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Snakebite Antivenom Development Is Stuck in the 19th Century--What's Next?

Doctors Without Borders now describes snakebites as "one of the world's most neglected public health emergencies"

By Jeremy Hsu | Nov 17, 2015

Modern medicine can grow kidneys from scratch, halt the spread of infectious diseases such as Ebola and diagnose the cause of a cough with a smartphone, yet snakebites still thwart us. Every year venom from snakes kills nearly 200,000 people and leaves hundreds of thousands disfigured or disabled, making these legless squamates the second deadliest animal. Only mosquitoes may kill more people every year (by spreading the protozoa that cause malaria).

Venomous snakes recently slithered their way back into the news when it came to light that leaders in the pharmaceutical world had ceased developing antidotes. French drug company Sanofi Pasteur, for example, made headlines in September, when Doctors Without Borders pointed out that the final batch of FAV-Afrique—the only antivenom proved to effectively treat snakebite victims in sub-Saharan Africa—expires in June 2016. Sanofi, its sole manufacturer, had ended production in 2014 because the drug was not making enough money. Others in the industry had already made similar moves, including Behringwerke and Wyeth Pharmaceuticals (now part of Pfizer).

The treatment situation has become so dire that Doctors Without Borders now describes snakebites as "one of the world's most neglected public health emergencies." And in October dozens of experts at the 18th World Congress of the International Society on Toxinology in Oxford, England, called for the World Health Organization to relist snakebite as a neglected tropical disease. Most bites occur in Africa and Southeast Asia.

Antivenom development is stuck in the 19th century because the field is underfunded, says David Williams, a clinical toxinologist and herpetologist who heads the Australian Venom Research Unit at the University of Melbourne and is also CEO of the Australian nonprofit Global Snakebite Initiative. To isolate compounds for treatment, researchers typically inject subtoxic levels of venom into animals, collect the antibodies formed by the immune response and purify the result. Antivenom must be tailored to an array of toxins across different regional snake species. No universal antidote exists.

Despite constraints, small research groups around the world are quietly working away at new, exciting solutions—waiting for a windfall of money and momentum. The most innovative of them is a targeted antivenom designed for sub-Saharan Africa that could serve as a blueprint for making cheaper compounds to counter bites from snakes found in other regions. Researchers from the U.K., Costa Rica and Spain started with proven "base antivenom" for three snakes and have begun screening it against toxins from additional snakes. Venom proteins that fail to bind to the base antivenom are screened for toxicity; only proteins identified as dangerous toxins become part of the immunizing mixture used to make the next antivenom batch more effective.

Such selective screening and iterative testing of specific proteins make for a stronger, targeted antidote compared with conventional antivenoms, which indiscriminately neutralize both toxic and nontoxic venom proteins. The group also plans to cut costs with a method pioneered in Costa Rica that requires fewer manufacturing steps. "Our goal is to make a product for sub-Saharan Africa that is cheaper or as cheap as $35 a vial," says Robert Harrison, head of the Alistair Reid Venom Research Unit at the Liverpool School of Tropical Medicine in England. Sanofi's product costs $150 per vial.

Other animals—and bacteria—may provide alternative antivenom. An opossum protein first identified in the 1990s has since been shown to protect mice from snake toxins that can cause widespread internal bleeding. Moreover, the protein neutralized hemorrhagic toxins from venomous snakes in both the U.S. and Pakistan. The finding suggests that the protein might possibly defend against all hemorrhagic snake toxins, says Claire Komives, a chemical engineer at San José State University. Komives has already demonstrated that she can engineer Escherichia coli bacteria to make the protein—which could reduce the cost of treatment to around $10 a dose. "I'm trying to make it in bacteria because we can scale [up production] cheaply," she says. To fund her research, Komives has turned to the crowdfunding service Experiment.com.

Research groups elsewhere have turned away from traditional antidote development altogether. Matthew Lewin, director of the Center for Exploration and Travel Health at the California Academy of Sciences, has begun screening existing fda-approved drugs for chemical ingredients that could form the basis of an injection or pill that stabilizes people bitten in the field or at least gives them time to reach a hospital. "If you had a pharmaceutical antidote, you could have it on your person," Lewin says. Many snakebite deaths happen when victims cannot reach hospitals or clinics to receive an intravenous antivenom treatment.

Similarly, Sakthivel Vaiyapuri, a pharmacology researcher at the University of Reading in England, is screening for molecules that block the effects of snake venom. He also hopes to eventually develop a cocktail of chemical inhibitors that could lead to a universal antidote.

Modernized antivenom treatments would represent a solid first step toward reducing deaths from snakebites. Yet in the end, the best treatments in the world

will fail without funding and distribution. “If the ministries of health responsible for health and well-being don't prioritize snakebite treatment,” says Williams of the Global Snakebite Initiative, “you're banging your head against a brick wall.”

http://www.medscape.com/viewarticle/854458

Supplements for Prostate Cancer: 'Junk' Science?

Hello. I'm Dr Gerald Chodak for Medscape. Today I want to talk about the potential value or role of “prostate-complex” supplements for men who are getting radiation therapy for localized prostate cancer.

Gerald Chodak, MD|November 20, 2015

Zaorsky and coworkers presented their data[1] at the recent American Society for Radiation Oncology (ASTRO) meeting; they analyzed about 2200 men who had received radiation therapy sometime between 2001 and 2010. They looked at whether or not supplements were reported as being ingested, and they analyzed the information in terms of biochemical recurrence, metastatic disease, overall survival, and cancer-specific survival at 5 years.

Their finding was that there was no significant difference in outcomes for the men taking supplements. On the basis of that, they have made statements—or, the lead author made a statement—that the supplements were junk and that their study supports that conclusion.[2]

Now, over the years, I have done a number of commentaries on supplements for men with prostate cancer, and I have been very critical of any that made recommendations that weren't based on well-designed trials. At the same time, I think we have to be careful when we are critical that we use data based on a well-designed trial; and, unfortunately, this trial does not support or prove anything.

There were many methodologic problems with the design of this trial. It was retrospective, it was completely uncontrolled, and the number of supplements taken was somewhere up to 50 different supplements that were used by the various individuals. There is nothing that controlled dose, duration of therapy, whether or not there was significant compliance, when it was started, or when it was stopped, and so these problems simply point out the fact that we really don't know much about whether or not people were taking something that contained an active ingredient or not.

It is quite possible, based on a recent analysis in New York, that a lot of the supplements claiming to contain certain ingredients, in fact, don't contain either the amount or the specific item that has been mentioned.[3]

The bottom line here is that unless we do a properly designed, well controlled, randomized trial in which we know whether people are getting a real product or not, only with that kind of analysis are we going to be able to make any conclusion about whether these supplements are beneficial for men with prostate cancer. Until then, I think the only thing we can tell patients is: Number one, we have absolutely no proof that supplements help men with prostate cancer; number two, we know from a variety of randomized trials of supplements that there can be harm, depending on a variety of factors; and number three, before someone takes a supplement when being treated for prostate cancer, the best advice for them is to have a discussion with the doctor in charge, at least to make them aware of what they are taking and also to discuss the basis or reasoning behind their action.

I look forward to your comments. Thank you.

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Earth not due for a geomagnetic flip in the near future

Researchers find geomagnetic field intensity is double the long-term historical average

The intensity of Earth's geomagnetic field has been dropping for the past 200 years, at a rate that some scientists suspect may cause the field to bottom out in 2,000 years, temporarily leaving the planet unprotected against damaging charged particles from the sun. This drop in intensity is associated with periodic geomagnetic field reversals, in which the Earth's North and South magnetic poles flip polarity, and it could last for several thousand years before returning to a stable, shielding intensity.

With a weakened geomagnetic field, increased solar radiation might damage electronics -- from individual pacemakers to entire power grids -- and could induce genetic mutations. A reversal may also affect the navigation of animals that use Earth's magnetic field as an internal compass.

But according to a new MIT study in the Proceedings of the National Academy of Sciences, the geomagnetic field is not in danger of flipping anytime soon: The researchers calculated Earth's average, stable field intensity over the last 5 million years, and found that today's intensity is about twice that of the historical average. This indicates that the current field intensity has a long way to fall before reaching an unstable level that would lead to a reversal.

"It makes a huge difference, knowing if today's field is a long-term average or is way above the long-term average," says lead author Huapei Wang, a postdoc in

MIT's Department of Earth, Atmospheric and Planetary Sciences. "Now we know we are way above the unstable zone. Even if the [field intensity] is dropping, we still have a long buffer that we can comfortably rely on."

Flip-flopping through history

Earth has undergone multiple geomagnetic reversals over its lifetime, flip-flopping its polarity at random intervals. "Sometimes you won't have a flip for about 40 million years; other times there will be 10 flips in 1 million years," Wang says. "On average, the duration between two flips is a few hundred thousand years. The last flip was around 780,000 years ago, so we are actually overdue for a flip."

The most obvious sign of an impending reversal is a geomagnetic field intensity that's significantly below its historical, long-term average -- a sign that the planet is tipping toward an unstable state. While satellites and ground-based observatories have made accurate measurements over the last 200 years of the current field intensity, there are less reliable estimates over the last few million years.

Wang and his colleagues, from Rutgers University and France, sought to measure Earth's paleomagnetic field using ancient rocks erupted from volcanoes on the Galapagos Islands -- an ideal site, since the island chain is on the equator. As Earth's magnetic field, in its stable configuration, is a dipole, the intensity of the field should be the same at both poles, and half that intensity at the equator.

Wang reasoned that knowing the paleomagnetic field intensity at the equator and the poles would therefore give an accurate estimate of the planet's average historical intensity.

Rocks from a dipole

Wang obtained samples of ancient volcanic lavas from the Galapagos, while his colleagues from the Scripps Institution of Oceanography at the University of California at San Diego excavated similarly aged rocks from Antarctica. Such volcanic rocks retain information on the geomagnetic field intensity at the time they cooled.

The two teams brought the samples back to their respective labs, and measured the rocks' natural remanent magnetization, or orientation of ferromagnetic particles. They then heated the rocks, and cooled them in the presence of a known magnetic field, measuring the rocks' magnetization after cooling.

A rock's remanent magnetization is proportional to the magnetic field in which it cooled. Therefore, using the data from their experiments, the researchers were able to calculate the peak distribution of the ancient geomagnetic field intensity, both at the equator -- about 15 microtesla -- and the poles -- about 30 microtesla. Today's field intensities at the same locations are around 30 microtesla and 60 microtesla, respectively -- double the historical, long-term values.

"That means today's value is anomalously high, and even if it's dropping, it's dropping to a long-term average, not from an average to zero," Wang says.

Far from zero

So why have scientists assumed that Earth's geomagnetic field is dropping to a precipitous low? It turns out this assumption is based on flawed historical data, Wang says.

Scientists have estimated paleomagnetic intensities at various latitudes around the Earth, but Wang's is the first data from equatorial regions. However, Wang found that scientists were misinterpreting how rocks recorded their magnetic fields, leading to inaccurate estimates of paleomagnetic intensity. Specifically, scientists were assuming that as individual ferromagnetic grains of rocks cooled, their unpaired electron spins assumed a uniform orientation, reflecting the magnetic field intensity.

However, this effect only holds true up to a certain size. In larger grains, unpaired electron spins assume various orientations in different domains of the grain, thereby complicating the field intensity picture.

Wang developed a method to correct for such multidomain effects, and applied the method to his Galapagos lavas. The results, he says, are more reliable than previous estimates of the paleomagnetic field.

As for when Earth may experience its next flip, Wang says the answer is still up in the air. "What I can say is, if you keep a constant present-day decrease rate, it will take another 1,000 years for the field to drop to its long-term average," Wang says. "From there, the field intensity may go up again. There's really no way to predict what will happen after that, given the random nature of the magnetohydrodynamic process of the geodynamo."

http://www.eurekalert.org/pub_releases/2015-11/uoc-ltc112015.php

Loneliness triggers cellular changes that can cause illness, study shows

Loneliness is more than a feeling: For older adults, perceived social isolation is a major health risk that can increase the risk of premature death by 14 percent.

Researchers have long known the dangers of loneliness, but the cellular mechanisms by which loneliness causes adverse health outcomes have not been well understood. Now a team of researchers, including UChicago psychologist and leading loneliness expert John Cacioppo, has released a study shedding new light on how loneliness triggers physiological responses that can ultimately make us sick.

The paper, which appears Nov. 23 in the Proceedings of the National Academy of Sciences, shows that loneliness leads to fight-or-flight stress signaling, which can ultimately affect the production of white blood cells.

Along with Cacioppo, the research team includes Steven W. Cole of UCLA and John P. Capitanio of the California National Primate Research Center at the University of California, Davis. The study examined loneliness in both humans and rhesus macaques, a highly social primate species.

Previous research from this group had identified a link between loneliness and a phenomenon they called "conserved transcriptional response to adversity" or CTRA. This response is characterized by an increased expression of genes involved in inflammation and a decreased expression of genes involved in antiviral responses. Essentially, lonely people had a less effective immune response and more inflammation than non-lonely people.

For the current study, the team examined gene expression in leukocytes, cells of the immune system that are involved in protecting the body against bacteria and viruses.

As expected, the leukocytes of lonely humans and macaques showed the effects of CTRA--an increased expression of genes involved in inflammation and a decreased expression of genes involved in antiviral responses. But the study also revealed several important new pieces of information about loneliness' effect on the body.

First, the researchers found that loneliness predicted future CTRA gene expression measured a year or more later. Interestingly, CTRA gene expression also predicted loneliness measured a year or more later. Leukocyte gene expression and loneliness appear to have a reciprocal relationship, suggesting that each can help propagate the other over time. These results were specific to loneliness and could not be explained by depression, stress or social support.

Next, the team investigated the cellular processes linking social experience to CTRA gene expression in rhesus macaque monkeys at the California National Primate Research Center, which had been behaviorally classified as high in perceived social isolation. Like the lonely humans, the "lonely like" monkeys showed higher CTRA activity. They also showed higher levels of the fight-or-flight neurotransmitter, norepinephrine.

Previous research has found that norepinephrine can stimulate blood stem cells in bone marrow to make more of a particular kind of immune cell--an immature monocyte that shows high levels of inflammatory gene expression and low levels of antiviral gene expression. Both lonely humans and "lonely like" monkeys showed higher levels of monocytes in their blood.

More detailed studies of the monkey white blood cells found that this difference stemmed from expansion of the pool of immature monocytes. In an additional study, monkeys repeatedly exposed to mildly stressful social conditions (unfamiliar cage-mates) also showed increases in immature monocyte levels. These analyses have finally identified one reason why CTRA gene expression is amplified in the white blood cell pool: increased output of immature monocytes.

Finally, the researchers determined that this monocyte-related CTRA shift had real consequences for health. In a monkey model of viral infection, the impaired antiviral gene expression in "lonely like" monkeys allowed simian immunodeficiency virus (the monkey version of HIV) to grow faster in both blood and brain.

Taken together, these findings support a mechanistic model in which loneliness results in fight-or-flight stress signaling, which increases the production of immature monocytes, leading to up-regulation of inflammatory genes and impaired anti-viral responses. The "danger signals" activated in the brain by loneliness ultimately affect the production of white blood cells. The resulting shift in monocyte output may both propagate loneliness and contribute to its associated health risks.

The team plans to continue research on how loneliness leads to poor health outcomes and how these effects can be prevented in older adults.

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High-fat diet prompts immune cells to start eating connections between neurons

When a high-fat diet causes us to become obese, it also appears to prompt normally bustling immune cells in our brain to become sedentary and start consuming the connections between our neurons, scientists say.

AUGUSTA, Ga. - The good news is going back on a low-fat diet for just two months, at least in mice, reverses this trend of shrinking cognitive ability as weight begins to normalize, said Dr. Alexis M. Stranahan, neuroscientist in the Department of Neuroscience and Regenerative Medicine at the Medical College of Georgia.

"Microglia eating synapses is contributing to synapse loss and cognitive impairment in obesity," Stranahan said. "On the one hand, that is very scary, but it's also reversible, meaning that if you go back on a low-fat diet that does not

even completely wipe out the adiposity, you can completely reverse these cellular processes in the brain and maintain cognition."

Stranahan is corresponding author of the study in the journal Brain, Behavior, and Immunity, which provides some of the first evidence of why fat is bad for the brain.

The trouble appears to start with too much fat in the body producing chronic inflammation, which stimulates microglia to have an autoimmune response. Microglia, like macrophages in the body, are known for their ability to ingest trash and infectious agents in the brain, and their highly acidic interior gets rids of it, which helps support the function and health of neurons. But as mice get obese, their microglia seem focused on overeating.

"Normally in the brain, microglia are constantly moving around. They are always moving around their little fingers and processes. What happens in obesity is they stop moving," Stranahan said. "They draw in all their processes; they basically just sit there and start eating synapses. When microglia start eating synapses, the mice don't learn as effectively," Stranahan said.

The study looked at normal male mice: One group ate a diet in which about 10 percent of the calories came from saturated fat, and another consumed chow that was 60 percent fat. To ensure other factors were equal, the researchers chose chows that had similar levels of other key ingredients such as macronutrients and protein. The chows were on par with a healthy diet versus a fast-food diet in humans. "If you look at the lipid breakdown for the two diets, these guys are getting crazy, crazy amounts," Stranahan said of the high-fat-fare mice.

At four, eight and 12 weeks, the MCG scientists took a series of metabolic measures, such as weight, food intake, insulin and serum glucose levels. They also measured in the hippocampus, the center of learning and memory, levels of synaptic markers, proteins found at synapses that correlate with the number of synapses.

"This gives us a window into what is occurring at the level of the synapse and also microglial activation," Stranahan said. And, they measured levels of inflammatory cytokines, which microglia produce when "they start getting activated and angry."

All levels in both groups were essentially the same at four weeks. The mice on a high-fat diet were fatter, but other measures were normal at eight weeks. By 12 weeks the fat-eating mice were obese, had elevated cytokine levels and a reduction in the markers for synapse number and function.

"When you get out to 12 weeks, you start seeing great increases in peripheral obesity. While you don't see insulin resistance, you also start seeing loss of synapses and increases in inflammatory cytokines in the brain," Stranahan said.

At that point, the research team switched half the mice on the high-fat diet to the low-fat regimen. It took about two months for their weight to return to normal, although their overall fat pad remained larger than their peers who had never gained weight. That fat layer makes it easier to gain weight in the future, Stranahan notes. As with most people, the mice that remained on the low-fat diet slowly accumulated a little weight as they aged.

Meanwhile, the group that stayed on the high-fat diet kept getting fatter, more inflamed and losing synapses, she said. Their microglia's little processes, or protrusions, which normally help monitor synaptic function and help these cells move, continued to wither. Dendritic spines on neurons, which get input from synapses, similarly withered on the high-fat diet, but like the microglia processes, were restored with the lower-fat fare.

"That is very promising," said Stranahan. The findings also point to some potential new purposes for existing drugs now used for conditions such as rheumatoid arthritis and Crohn's disease, which block specific inflammatory cytokines and tumor necrosis factor alpha, both of which are elevated in the brains of the fat mice.

Obesity yields extreme overkill in microglia, which are typically extremely discriminating and helpful to neurons. During development, for example, they will prune a synapse that isn't functioning. "That is one way the developing brain refines itself. It allows you to keep only those synapses that you need or the synapses you have been using. Fat dramatically alters their dynamic.

"Instead of doing garbage disposal, they are taking your mailbox, your front door, your kitchen sink and all the stuff that you need, and not doing their job of getting rid of trash," Stranahan said.

She notes that the high-fat-eating mice actually ate less chow and consumed the same amount of calories as mice eating low fat. "The entire metabolic phenotype is driven by diet composition rather than the amount of calories," Stranahan said. If high-fat-eating mice had greater variety in their diet, such as a sugar-water option, they might also consume more total calories, similar to the sensory-specific satiety phenomenon in humans, she said.

http://www.eurekalert.org/pub_releases/2015-11/sumc-avm111715.php

Ancient viral molecules essential for human development, Stanford researchers say

Genetic material from ancient viral infections is critical to human development, according to researchers at the Stanford University School of Medicine.

They've identified several noncoding RNA molecules of viral origins that are necessary for a fertilized human egg to acquire the ability in early development to

become all the cells and tissues of the body. Blocking the production of this RNA molecule stops development in its tracks, they found.

The discovery comes on the heels of a Stanford study earlier this year showing that early human embryos are packed full of what appear to be viral particles arising from similar left-behind genetic material.

"We're starting to accumulate evidence that these viral sequences, which originally may have threatened the survival of our species, were co-opted by our genomes for their own benefit," said Vittorio Sebastiano, PhD, an assistant professor of obstetrics and gynecology. "In this manner, they may even have contributed species-specific characteristics and fundamental cell processes, even in humans."

Sebastiano is a co-lead and co-senior author of the study, which will be published online Nov. 23 in Nature Genetics. Postdoctoral scholar Jens Durruthy-Durruthy, PhD, is the other lead author. The other senior author of the paper is Renee Reijo Pera, PhD, a former professor of obstetrics and gynecology at Stanford who is now on the faculty of Montana State University.

Sebastiano and his colleagues were interested in learning how cells become pluripotent, or able to become any tissue in the body. A human egg becomes pluripotent after fertilization, for example. And scientists have learned how to induce other, fully developed human cells to become pluripotent by exposing them to proteins known to be present in the very early human embryo. But the nitty-gritty molecular details of this transformative process are not well understood in either case.

An ancient infection

The researchers knew that a type of RNA molecules called long-intergenic noncoding, or lincRNAs, have been implicated in many important biological processes, including the acquisition of pluripotency. These molecules are made from DNA in the genome, but they don't go on to make proteins. Instead they function as RNA molecules to affect the expression of other genes.

Sebastiano and Durruthy-Durruthy used recently developed RNA sequencing techniques to examine which lincRNAs are highly expressed in human embryonic stem cells. Previously, this type of analysis was stymied by the fact that many of the molecules contain highly similar, very repetitive regions that are difficult to sequence accurately.

They identified more than 2,000 previously unknown RNA sequences, and found that 146 are specifically expressed in embryonic stem cells. They homed in on the 23 most highly expressed sequences, which they termed HPAT1-23, for further study. Thirteen of these, they found, were made up almost entirely of genetic material left behind after an eons-ago infection by a virus called HERV-H.

HERV-H is what's known as a retrovirus. These viruses spread by inserting their genetic material into the genome of an infected cell. In this way, the virus can use the cell's protein-making machinery to generate viral proteins for assembly into a new viral particle. That particle then goes on to infect other cells. If the infected cell is a sperm or an egg, the retroviral sequence can also be passed to future generations.

HIV is one common retrovirus that currently causes disease in humans. But our genomes are also littered with sequences left behind from long-ago retroviral infections. Unlike HIV, which can go on to infect new cells, these retroviral sequences are thought to be relatively inert; millions of years of evolution and accumulated mutations mean that few maintain the capacity to give instructions for functional proteins.

After identifying HPAT1-23 in embryonic stem cells, Sebastiano and his colleagues studied their expression in human blastocysts -- the hollow clump of cells that arises from the egg in the first days after fertilization. They found that HPAT2, HPAT3 and HPAT5 were expressed only in the inner cell mass of the blastocyst, which becomes the developing fetus. Blocking their expression in one cell of a two-celled embryo stopped the affected cell from contributing to the embryo's inner cell mass. Further studies showed that the expression of the three genes is also required for efficient reprogramming of adult cells into induced pluripotent stem cells.

Sequences found only in primates

"This is the first time that these virally derived RNA molecules have been shown to be directly involved with and necessary for vital steps of human development," Sebastiano said. "What's really interesting is that these sequences are found only in primates, raising the possibility that their function may have contributed to unique characteristics that distinguish humans from other animals."

The researchers are continuing their studies of all the HPAT molecules. They've learned that HPAT-5 specifically affects pluripotency by interacting with and sequestering members of another family of RNAs involved in pluripotency called let-7.

"Previously retroviral elements were considered to be a class that all functioned in basically the same way," said Durruthy-Durruthy. "Now we're learning that they function as individual elements with very specific and important roles in our cells. It's fascinating to imagine how, during the course of evolution, primates began to recycle these viral leftovers into something that's beneficial and necessary to our development."

Other Stanford authors are postdoctoral scholars Mark Wossidlo, PhD, Jonathan Davila, PhD, and Moritz Mall, PhD; research associate Diana Cepeda, PhD; former postdoctoral

scholar Jun Cui, PhD; graduate student Edward Grow; Wing Wong, PhD, professor of statistics and health research; and Joanna Wysocka, PhD, professor of chemical and systems biology and of developmental biology.

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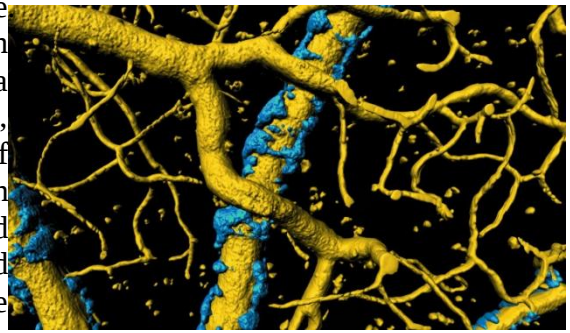
Neuroscientists gain insight into cause of Alzheimer's symptoms

Amyloid plaques may be strangling blood flow

Virginia Tech Carilion Research Institute scientists have uncovered a mechanism in the brain that could account for some of the neural degeneration and memory loss in people with Alzheimer's disease. The researchers, together with scientists at the University of Alabama at Birmingham School of Medicine, discovered that a common symptom of Alzheimer's disease - the accumulation of amyloid plaques along blood vessels - could be disrupting blood flow in the brain. The results were published Monday in the journal Brain.



Virginia Tech Carilion Research Institute scientists have uncovered a mechanism in the brain that could account for some of the neural degeneration and memory loss in people with Alzheimers disease. A buildup of misfolded proteins causes an exoskeleton (in blue) to form around blood vessels (in gold) in the brain. **Virginia Tech**

"We've always been interested in how glial cells interact with blood vessels," said Harald Sontheimer, director of the Center for Glial Biology in Health, Disease, and Cancer at the Virginia Tech Carilion Research Institute and senior author of the paper. "Astrocytes are the most populous cell type in the brain and even outnumber neurons."

Sontheimer also noted the importance of astrocyte function in the brain.

"Astrocytes serve many support functions, such as shuttling nutrients from blood vessels to nerve cells or removing their waste products," said Sontheimer, who is also the I. D. Wilson Chair in Virginia Tech's College of Science. "They also control the diameter of blood vessels to assure proper nutrient and oxygen delivery to the brain and maintenance of the blood-brain barrier. In response to injury and disease, however, astrocytes become reactive and change many of their supportive properties."

Sontheimer's team discovered that the astrocytes' blood flow regulation is disrupted by plaques formed of misfolded amyloid protein around blood vessels. In a healthy brain, amyloid protein fragments are routinely broken down and eliminated. The presence of amyloid proteins around blood vessels in the brain is a hallmark of Alzheimer's disease, yet it wasn't understood if the proteins did any harm. Now, Sontheimer's team has found that they do.

"We found that amyloid deposits separated astrocytes from the blood vessel wall," said Stefanie Robel, a research assistant professor at the Virginia Tech Carilion Research Institute and a coauthor of the paper. "We also found that these amyloid deposits form an exoskeleton around the blood vessels, a kind of cast that reduces the pliability of the vessels."

The exoskeleton is known as a vascular amyloid. Its inelasticity might result in lower blood flow, which could account for Alzheimer's symptoms, such as memory lapses, impaired decision-making, and personality changes.

"Vascular amyloid may be the culprit in Alzheimer's disease symptoms, especially considering that the amyloid exoskeleton might limit the supply of oxygen and glucose to the brain regions that need them most," Sontheimer said. "This could also explain the cognitive decline in people with Alzheimer's disease, as the disease is associated with reduced cerebral blood flow."

While the scientists don't fully understand the role of vascular amyloid in Alzheimer's disease, they now have a possible therapeutic target to study.

"It may be helpful to remove the deposits to allow for appropriate blood flow," Robel said. "The problem is we don't know. It might be harmful to remove vascular amyloid at late stages of the disease; maybe they're actually holding the vessels together."

The researchers' next step will be to examine blood vessels once the amyloid deposits are removed. "Vascular amyloid is strangling the blood vessels," Sontheimer said. "By removing them, maybe we'll be able to restore blood flow regulation. Perhaps it'll turn out vascular amyloid is preventing further degeneration. Whatever the case, we'll certainly learn something new."

http://nyti.ms/1NhxzqQ

F.D.A. Targets Inaccurate Medical Tests, Citing Dangers and Costs

Inaccurate and unreliable medical tests are prompting abortions, promoting unnecessary surgeries, putting tens of thousands of people on unneeded drugs and raising medical costs, the Food and Drug Administration has concluded.

By ROBERT PEAR NOV. 23, 2015

WASHINGTON - Life-threatening diseases go undetected in some cases. In others, patients are treated for conditions they do not have. “Patients have been demonstrably harmed or may have been harmed by tests that did not meet F.D.A. requirements,” federal investigators concluded in a report to Congress last week.

The findings come at a time when the use of laboratory-developed tests is booming, the Obama administration is seeking new regulatory powers and even Republicans in Congress are working on legislation to set stricter standards. The new standards, whether set by Congress or by the administration, would be the most significant change in the regulation of laboratories since 1988, lawyers say.

In 20 case studies — half involving tests used to diagnose and treat cancer, others focused on heart disease, autism and Lyme disease — the F.D.A. laid out a compendium of serious problems.

One blood test to help detect ovarian cancer was never shown to be effective, the report said, but was used anyway. False-positive tests may have led to "unnecessary surgery to remove healthy ovaries."

Pregnant women have considered or had abortions because other tests inaccurately indicated abnormalities in the fetus.

Several tests now on the market detect a genetic variant that was once thought to increase the risk of heart disease, a link that has not been confirmed. Yet more than 150,000 people have been given these tests, the report said, and "many were likely over- or undertreated with statins," cholesterol-lowering drugs, at a cost estimated at more than $2.4 billion.

"The problems are more prevalent than people want to recognize," said Dr. Jeffrey E. Shuren, the director of the Center for Devices and Radiological Health at the F.D.A. "Doctors and patients rely on these tests to make well-informed health care decisions. If they get inaccurate results, they can make the wrong decisions, and people get hurt as a result."

Dr. Shuren said officials did not know how many people might have been harmed, because information on "adverse events" associated with laboratory-developed tests is not systematically collected or reported — a gap that many in Congress and the administration want to close.

Inaccurate test results pose a significant threat to President Obama's plan to develop treatments tailored to the genetic characteristics of individuals. Many of the new "personalized medicines" are used with a diagnostic test that identifies patients who are most likely to benefit, or to suffer serious side effects. If the tests are unreliable, the treatments could be ineffective.

The maker of one of the tests cited by the F.D.A., Genomic Health of Redwood City, Calif., rejected the criticism. Victoria Steiner, a spokeswoman for the company, said that "a wealth of evidence has supported use of our test to help guide chemotherapy treatment decisions in more than 500,000 breast cancer patients to date."

Diagnostic tests are now regulated differently depending on where they were developed and manufactured. Products that will be sold to multiple labs — "commercial test kits" — are typically subject to review by the F.D.A. before they go on the market. Manufacturers are supposed to inform the government if they learn that their products may have contributed to a death or a serious injury, and they may have to notify the government if they recall defective products.

But for tests manufactured and used within a single laboratory, the agency has not actively enforced regulatory requirements, even though doctors around the country may submit samples to that lab for testing.

The Obama administration is moving to assert its enforcement authority over such laboratory-developed tests, saying they have become more complex, more widely used and more similar to commercial tests that the government has regulated for nearly 40 years.

Democrats and consumer groups have generally supported the efforts to regulate or legislate. "Patients and their physicians should be able to trust the results of their tests, regardless of how or where a test is developed or performed," said Representative Frank Pallone Jr. of New Jersey, the senior Democrat on the House Energy and Commerce Committee. "It does not make sense to regulate tests differently based on who develops them."

Republicans are divided between those who are willing to consider a larger federal role and others who are skeptical.

"This is a tough area for conservative Republicans who think that government is too big and costs too much," said Representative John Shimkus, Republican of Illinois. He indicated that he was willing to consider legislation because "the volume and complexity of these tests have grown exponentially," and federal standards may be needed to ensure that the tests do what they are supposed to do.

But Representative Michael C. Burgess, Republican of Texas and a physician, expressed concern that the proposals "could stifle medical innovation and open the door to federal regulation of the practice of medicine."

Jeffrey N. Gibbs, a Washington lawyer who represents medical device companies and laboratories, said he had seen a shift in the past six months: People once adamantly opposed to the regulation of laboratory-developed tests are now open to the idea.

"It is more likely that the F.D.A. will have a role in regulating laboratory-developed tests as a result of either congressional action or a guidance document issued by the agency," Mr. Gibbs said.

The American Clinical Laboratory Association, a trade group, contends that "the F.D.A. lacks the statutory authority to regulate laboratory-developed tests."

But Jayson S. Slotnik, a consultant to drug and device companies, said: "There will be more regulation, and it need not stunt innovation. The right regulation would separate good from bad tests and encourage use of the better ones."

http://www.bbc.com/news/science-environment-34809804

DNA study finds London was ethnically diverse from start

A DNA study has confirmed that London was an ethnically diverse city from its very beginnings, BBC News has learned.

By Pallab Ghosh Science correspondent, BBC News

The analysis reveals what some of the very first Londoners looked like and where they came from. These initial results come from four people: two had origins from outside Europe, another was from continental Europe and one was a native Briton.

The researchers plan to analyse more of the 20,000 human remains stored at the Museum of London. According to Caroline McDonald, who is a senior curator at the museum, London was a cosmopolitan city from the moment it was created following the Roman invasion 2,000 years ago.

"The thing to remember with the original Londoners is that they were not born here. Every first-generation Londoner was from somewhere else - whether it was somewhere else in Britain, somewhere else on the continent, somewhere else in the Mediterranean, somewhere else from Africa," she said. "So the stories we can tell about our ancient population are absolutely relevant to modern contemporary London because these are our stories - these are people just like us."

Working with scientists at Durham University and an ancient DNA lab at McMaster University in Canada, museum researchers were able to reconstruct the DNA of four individuals.

They come from a collection of 20,000 human remains from London stretching back 5,500 years. Each of these individuals are stored in their own cardboard box in a storehouse at the museum. The development of DNA analysis techniques now means that "flesh can be put on the bones" of the history of these Londoners: telling us where they came from, how they lived and how they died.

Further analyses will greatly add to our knowledge of the history of the city and enable researchers to view events through the eyes of people that lived in it at the time, according to Ms McDonald.

"Their stories are written in their bones and these were stories we did not realise until we did this scientific analysis," she told BBC News.

The Lant Street teenager

The most complete skeleton studied was that of a 14-year-old girl, who the museum curators have named "The Lant Street teenager". Analysis of her DNA and chemicals in her teeth show that she grew up in North Africa. Her mitochondrial DNA lineage (passed down on the maternal line only) is common in southern and Eastern Europe. The teenager had blue eyes and yet there were things about her skeleton that suggested some she had Sub-Saharan African ancestry. Like many people living in the capital today, she had travelled a long distance to be in London.

The Mansell Street man

Archaeologists build up a picture of individuals from the belongings they are buried with. But "The Mansell Street man" was found with nothing. According to Dr Rebecca Redfern, another Museum of London curator, until the emergence of new ancient DNA and chemical analysis techniques, these were the people who had slipped through the cracks of history.

"Most of the human remains in our collection don't have any coffin plates or any sort of biographical information, so by doing these types of studies we are able to show where people came from and learn more about them as a person, about aspects of their physical appearance, and so we can really give people back their voices," she said. The analysis showed that Mansell Street man was over 45 years old with very dark brown hair and brown eyes. His mitochondrial DNA line was from North Africa and his remains show African traits as well.

However, the chemical make-up of his teeth shows he grew up in London. His skeleton indicates that he had a form of bone disease that today is associated with diabetes caused by a protein-rich diet. That has come as a huge surprise to researchers because in modern populations this is a disease that mostly afflicts white males from the West. So the discovery will be of great interest to medical researchers.

The Gladiator

This man was possibly a gladiator. His skull was found in a pit along with the heads of 38 other men aged between 18 and 45 - all of whom had met a violent end. This particular individual was 36-45 when he died. He had suffered serious injuries to his skull that had healed, so he had led a violent life up to his death.

His mother's ancestral line is common in Eastern Europe and the Middle East. The Gladiator was not born in London, but he met a tragic end in the city. His head was removed from his body and probably left exposed in these pits for passers-by to see.

The Harper Road woman

"The Harper Road" woman was a first-generation Londoner. She had brown hair and brown eyes and died a handful of years after the city had been settled - shortly after Britain had been invaded by the Roman Empire in AD 43.

She is buried with Roman pottery and belongings. When researchers checked the chemicals in her teeth, they confirmed she had been born in Britain. Ms McDonald was intrigued by the fact that a native Briton adopted a Roman lifestyle within a few years of the conquest.

"What this is telling us is that people's identities were very, very fluid... her family wanted to portray a certain Roman style of identity. The Harper Road woman would have adapted her identity depending on who she was meeting - the way that we all do," she said. An added twist to the Harper Road woman's tale is that her chromosomes show that she was genetically a male - even though physically she was a woman - another feature that will intrigue modern-day researchers.

Waiting in the wings are thousands more people in the Museum of London's store house that the researchers are eager to learn more about. Next on their list are more Roman Londoners, then a group of Napoleonic soldiers and marines that were buried in Greenwich, followed by a group of medieval monks.

"We would like to do an awful lot more because everyone has their own story to tell - so the more people we are able to analyse the more stories we can tell about London," says Dr Redfern.

The research, and skeletons used for analysis will form a new display at the Museum of London opening on 27 November 2015.

http://nyti.ms/1Owwomq

A Step Closer to the Defeat of Polio

Three years have passed since a case of Type 3 wild polio virus has been detected in the world, which means that particular viral subtype has most likely disappeared forever, the World Health Organization announced this month.

By DONALD G. McNEIL Jr.

Its demise could speed up the drive to eliminate polio, which has gone on for 27 years and now costs more than $1 billion a year. The last known Type 3 polio case was an 11-month-old boy in northern Nigeria who became paralyzed on Nov. 10, 2012.

When vaccines were first invented in the 1950s, there were three polio strains, which had nicknames. Type 1, by far the most common, was named Brunhilde, after a chimpanzee in the lab of the scientist leading the work. Type 2 was Lansing, after the Michigan city where it was isolated from a dying patient. Type 3 was Leon, after a Los Angeles boy who died of it. The names later fell out of favor.

In 2009, after experts waited a decade to be sure that Type 2 was gone forever, they began removing that strain from the trivalent oral vaccine, which works against all three types.

The three strains of weakened live virus in the oral vaccine compete with one another to attach to receptors in the gut. Removing one type of polio virus meant children developed full immunity after fewer doses.

Once experts are sure Type 3 is gone, they may decide to switch to a monovalent vaccine containing only Type 1. But all types of polio may be eradicated even before that happens. Wild-type polio, caused by circulating viruses, is now found in only two countries, Pakistan and across the border in Afghanistan.

And cases are declining sharply in both countries as the Pakistani military has expanded its power, fighting its way into Taliban-controlled areas where most of the vaccine resistance has been. When families are displaced, children are vaccinated at highway checkpoints and border crossings.

As of Nov. 17, only 56 cases had been detected, far fewer than the 290 that had been found by the same date in 2014.

Wild-type cases may soon be outnumbered by vaccine-derived polio. Those cases occur when a weakened vaccine strain mutates enough to cause paralysis.

Seventeen cases in five other countries have been detected this year. Those outbreaks are usually stopped by giving all children in the region injections of killed vaccine and follow-up doses of the oral one.

http://bit.ly/1RcGqEt

Water Bears Are the Master DNA Thieves of the Animal World

Foreign genes from bacteria, fungi and plants may have bestowed these animals with their ability to tolerate boiling, freezing and the vacuum of space

By Rachel Nuwer

Tardigrades are animals that thrive in extremes. Also known as water bears or moss piglets, the aquatic, microscopic invertebrates can survive freezing and boiling temperatures as well as the harsh conditions of outer space. A dried-out tardigrade can be reanimated just by adding water—even decades later. They're found on every continent including Antarctica, and they live in environments ranging from the deepest ocean trenches to the hottest deserts to the tops of the Himalaya.

Now scientists have discovered that tardigrades possess yet another extreme claim to fame: Their genome contains the most foreign DNA of any animal species known.

Rather than inheriting all of their genes from their ancestors, tardigrades get a whopping one-sixth of their genetic makeup from unrelated plants, bacteria, fungi and archaeans, researchers report today in PNAS. The bizarre mashup highlights the fact that species can take shape in much less linear ways that commonly imagined.

"When most people think of the diversity of life and flow of genetic information, they picture a tree with big branches generating smaller ones, but without any connection between the limbs," says study leader Thomas Boothby, a Life Sciences Research Foundation postdoctoral fellow at the University of North Carolina, Chapel Hill. "We're beginning to realize that instead of the tree of life, it might be more appropriate to think of the web of life."

Boothby turned to the tardigrade genome in the hopes of uncovering the most basic underpinnings of the creatures' extreme survival strategies. To catalog every gene, he and his colleagues first extracted and sequenced many short chunks of DNA from thousands of tardigrades. Using a computer program, they stitched those sequences back together to produce the code in its entirety.

"When we did that, we initially saw that there were a lot of genes that looked like they didn't come from animals," Boothby says. "Our gut reaction was that we messed something up and must have contaminated our sample."

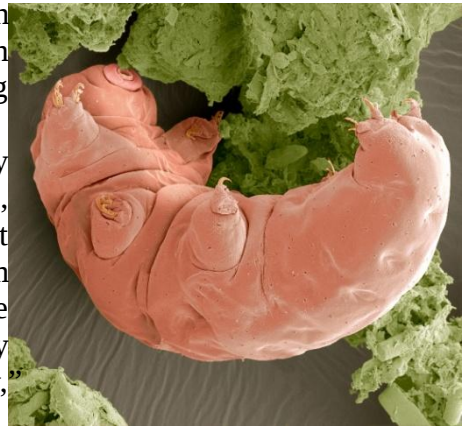
To double check, the team turned to the polymerase chain reaction, a method that amplifies targeted regions of genetic material only if they match with specific primers. In this case, they wanted to see if they could amplify animal and bacterial genes as single units, which would only be possible if they were physically linked within the same genome. "We did that for over 100 genes, with 98-percent success," Boothby says.

Convinced their reading of the genome was correct, the team then reconstructed the evolutionary ancestry of specific gene sequences. This confirmed that what looked like foreign genes actually were just that, rather than look-a-likes developed by tardigrades themselves.

"The results told us pretty unambiguously that genes that look foreign really are coming from non-animals," Boothby says.

All told, the tardigrade genes are made of 17.5 percent foreign material. Most of those strange genes have bacterial origins—thousands of species are represented within the tardigrade's genetic makeup. Many of the genes are known or suspected to play roles in stress tolerance for their original owners.

"I think the findings are extremely surprising," says Andrew Roger, a biologist at Dalhousie University in Canada. That an animal could acquire such a large proportion of its genes from foreign sources is "amazing and unprecedented."



Tardigrades get up to 17.5 percent of their genes from unrelated organisms. **STEVE GSCHMEISSNER/Science Photo Library/Corbis**

In some cases, foreign genes have actually replaced tardigrade ones, while in others, tardigrades kept their own versions but incorporated single or multiple copies from one or several bacteria species. "We speculate that this wasn't a one-time event, but probably was ongoing and may still be happening today," Boothby says.

Researchers have known for years that bacteria and other microbes can engage in horizontal gene transfer—the swapping of genetic material between unrelated species. But only recently have scientists begun to realize that this method of genetic development can also occur in animals.

Compared to tardigrades, other animals' genomes, including humans, contain very little foreign material. Until now, rotifers—another microscopic aquatic animal—held the record at 8 to 9 percent. For tardigrades and rotifers, the heavy dose of foreign genes likely plays a significant role in bestowing them with superior survival skills.

"If they can acquire DNA from organisms already living in stressful environments, they may be able to pick up some of the same tricks," Boothby says. But precisely how tardigrades managed to cobble together so much foreign genetic material remains unknown.

Boothby and his colleagues suspect that the animals' ability to dry out and reanimate might play a role. When tardigrades desiccate, their genomes fragment. After life-giving liquid restores them, the membranes surrounding their cells remain leaky for a while, and as the cells quickly work to repair their own genomes, they may accidentally work in some DNA from the environment.

"This paper confirms the importance of the study of the whole genome, here applied to an unusual but very interesting and often-neglected animal model," says Roberto Bertolani, an evolutionary zoologist at the University of Modena and Reggio Emilia in Italy.

"One interesting point that the authors make is the possible relationship between desiccation, membrane leakiness and DNA breakages that may predispose these animals to incorporate and integrate many foreign genes."

For now that's just a hypothesis, so Boothby plans to investigate this and other lingering questions. His work with this extreme creature could even give humans a better shot at survival: Studying tardigrade genes may one day aid development of pharmaceuticals and vaccines that no longer have to be kept on ice and instead can be dried out and reanimated on the spot in a rural clinic or crisis zone.

http://www.eurekalert.org/pub_releases/2015-11/uoy-hnd112415.php

Human nature's dark side helped us spread across the world

New research by an archaeologist at the University of York suggests that betrayals of trust were the missing link in understanding the rapid spread of our own species around the world

Human nature's dark side helped us spread across the world. New research by an archaeologist at the University of York suggests that betrayals of trust were the missing link in understanding the rapid spread of our own species around the world.

Dr Penny Spikins, of the University's Department of Archaeology, says that the speed and character of human dispersals changed significantly around 100,000 years ago. Before then, movement of archaic humans were slow and largely governed by environmental events due to population increases or ecological changes. Afterwards populations spread with remarkable speed and across major environmental barriers.

But Dr Spikins, a senior lecturer in the Archaeology of Human Origins, relates this change to changes in human emotional relationships. In research published in Open Quaternary, she says that neither population increase nor ecological changes provide an adequate explanation for patterns of human movement into new regions which began around 100,000 years ago.

She suggests that as commitments to others became more essential to survival, and human groups ever more motivated to identify and punish those who cheat, the 'dark' side of human nature also developed. Moral disputes motivated by broken trust and a sense of betrayal became more frequent and motivated early humans to put distance between them and their rivals.

According to Dr Spikins, the emotional bonds which held populations together in crisis had a darker side in heartfelt reactions to betrayal which we still feel today. Larger social networks made it easier to find distant allies with whom to start new colonies, and more efficient hunting technology meant that anyone with a grudge was a danger but it was human emotions which provided the force of repulsion from existing occupied areas which we do not see in other animals.

Early species of hominin were limited in distribution to specific environments such as grasslands and open woodland. The expansion of Homo erectus out of Africa into Asia around 1.6 million years ago appears to have been caused by the need to find more large scale grasslands. By contrast, Neanderthals occupied cold and arid parts of Europe. All archaic species adapted slowly to new opportunities for settlement and were often deterred by environmental and climatic barriers.

After 100,000 years ago, however, dispersal into distant, risky and inhospitable areas became relatively more common compared with movements into already occupied regions. Most notably, the spread of modern human populations was not inhibited by biogeographical barriers. Populations moved into cold regions of Northern Europe, crossed significant deltas such as the Indus and the Ganges, deserts, tundra and jungle environment and even made significant sea crossings to reach Australia and the Pacific islands.

Dr Spikins argues that betrayals of trust resulting from moral disputes were a significant reason for such risky dispersals into apparently unwelcoming environments with a desire to avoid physical harm from disgruntled former friends and allies being a key motivation. Offenders and any allies within their social network would feel driven to get out of harm's way.

She says: "Active colonisations of and through hazardous terrain are difficult to explain through immediate pragmatic choices. But they become easier to explain through the rise of the strong motivations to harm others even at one's own expense which widespread emotional commitments bring.

"Moral conflicts provoke substantial mobility -- the furious ex ally, mate or whole group, with a poisoned spear or projectile intent on seeking revenge or justice, are a strong motivation to get away, and to take almost any risk to do so.

"While we view the global dispersal of our species as a symbol of our success, part of the motivations for such movements reflect a darker, though no less 'collaborative', side to human nature."

http://www.eurekalert.org/pub_releases/2015-11/s-chi112415.php

Complex humor is no laughing matter

Jokes with too many mind-twists not found to be funny

Since the earliest times, laughter and humor have performed important functions in human interaction. They help to expedite courtship, improve conversational flow, synchronize emotional states and enhance social bonding. Jokes, a structured form of humor, give us control over laughter and are therefore a way to elicit these positive effects intentionally. In order to comprehend why some jokes are perceived as funny and others are not, Robert Dunbar and colleagues at Oxford University investigated the cognitive mechanism underlying laughter and humor. The research is published in Springer's journal Human Nature.

The ability to fully understand other people's often unspoken intentions is called mentalizing, and involves different levels of so-called intentionality. For example, an adult can comprehend up to five such levels of intentionality before losing the plot of a too-complex story. Conversations that share facts normally involve only three such levels. Greater brain power is needed when people chat about the social behavior of others, because it requires them to think and rethink themselves into the shoes of others.

The best jokes are thought to build on a set of expectations and have a punchline to update the knowledge of the listener in an unexpected way. Expectations that involve the thoughts or intentions of people other than the joke-teller or the audience, for example the characters in the joke, are harder to pin down. Our natural ability to handle only a limited number of mindstates comes into play.

In order to shed light on how our mental ability limits what we find funny, the researchers analyzed the reaction of 55 undergraduates from the London School of Economics to 65 jokes from an online compilation of the 101 funniest jokes of all time. The collection mostly consisted of jokes from successful stand-up

comedians. Some jokes in the compilation were mere one-liners, while others were longer and more complex. A third of the jokes were factual and contained reasonably undemanding observations of idiosyncrasies in the world. The rest involved the mindstates of third parties. The jokes were rated on a scale from one to four (not at all funny to very funny).

The research team found that the funniest jokes are those that involve two characters and up to five back-and-forth levels of intentionality between the comedian and the audience. People easily loose the plot when jokes are more complex than that. The findings do not suggest that humor is defined by how cleverly a joke is constructed, but rather that there is a limit to how complex its contents can be to still be considered funny. According to Dunbar, increasing the mentalizing complexity of the joke improves the perceived quality, but only up to a certain point: stand-up comedians cannot afford to tell intricate jokes that leave their audience feeling as if they've missed the punchline.

"The task of professional comics is to elicit laughs as directly and as fast as possible. They generally do this most effectively when ensuring that they keep within the mental competence of the typical audience member," says Dunbar. "If they exceed these limits, the joke will not be perceived as funny."

It is likely that everyday conversational jokes do not involve as many intentional levels as those that have been carefully constructed by professional comedians. Further research needs to be conducted in this area. However, Dunbar's findings shed some light on the mechanics of language-based humor and therefore on the workings of our mind.

Reference: Dunbar, R.I.M. et al (2015). The Complexity of Jokes Is Limited by Cognitive Constraints on Mentalizing, Human Nature, DOI 10.1007/s12110-015-9251-6

http://www.eurekalert.org/pub_releases/2015-11/uoc-sff112415.php

Stored fat fights against the body's attempts to lose weight

The fatter we are, the more our body appears to produce a protein that inhibits our ability to burn fat, suggests new research published in the journal Nature Communication.

The findings may have implications for the treatment of obesity and other metabolic diseases.

Most of the fat cells in the body act to store excess energy and release it when needed but some types of fat cells, known as brown adipocytes, function primarily for a process known as thermogenesis, which generates heat to keep us warm. However, an international team of researchers from the Wellcome Trust-Medical Research Council Institute of Metabolic Sciences at the University of Cambridge, UK, and Toho University, Japan, have shown that a protein found in the body, known as sLR11, acts to suppress this process.

Researchers investigated why mice that lacked the gene for the production of this protein were far more resistant to weight gain. All mice - and, in fact, humans - increase their metabolic rate slightly when switched from a lower calorie diet to a higher calorie diet, but mice lacking the gene responded with a much greater increase, meaning that they were able to burn calories faster.

Further examinations revealed that in these mice, genes normally associated with brown adipose tissue were more active in white adipose tissue (which normally stores fat for energy release). In line with this observation, the mice themselves were indeed more thermogenic and had increased energy expenditure, particularly following high fat diet feeding.

The researchers were able to show that sLR11 binds to specific receptors on fat cells - in the same way that a key fits into a lock - to inhibit their ability to activate thermogenesis. In effect, sLR11 acts as a signal to increase the efficiency of fat to store energy and prevents excessive energy loss through unrestricted thermogenesis.

When the researchers examined levels of sLR11 in humans, they found that levels of the protein circulating in the blood correlated with total fat mass - in other words, the greater the levels of the protein, the higher the total fat mass. In addition, when obese patients underwent bariatric surgery, their degree of postoperative weight loss was directly proportional to the reduction in their sLR11 levels, suggesting that sLR11 is produced by fat cells.

In their paper the authors suggest that sLR11 helps fat cells resist burning too much fat during 'spikes' in other metabolic signals following large meals or short term drops in temperature. This in turn makes adipose tissue more effective at storing energy over long periods of time.

There is growing interest in targeting thermogenesis with drugs in order to treat obesity, diabetes and other associated conditions such as heart disease. This is because it offers a mechanism for disposing of excess fat in a relatively safe manner. A number of molecules have already been identified that can increase thermogenesis and/or the number of fat cells capable of thermogenesis. However to date there have been very few molecules identified that can decrease thermogenesis. These findings shed light on one of the mechanisms that the body employs to hold onto stored energy, where sLR11 levels increase in line with the amount of stored fat and act to prevent it being 'wasted' for thermogenesis.

Dr Andrew Whittle, joint first author, said: "Our discovery may help explain why overweight individuals find it incredibly hard to lose weight. Their stored fat is actively fighting against their efforts to burn it off at the molecular level."

Professor Toni Vidal-Puig, who led the team, added: "We have found an important mechanism that could be targeted not just to help increase people's

ability to burn fat, but also help people with conditions where saving energy is important such as anorexia nervosa."

Jeremy Pearson, Associate Medical Director at the British Heart Foundation (BHF), which helped fund the research, said: "This research could stimulate the development of new drugs that either help reduce obesity, by blocking the action of this protein, or control weight loss by mimicking its action. Based on this promising discovery, we look forward to the Cambridge team's future findings.

"But an effective medicine to treat obesity, which safely manages weight loss is still some way off. In the meantime people can find advice on healthy ways to lose weight and boost their heart healthy on the BHF website - bhf.org.uk."

The study was part-funded in part by the British Heart Foundation, the Wellcome Trust, the Medical Research Council and the Biotechnology and Biological Sciences Research Council.

Whittle, AJ, Jiang, M, et al. Soluble LR11/SorLA represses thermogenesis in adipose tissue and correlates with BMI in humans. Nature Communications; 20 November 2015

http://www.eurekalert.org/pub_releases/2015-11/uoca-rbt112415.php

Reducing body temperature saves neurological functions in cardiac arrest patients

Therapeutic hypothermia effective on patients with 'nonshockable' cardiac arrests

AURORA, Colo. - Survivors of cardiac arrest who remain in comas have better survival and neurological outcomes when their body temperatures are lowered, according to new research by Dr. Sarah Perman at the University of Colorado Anschutz Medical Campus. Therapeutic hypothermia involves decreasing the body temperature to protect the brain when blood flow is reduced from a cardiac arrest, when the heart stops pumping and the patient has no pulse.

Previous studies have shown the therapy effective on patients with so-called `shockable' heart rhythms like ventricular fibrillation. But Perman's research demonstrates that it's also effective on patients with `nonshockable' rhythms when there is no pulse and the patient is in a coma.

"Prior to our study, there was minimal data to support the use of this treatment on patients with nonshockable rhythms," said Perman, an assistant professor of emergency medicine at the University of Colorado School of Medicine. "As a result, the therapy was not widely used with these patients."

Every year, 530,000 Americans suffer cardiac arrest and 300,000 of them happen outside of a hospital. Perman, a clinical expert in cardiac arrest and post-arrest care, and her colleagues looked at data from 519 patients who had nonshockable heart rhythms between 2000 and 2013. They found those who received therapeutic hypothermia were 2.8 times as likely to survive to be discharged from the hospital and 3.5 times more likely to have better neurological outcomes - returning to their baseline mental state - than those who did not have the treatment.

Physicians who use the technique employ cooling wraps to drop the patients' temperature from approximately 37 degrees Celsius to 33 degrees Celsius (91.4 degrees F). The therapy has shown to reduce damage to the brain following a cardiac arrest, though scientists continue to investigate why this occurs.

Landmark trials in 2002 studying shockable patients found 49 percent of those who received therapeutic hypothermia had good neurological outcomes as opposed to 26 percent who did not receive the treatment. Another trial showed 55 percent of patients with good neurological outcome against 39 percent who didn't have the therapy.

"Neurologic injury after cardiac arrest is devastating," said Perman, who like most physicians at CU Anschutz is both an active researcher and practicing clinician. "We have one chance to give some form of neuroprotection, and that's immediately after the arrest."

She said therapeutic hypothermia should be more widely used in comatose patients to protect neurological function. "We know that patients benefit from this therapy," said Perman, noting the importance of delivering meaningful research from the laboratory directly to the patient. "Therefore, one of our next challenges is to tailor the hypothermia treatment to the patient's specific injury in order to improve outcomes further." The study was published in the latest edition of the journal Circulation. It was funded by the National Institutes of Health.

http://www.eurekalert.org/pub_releases/2015-11/qmuo-nsd112315.php

New strategy discovered for treating arthritis

An early study by Queen Mary University of London suggests that arthritic cartilage, previously thought to be impenetrable, could be treated by a patient's own 'microvesicles' that can travel into cartilage cells and deliver therapeutic agents

Arthritis patients could one day benefit from a novel form of medicine, according to researchers at Queen Mary University of London (QMUL). Their early study indicates that arthritic cartilage, previously thought to be impenetrable to therapies, could be treated by a patient's own 'microvesicles' that are able to travel into cartilage cells and deliver therapeutic agents.

Microvesicles are very small subcellular structures (0.05 to 1 micrometer in diameter) that consist of fluid enclosed by a membrane. They are released by cells in copious numbers to transfer lipids and proteins to target cells, yet their role in disease has been poorly understood.

Some white blood cells' microvesicles tend to accumulate in large numbers in the joints of rheumatoid arthritis patients. The biological impact of these

microvesicles has been intriguing to researchers, because they are known to contain over 300 types of protein that vary in different situations.

Lead author Professor Mauro Perretti from QMUL's William Harvey Research Institute said: "Cartilage has long been thought to be impenetrable to cells and other small structures, leading to strong limitations in our abilities to deliver therapies for arthritis. To our surprise, we've now discovered that vesicles released from white blood cells can 'travel' into the cartilage and deliver their cargo, and that they also have a protective effect on cartilage affected by arthritis.

"Our study indicates that these vesicles could be a novel form of therapeutic strategy for patients suffering from cartilage damage due to a range of diseases, including osteoarthritis, rheumatoid arthritis and trauma. Treating patients with their own vesicles may only require a day in hospital, and the vesicles could even be 'fortified' with other therapeutic agents, for example, omega-3 fatty acids or other small molecules."

The study, published in Science Translational Medicine and funded by Arthritis Research UK, the Nuffield Foundation (Oliver Bird Fund) and the Wellcome Trust, examined the role of microvesicles in mice models and human cartilage cells, investigating their effect on experimental arthritic disease.

Mice were genetically modified to have reduced vesicle production. These mice exhibited cartilage damage from inflammatory arthritis, but showed reduced cartilage degradation when treated with microvesicles. The microvesicles were also found to lead to cartilage protection when repeated in human cells.

The researchers additionally found that one particular cellular receptor, known as 'FPR2/ALX', played a role in protecting cartilage tissue and could therefore be targeted by new small molecules for the treatment of cartilage erosive diseases.

Arthritis Research UK's Medical Director, Stephen Simpson said: "By using the body's own transport system to get new and current therapeutic agents directly into the cartilage, holds the promise that we will be able to reduce joint damage more effectively than ever. A healthy and intact joint results in less pain and disability improving the quality of life of millions of people living with arthritis in the UK."

The authors say that these early results reveal a possible new therapeutic approach for treating damaged cartilage of arthritic joints. Further studies in humans will be needed to confirm the therapeutic potential of the new approach.

'Neutrophil-derived microvesicles enter cartilage and protect the joint in inflammatory arthritis'. Sarah E. Headland, Hefin R. Jones, Lucy V. Norling, Andrew Kim, Patricia R. Souza, Elisa Corsiero, Cristiane D. Gil, Alessandra Nerviani, Francesco Dell'Accio, Costantino Pitzalis, Sonia M. Oliani, Lily Y. Jan, Mauro Perretti. Science Translational Medicine. 25 November 2015

http://www.eurekalert.org/pub_releases/2015-11/osu-dco112315.php

Discovery could open door to frozen preservation of tissues, whole organs

Vitrification could ultimately allow a much wider use of extreme cold to preserve tissues

CORVALLIS, Ore. - Researchers in the College of Engineering at Oregon State University have discovered a new approach to "vitrification," or ice-free cryopreservation, that could ultimately allow a much wider use of extreme cold to preserve tissues and even organs for later use. The findings were announced today in PLOS ONE, in work supported by the National Science Foundation.

"This could be an important step toward the preservation of more complex tissues and structures," said Adam Higgins, an associate professor in the OSU School of Chemical, Biological and Environmental Engineering, and expert on medical bioprocessing.

Cryopreservation has already found widespread use in simpler applications such as preserving semen, blood, embryos, plant seeds and some other biological applications. But it is often constrained by the crystallization that occurs when water freezes, which can damage or destroy tissues and cells, Higgins said. This is similar to what happens to some food products when they are stored in a freezer, and lose much of their texture when thawed.

To address this, researchers have used various types of cryoprotectants that help reduce cell damage during the freezing process - among them is ethylene glycol, literally the same compound often used in automobile radiators to prevent freezing. A problem, Higgins said, is that many of these cryoprotectants are toxic, and can damage or kill the very cells they are trying to protect from the forces of extreme cold.

In the new OSU research, the engineers developed a mathematical model to simulate the freezing process in the presence of cryoprotectants, and identified a way to minimize damage. They found that if cells are initially exposed to a low concentration of cryoprotectant and time is allowed for the cells to swell, then the sample can be vitrified after rapidly adding a high concentration of cryoprotectants. The end result is much less overall toxicity, Higgins said.

The research showed that healthy cell survival following vitrification rose from about 10 percent with a conventional approach to more than 80 percent with the new optimized procedure. "The biggest single problem and limiting factor in vitrification is cryoprotectant toxicity, and this helps to address that," Higgins said. "The model should also help us identify less toxic cryoprotectants, and ultimately

open the door to vitrification of more complex tissues and perhaps complete organs."

If that were possible, many more applications of vitrification could be possible, especially as future progress is made in the rapidly advancing field of tissue regeneration, in which stem cells can be used to grow new tissues or even organs.

Tissues could be made in small amounts and then stored until needed for transplantation. Organs being used for transplants could be routinely preserved until a precise immunological match was found for their use. Conceptually, a person could even grow a spare heart or liver from their own stem cells and preserve it through vitrification in case it was ever needed, Higgins said.

Important applications might also be found in new drug development.

Drug testing is now carried out with traditional cell culture systems or animal models, which in many cases don't accurately predict the effect of the drug in humans. To address this, researchers are developing "organs-on-a-chip," or microfluidic chambers that contain human cells cultured under conditions that mimic native tissues or organs.

These new "organ-on-a-chip" systems may be able to more accurately predict drug responses in humans, but to deploy them, cells must be preserved in long-term storage. The new research could help address this by making it possible to store the systems in a vitrified state.

http://dx.plos.org/10.1371/journal.pone.0142828

http://www.eurekalert.org/pub_releases/2015-11/esoc-hdp112315.php

Heart disease patients who sit a lot have worse health even if they exercise

Patients with coronary artery disease spend an average of 8 hours each day sitting -- men were more sedentary than women

Sophia Antipolis - Patients with heart disease who sit a lot have worse health even if they exercise, reveals research published today in the European Journal of Cardiovascular Prevention.[1]

Get up and move every 30 minutes to improve health.

"Limiting the amount of time we spend sitting may be as important as the amount we exercise," said lead author Dr Stephanie Prince, post-doctorate fellow in the Division of Prevention and Rehabilitation, University of Ottawa Heart Institute, Ontario, Canada. "Sitting, watching TV, working at a computer and driving in a car are all sedentary behaviours and we need to take breaks from them."

Previous research has shown that being sedentary increases the risk of cardiovascular disease but until now its effect on patients with established heart disease was unknown.

The current study investigated levels of sedentary behaviour and the effect on health in 278 patients with coronary artery disease. The patients had been through a cardiac rehabilitation programme which taught them how to improve their levels of exercise in the long term.

Patients wore an activity monitor during their waking hours for nine days. The monitors allowed the researchers to measure how long patients spent being sedentary, or doing light, moderate or vigorous levels of physical activity.

The researchers also assessed various markers of health including body mass index (BMI, in kg/m2) and cardiorespiratory fitness. Next they looked at whether the amount of time a person spent being sedentary (which was mainly sitting) was related to these markers of health.

The researchers found that patients with coronary artery disease spent an average of eight hours each day being sedentary. "This was surprising given that they had taken classes on how to exercise more," said Dr Prince. "We assumed they would be less sedentary but they spent the majority of their day sitting."

Men spent more time sitting than women - an average of one hour more each day. This was primarily because women tended to do more light intensity movement - things like light housework, walking to the end of the drive, or running errands.

Dr Prince said: "Women with coronary artery disease spend less time sitting for long periods but we need to do more research to understand why. There is some research from the past which suggests that at around the age of 60 men become more sedentary than women and may watch more TV."

The researchers found that patients who sat more had a higher BMI. They also had lower cardiorespiratory fitness, which was assessed using VO2 peak. This is the maximum rate at which the heart, lungs and muscles use oxygen during an exercise test (also called aerobic capacity).

"These relationships remained even when we controlled for an individual's age, gender or physical activity levels," said Dr Prince. "In other words, people who sat for longer periods were heavier and less fit regardless of how much they exercised." Practical tips to get moving:

Get up and move every 30 minutes
Stand up during TV commercials or, even better, do light exercises while watching TV
Set a timer and take regular breaks from your desk
Take lunch breaks outside instead of in front of the computer
Go to bed instead of sitting in front of the TV and get the benefits of sleeping
Monitor your activity patterns to find out when you are most sedentary.

Dr Prince emphasised that sitting less was not a replacement for exercise. "It's important to limit prolonged bouts of sitting and in addition to be physically

active," she said. "Sedentary time may be another area of focus for cardiac rehabilitation programmes along with exercise."

SOURCES OF FUNDING: Stephanie Prince is funded by a Strategic Endowed Research Fellowship from the University of Ottawa Heart Institute Foundation and a Canadian Institutes of Health Research Fellowship. The ECO-PCR study is funded by the Heart and Stroke Foundation of Ontario (Grant #000109).

DISCLOSURES: The authors declare no conflicts of interest and have nothing to disclose.

[1]Prince SA, Blanchard CM, Grace SL, Reid RD. Objectively-measured sedentary time and its association with markers of cardiometabolic health and fitness among cardiac rehabilitation graduates. European Journal of Preventive Cardiology. 2015: DOI: 10.1177/2047487315617101

http://www.eurekalert.org/pub_releases/2015-11/jhu-sgf112415.php

Scientists get first glimpse of black hole eating star, ejecting high-speed flare

Johns Hopkins astrophysicist leads team observing 'extremely rare' event

An international team of astrophysicists led by a Johns Hopkins University scientist has for the first time witnessed a star being swallowed by a black hole and ejecting a flare of matter moving at nearly the speed of light.

The finding reported Thursday in the journal Science tracks the star -- about the size of our sun -- as it shifts from its customary path, slips into the gravitational pull of a supermassive black hole and is sucked in, said Sjoert van Velzen, a Hubble fellow at Johns Hopkins.

"These events are extremely rare," van Velzen said. "It's the first time we see everything from the stellar destruction followed by the launch of a conical outflow, also called a jet, and we watched it unfold over several months."

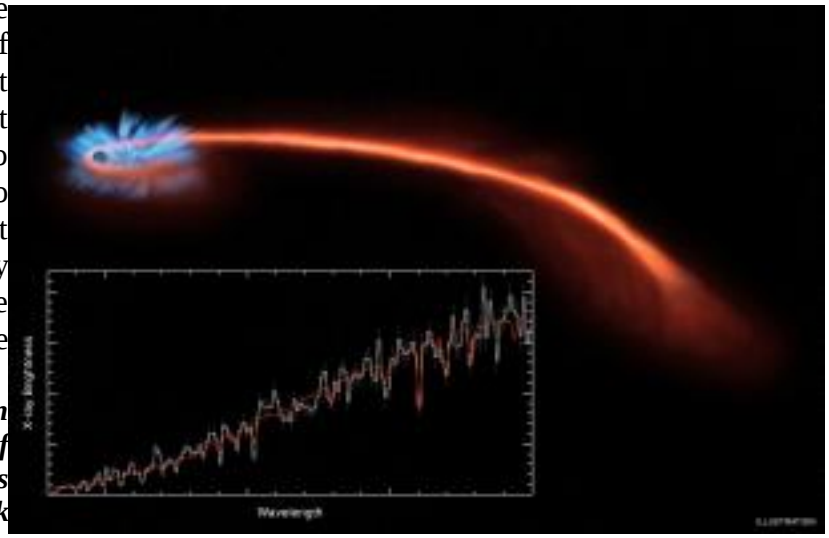
Black holes are areas of space so dense that irresistible gravitational force stops the escape of matter, gas and even light, rendering them invisible and creating the effect of a void in the fabric of space. Astrophysicists had predicted that when a black hole is force-fed a large amount of gas, in this case a whole star, then a fast-moving jet of plasma - elementary particles in a magnetic field - can escape from near the black hole rim, or "event horizon." This study suggests this prediction was correct, the scientists said.

"Previous efforts to find evidence for these jets, including my own, were late to the game," said van Velzen, who led the analysis and coordinated the efforts of 13 other scientists in the United States, the Netherlands, Great Britain and Australia.

Supermassive black holes, the largest of black holes, are believed to exist at the center of most massive galaxies. This particular one lies at the lighter end of the supermassive black hole spectrum, at only about a million times the mass of our sun, but still packing the force to gobble a star.

The first observation of the star being destroyed was made by a team at the Ohio State University, using an optical telescope in Hawaii. That team announced its discovery on Twitter in early December 2014.

After reading about the event, van Velzen contacted an astrophysics team led by Rob Fender at the University of Oxford in Great Britain. That group used radio telescopes to follow up as fast as possible. They were just in time to catch the action.



The illustration shows a disk of stellar debris around the black hole in the upper left of the illustration, and a long tail of debris that has been flung away from the black hole.

The X-ray spectrum obtained with Chandra (seen in the inset box) and XMM-Newton both show clear evidence for absorption lines, i.e. dips in X-ray intensity over a narrow range of wavelengths. In an X-ray light version of the Doppler Shift, the absorption lines are shifted to bluer wavelengths than expected, giving evidence for a wind blowing towards us and away from the black hole.

The presence of a wind moving away from the black hole is shown as the bluish white lines in the artist's illustration. The wind is not moving fast enough to escape the black hole's gravitational grasp. An alternative explanation for the relatively low speed is that gas from the disrupted star is following an elliptical orbit around the black hole and is observed at the greatest distance from the black hole where it is traveling the slowest. These results confirm recent theoretical predictions for the structure and evolution of tidal disruptions events. **Image credit: NASA/CXC/U. Michigan/J. Miller et al.; Illustration: NASA/CXC/M. Weiss**

By the time it was done, the international team had data from satellites and ground-based telescopes that gathered X-ray, radio and optical signals, providing a stunning "multi-wavelength" portrait of this event.

It helped that the galaxy in question is closer to Earth than those studied previously in hopes of tracking a jet emerging after the destruction of a star. This

galaxy is about 300 million light years away, while the others were at least three times farther away. One light year is 5.88 trillion miles.

The first step for the international team was to rule out the possibility that the light was from a pre-existing expansive swirling mass called an "accretion disk" that forms when a black hole is sucking in matter from space. That helped to confirm that the sudden increase of light from the galaxy was due to a newly trapped star.

"The destruction of a star by a black hole is beautifully complicated, and far from understood," van Velzen said. "From our observations, we learn the streams of stellar debris can organize and make a jet rather quickly, which is valuable input for constructing a complete theory of these events."

Van Velzen last year completed his doctoral dissertation at Radboud University in the Netherlands, where he studied jets from supermassive black holes. In the last line of the dissertation, he expressed his hope to discover these events within four years. It turned out to take only a few months after the ceremony for his dissertation defense.

Van Velzen and his team were not the only ones to hunt for radio signals from this particular unlucky star. A group at Harvard observed the same source with radio telescopes in New Mexico and announced its results online. Both teams presented results at a workshop in Jerusalem in early November. It was the first time the two competing teams had met face to face.

"The meeting was an intense, yet very productive exchange of ideas about this source," van Velzen said. "We still get along very well; I actually went for a long hike near the Dead Sea with the leader of the competing group."

Support for this study came from sources including NASA, the Netherlands Foundation for Scientific Research (NOW), the European Research Council, the International Centre for Radio Astronomy Research, the Alfred P. Sloan Foundation and the Australian Research Council.

http://www.eurekalert.org/pub_releases/2015-11/b-rwb112415.php

Recent Western blood pressure guidelines may boost stroke risk in Asian patients

Link between blood pressure and stroke much stronger in Asia than it is in Europe/North America

European and North American blood pressure guidelines, issued last year, may actually boost the stroke risk if used for Asian patients, particularly the elderly, suggests an expert opinion published online in the journal Heart Asia.

High blood pressure is a key risk factor for stroke, but the link between the two is much stronger in Asians than it is in Europeans or North Americans, say the experts. The global number of people with poorly controlled high blood pressure has risen from 600 million in 1980 to almost 1 billion in 2008, and predicted to rise a further 60% to 1.56 billion by 2025.

The prevalence of high blood pressure in Asian countries has risen sharply in the past 30 years, and particularly over the past decade, as a result of increasing urbanisation and the adoption of a Western lifestyle

High blood pressure among Asian populations has unique features in terms of the response to drug treatment, risk of complications, and outcomes, say the authors. This leads to disproportionately high rates of death and ill health from stroke compared with Western populations.

"Although evidence-based and qualified guidelines have been recently released from Europe and North America, the unique features of Asian hypertensive patients raise concerns on the real clinical applicability of these guidelines to Asian populations," write the authors.

The latest Western guidelines increased target blood pressure to 140/90 mmHg for patients at high risk of cardiovascular disease and renal failure, but this may be too high for Asian populations warn, the authors. Some Asian guidelines have recommended more stringent targets in these patients, they say.

Treating high blood pressure in elderly Asian patients is particularly challenging, they say. And the threshold for systolic blood pressure recommended by Western guidelines could boost the risk of stroke in these patients. A threshold below 140/90 mmHg might be more appropriate, they suggest.

"The paucity of data on the correct definition of the most appropriate [blood pressure] target in elderly patients, highlighted by the few available trials, should be perceived as a stimulus for future research in Asia, not as an argument for questioning the benefit of treatment," they write.

http://nyti.ms/1lS5Gvj

Scientists Link Moon's Tilt and Earth's Gold

The moon's orbit is askew, and two planetary scientists believe that they have come up with a good reason.

By KENNETH CHANG NOV. 27, 2015

Intriguingly, their idea also explains why gold and platinum are found in the Earth's crust, well within diggable reach.

The moon is believed to have formed out of a giant cataclysmic collision early in the history of the solar system when an interplanetary interloper the size of Mars slammed into Earth and lofted a ring of debris circling over the Equator. The debris coalesced into the moon.At its birth, the moon was quite close to the Earth, probably within 20,000 miles. Because of the tidal pulls between the Earth and moon, the moon's orbit has slowly been spiraling outward ever since, and as it does, Earth's pull diminishes, and the pull of the sun becomes more dominant.

By now, with the moon a quarter million miles from Earth, the sun's gravity should have tipped the moon's orbit to lie in the same plane as the orbits of the planets. But it has not. The moon's orbit is about 5 degrees askew.

"That the lunar inclination is as small as it is gives us some confidence that the basic idea of lunar formation from an equatorial disk of debris orbiting the proto-Earth is a good one," said Kaveh Pahlevan, a planetary scientist at the Observatory of the Côte d'Azur in Nice, France. "But the story must have a twist."

Writing in this week's issue of the journal Nature, Dr. Pahlevan and his observatory colleague Alessandro Morbidelli propose the twist.

The moon did indeed form in the Earth's equatorial plane, the scientists said, but then a few large objects, perhaps as large as the moon, zipping through the inner solar system repeatedly passed nearby over a few tens of millions of years and tipped the moon's orbit.

A series of computer simulations show that the idea is plausible. "This mechanism works for a broad range of physical conditions," Dr. Pahlevan said.

Eventually the crisscrossing mini-planets would have been tossed out of the solar system, swallowed by the sun, or slammed into the Earth or the other planets.

Robin M. Canup, a planetary scientist at the Southwest Research Institute in Boulder, Colo., who wrote an accompanying commentary in Nature, said the thousands of close passes that typically occur before an impact were a "really new realization" by Dr. Pahlevan and Dr. Morbidelli. "While a single scattering event will only change the moon's tilt slightly," Dr. Canup said, "it's the cumulative effect of these many passes that can produce this tilt."

The scars of one or more moon-size objects hitting Earth would have long been erased by the tectonics of the shifting surface, but those impacts would explain the gold, platinum and other precious metals in the Earth's crust but not on the moon.

Metals on the early Earth should have sunk to the interior. Thus, planetary scientists think that after the moon was created, later collisions that provided the last 1 percent or so of the Earth's mass added a veneer of precious metals.

A dearth of lunar metals argues for a few large metal-rich objects hitting the Earth rather than many small ones.

The computer simulations show that the chances of the moon's getting hit are low. In the simulations, if there was one object buzzing by, the moon was hit 9 percent of the time. With four objects, the chances of a lunar impact rose to 25 percent.

"Not an overly likely outcome, which is good," Dr. Canup said.

Scientists including Dr. Canup had proposed other explanations for the tilt. "I would say those relied on certainly more complex processes and required rather narrow sets of conditions for success," Dr. Canup said. "I think where this has really stepped in is it's a very simple mechanism."

http://bit.ly/1XABuAz

NASA's 'Chemical Laptop' could help future rovers find life on alien planets

NASA scientists have a new device up their sleeves to help find life on other planets.

By Dante D'Orazio

The rectangular box is being called the "Chemical Laptop," but it's really more of a portable, automated chemistry lab that can be built into future NASA rovers.

The Chemical Laptop has one primary goal, according to NASA: to find molecules associated with life. Specifically, it's designed to find amino acids and fatty acids, which are key to proteins and cell membranes, respectively, in life here on Earth.

Samples obtained on Mars or elsewhere need to be dissolved in water before they can be analyzed. The Chemical Laptop uses something researchers are likening to an espresso machine to heat up and dissolve the samples in water. Dyes and other chemical additives will be used to help mark molecules in the samples, and anything that's obtained will be analyzed by a laser in the device.

But the tool won't just be able to tell if there are amino acids or fatty acids on an alien planet. It can determine additional information that could help determine whether those amino acids actually came from a life form.

"It can tell if amino acids came from life forms"

A particular amino acid can come in either a left- and right-handed variety; the two versions, called enantiomers, have identical physical properties, but they are mirror images of each other. Here on Earth, life has evolved to almost exclusively use the left-handed versions. Many biological reactions will retain the "handedness" of a molecule — for whatever reason, left-handed came to dominate life that we know. But it's equally possible that right-handed amino acids could dominate life on another planet. What's not likely is that an alien life form would use an equal mixture of the two — if a sample contained an equal mix, the molecules probably didn't come from life.

Since the left- and right-handed versions are so similar, they can be difficult to distinguish — especially on a faraway planet. To solve this problem, some of the dyes used by the Chemical Laptop only work with left- or right-handed amino acids. That will then let researchers see the composition of a sample, and determine if it's likely life existed on the planet.

Jessica Creamer, of NASA's Jet Propulsion Laboratory, says in a statement that if an excess of one was found, "That would be the best evidence so far that life exists on other planets." She added that the Chemical Laptop "would be the most sensitive device of its kind to leave Earth," if and when it's implemented on future

missions. So far, a version of the device has already been demonstrated here on Earth — now it just needs its chance in space.

http://bit.ly/1XABuAz

An old scourge, syphilis, making a comeback

Reported cases of syphilis appear to be making a comeback

Kuchikomi Nov. 29, 2015 - 06:20AM JST

TOKYO - The Japanese word for syphilis, "baidoku," literally translates as "plum poison." It was so named from the chancres (painless ulcerations) that appear on the skin in the disease's primary stage, which were thought to resemble plum blossoms.

Nikkan Gendai (Nov 27) notes that according to the Shinjuku-based National Institute of Infectious Diseases, reported cases of this ancient scourge of mankind appear to be making a comeback. While 831 cases were reported in 2008, the number declined to 621 in 2010. By the end of October this year, the count was up to 2,037—up from 1,670 for all of 2014.

Most disconcerting, perhaps, is that the largest demographic turned out to be females in the 20 to 24 years age group: the 177 reported cases represented a 2.7-fold increase over the year before. "We're in the midst of a worldwide pandemic," says Dr Yasuhiko Onue, an authority on sexually transmitted diseases. "Among the carriers I believe are also women from Asian countries visiting Japan."

Koichiro Fujita, professor emeritus at Tokyo Medical and Dental University, tells the newspaper, "It's spreading because more people are engaging in sex without taking precautions. Young females lacking knowledge of the ways of the world are overly trusting, and are persuaded by males to have sex with them without use of a condom."

The decline in fears over contracting AIDS appears to be a main factor, says Fujita. "When HIV was a concern, warnings were ubiquitous, and young people became more conscientious about use of condoms," he explains. "But more recently there's been less concern over contracting HIV. And at the same time people regard syphilis as 'a disease of olden times,' and they're not taking the necessary precautions."

Another contributing factor, Dr Fujita believes, is the insufficiency of vitamin B, which may be responsible for weakening of the surface membrane of the genitals and lowered resistance to infection. Syphilis can also be spread via oral sex.

Unlike gonorrhea, syphilis in its early stages can be asymptomatic, and if a woman is infected during pregnancy, miscarriages or stillbirths are not uncommon. If the fetus does survive, should the syphilis bacteria infect its brain, mental impairment can result.

"It's very difficult to tell if a woman's been infected from a superficial glance," says Dr Fujita. "Some of them tend to have rather sickly complexions. During sex, some of them may have telltale wartlike bumps, or inflammation, on their genitals. "Some doctors overseas say they can detect infection from the characteristic odor. In any case, they should undergo a blood test as part of a full physical examination, and specifically request the doctor to look for signs of syphilis.

Tertiary cases of syphilis are a relative rarity but if allowed to go untreated a carrier can suffer a fatal aneurysm. Should you find yourself tested positive, Nikkan Gendai advises, you should also inform all of your recent sexual partners, whether they are amateurs or pros.

http://www.eurekalert.org/pub_releases/2015-11/btif-atk112515.php

Aspirin targets key protein in neurodegenerative diseases

A breakdown product of aspirin blocks cell death associated with Alzheimer's, Parkinson's and Huntington's disease

ITHACA, NY - A new study finds that a component of aspirin binds to an enzyme called GAPDH, which is believed to play a major role in neurodegenerative diseases, including Alzheimer's, Parkinson's and Huntington's diseases.

Researchers at the Boyce Thompson Institute and John Hopkins University discovered that salicylic acid, the primary breakdown product of aspirin, binds to GAPDH, thereby stopping it from moving into a cell's nucleus, where it can trigger the cell's death. The study, which appears in the journal PLOS ONE, also suggests that derivatives of salicylic acid may hold promise for treating multiple neurodegenerative diseases.

Senior author Daniel Klessig, a professor at Boyce Thompson Institute and Cornell University, has studied the actions of salicylic acid for many years, but primarily in plants. Salicylic acid is the critical hormone for regulating the plant immune system. Previous studies have identified several targets in plants that are affected by salicylic acid, and many of these targets have equivalents in humans.

In the new study, the researchers performed high-throughput screens to identify proteins in the human body that bind to salicylic acid. GAPDH (Glyceraldehyde 3-Phosphate Dehydrogenase) is a central enzyme in glucose metabolism, but plays additional roles in the cell. Under oxidative stress--an excess of free radicals and other reactive compounds--GAPDH is modified and then enters the nucleus of neurons, where it enhances protein turnover, leading to cell death.

The anti-Parkinson's drug deprenyl blocks GAPDH's entry into the nucleus and the resulting cell death. The researchers discovered that salicylic acid also is effective at stopping GAPDH from moving into the nucleus, thus preventing the cell from dying.

"The enzyme GAPDH, long thought to function solely in glucose metabolism, is now known to participate in intracellular signaling," said co-author Solomon Snyder, professor of neuroscience at Johns Hopkins University in Baltimore. "The new study establishes that GAPDH is a target for salicylate drugs related to aspirin, and hence may be relevant to the therapeutic actions of such drugs."

Furthermore, they found that a natural derivative of salicylic acid from the Chinese medical herb licorice and a lab-synthesized derivative bind to GAPDH more tightly than salicylic acid. Both are more effective than salicylic acid at blocking GAPDH's movement into the nucleus and the resulting cell death.

Earlier this year, Klessig's group identified another novel target of salicylic acid called HMGB1 (High Mobility Group Box 1), which causes inflammation and is associated with several diseases, including arthritis, lupus, sepsis, atherosclerosis and certain cancers. Low levels of salicylic acid block these pro-inflammatory activities, and the above mentioned salicylic acid derivatives are 40 to 70 times more potent than salicylic acid at inhibiting these pro-inflammatory activities.

"A better understanding of how salicylic acid and its derivatives regulate the activities of GAPDH and HMGB1, coupled with the discovery of much more potent synthetic and natural derivatives of salicylic acid, provide great promise for the development of new and better salicylic acid-based treatments of a wide variety of prevalent, devastating diseases," said Klessig.

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