-2.4 billion years ago, and the second during the Late Neoproterozoic Era around 750 to 540 million years ago. The latter is thought to have been the cause for the emergence of animals during the so-called 'Cambrian explosion' around 540 to 520 million years ago.

An international team of researchers led by Professor Robert Frei from the Department of Geoscience and Natural Resource Management at the University of Copenhagen has just released a study indicating evidence for the presence of small concentrations of oxygen on Earth already 3.8 billion years ago. The researchers analysed Earth's oldest Banded Iron Formations (BIFs) from Western Greenland. BIFs are marine chemical sediments originally comprised of alternating layers of silica and Fe-hydroxides and are widely used as geochemical archives. The reason for this is that they retain information on the composition and presence of oxygenation/reduction processes in ambient seawater and on the interaction of the atmosphere with Earth's surface.

The research team used concentrations and isotope compositions, i.e. variations of the same elements with different atomic weight, of the elements chromium (Cr) and uranium (U) present in the BIFs. Chromium and uranium were used as these elements weather rapidly when continental landmasses are exposed to reactive oxygen species (ROS) such as oxygen (O_2). After weathering, they are transported to the oceans by rivers, where they are deposited with chemical sediments and serve as geochemical signals of weathering by ROS.

The fact that the analyses of the BIF layers from Western Greenland show elements that require presence of oxygen in the atmosphere opens up for the possibility of evolution of the earliest primitive photosynthetic life forms as early as 3.8 billion years ago. As Robert Frei explains: "It is generally believed that the Early Earth was a completely anoxic, but our study shows that the surface of the Earth was exposed to a low oxygen atmosphere already this time. This has far reaching implications for how we investigate the pace of evolution of life and its biodiversity on our planet."

You can read more about this important scientific discovery in the article just published in Nature's Scientific Reports *"Oxidative elemental cycling under the low O_2 Eoarchean atmosphere" by Robert Frei, Sean A. Crowe, Michael Bau, Ali Polat, David A. Fowle, and Lasse N. Døssing.http://www.nature.com/articles/srep21058)*

http://www.bbc.com/news/health-35586834

Excitement at new cancer treatment

A therapy that retrains the body's immune system to fight cancer has provoked excitement after more than 90% of terminally ill patients reportedly went into remission.

By James Gallagher Health editor, BBC News website

White blood cells were taken from patients with leukaemia, modified in the lab and then put back. But the data has not been published or reviewed and two patients are said to have died from an extreme immune response. Experts said the trial was exciting, but still only "a baby step."

The news bubbled out of the American Association for the Advancement of Science's annual meeting in Washington DC. The lead scientist, Prof Stanley Riddell from the Fred Hutchinson Cancer Research Centre in Seattle, said all other treatments had failed in these patients and they had only two-to-five months to live. He told the conference that: "The early data is unprecedented."

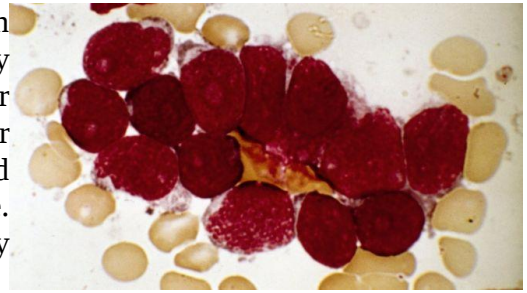


Image copyright SPL

Re-training

In the trial, cells from the immune system called killer t-cells were taken out of dozens of patients. The cells normally act like bombs destroying infected tissue.

The researchers genetically modified the t-cells to engineer a new targeting mechanism - with the technical name of chimeric antigen receptors - to target acute lymphoblastic leukaemia. Prof Riddell told the BBC: "Essentially what this process does is, it genetically reprograms the T-cell to seek out and recognise and destroy the patient's tumour cells.

"[The patients] were really at the end of the line in terms of treatment options and yet a single dose of this therapy put more than ninety percent of these patients in complete remission where we can't detect any of these leukaemia cells."

But one cancer expert told me they still felt in the dark on the full significance of the study, as the data is not available. Also seven of the patients developed cytokine release syndrome so severe that they required intensive care, and a further two patients died.

While those odds may be acceptable if facing terminal cancer, the side-effects are much greater than conventional leukaemia treatments such as chemotherapy and radiotherapy, which work in the majority of patients.

Analysis

By James Gallagher, health editor, BBC News website

The field of immunotherapy - harnessing the immune system to attack cancer - is coming of age.

The significance of today's development is hard to ascertain while the data is unpublished - but the field is undoubtedly making giant strides.

Drugs called checkpoint inhibitors, such as pembrolizumab and ipilimumab, take the brakes off the immune system so it attacks cancer.

They are already being used by doctors.

And other experimental techniques are coming to fruition to allow doctors to change a patient's own cells to engineer a designer immune system to kill cancer.

It's an exciting time that is likely to see immunotherapy soon join chemotherapy, radiotherapy and surgery as major weapons in the fight against cancer.

There is also a big difference between using such approaches on a blood cancer like leukaemia and "solid" tumours such as breast cancer.

Dr Alan Worsley, from Cancer Research UK, said that while the field was incredibly exciting, "this is a baby step". He told the BBC: "We've been working for a while using this type of technology, genetically engineering cells. So far it's really shown some promise in this type of blood cancer.

"We should say that in most cases standard treatment for blood cancer is quite effective, so this is for those rare patients where that hasn't worked.

"The real challenge now is how do we get this to work for other cancers, how do we get it to work for what's known as solid cancers, cancers in the tissue?"

http://www.bbc.com/news/science-environment-35587680

Iron meteorites 'buried in Antarctica' by the Sun

New research suggests there could be a layer of iron-rich meteorites hidden just under the Antarctic ice.

By Jonathan Webb Science reporter, BBC News

The churning of glaciers spews many space rocks out on to the surface in Antarctica, but compared to elsewhere on Earth, few of them are made of iron.

Based on modelling and lab experiments, scientists say the missing metallic rocks might be burying themselves, by melting the ice as sunlight heats them. To prove their idea, the team now wants to look for the rocks themselves.

Antarctica is one of the best places to hunt for meteorites **Antarctic Search for Meteorites Program/Katherin**

"The study is proposing a hypothesis - these samples should be there. We just have to go and locate them," said Dr Katherine Joy from the University of Manchester, a co-author of the paper published in Nature Communications.

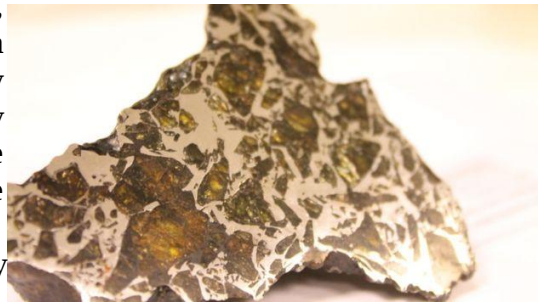
The idea is, they never make it to the surface - they're forever trapped, 50-100cm or so below the iceDr Katherine Joy, University of Manchester

Antarctica is known by meteorite specialists as a fruitful hunting ground, because the rocks are collected from their landing sites by glacial flows and transported to concentrated dumping-grounds.

"The great thing about Antarctica is they fall on the ice, and then the ice progressively moves away from the plateau. And where it hits these barriers, along the Transantarctic Mountains, the ice gets moved up," Dr Joy told the BBC.

"So this continuous conveyor belt has delivered meteorites from the interior fall sites to the 'meteorite stranding zones' for the past couple of million years or so."

Among this Antarctic haul, however, researchers have noticed that iron-rich meteorites - whether partly or wholly made of the metal - are surprisingly scarce, compared to the percentage collected in other places around the world.



Dr Joy and her colleagues think they may have discovered why.

Wholly iron and stony-iron meteorites, like this one, are less common in Antarctica than elsewhere **Mark Nottingham/Earth and Solar System**

They froze two small meteorites of similar size and shape, one made of iron and the other rocky and non-metallic, inside blocks of ice. A special lamp was trained on the ice from above, to mimic the rays of the Sun.

Both meteorites, on repeated trials, melted their way downward through the ice block. But because the metal conducts heat more efficiently, the iron meteorite sank further, faster.

The researchers then expanded that observation using a mathematical simulation. Their model showed that this Sun-driven burrowing would be enough to cause iron-rich rocks to sink so much during the long summer days that, over the course of the year, it would account fairly precisely for the lack of iron space rocks welling their way to the surface of the Antarctic "stranding zones".

"The idea is, they never make it to the surface. They're forever trapped, 50-100cm or so below the ice," Dr Joy explained.

That means, if the team's findings are to be believed, that the hunt is on.

Failed planets

As Dr Joy's Manchester colleague Geoffrey Evatt put it: "The challenge is now set - to be the first team to locate this reserve of meteorites and retrieve samples from it."

Of all the meteorites gathered from Antarctica, only a handful - so far - have been pulled out from beneath the ice. This is mostly for practical reasons, Dr Joy said.

"When it's very cold... picking up the sample in a controlled way is difficult enough with things sitting on the surface. To access ones that are subsurface - nobody's really tried to do that so far."

So it will not be easy, but the team hopes that radar and metal detectors might help target the search. And the potential rewards are high. "Every meteorite we find tells us something new about the Solar System," Dr Joy said.

Some are carbon-rich or rocky remnants from long before any planet clumped together; others - like iron and rocky-iron meteorites - offer clues from a more intermediate stage, when baby planets with cores, mantles and crusts were trying to form.

"The iron group represents meteorites that were once the cores and the internal structures of different planetesimals. "We think there were probably hundreds of these early planets, that formed in the solar system but never really got big enough and were broken up in collision events."

http://nyti.ms/20LjK7a

China Telescope to Displace 9,000 Villagers in Hunt for Extraterrestrials

More than 9,000 Chinese villagers are leaving their homes to make way for aliens — or for the possible echoes of them, at least.

By EDWARD WONG FEB. 17, 2016

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BEIJING - It is not a colonization plan from outer space. The Chinese government is relocating the villagers as it finishes building the world's biggest radio telescope, one of whose purposes is to detect signs of extraterrestrial life.

The telescope will be 500 meters, or 1,640 feet, in diameter, making it by far the largest instrument of its kind in the world. It is called FAST, short for 500-meter aperture spherical telescope, and will cost an estimated 1.2 billion renminbi, or $184 million, to erect. The government hopes to complete it by September.

The mass relocation was announced on Tuesday in a report by Xinhua, the state news agency. The report said officials were moving 2,029 families, a total of 9,110 people, who live within about three miles of the telescope in the area of Pingtang and Luodian Counties in the southwestern province of Guizhou. Depopulating the area will create "a sound electromagnetic wave environment" for the telescope, Xinhua said.

Officials plan to give each person the equivalent of $1,800 for housing compensation, the report said. Guizhou is one of China's poorest provinces.

Forced relocations for large projects are common across China, and so are complaints about them and about the amount of compensation offered.

The Three Gorges Dam displaced more than one million people along the Yangtze River, for example, and the middle route of the gargantuan South-North Water Diversion Project has resulted in the relocation of 350,000 people to make way for a series of canals.

The Chinese government has announced ambitious plans for its space program, at a time when the American one's direction is uncertain. China aims to put an astronaut on the moon and a space station in orbit. The FAST project is another important element in the larger plan.

Some official Chinese news reports about the project have emphasized the search for alien life, but the telescope's main scientific work will be somewhat less romantic, gathering large amounts of new data on a wide range of physical phenomena in space including pulsars, galaxies, black holes and gas clouds.

The telescope is being built in a wide depression among karst hills. The site is far from any large city, and ideal for picking up radio transmissions from the sky, the Xinhua report said. Scientists began looking for a suitable site for the project in 1994.

If the truth is out there, some Chinese scientists are confident that the giant telescope will find it.

For decades, professional and amateur scientists have combed the data gathered by the largest currently operational radio telescope in the world, the 53-year-old Arecibo Observatory in Puerto Rico, hoping to find traces of intelligent life that, like mankind, may be advertising its existence to the universe through radio emissions.

But they have yet to find any sign.

"With a larger signal receiving area and more flexibility, FAST will be able to scan two times more sky area than Arecibo, with three to five times higher sensitivity," Li Di, a chief scientist with the National Astronomical Observatories under the Chinese Academy of Sciences, told China Daily last year.

The new telescope should be able to pick up all kinds of radio signals more clearly from sources much farther away than can the Arecibo dish, which is 300 meters (about 1,000 feet) in diameter.

In November, scientists successfully tested the new telescope's "retina," which weighs 33 tons and is suspended 460 to 525 feet above the reflector dish, which was half-finished at the time, China Daily reported.

The telescope is made up of 4,500 mostly triangular panels that measure about 36 feet on a side, the report said, which together create an immense parabolic dish. Scientists will be able to adjust the panels' positions to alter the shape of the dish and reflect radio signals from distant parts of the universe to a single focal point for detection and study.

Mr. Li told China Daily that engineers were aiming to install all the panels by June and complete debugging the antenna by September.

"Ultimately, exploring the unknown is the nature of mankind," he said, adding that it was "as visceral as feeding and clothing ourselves."

"It drives us to a greater future," he said.

http://www.eurekalert.org/pub_releases/2016-02/aaon-cam021116.php

Common antibiotics may be linked to temporary mental confusion

Antibiotics may be linked to a serious disruption in brain function, called delirium, and other brain problems, more than previously thought

MINNEAPOLIS - Antibiotics may be linked to a serious disruption in brain function, called delirium, and other brain problems, more than previously thought, according to a "Views and Reviews" article published in the Feb. 17, 2016, online issue of *Neurology*®, a medical journal of the American Academy of Neurology.

Delirium causes mental confusion that may be accompanied by hallucinations and agitation. Medications are often the cause of delirium, but antibiotics are not necessarily the first medications doctors may suspect.

"People who have delirium are more likely to have other complications, go into a nursing home instead of going home after being in the hospital and are more likely to die than people who do not develop delirium," said author Shamik Bhattacharyya, MD, of Harvard Medical School and Brigham and Women's Hospital in Boston, Mass., and a member of the American Academy of Neurology. "Any efforts we can make to help identify the cause of delirium have the potential to be greatly beneficial."

For the study, researchers reviewed all available scientific reports and found case reports on 391 patients, over seven decades, who were given antibiotics and later developed delirium and other brain problems. A total of 54 different antibiotics were involved, from 12 different classes of antibiotics ranging from commonly used antibiotics such as sulfonamides and ciprofloxacin to intravenous antibiotics such as cefepime and penicillin.

About 47 percent had delusions or hallucinations, 14 percent had seizures, 15 percent had involuntary muscle twitching and 5 percent had loss of control of body movements. Plus, EEG, a test that detects electrical activity in the brain, was abnormal in 70 percent of the cases. 25 percent of the people who developed delirium had kidney failure.

The researchers identified three types of delirium and other brain problems related to antibiotics.

Type 1 was characterized by seizures and most often associated with penicillin and cephalosporins. Type 2 was marked by symptoms of psychosis and associated with procaine penicillin, sulfonamides, fluoroquinolones and macrolides. Both Type 1 and Type 2 had a quick onset of symptoms, within days. Once antibiotics were stopped, symptoms also stopped within days.

Type 3 was characterized by abnormal brain scans and impaired muscle coordination and other signs of brain dysfunction, and was only associated with the drug metronidazole. The beginning of noticeable symptoms took weeks instead of days. Symptoms also took longer to go away once the antibiotic was stopped.

Bhattacharyya noted that all of the patients had an active infection that could not be ruled out as the cause of the delirium and other brain problems. A scale used to determine whether side effects can be attributed to a drug found that the association was possible in most cases. When infections that affected the central nervous system were not included, the association was probable.

"More research is needed, but these antibiotics should be considered as a possible cause of delirium," said Bhattacharyya. "Recognition of different patterns of toxicity could lead to a quicker diagnosis and hopefully prevent of some of the negative consequences for people with delirium and other brain problems."

To learn more about brain health, visit http://www.aan.com/patients.

http://www.eurekalert.org/pub_releases/2016-02/nu-npo021716.php

New predictor of cancer

When your biological age is older than your chronological age, the risk of getting and dying of cancer rises

Discrepancy between the two ages could become early warning sign of cancer

If your biological age is 2.2 years older than your actual age, you have a higher chance of dying from cancer

Epigenetic age is new way to measure biological age

CHICAGO --- Epigenetic age is a new way to measure your biological age. When your biological (epigenetic) age is older than your chronological age, you are at increased risk for getting and dying of cancer, reports a new Northwestern Medicine study. And the bigger the difference between the two ages, the higher your risk of dying of cancer.

"This could become a new early warning sign of cancer," said senior author Dr. Lifang Hou, who led the study. "The discrepancy between the two ages appears to be a promising tool that could be used to develop an early detection blood test for cancer."

Hou is chief of cancer epidemiology and prevention in preventive medicine at Northwestern University Feinberg School of Medicine and co-leader of the cancer prevention program at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

"People who are healthy have a very small difference between their epigenetic/biological age and chronological age," Hou said. "People who develop

cancer have a large difference and people who die from cancer have a difference even larger than that. Our evidence showed a clear trend."

A person's epigenetic age is calculated based on an algorithm measuring 71 blood DNA methylation markers that could be modified by a person's environment, including environmental chemicals, obesity, exercise and diet. This test is not commercially available but is currently being studied by academic researchers, including a team at Northwestern.

In DNA methylation, a cluster of molecules attaches to a gene and makes the gene more or less receptive to biochemical signals from the body. The gene itself -- your DNA code -- does not change.

This is the first study to link the discrepancy between epigenetic age and chronological age with both cancer development and cancer death using multiple blood samples collected over time. The multiple samples, which showed changing epigenetic age, allowed for more precise measurements of epigenetic age and its relationship to cancer risk. Other studies have looked at blood samples collected only at a single time point.

The final paper was published Feb. 15 in *EBioMedicine*.

The study was a longitudinal design with multiple blood samples collected from 1999 to 2013. Scientists used 834 blood samples collected from 442 participants who were free of cancer at the time of the blood draw.

For each one-year increase in the discrepancy between chronological and epigenetic ages, there was a 6 percent increased risk of getting cancer within three years and a 17 percent increased risk of cancer death within five years. Those who will develop cancer have an epigenetic age about six months older than their chronological age; those who will die of cancer are about 2.2 years older, the study found.

"Our results suggest future researchers should focus on the epigenetic-chronological age discrepancy for its potential to show a big picture snapshot of human health and disease at a molecular level," said first author Yinan Zheng, a predoctoral fellow at Feinberg.

Northwestern scientists now are studying whether individuals can lower their epigenetic age through lifestyle improvements such as increasing exercise and having a healthier diet, noted Brian Joyce, co-first author and predoctoral fellow at Feinberg.

The study is titled "Blood Epigenetic Age may Predict Cancer Incidence and Mortality."

The research was funded by the Epidemiology Research and Information Center, U.S. Department of Veterans Affairs grant NIEHS R01-ES015172. Additional funding support was provided by the Northwestern University Robert H. Lurie Comprehensive Cancer Center Rosenberg Research Fund.

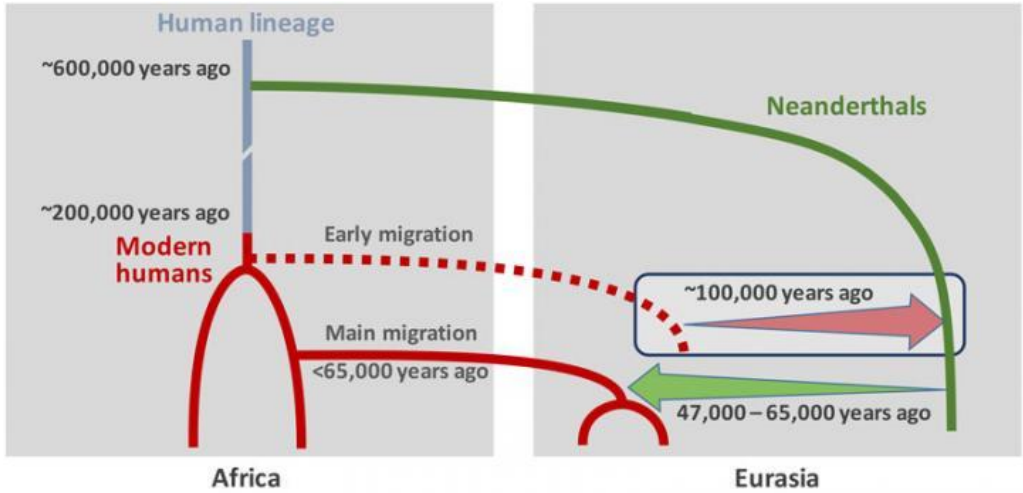
http://www.eurekalert.org/pub_releases/2016-02/m-egf021616.php

Early gene flow from modern humans into Neanderthals

Researchers find first genetic evidence of modern human DNA in a Neanderthal individual

Using several different methods of DNA analysis, an international research team has identified an interbreeding event between Neanderthals and modern humans that occurred an estimated 100,000 years ago, which is tens of thousands of years earlier than other such events previously documented. They suggest that some modern humans left Africa early and mixed with Neanderthals. These modern humans later became extinct and are therefore not among the ancestors of present-day people outside Africa who left Africa about 65,000 years ago.

"We knew from Neanderthal DNA found in the genomes of humans outside Africa that Neanderthals and humans have interbred. This interbreeding is estimated to have happened less than 65,000 years ago, around the time that modern human populations spread across Eurasia from Africa. We now find evidence for a modern human contribution to the Neanderthal genome. This is likely the result of much earlier interbreeding", says Sergi Castellano from the Max Planck Institute for Evolutionary Anthropology, who co-led the study.



Scenario of interbreeding between modern humans and Neanderthals: Neanderthal DNA in present-day humans outside Africa originates from interbreeding that occurred 47,000 - 65,000 years ago (green arrow). Modern human DNA in Neanderthals is likely a consequence of earlier contact between the two groups roughly 100,000 years ago (red arrow). **Credit: Ilan Gronau**

Martin Kuhlwilm, co-first author of the new paper, identified the regions of the Altai Neanderthal genome that come from modern humans. "I was looking to see

if I could find regions in the genome where the Neanderthal genome from Siberia has sequences resembling those in humans. We know that contemporary non-Africans have traces of Neanderthal in them, so they were not useful to us. So we instead used genomes of contemporary individuals from across Africa to identify mutations which most of them have in common. Some of these mutations occur together in regions of the Altai Neanderthal genome, a sign of interbreeding," adds Kuhlwilm, who did this work at Max Planck Institute for Evolutionary Anthropology.

In addition to Kuhlwilm and Castellano, the team included several other members of the Max Planck Institute for Evolutionary Anthropology, including Svante Pääbo and Matthias Meyer. The team also included Adam Siepel, who is Chair of CSHL's Simons Center for Quantitative Biology and co-lead the study, and a former member of Siepel's Lab, Ilan Gronau, who is now at the Herzliya Interdisciplinary Center, Israel. Melissa Hubisz, a Ph.D. student with Siepel at Cornell University, also made major contributions to the work. The full international research team included 15 additional co-authors.

The team's evidence of "gene flow" from descendants of modern humans into the Neanderthal genome applies to one specific Neanderthal, whose remains were found in a cave in the Altai Mountains in southern Siberia, near the Russia-Mongolia border. Two Neanderthals from European caves that were sequenced for this study -- one from Croatia, another from Spain -- both lack DNA derived from modern humans. The team also analyzed the genome of another extinct human, a Denisovan, whose remains were found in the same cave in the Altai Mountains as the Neanderthal bone. Unlike the Neanderthal individual, the Denisovan individual did not carry any modern human DNA. That does not mean modern humans never mated with Denisovans or European Neanderthals. What it does mean, Siepel clarifies, is that "the signal we are seeing in the Altai Neanderthal probably comes from an interbreeding event that occurred after this Neanderthal lineage diverged from its European cousins, a little more than 100,000 years ago."

Separate paths

The modern human DNA sequences in the Altai Neanderthal appear to derive from a modern human group that separated early from other humans, "about the time present-day African populations diverged from one another, around 200,000 years ago," adds Gronau, co-first author of this work.

The modern human who contributed genes to this particular Neanderthal individual must have come from a population that left Africa long before the migration of the ancestors of present-day Europeans and Asians from Africa less than 65,000 years ago, the scientists say. Thus, there must have been a long lag between when this group branched off the modern human family tree, roughly 200,000 years ago, and when they left their genetic mark in the Altai Neanderthal, about 100,000 years ago, before themselves being lost to extinction.

Original paper

Martin Kuhlwilm, Ilan Gronau, Melissa J. Hubisz, Cesare de Filippo, Javier Prado, Martin Kircher, Qiaomei Fu, Hernán A. Burbano, Carles Lalueza-Fox, Marco de la Rasilla, Antonio Rosas, Pavao Rudan, Dejana Brajkovic, Zeljko Kucan, Ivan Gušic, Tomas Marques-Bonet, Aida M. Andrés, Bence Viola, Svante Pääbo, Matthias Meyer, Adam Siepel and Sergi Castellano ***Ancient gene flow from early modern humans into Eastern Neanderthals***

Nature; 17 February, 2016 (DOI 10.1038/nature16544)

http://www.eurekalert.org/pub_releases/2016-02/aha-int021016.php

Imaging, not time, may determine who is right for stroke clot removal

Brain imaging may accurately identify patients likely to benefit from stroke clot removal instead of relying on the time since symptoms began as an indicator of treatment eligibility

LOS ANGELES - Brain imaging may accurately identify patients likely to benefit from stroke clot removal instead of relying on the time since symptoms began as an indicator of treatment eligibility, according to research presented at the American Stroke Association's International Stroke Conference 2016.

An ischemic stroke is caused by lack of blood reaching part of the brain. Endovascular treatment - which mechanically removes the blood clot blocking the path to the brain - benefits patients when performed within six hours of symptom onset. Drug treatment to bust the clot is beneficial up to 4.5 hours.

Here, researchers show that brain imaging can select patients who could benefit from clot removal up to 18 hours after stroke symptoms begin.

Researchers evaluated data on 102 patients who had endovascular therapy up to 18 hours after the start of their stroke and had a CT Perfusion (CTP) imaging scan before treatment that showed where a large area of brain tissue may be safely salvaged.

Good recovery - defined as little to no disability - was achieved in 71.4 percent of the patients treated within six hours and 61.7 percent of patients treated beyond six hours of stroke onset. There was no significant association between time to treatment and good outcomes when CT perfusion imaging shows a salvageable brain tissue.

"Using this image-based selection, we would be able to look at any patient who comes through the door to identify the ones likely to benefit from these therapies, regardless of what the clock shows," said Jenny Tsai, M.D., C.M., study author and Neuroimaging and Vascular Neurology Fellow at the Stanford Stroke Center.

The facility is part of the University of Stanford's School of Medicine in Stanford, California.

"This is important because we want to offer the best treatments to every patient who suffers stroke and who may benefit from them. One of the best ways to do this is to have an objective imaging tool to evaluate every single patient," she said.

Researchers analyzed patient data from the clinical study CT Perfusion to predict Response to recanalization in Ischemic Stroke Project (CRISP). The two-year study focused on adults 18 and older and finished in 2014. It was funded by the NIH and conducted at six U.S. medical sites with the goal of developing a practical tool to identify acute stroke patients likely to benefit from endovascular therapy. "We now have a very effective treatment for the large and disabling acute strokes," Tsai said. "And we know that there are patients likely to benefit from interventional treatments who are not being captured using basic imaging and time criteria alone. We need to do better."

Stroke is the No. 5 cause of death and a leading cause of disability in the United States, according to the American Stroke Association.

Co-authors are Michael Mlynash, M.D., M.S.; Soren Christensen, Ph.D.; Stephanie Kemp; Nishant Mishra, M.D., Ph.D.; Christian Federau, M.D.; Dipl. Phys. ETH; Sun Kim, M.D.; Michael Frankel, M.D.; Seena Dehkharghani, M.D.; Thomas Devlin, M.D.; Dileep Yavagal, M.D.; Naveed Akhtar, M.D.; Tudor Jovin, M.D.; Raul Nogueira, M.D.; Roland Bammer, Ph.D.; Matus Straka, Ph.D.; Gregory Zaharchuk, M.D., Ph.D; Gregory Albers, M.D.; Michael Marks, M.D.; and Maarten Lansberg, M.D., Ph.D. Author disclosures are on the abstract. The study was funded by the National Institutes of Health.

http://www.eurekalert.org/pub_releases/2016-02/nion-ddm021716.php

Diabetes drug may prevent recurring strokes

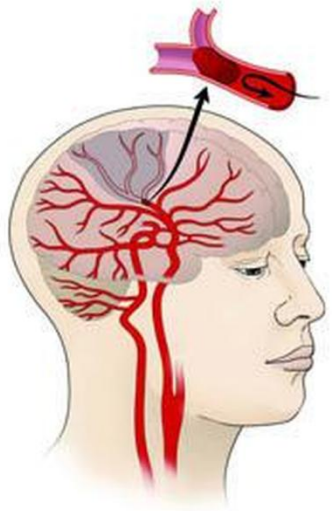
NIH-funded global study suggests novel approach for preventing repeated cardiovascular events

Pioglitazone, a drug used for type 2 diabetes, may prevent recurrent stroke and heart attacks in people with insulin resistance but without diabetes. The results of the Insulin Resistance Intervention after Stroke (IRIS) trial, presented at the International Stroke Conference 2016 in Los Angeles and published in the *New England Journal of Medicine*, suggest a potential new method to prevent stroke and heart attack in high-risk patients who have already had one stroke or transient ischemic attack. This large, international study was supported by the National Institutes of Health's National Institute of Neurological Disorders and Stroke (NINDS).

The IRIS trial is the first study to provide evidence that a drug targeting cell metabolism may prevent secondary strokes and heart attacks even before diabetes develops. Insulin regulates metabolism and keeps blood sugar levels from getting too high, along with many other processes, in the body. Insulin resistance is a condition in which the body produces insulin but does not use it effectively.

"This study represents a novel approach to prevent recurrent vascular events by reversing a specific metabolic abnormality thought to increase the risk for future heart attack or stroke," said Walter J. Koroshetz, M.D., director of the NINDS.

"The IRIS trial supports the value of more research to test the vascular benefits of other interventions such as exercise, diet and medications that have similar effects on metabolism as pioglitazone," said Walter N. Kernan, M.D. professor of general medicine at Yale University School of Medicine, New Haven, Connecticut, and lead author of the study.



Ischemic stroke occurs when a brain blood vessel gets blocked. The gray area represents brain tissue that is not receiving nutrients as a result of the stroke. **Courtesy of the NINDS.**

More than 3000 patients from seven countries who had experienced an ischemic stroke or transient ischemic attack within the previous six months were randomized to receive pioglitazone or placebo for up to five years in addition to standard care. Ischemic stroke and transient ischemic attacks can occur when a cerebral blood vessel becomes blocked, cutting off the delivery of oxygen and nutrients to brain tissue.

In this study, stroke or heart attack occurred in 9 percent of participants taking pioglitazone and 11.8 percent of patients on placebo, which was a relative decrease of 24 percent. The results suggest that 28 strokes or heart attacks may be prevented for every 1000 patients who take pioglitazone for up to five years.

Insulin resistance is a hallmark of type 2 diabetes but also occurs in more than 50 percent of people with ischemic stroke who do not have diabetes. People with diabetes are known to have increased risk of stroke. Previous research suggested that insulin resistance increases risk for stroke, but the IRIS trial was the first to treat it and suggested that the therapy reduced the risk of recurrent stroke and heart attacks. However, pioglitazone is not FDA-approved for the uses studied in the IRIS trial.

In this study, pioglitazone also reduced the risk of diabetes by 52 percent in the study participants. The study evidenced an additional known side effect of the drug, which is an increased risk of bone fractures. To help doctors and patients choose the best strategy for preventing recurring strokes, future studies will

attempt to identify a person's risk of bone fractures due to pioglitazone. As approved for use in medical practice, the drug also carries additional side effects (drug label). "More research is needed to determine the mechanisms by which pioglitazone decreases risk for stroke and heart attack and increases bone fracture risk, with the hope of developing strategies that maximize benefit and minimize serious side effects in our patients," said Dr. Kernan.

This work was supported by the NINDS (NS04486).

References: *Kernan WN et al. Pioglitazone after Ischemic Stroke or Transient Ischemic Attack.* New England Journal of Medicine. *February 17, 2016.*

http://bit.ly/1Re0AEe

Sound wave therapy is first alternative to Viagra in 15 years

STAND aside Viagra: a sound wave therapy that treats erectile dysfunction offers men the first alternative to the little blue pill in 15 years.

Viagra and similar drugs work by increasing blood flow to the penis, but men who use them have to plan sex around the drugs, and side effects can include headaches, dizziness, nasal congestion and sudden hearing loss. An alternative, called extra-corporeal shock wave therapy (ESWT), could provide a longer-term solution, according to several studies discussed this month at a meeting of the European Society for Sexual Medicine in Madrid, Spain.

One study of ESWT involved 112 men with erectile dysfunction. Half received five weekly doses of low-intensity sound waves directed at six sites along their penis. The other half received a placebo. At the start of the study, none of the men were able to have penetrative sex without medication. By the end, 57 per cent of the treated men said they were having intercourse, compared with 9 per cent of the men who received the placebo (*Scandinavian Journal of Urology*, doi.org/bch9).

The treatment seems to increase blood flow to the penis by encouraging the growth of new blood vessels, says Ilan Gruenwald of the Rambam Medical Center in Haifa, Israel. If this proves true, it suggests the treatment could be long-lasting.

Another study found that ESWT improves erectile function in men who do not respond to traditional drugs. Other small trials have also reported positive results.

The treatment is unlikely to cause any harm because the sound waves are of such low energy, says Delphine Behr-Roussel of Versailles Saint-Quentin-en-Yvelines University in France, who is studying the effects of ESWT in rats.

Although ESWT is offered in some clinics around the world, Trinity Bivalacqua at Johns Hopkins University and Hospital in Baltimore, Maryland, says that he would not offer it to his patients just yet, because treatment protocols need to be standardised. However, he is hopeful for the future of the therapy. “I’ve been a sceptic, but I’m becoming a believer,” he says.

http://www.eurekalert.org/pub_releases/2016-02/uoo-nct021816.php

New charts to assess head circumference at birth will be valuable tool in Zika crisis

Charts that enable healthcare professionals worldwide to assess the weight, length and head circumference of newborns from 24 to 42 weeks of gestation

In the medical journal *The Lancet*, the INTERGROWTH-21st Consortium, led by researchers at the University of Oxford, publish the final set of charts that enable healthcare professionals worldwide to assess the weight, length and head circumference of newborns from 24 to 42 weeks of gestation, and which apply to all babies, regardless of race or ethnicity.

José Villar, Professor of Perinatal Medicine at Oxford University, who led the study, said: 'The size of babies in relation to their gestational age at birth is a very important and easy to obtain marker of their health, nutritional status, chances of survival in the first years of life and future well-being. For the first time in history, health workers can now screen all babies around the world using the same charts to determine whether their growth in the womb was restricted or excessive.'

These charts were derived from a healthy population and are specific for the gestational age of the baby at birth. Failing to take gestational age at birth into account when assessing the size of newborns can result in the wrong diagnosis being made. These charts are unique because, for the first time, they include measures of head circumference at birth across populations that were obtained using rigorous methodology and standardised procedures. This is extremely important in the context of the Zika virus outbreak, as reliable information on the head circumference of newborns according to their gestational age is required so as to screen for microcephaly, which has been attributed to the viral infection.

Stephen Kennedy, Professor of Reproductive Medicine at Oxford University, who co-led the study, said: 'It is now clear that the authorities may have been over-reporting the number of babies suspected of having microcephaly because they have been using a single cut-off for term babies to define what is a normally grown baby's head without taking the gestational age at birth into account.'

The researchers say thousands of mothers of newborn babies in the affected regions are being made avoidably anxious because the current definition of suspected microcephaly lacks specificity. This was first recognised in a commentary to *The Lancet*, published on 5 February 2016, from a leading group of Brazilian researchers, who said: '...[W]e recommend use of a consistent set of diagnostic criteria for suspected microcephaly that take into account gestational age for term and preterm babies; such criteria are provided by the INTERGROWTH-21st standards.'

The complete set of charts is available free of charge at https://intergrowth21.tghn.org/. They will: 1) improve the assessment of individual babies at birth worldwide; 2) facilitate much-needed research to elucidate the suspected association with the Zika virus; and 3) make comparisons across populations around the world. The charts have been produced with supporting information in Spanish and Portuguese.

http://www.eurekalert.org/pub_releases/2016-02/cp-wdw021816.php

Why do we still have mitochondrial DNA?

The mitochondrion isn't the bacterium it was in its prime, say two billion years ago.

Since getting consumed by our common single-celled ancestor the "energy powerhouse" organelle has lost most of its 2,000+ genes, likely to the nucleus. There are still a handful left--depending on the organism--but the question is why. One explanation, say a mathematician and biologist who analyzed gene loss in mitochondria over evolutionary time, is that mitochondrial DNA is too important to encode inside the nucleus and has thus evolved to resist the damaging environment inside of the mitochondrion. Their study appears February 18 in Cell Systems.

"It's not that the 'lost' genes no longer exist in many cases, it's that the nucleus produces the proteins and the proteins go into the mitochondria, but why bother having anything in the mitochondria when you could have it all in the nucleus?" says co-author Ben Williams, a postdoctoral fellow at the Whitehead Institute for Biomedical Research. "It's like saying you have a central library with all your books in it, but we're going to keep 10 of them off site in a leaky shed."

Despite our long-term relationship with mitochondria, a lot of how our cells and these commensal organelles work together is still mysterious and controversial. We know that acquiring mitochondria may have sparked one of the most important evolutionary events in history by giving the common ancestor of eukaryotes (our kingdom of life) the energy to go multicellular.

And we know that each of our cells can possess dozens or hundreds of mitochondria, which are essential for powering everything from our muscles to our brain.

But what's strange is that in nearly all multicellular organisms, mitochondria have stayed independent by holding on to a few vital genes--despite the fact it may be safer for the cell to store these genes in the nucleus.

To figure out what makes the few genes in mitochondria so essential, Williams and lead author Iain Johnston, a research fellow at the University of Birmingham, took all of the data generated about mitochondrial genes and threw them into a computer. After a few weeks, with the algorithm Johnston developed, the computer threw back a timeline for mitochondrial gene loss over evolutionary history.

"The hypotheses underlying potential reasons for mitochondria to keep their own genes have been debated for decades, and this is the first data-driven approach to address this question," says Johnston. "It's facilitated by the fact that there are thousands of mitochondrial genomes from across a very wide diverse set of taxa available so now we can harness the data and let it speak for itself."

The analysis revealed that the genes that are retained in the mitochondria are related to building the organelle's internal structure, are otherwise at risk of being misplaced by the cell, and the DNA in these genes use a very ancient pattern that allows the mitochondrial DNA to strongly bond together and resist breaking apart. Williams and Johnston believe this design, not typically found in our own DNA, is likely what keeps the mitochondrial genes from breaking apart during mitochondrial energy production.

As energy is produced within the mitochondria, in the form of ATP, free radicals are emitted--the same free radicals that are a common byproduct of radiation. In essence, the power produced by the mitochondria comes with a certain amount of destruction, and it could be that the mitochondria are capable of withstanding this damage.

"You need specialists who can work in this ridiculously extreme environment because the nucleus is not necessary the best fit," says Williams.

The investigators also observed that the mitochondrial gene loss that's taken place across the eukaryote kingdom has followed the same pattern. This is a lesson that evolution may follow the same path many times over, and it's not always this entirely random process.

In the cellular environment, the evolution of mitochondrial gene loss became nearly predictable between different organisms.

"If we can harness data on what evolution has done in the past and make predictive statements about where it's going to go next, the possibility for exploring synthetic biology and disease are massive," says Johnston.

Using their algorithm, the duo next plans to explore the reasons for chloroplasts as well as where mitochondrial diseases, which are often quite devastating, fit into this bigger picture.

While this study doesn't close the door on why we still have mitochondrial DNA, the authors say it does find a middle ground for many different arguments in the debate.

Cell Systems, Johnston and Williams: "Evolutionary inference across eukaryotes identifies multiple pressures favoring mtDNA gene retention"
http://dx.doi.org/10.1016/j.cels.2016.01.013

http://nyti.ms/1WA1rk0

In Zika Epidemic, a Warning on Climate Change

The global public health emergency involving deformed babies emerged in 2015, the hottest year in the historical record, with an outbreak in Brazil of a disease transmitted by heat-loving mosquitoes. Can that be a coincidence?

By JUSTIN GILLIS FEB. 20, 2016 Simon Romero contributed reporting.

Scientists say it will take them years to figure that out, and pointed to other factors that may have played a larger role in starting the crisis. But these same experts added that the Zika epidemic, as well as the related spread of a disease called dengue that is sickening as many as 100 million people a year and killing thousands, should be interpreted as warnings.

Over the coming decades, global warming is likely to increase the range and speed of the life cycle of the particular mosquitoes carrying these viruses, encouraging their spread deeper into temperate countries like the United States.

Recent research suggests that under a worst-case scenario, involving continued high global emissions coupled with fast population growth, the number of people exposed to the principal mosquito could more than double, to as many as 8 billion or 9 billion by late this century from roughly 4 billion today.

"As we get continued warming, it's going to become more difficult to control mosquitoes," said Andrew Monaghan, who is studying the interaction of climate and health at the National Center for Atmospheric Research in Boulder, Colo. "The warmer it is, the faster they can develop from egg to adult, and the faster they can incubate viruses."

Already, climate change is suspected - though not proved - to have been a factor in a string of disease outbreaks afflicting both people and animals. These include the spread of malaria into the highlands of eastern Africa, the rising incidence of Lyme disease in North America, and the spread of a serious livestock ailment called bluetongue into parts of Europe that were once too cold for it to thrive.

In interviews, experts noted that no epidemic was ever the result of a single variable. Instead, epidemics always involve interactions among genes, ecology, climate and human behavior, presenting profound difficulties for scientists trying to tease apart the contributing factors. "The complexity is enormous," said Walter J. Tabachnick, a professor with the Florida Medical Entomology Laboratory, a unit of the University of Florida in Vero Beach.

The epidemics of Zika and dengue are cases in point. The viruses are being transmitted largely by the yellow fever mosquito, Aedes aegypti. That creature adapted long ago to live in human settlements, and developed a concomitant taste for human blood.

Cities in the tropics, the climate zone most favorable to the mosquito, have undergone explosive growth: Humanity passed a milestone a few years ago when more than half the population had moved to urban areas. But spending on health care and on basic public health infrastructure, like water pipes and sewers, has not kept pace. Mosquito control has also faltered in recent decades.

The mosquito lays its eggs in containers of water, of a sort that are especially common in the huge slums of Latin American cities. With unreliable access to piped water, people there store water in rooftop cisterns, buckets and the like. Old tires and other debris can also become mosquito habitat.

Water storage near homes is commonplace in areas where Zika has spread rapidly, like the cities of Recife and Salvador in northeastern Brazil, and where dengue experienced a surge in 2015, like São Paulo, Brazil's largest state. Altogether, dengue killed at least 839 people in Brazil in 2015, a 40 percent increase from the previous year. Worldwide, dengue is killing more than 20,000 people a year.

Several experts said in interviews that a main reason for the disease outbreaks was most likely the expansion of the number of people at risk, through urbanization, population growth and international travel. They see the changing climate as just another stress on top of a situation that was already rife with peril. While they do not understand to what degree rising temperatures and other weather shifts may have contributed to the outbreaks, they do understand some of the potential mechanisms.

The mosquitoes mostly live on flower nectar, but the female of the species needs a meal of human blood to have enough protein to lay her eggs. If she bites a person infected with dengue, Zika or any of several other diseases, she picks up the virus. The virus has to reproduce in the mosquito for a certain period before it can be transmitted to another person in a subsequent bite. The higher the air temperature, the shorter that incubation period. Moreover, up to a point, higher temperatures cause the mosquitoes to mature faster.

With rising temperatures, "You're actually speeding up the whole reproductive cycle of the mosquitoes," said Charles B. Beard, who heads a unit in Fort Collins, Colo., studying insect-borne diseases for the Centers for Disease Control and Prevention in Atlanta. "You get larger populations, with more generations of mosquitoes, in a warmer, wetter climate. You have this kind of amplification of the risk."

Aedes aegypti is present across the southern tier of the United States. Brief outbreaks of dengue have occurred recently at the warmest margins of the country, and one is underway in Hawaii. But with pervasive window screens and air-conditioning, the risk of disease transmission is far less for most Americans than for people in poorer countries.

The mosquito does not thrive in areas with cold winters. Some research suggests that continued climatic warming could allow the mosquito to colonize more of North America in coming decades, though how much of a disease risk that would represent is anybody's guess.

The yellow fever mosquito competes with a cousin, the Asian tiger mosquito, that has also colonized the United States, and is more tolerant of cold weather. Whether one would beat out the other in a hotter climate is unclear. Likewise, it is unclear how effective the Asian tiger mosquito might become at transmitting Zika or dengue viruses. In principle, the risk from continued global warming applies not just to temperate countries, but to cities at high altitude in tropical countries. Researchers are keeping a close eye on Mexico City, for instance.

With 21 million people in the city and its suburbs, Mexico City is the largest metropolis of the Western Hemisphere. While the lowlands of Mexico are plagued by yellow fever mosquitoes and the viruses they transmit, the country's capital sits on a mountain plain that has — up to now — been too cold for the mosquitoes. But temperatures are rising, and the mosquitoes have recently been detected in low numbers near Mexico City. "The mosquito is just down the hill, literally," Dr. Monaghan said. "I think all the potential is there to have virus transmission if climatic conditions become a bit more suitable."

http://bit.ly/1TxAq2D

Ransomware threat highlighted by Los Angeles hospital payout

Bitcoin is making it easier for cybercriminals to profit from their attacks

Extortion is bigger business than ever, and now it doesn't have to rely on people depositing bags stuffed with cash. Earlier this month, cybercriminals attacked a hospital in Los Angeles, then demanded payment in bitcoin to let the hospital regain access to their computers. It's the most high-profile case yet of cyber-extortion using software known as ransomware.

The attack on Hollywood Presbyterian Medical Center effectively knocked it offline. As a result, patients had to be diverted to other hospitals, medical records were kept using pen and paper, and staff resorted to communicating by fax.

The attackers demanded 9000 bitcoins – around $3.6 million. After a two-week stand-off, the hospital yesterday paid out $17,000.

Malware can infect computers when someone clicks on a link to a booby-trapped website, or opens an attachment in a phishing email. In a ransomware attack, the malicious software typically encrypts all of the files stored on a system – making them unusable – and demands payment to decrypt them.

"Ransomware has really exploded in the last couple of years," says Steve Santorelli, a former UK police detective who now works for Team Cymru, a threat intelligence firm based in Florida. One ransomware package, CryptoLocker 3.0, is thought to have earned attackers $325 million in 2015 alone.

"These guys are crazy sophisticated," says Jake Williams, the founder of cybersecurity firm Rendition Infosec. Some even have online helpdesks that can be accessed via the anonymising web browser Tor, and will decrypt one of the victim's files to prove that they have the key.

Williams says his company has worked with several healthcare providers who have been attacked. When clients don't have their files backed up and the ransom is relatively small – hundreds of dollars, say – the firm advises paying up. "We tell them before the attackers realise they've got a much bigger fish on the hook, go ahead and pay immediately," he says. "In every case we've worked with, if you pay the ransom, within a couple of hours you get the decryption key and are able to decrypt your files."

Ransom by bitcoin

Ross Anderson, a security researcher at the University of Cambridge, says bitcoin has helped cybercriminals to access payments without being caught. "In the old days, collecting ransom was really hard. The police would just put a radio tracker in the carpet bag full of £20 notes and they would always get the guy. Now it's possible to collect ransoms by bitcoin, lots of people are doing it."

This is not to say the criminals can't be tracked down. "Good cybercrime investigation is about turning over thousands of little rocks looking for the mistakes that the criminals have made," says Santorelli. "And they always make mistakes." Williams says in some cases his firm has been able to trace attackers to locations in eastern Europe.

Protecting against ransomware is easy: back up your files frequently and make sure your network is segmented – divided up in such a way that an attack on one machine can't spread. "Professionally run operations are not really at risk from ransomware," says Anderson. "You can always go back to yesterday's data."

It would appear that Hollywood Presbyterian was not so well prepared, and it shut down its network after the infection. "It sounds like they're pretty disorganised there, from an IP security perspective," says Williams.

Although ransomware typically encrypts files, the goal of some attacks may be to grab medical records. "We've seen malware in healthcare environments that's been able to steal patients' information," says Williams.

Many more hospitals may have been attacked by cybercriminals, but we never hear about it because they keep things under wraps. "People don't want to rock consumer confidence, and having your medical history stolen is pretty horrific," says Santorelli. "This is going to be devastating to the victims."

As long as security weaknesses exist, there will be criminals eager to exploit them for profit, says Williams. School districts and police departments have also been targeted. "Until healthcare in particular and some of our other critical infrastructure start taking this seriously, you're going to see these attacks for sure."

http://bit.ly/1TxAq2D

Zika May Increase Risk of Mental Illness, Researchers Say

Health experts warn that microcephaly may be only the most obvious consequence of the spread of the Zika

By DONALD G. McNEIL Jr. FEB. 18, 2016

A baby with a shrunken, misshapen head is surely a heartbreaking sight. But reproductive health experts are warning that microcephaly may be only the most obvious consequence of the spread of the Zika virus.

Even infants who appear normal at birth may be at higher risk for mental illnesses later in life if their mothers were infected during pregnancy, many researchers fear. The Zika virus, they say, closely resembles some infectious agents that have been linked to the development of autism, bipolar disorder and schizophrenia.

Schizophrenia and other debilitating mental illnesses have no single cause, experts emphasized in interviews. The conditions are thought to arise from a combination of factors, including genetic predisposition and traumas later in life, such as sexual or physical abuse, abandonment or heavy drug use.

But illnesses in utero, including viral infections, are thought to be a trigger.

"The consequences of this go way beyond microcephaly," said Dr. W. Ian Lipkin, who directs The Center for Infection and Immunity at Columbia University.

Among children in Latin America and the Caribbean, "I wouldn't be surprised if we saw a big upswing in A.D.H.D., autism, epilepsy and schizophrenia," he added. "We're looking at a large group of individuals who may not be able to function in the world."

Researchers in Brazil are investigating thousands of reports of microcephalic births. While there is no solid proof that Zika virus is the cause, virologists studying the outbreak strongly suspect it.

Although the virus was discovered in 1947, there has been no research into its long-term consequences. Scientists are left to draw inferences from what is known of similar infections. In interviews, psychiatric researchers specializing in fetal development agreed with Dr. Lipkin's pessimistic prognosis.

A viral attack early in pregnancy can kill a fetus or stunt the growing brain, producing microcephaly, they explained. An infection later in the fetus's development, when the brain is nearly fully formed, can do damage that is less obvious but still significant. "It is pretty scary," said Dr. Urs Meyer, a behavioral neurobiologist at the Swiss Federal Institute of Technology in Zurich who studies the consequences of fetal infections in lab animals. "These problems are on a continuous scale, and whether you end up with autism or schizophrenia is complex — and we really can't predict it."

Evidence has increased for years that mental illnesses may be linked to exposure during pregnancy to viruses like rubella, herpes and influenza, and to parasites like Toxoplasma gondii. "It can happen with a variety of viruses and other infectious agents, but we don't know how often," said Dr. E. Fuller Torrey, executive director of the Stanley Medical Research Institute in Chevy Chase, Md.

Dr. Torrey noted that Rosemary Kennedy, sister of President of John F. Kennedy, was born in 1918 during the Spanish flu epidemic. She suffered mental disabilities as a child and developed schizophrenia-like symptoms at age 20. Although some historians have attributed her disabilities to a lack of oxygen at birth, Dr. Torrey believes that viral infection in utero is "the most likely" explanation.

The possibility that in utero infection could contribute to mental illness first emerged with an observation in 1988 by Finnish researchers that children born during the 1957 "Asian flu" epidemic had high rates of schizophrenia later in life.

Researchers have long noted that schizophrenia is highest in adults who were born in winter and early spring — just after the peak of flu season.

But estimates of the size of the risk vary. One 2011 analysis of other studies estimated that maternal infections of any kind account for 6 percent of all cases of schizophrenia. (Researchers have done very large studies in Finland, Sweden and Denmark because they have cradle-to-grave records on millions of citizens.)

By contrast, a 2001 study of adults born to mothers infected with rubella, or German measles, during the last American epidemic, which lasted from 1964 to 1965, found that 20 percent had schizophrenia symptoms. The expected rate among adults is below 1 percent.

Dr. Alan S. Brown, director of birth cohort studies at the Columbia University Medical School and leader of that study, said it was "certainly possible" that Zika poses a similar risk, "although ideally you'd want a controlled study."

Although children may be troubled, the hallucinations, voices and paranoia of true schizophrenia do not normally emerge until late adolescence, "when there is a lot of rearranging and pruning in the brain," said Dr. Robert H. Yolken, a developmental neurovirologist at Johns Hopkins University, who also believes that Zika increases mental illness risk.

The effects of Zika mimic those of rubella, some experts noted: Both cause only a mild rash in adults, but can cause stillbirths, microcephaly and eye malformations in newborns. In the 1964-65 rubella epidemic, about 20,000 newborns suffered consequences, including 11,000 born deaf, 3,500 born blind — and at least 1,800 in whom mental problems were later diagnosed.

That epidemic infected an estimated 12 million Americans. More than 500 million people live in the countries of Latin America and the Caribbean to which the World Health Organization has predicted that Zika will spread.

Dr. Stanley A. Plotkin, a rubella expert, said it was possible that children who survive maternal Zika infections with no signs of microcephaly could still suffer mental deficits as they grow.

“Any virus in the blood of a pregnant woman is a risk to the fetus, so ultimately there may be damage,” he said. His own work as a pediatrician showed that many children who survived the 1964-65 epidemic “suffered from autism, learning disabilities and behavioral disabilities.”

The Zika virus seems to zero in on nerve cells even more than does rubella, which also causes heart defects, for example.

Pathologists in Ljubljana, Slovenia, who dissected a microcephalic fetus aborted at 32 weeks by a European woman who had become pregnant in Brazil reported last week that they found “severe fetal brain injury associated with ZIKV infection with vertical transmission” — meaning the Zika virus had come from the mother’s infection.

But a pathogen may not even have to reach the fetus to cause damage.

Flu viruses do not cross the placenta, Dr. Meyer of the Swiss Institute noted, but the mother’s immune reaction creates a storm of cytokines, some of which do. Cytokines are small “signaling” proteins that can cause cells to stop growing.

How much damage is done depends not just on the virus and the mother’s immune response, but on which stage of pregnancy the infection strikes.

First-trimester infections may cause brain tissue to calcify and die; later ones may have subtler, but still insidious, effects.

For example, Dr. Lipkin of the Columbia immunity center said his lab in 2010 infected pregnant mice with a synthetic RNA virus that replicated in fetal mouse brains. The results were wildly unpredictable.

“If you infected them halfway through gestation, the offspring were withdrawn — they sat in a corner of their cage and didn’t interact at all,” he said. “If you did it two-thirds of the way through, they were hyperactive.”

Reports suggest that Brazil, which was facing economic crises even before the Zika outbreak, has little capacity to cope with a surge of mentally disabled children.

European researchers initially paid little attention to the South American outbreak, Dr. Meyer said. But that has changed.

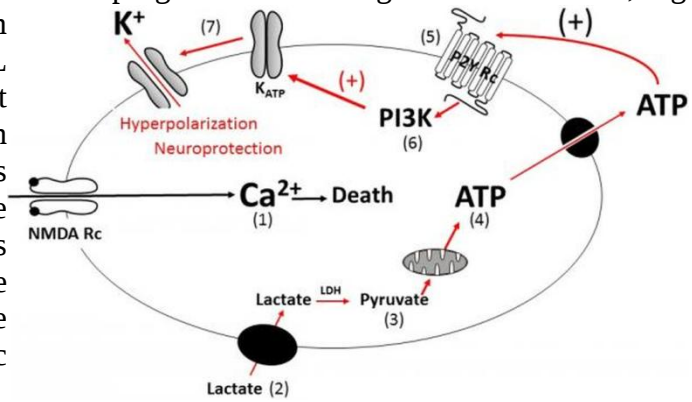
“The information we’re hearing now is just overwhelming,” he said. “A whole generation of children might be affected.”

http://www.eurekalert.org/pub_releases/2016-02/epfd-haw021816.php

How a waste product of exercise protects neurons from trauma damage

Researchers led by EPFL have found how lactate, a waste product of glucose metabolism can protect neurons from damage following acute trauma such as stroke or spinal cord injury.

Stroke or spinal cord injury can cause nerve cells to receive excessive stimulation, which ultimately damages and even kills them. This process is known as excitotoxicity, and it is one of the reasons why time following such trauma is critical, while it also implicated in progressive neurodegenerative diseases, e.g. Alzheimer's disease. A team of scientists led by EPFL has now discovered that lactate, which is produced in the brain and even muscles after intense exercise, can be used to protect neurons against excitotoxicity. The study is published in the Nature journal Scientific Reports.



Step-by-step description of how lactate protects neurons against excitotoxicity: (1) Excessive glutamate activity triggers a strong influx of calcium (Ca2+) into the neuron through NMDA receptors, which leads to cell death. (2) Lactate is transported into the neuron and (3) converted to pyruvate by the enzyme lactate dehydrogenase (LDH). (4) Pyruvate is then transported into mitochondria by the mitochondrial pyruvate carrier (MPC) where it generates ATP. (5) ATP is then released through pannexins and activates the receptor P2Y, which (6) activates the PI3K pathway. (7) This triggers the opening of potassium channels (K+), which causes the neuron to hyperpolarize, decreasing the neuron's excitability, and thus protecting it from excitotoxic damage.
Pascal Jourdain (EPFL)

Following acute trauma such as a stroke or spinal cord injury, a certain type of receptors go into overdrive and overwhelm the target neuron with a barrage of electrical signals. This causes a build-up of calcium ions inside the neuron, which triggers toxic biochemical pathways that ultimately damage or kill it.

The receptors that cause this are called NMDA receptors, and interact with the neurotransmitter glutamate. NMDA receptors are a major target in research and medicine, as they are implicated in a number of disorders, including epilepsy, schizophrenia, Parkinson's and even Alzheimer's.

A team of researchers led by Pierre Magistretti from EPFL and the King Abdullah University of Science and Technology, investigated the effects of glutamate on cultured neurons from the brains of mice. The scientists used a new, non-invasive imaging technique called Digital Holographic Microscopy that can visualize cells structure and dynamics with nanometer-level resolution.

Previous studies have suggested that, lactate could protect neurons against excitotoxicity. Lactate is produced in the brain and in muscles after intense exercise as a waste product of glucose metabolism. Nonetheless, how lactate protects neurons has eluded scientists until now.

The researchers tested the effects of glutamate on the mouse neurons with and without lactate. The results were revealing: glutamate killed 65% of the neurons, but when with lactate, that number dropped to 32%.

The researchers then aimed to determine how lactate protects neurons. By using different receptor blockers on the mouse neurons, they determined that lactate triggers the production of ATP, the cell's energy molecule. In turn, the produced ATP binds and activates another type of receptor in the neuron, which turns on a complex cascade of defense mechanisms. As a result, the neuron can withstand the onslaught of signals from the NMDA receptor.

The breakthrough can advance our understanding of neuroprotection, which could lead to improved pharmacological ways to ameliorate the irreparable damage caused by stroke, spinal cord injury, and other trauma.

This work involved a collaboration of EPFL's Brain Mind Institute with the King Abdullah University of Science and Technology, and the University Hospital of Lausanne (CHUV). It was funded by the FNRS and the NCCR Synapsy.

Jourdain P, Allaman I, Rothenfusser K, Fiumelli H., Marquet P, Magistretti PJ. L-Lactate protects neurons against excitotoxicity: implication of an ATP-mediated signaling cascade. Scientific Reports 6:21250, 19 February 2016. DOI: 10.1038/srep2125019

http://www.eurekalert.org/pub_releases/2016-02/aha-ndr021016.php

New drug reverses the effects of blood thinner in patients with brain hemorrhage

New medication reverses the blood-thinning effects of the anticoagulant dabigatran in patients suffering a brain bleed, potentially limiting the extent of bleeding

LOS ANGELES - A new medication reverses the blood-thinning effects of the anticoagulant dabigatran in patients suffering a brain bleed, potentially limiting the extent of bleeding, according to research presented at the American Stroke Association's International Stroke Conference 2016.

Dabigitran is prescribed to people with atrial fibrillation to prevent blood clots from forming in the heart and traveling to the brain causing a stroke. Patients on blood-thinning drugs, such as dabigatran (Pradaxa), who suffer a type of bleeding that occurs inside the skull (intracranial hemorrhage) are at high risk of complications or disability. Idarucizumab (Praxbind) is an antibody that chemically binds and neutralizes the blood-thinning effects of dabigatran.

An interim analysis of the first 90 patients in a study called RE-VERSE AD (REVERSal Effects of idarucizumab in patients on Active Dabigatran) showed that idarucizumab effectively reversed dabigatran's anticoagulant effects, said Richard A. Bernstein, M.D., Ph.D., lead study author and director of the stroke program at Northwestern Memorial Hospital in Chicago, Illinois.

Bernstein presented the results of 90 brain hemorrhage patients enrolled in the REVERSE-AD study. This included 11 men and seven women (average age 79).

In patients who received two 2.5-gram of idarucizumab infusions in a 15-minute period, blood tests revealed that dabigatran's blood-thinning effect was 100 percent reversed in all 18 patients with brain bleed.

"This is definitely good news," Bernstein said. "Idarucizumab rapidly and completely reverses the effect of dabigatran in patients with brain hemorrhage. Once the dabigatran is reversed, we can focus on taking care of the patient without worrying about the blood thinner."

The new results are part of a large on-going phase III study testing idarucizumab in a range of patients who take dabigatran and have dangerous bleeding or need urgent surgery or other procedures that carry serious bleeding risks.

Idarucizumab was approved by the U.S. Food and Drug Administration in October 2015 as the first medicine designed to reverse dabigatran.

Researchers say before idarucizumab was available, patients on dabigatran who needed emergency surgery were given purified clotting factors, which carry the risk of patients' clotting systems forming dangerous blood clots.

"Idarucizumab gets rid of the dabigatran, but doesn't seem to carry with it any tendency to increase clotting. This should make perioperative management easier and safer," Bernstein said.

Idarucizumab's success so far might persuade more people to take a blood thinner when their doctors recommend it. "The biggest problem we face in preventing stroke in patients with atrial fibrillation is that almost half of patients don't take any blood thinner at all," Bernstein said. "I see the biggest impact of idarucizumab as providing reassurance to patients that if bleeding while taking dabigatran does occur, we can quickly reverse the dabigatran. This reassurance could lead to more strokes prevented by increasing the use of an effective blood thinner."

Co-authors are Charles V. Pollack Jr., M.D.; Jeffrey I. Weitz, M.D.; Paul A. Reilly, Ph.D.; John Eikelboom, M.B.B.S., M.Sc.; Menno V. Huisman, M.D., Ph.D.; Pieter W. Kamphuisen,

M.D., Ph.D.; Jörg Kreuzer, M.D.; Jerrold H. Levy, M.D. and Thorsten Steiner, M.D., Ph.D. Author disclosures are on the abstract.

The study was funded by Boehringer Ingelheim. Praxbind and Pradaxa are both marketed by Boehringer Ingelheim of Ridgefield, Connecticut.

http://bit.ly/21hXmnQ

New underground plant hides from the sun and parasitises fungi

It's a low-down, dirty cheat. A newly discovered Japanese plant spends most of its life hidden underground and steals nutrients from fungi rather than getting its energy from the sun.

Kenji Suetsugu of Kobe University came across the previously unknown plant in an evergreen forest on the subtropical Japanese island of Yakushima while documenting other fungi-parasitising – mycoheterotrophic – plants in Japan.

The plant's stem is about 3-9 centimetres long and has between nine and 15 purple star-shaped flowers, which push up above the ground. Suetsugu has named it *Sciaphila yakushimensis* after the island.

***The flowers of* Sciaphila yakushimensis *(left) and* Sciaphila japonica *poke above the ground* Yamashita Hiroaki**

The plant can't photosynthesise and, like other mycoheterotrophs, steals the carbon it needs from a fungal host. The parasitic plant attracts strands of mycorrhizal fungus into its many hairy roots and then feeds off fungus growing inside the roots.

Life in the dark

Its parasitic lifestyle is an adaptation to the forest understorey, where the sun's rays struggle to penetrate and so photosynthetic plants are rare, says Suetsugu.

Because it doesn't rely on photosynthesising the sun's light for its energy, it can stay underground, reducing the risk of being eaten by aboveground herbivores. It only pokes through the leaf litter to flower and fruit.

Vast fungal networks in the forest soil are linked up with plant roots and usually get their carbon from trees, in exchange for water and minerals that their tiny hairs extract from soil. But mycoheterotrophs taps into this network and get the carbon from fungi, which got it from other plants to start with. "These mycoheterotrophs are extremely rare and could not survive without a flourishing forest, sustained by species-rich underground fungal networks," says Suetsugu.

Rare but not protected

Given that it only seems to have two small populations, the new species can be considered critically endangered, Suetsugu says. Other mycoheterotrophic plant species have recently been found in the area, but many are not yet officially protected.

Such plants are dependent on their host fungi, so Suetsugu says it will be necessary to conserve entire ecosystems to protect these rare plants. He recommends that regulators should restrict logging and construction to preserve these and other endemic species in the forest habitats of Yakushima.

Constantijn Mennes at the Naturalis Biodiversity Center in Leiden, the Netherlands, says there is still a substantial amount of undescribed biodiversity, even in flowering plants.

"This observation adds to a large list of critically endangered mycoheterotrophic species, like species of *Kupea* and *Kihansia* in Africa," he says.

Journal reference: Journal of Japanese Botany, *Vol. 91 No. 1*

http://bit.ly/1SJG1CQ

Exoplanet Census Suggests Earth Is Special after All

A new tally proposes that roughly 700 quintillion terrestrial exoplanets are likely to exist across the observable universe—most vastly different from Earth

By Shannon Hall on February 19, 2016

More than 400 years ago Renaissance scientist Nicolaus Copernicus reduced us to near nothingness by showing that our planet is not the center of the solar system. With every subsequent scientific revolution, most other privileged positions in the universe humans might have held dear have been further degraded, revealing the cold truth that our species is the smallest of specks on a speck of a planet, cosmologically speaking. A new calculation of exoplanets suggests that Earth is just one out of a likely 700 million trillion terrestrial planets in the entire observable universe. But the average age of these planets—well above Earth's age—and their typical locations—in galaxies vastly unlike the Milky Way—just might turn the Copernican principle on its head.

Astronomer Erik Zackrisson from Uppsala University and his colleagues created a cosmic compendium of all the terrestrial exoplanets likely to exist throughout the observable universe, based on the rocky worlds astronomers have found so far. In a powerful computer simulation, they first created their own mini universe containing models of the earliest galaxies. Then they unleashed the laws of physics—as close as scientists understand them—that describe how galaxies grow, how stars evolve and how planets come to be. Finally, they fast-forwarded through 13.8 billion years of cosmic history. Their results, published to the preprint server arXiv (pdf) and submitted to *The Astrophysical Journal*, provide a

tantalizing trove of probable exoplanet statistics that helps astronomers understand our place in the universe. “It's kind of mind-boggling that we're actually at a point where we can begin to do this,” says co-author Andrew Benson from the Carnegie Observatories in California. Until recently, he says, so few exoplanets were known that reasonable extrapolations to the rest of the universe were impossible. Still, his team’s findings are a preliminary guess at what the cosmos might hold. “It's certainly the case that there are a lot of uncertainties in a calculation like this. Our knowledge of all of these pieces is imperfect,” he adds.

Take exoplanets as an example. NASA’s Kepler space telescope is arguably one of the world’s best planet hunters, but it uses a method so challenging that it is often compared with looking across thousands of kilometers to see a firefly buzzing around a brilliant searchlight. Because the telescope looks for subtle dimming in a star’s light from planets crossing in front of it, Kepler has an easier time spotting massive planets orbiting close to their stars.

Thus, the catalogue of planets Kepler has found lean heavily toward these types, and smaller, farther-out planets are underrepresented, leaving our knowledge of planetary systems incomplete. Astronomers do use other techniques to search for smaller planets orbiting at farther distances, but these methods are still relatively new and have not yet found nearly as many worlds as Kepler. In addition, “everything we know about exoplanets is from a very small patch in our galaxy,” Zackrisson says, within which most stars are pretty similar to one another in terms of how many heavy elements they contain and other characteristics. The team had to extrapolate in order to guess how planets might form around stars with fewer heavy elements, such as those found in small galaxies or the early universe.

The scientists also have similar concerns about the galactic and cosmological inputs of their model but nonetheless they suspect that their final numbers are accurate to within an order of magnitude. With the estimated errors taken into account, the researchers conclude that Earth stands as a mild violation of the Copernican principle. Our pale blue dot might just be special after all. “It's not too much of a fluke that we could arise in a galaxy like the Milky Way, but nevertheless, it's just enough to make you think twice about it,” says Jay Olson from Boise State University, who was not involved in the study. Both he and Zackrisson think the Copernican principle could be saved by some unknown caveat to the findings. “Whenever you find something that sticks out…” Zackrisson says, “…that means that either we are the result of a very improbable lottery draw or we don’t understand how the lottery works.”

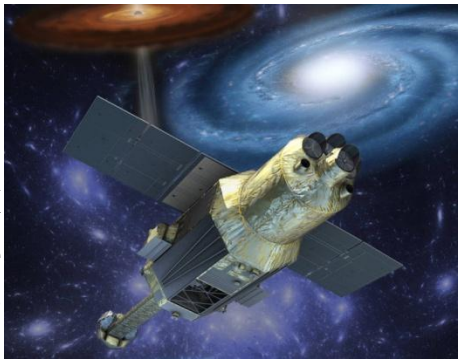
But Max Tegmark from the Massachusetts Institute of Technology, who also was not part of the research, thinks Earth is a colossal violation of the Copernican principle—not because of its location but because of its young age. “If you have these civilizations that had a 3.5-billion-year head start on us, why haven't they colonized our galaxy?” asks Tegmark. “To me, the most likely explanation is that if the planets are a dime a dozen, then highly intelligent life evolves only rarely.” So should we feel insignificant? Should we be reduced to near nothingness? Not at all, he says. “It might be that one day in the distant future much of our universe will be teeming with life because of what we did here.”

http://tcrn.ch/1mQmlz9

Japan Launches Observatory To Study Black Holes And Dying Stars

This week the Japan Aerospace Exploration Agency (JAXA) successfully launched a new space observatory designed to study black holes, dying stars and the history of galaxy clusters.

Posted 17 hours ago by Emily Calandrelli (@TheSpaceGal)



The X-ray Astronomy Satellite, known as ASTRO-H, will be able to detect X-rays more than 10 times fainter than its telescope predecessor, Suzaku.

ASTRO-H was launched on the Japanese launch vehicle H-IIA from Tanegashima Launch Center on Wednesday, February 17th at 3:45 am EST. Within hours, the satellite deployed its solar arrays and was functioning normally.

It’s tradition for Japan’s astronomy satellites to be given a provisional name before launch and be renamed once they’re in orbit. After its successful launch, JAXA announced ASTRO-H was renamed to Hitomi, a Japanese word that refers to an eye’s pupil, which is like an aperture collecting light for an eye.

Celestial bodies in the universe emit radiation in many different forms. Perhaps the most obvious form is the kind we can see with our own eyes – visible light. The Hubble Space Telescope, for example, was an optical telescope that collected visible light and could study the universe in the visible spectrum.

In contrast, Hitomi is designed to study celestial bodies that emit X-rays. X-rays are a form of extremely high energy radiation and are generated by high energy events in the universe like black holes, neutron stars, supernova explosions and galaxy clusters. While visible light spans an energy range from 2 electron volts (eV) to 3 eV, Hitomi is equipped with 4 co-aligned X-ray telescopes that are capable of detecting 300 eV to 600,000 eV.

Hitomi is the sixth in a series of JAXA X-ray astronomy satellites. With technology improvements and state-of-the-art instruments, Hitomi will be able to provide a higher-resolution image of the universe in the X-ray spectrum than ever before. This is achieved with precise pointing (looking at a very small section of the sky) and the ability to measure and distinguish a wide range of frequencies in the X-ray spectrum.

The astronomy satellite was an international project lead by JAXA with contributions from Europe, Canada and NASA. In return for their contributions, space agencies are able to compete for a certain percentage of observational time on Hitomi.

As technologies improve, scientists are able to view the universe in ways they've never seen before. With Hitomi, astronomers will be able to view the X-ray side of the universe with higher precision and resolution than they've achieved with prior telescopes.

As data comes in from Japan's latest X-ray satellite, astronomers around the world hope to learn about the evolution of the largest structures in the cosmos, the behavior of black holes and the matter around them, and the internal structure of neutron stars.

http://bit.ly/1UfR2LI

Naked Mole Rats Were Thought to Be Impervious to Cancer, Until They Got It This Month

Veterinarians from the Brookfield Zoo in Chicago discovered two mole rats with cancerous masses

Aimée Lutkin

Image via *AP*.

But before we get to the science, let's say what we're all thinking—that rodent looks like a penis with feet.

Great, now that that's out of the way, here's some cool stuff about the magical Naked Mole Rat that I had never even heard of before writing this post.

For example, researchers have never reported a case of cancer in one of these skittering phalluses, in zoos or in the wild. They've even straight up injected their cells with the same viruses that triggers tumors in mice, and nothing happened. Whatever else is up with them, their bodies are like, "Cancer schmancer."

Until! Early in February, veterinarians from the Brookfield Zoo in Chicago discovered two mole rats with cancerous masses, that they then sent samples of to researchers at the University of Washington School of Medicine. Pathologist Martha Delaney wrote to the *New York Times* that this is actually a great opportunity, rather than a sign that the end is nigh:

Now that we have two naked mole rats with cancer... we can study the colonies from which they came to elucidate why they are cancer prone, compared to other zoo and research colonies.

Environmental factors and aging are a big part of cancer research, so it's all a pretty exciting stuff. Except, bad news first—one of the cancer stricken naked mole rats has passed. Good news second—the other naked mole rat was pronounced cancer free at age 22! Please knit him a little sweater, or something.

http://www.eurekalert.org/pub_releases/2016-02/w-wah021716.php

Weight and height during adolescence may impact future risk of developing Non-Hodgkin's lymphoma

Higher body weight and taller stature during adolescence increase the risk of developing Non-Hodgkin's Lymphoma

A new analysis indicates that higher body weight and taller stature during adolescence increase the risk of developing Non-Hodgkin's Lymphoma (NHL), a type of cancer of the lymphatic system. The findings are published early online in CANCER, a peer-reviewed journal of the American Cancer Society.

Rates of NHL have increased worldwide, and research suggests that rising rates of obesity may be contributing to this trend. With this in mind, a team led by Merav Leiba, MD, of the Sheba Medical Center in Israel, examined whether adolescent weight and height might be associated with the risk of developing NHL later in life. The study included 2,352,988 teens aged 16 to 19 years old who were examined between 1967 and 2011. Their information was linked to the Israel National Cancer Registry, which included 4021 cases of NHL from 1967 through 2012.

Adolescent overweight and obesity was associated with a 25 percent increased risk of NHL in later life, compared with normal weight, and there was an association for multiple subtypes of NHL. "Obesity and overweight during adolescence are risk factors for future Non-Hodgkin Lymphoma," said Dr. Leiba. "It is important to be aware that overweight and obesity are not risk factors only for diabetes and cardiovascular disease but also for lymphomas."

There was also a stepwise gradient in NHL risk with increasing height. When compared with the mid-range height category, shorter individuals had a 25 percent reduced risk of NHL, whereas the tallest individuals had a 28 percent increased risk. In the end, excess height and weight were responsible for 6% and 3% of all NHL cases respectively. As for mechanism, height and excess nutrition in childhood may have impacts on inflammatory molecules and growth factors that

could support the development of NHL, but additional studies are needed to investigate these possibilities.

Article: "Adolescent weight and height are predictors of specific Non-Hodgkin's Lymphoma subtypes among a cohort of 2,352,988, 16-19 year olds." Merav Leiba, Adi Leiba, Lital Keinan-Boker, Abraham Avigdor, Estela Derazne, Hagai Levine, and Jeremy D. Kark. CANCER; Published Online: February 22, 2016 (DOI: 10.1002/cncr.29792).

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Vaccine Has Sharply Reduced HPV in Teenage Girls, Study Says

A vaccine introduced a decade ago to combat the sexually transmitted virus that causes cervical cancer has already reduced the virus's prevalence in teenage girls by almost two-thirds, federal researchers said Monday.

By JAN HOFFMAN FEB. 22, 2016

Even for women in their early 20s, a group with lower vaccination rates, the most dangerous strains of human papillomavirus, or HPV, have still been reduced by more than a third.

"We're seeing the impact of the vaccine as it marches down the line for age groups, and that's incredibly exciting," said Dr. Amy B. Middleman, the chief of adolescent medicine at the University of Oklahoma Health Sciences Center, who was not involved in the study. "A minority of females in this country have been immunized, but we're seeing a public health impact that is quite expansive."

The vaccine for human papillomavirus, a cause of cervical cancer, has proved effective, but immunization rates remain low. **Joe Raedle/Getty Images**

The news is likely to serve as a welcome energizer in the tumultuous struggle to encourage HPV vaccination in the United States. Despite the vaccine's proven effectiveness, immunization rates remain low — about 40 percent of girls and 20 percent of boys between the ages of 13 and 17. That is partly because of the implicit association of the vaccine with adolescent sexual activity, rather than with its explicit purpose: cancer prevention. Only Virginia, Rhode Island and the District of Columbia require the HPV vaccine.

Recent efforts have focused on recommending the vaccine for children ages 11 and 12, when their immune response is more robust than that of teenagers and when most states require two other vaccines — one for tetanus, diphtheria and pertussis, and the other for meningococcal disease. The immunization rates for those vaccines are 80 percent and higher.

About 14 million Americans become infected with HPV each year, and the vast majority will clear the virus. But some strains persist and can cause genital warts, as well as cervical, anal, penile, and mouth and throat cancers. The American Cancer Society estimates that 4,120 women will die of cervical cancer this year.

The latest research, published in Pediatrics, examined HPV immunization and infection rates through 2012, but just in girls. The recommendation to vaccinate boys became widespread only in 2011; they will be included in subsequent studies.

Using data from a survey by the Centers for Disease Control and Prevention, the study examined the prevalence of the virus in women and girls of different age groups during the pre-vaccine years of 2003 through 2006. (The vaccine was recommended for girls later in 2006.) Researchers then looked at the prevalence in the same age groups between 2009 and 2012.

By those later years, the prevalence of the four strains of HPV covered by the vaccine had decreased by 64 percent in girls ages 14 to 19. Among women ages 20 to 24, the prevalence of those strains had declined 34 percent. The rates of HPV in women 25 and older had not fallen.

"The vaccine is more effective than we thought," said Debbie Saslow, a public health expert in HPV vaccination and cervical cancer at the American Cancer Society. As vaccinated teenagers become sexually active, they are not spreading the virus, so "they also protect the people who haven't been vaccinated," she said.

There are several obstacles to greater coverage rates in the United States. In other countries, the vaccine is often given in two doses, particularly to girls younger than 15. In the United States, it is given in three doses. An immunization advisory committee to the C.D.C. will convene this week to learn more about the efficacy of the lower dose.

And in some countries, the vaccine is either mandatory or at least offered at school, its cost covered by a national health care system, making administration more streamlined and comprehensive. Such measures helped Rwanda achieve a 93 percent immunization rate in girls. Australia, where the vaccine is offered free to schoolgirls, accomplished a 92 percent reduction in genital warts in women under 21, a study showed. But in the United States, the vaccine is largely optional.

"Multiple studies have shown the importance of a strong provider recommendation for increasing vaccination coverage," said Dr. Lauri E. Markowitz, a medical epidemiologist at the National Center for Immunizations and Respiratory Diseases, a division of the C.D.C., who led the research for the latest study.

But studies show that many primary care providers either do not recommend the vaccine to parents and patients or do so halfheartedly. Some doctors are reluctant to discuss the vaccine because the conversation may dance uncomfortably around

sexual activity. They may want to use their limited appointment time for health topics that parents may be more willing to engage.

To try to shift focus to the vaccine's purpose, last month dozens of cancer centers endorsed the HPV vaccine as a safe, effective prevention strategy against types of cancer that result in 27,000 cases a year. The latest HPV vaccine protects against nine strains of the virus.

Many doctors are pressing for primary care providers to strongly recommend the HPV vaccine in tandem with the other two that preteen children now typically receive.

"The infection is sexually transmitted, but that doesn't need to be part of the conversation," said Dr. Joseph A. Bocchini Jr., a pediatric infectious disease specialist at Louisiana State University in Shreveport.

"If a parent is concerned, physicians should be prepared to talk about it," said Dr. Bocchini, a former chairman of an HPV vaccine working group for the committee that advises the C.D.C. on immunizations. "But we don't really discuss how people become infected with every vaccine-preventable disease."