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Can pure maple syrup help reduce chronic inflammation?

First-ever global symposium convenes to review latest science on natural sweetener

SAN FRANCISCO - The first-ever global symposium, solely dedicated to sharing the latest scientific discoveries on the potential health benefits of 100% pure maple products from Canada, took place on April 2 in San Francisco at the 253rd annual meeting of the American Chemical Society (ACS), the largest scientific society in the world. At the symposium, entitled "Chemistry and Biological Effects of Maple Food Products," scientists from around the world shared the results of their research that expands the science of maple's potential impact on several areas affected by chronic inflammation. These include metabolic syndrome, brain health and liver disease, as well as maple's emerging link to a healthy gut microbiome.

The global symposium was organized by Dr. Navindra Seeram, who currently serves as chairman of the Division of Agricultural and Food Chemistry of the American Chemical Society. Dr. Seeram has extensive experience examining the impact of phytonutrients in foods such as berries and pomegranates. In collaboration with the Federation of Quebec Maple Syrup Producers, Dr. Seeram has been studying the unique properties of maple in his laboratory at the University of Rhode Island since 2009. The results of his research stimulated the interest of the global scientific community, which has uncovered additional health benefits of pure maple products.

A new University of Rhode Island study, highlighted at the symposium, revealed the presence of inulin, a type of carbohydrate recently discovered for the first time in maple syrup. Inulin is a complex carbohydrate (natural dietary fiber) that acts as a prebiotic and works to encourage the growth of "good" or beneficial bacteria in the gut. Inulin joins the other beneficial polyphenols, vitamins and

minerals already identified in pure maple syrup. This latest discovery could allow maple to be classified as a functional food.

In addition, a new study conducted on animals, also revealed at the symposium, focused on the beneficial effect of a symbiotic (prebiotic and probiotic) maple sap drink in recovering gut flora balance, which can be lost for several reasons, including treatment with antibiotics.

"A healthy gut, with a balance of beneficial bacteria, helps to stimulate and support a healthy immune system. A healthy immune system, then, can help protect the body against chronic inflammation," said Dr. Seeram. "Chronic inflammation has been shown to have a potential link to brain conditions such as Alzheimer's disease. As such, this research provides additional information linking pure maple syrup, a unique natural sweetener, to brain health. However, additional animal studies, along with eventual human studies, would be required to confirm these initial findings."

This year, two newly discovered additional compounds with antioxidant properties and potential health benefits have been identified in the lignan family, bringing the total count of known phytonutrients in maple products to 65. This may help support discoveries made over the past few years on the inherent properties of maple syrup from Canada that comes directly from the sap of the maple tree, making it an all-natural product with unique health benefits. Discovered in 2011, a unique, polyphenolic molecule in maple syrup, Quebecol⁽¹⁾, and one of its analogues (isoquebecol, recently synthesized), have demonstrated that it significantly decreases the production of inflammation mediators.

"The 7,500 Quebec-based maple producers are committed to pursuing funding of new research to help further identify the positive health impacts of pure maple," said Serge Beaulieu, President of the Federation of Quebec Maple Syrup Producers. "This is why we have chosen to work with Dr. Seeram along with other researchers. Dr. Seeram's tremendous experience studying the impact of phytonutrients in plants and fruits has propelled maple research since he began

studying the natural sweetener in 2009. There is still much to discover about maple's health benefits, and the scientific community has only uncovered the tip of the iceberg. We will continue to allocate resources to research on maple products to discover its impacts on the human body."

Inflammation is a normal part of a healthy immune response, and is a biological process that helps heal injury and fight infection. When inflammation becomes uncontrolled or chronic, it plays a role in exacerbating a variety of health-related issues. There are several ways to help prevent and combat chronic inflammation. A diet rich in foods that contain polyphenols, such as green tea, red wine, fruits and vegetables - and potentially pure maple syrup from Canada - may be beneficial for supporting a healthy immune system.

The Federation of Quebec Maple Syrup Producers does not promote an increase of sugar consumption. When choosing a sweetener for moderate use, it appears that 100% pure maple syrup from Canada has more healthful compounds compared to some other sources of sugar.

⁽¹⁾ Li, L., & Seeram, N. P. (2011). Quebecol, a novel phenolic compound isolated from Canadian maple syrup. *Journal of Functional Foods*, 3(2), 125-128.

<http://bit.ly/2o14qs3>

Researcher creates chemical system that mimics early cell behavior

Artificial "proto-cells" grow, replicate, react to light, and even exhibit signs of natural selection

A Harvard researcher seeking a model for the earliest cells has created a system that self-assembles from a chemical soup into cell-like structures that grow, move in response to light, replicate when destroyed, and exhibit signs of rudimentary evolutionary selection.

While the system, developed by senior research fellow Juan Pérez-Mercader, mimics what one might conceive of as early cell behavior, a major caveat is that its main component is a molecule not typically found in living things.

Pérez-Mercader said that is by design. A physicist by training, Pérez-Mercader initiated the work to follow up on a paper he wrote in 2003 discussing mathematical models for some of the basic properties of life.

The recent work, described in the open-access journal *Scientific Reports*, is an attempt to use chemistry to translate those mathematical models into the real world, he said. "I am trying to build something that mimics life in a completely artificial way," Pérez-Mercader said. Pérez-Mercader came to Harvard to join the Origins of Life Initiative, a University-wide effort involving researchers across Schools and disciplines. Work ranges from investigations into the still-murky processes by which life first arose to study of exoplanets far from Earth.

Life has four main attributes, Pérez-Mercader said. It stores, communicates, uses, and replicates information—as in the data held in DNA. It has metabolism that allows it to make its own parts. It is capable of self-replication. And it is capable of evolving.

"Life ... does all those things based on chemistry. If there is any chemistry that does all of the above, and is not the known biochemistry, we are searching high and low for [it]," he said.

The ability to separate from the surrounding environment is a key component of any living system, Pérez-Mercader said. This allows the chemistry of life to occur in an encapsulated structure, which keeps it from diffusing into the surrounding environment. The work of other researchers in this area has included creating rudimentary cells via fat molecules, which are used in cell-building by living things. Pérez-Mercader sought to strip the process to its essentials to better understand the basics.

"You do need to have something that generates that compartmentalization. So we said: 'Can we build the compartment in a simple way?'" Pérez-Mercader said.

To create the system, Pérez-Mercader worked with Anders Albertsen, an associate of the Department of Earth and Planetary Sciences, and

Jan Szymanski, a former postdoctoral fellow at Harvard, to create a chemical soup made up of 2-hydroxypropyl methacrylate. They added ruthenium, a light-sensitive metal, to make the molecule respond to light. The modified molecule tends to link with others into long repeating chains called polymers, with one end repelling water and the other attracting it. That interaction with water causes the polymers to line up, and ultimately form vesicles.

The system is activated by blue light. Over the course of several hours of exposure, the monomers link together to form polymers, and the polymers line up to form spherical vesicles, with some approaching the size of natural cells. They grow due to osmosis until they pop and then begin growing again.

"By five hours the mixture changes," Pérez-Mercader said. "By six hours it becomes turbid. Out of the homogenous mixture develop these containers. The containers implode and grow again, they begin to do these very interesting things."

The regenerative behavior is what led Pérez-Mercader to the description "phoenix vesicles," after the mythical bird that burned up in its nest and was born again.

In addition to the ability to form spontaneously and replicate, the vesicles are attracted to light, and tend to cluster near the light source.

Over time, larger vesicles dominate the population, Pérez-Mercader said, indicating that a form of selection is at work.

Aside from any potential lessons about early life, Pérez-Mercader said the findings could be useful in creating a self-assembling delivery system in industry. He said he plans to continue the work with more complex vesicles and include some active chemistry in their interior.

"The implications for the origins of life to me are very interesting, though they still need to be explored," he said.

Anders N. Albertsen et al. Emergent Properties of Giant Vesicles Formed by a Polymerization-Induced Self-Assembly (PISA) Reaction, Scientific Reports (2017). DOI: 10.1038/srep41534

<http://bit.ly/2odexfo>

Meningitis bacteria adapting to STI niche, genetic analysis shows

Acquisition of DNA from relatives that cause gonorrhea

Neisseria meningitidis, a bacterium usually associated with meningitis and sepsis, is the cause of a recent cluster of sexually transmitted infections in Columbus, Ohio and in other US cities. The bacterium appears to be adapting to a urogenital environment, an analysis of the organism's DNA shows.

The DNA analysis helps doctors track the spread of this type of bacteria, distinguish it from others, anticipate which vaccines might be protective, and understand how it has evolved.

The findings are scheduled for publication in PNAS.

Genetic changes make this "clade" of *N. meningitidis* look more like relatives that are known to cause gonorrhea, says lead author Yih-Ling Tzeng, PhD, assistant professor of medicine (infectious diseases) at Emory University School of Medicine.

In particular, the bacteria have lost their outer coat-capsules, potentially enhancing their ability to stick to mucosal surfaces in the body, and have gained enzymes that promote growth in a low-oxygen environment.

Some good news is that the capsule-less organism is less likely to cause invasive diseases such as meningitis, because the capsule protects the bacteria against components of the immune system found in the blood, Tzeng says.

N. meningitidis is carried at the back of the nose and throat, without symptoms, in 5 to 10 percent of people. As its name suggests, when *N. meningitidis* invades other parts of the body, it can cause meningitis, an infection of the lining of the brain and spinal cord, as well as deadly bloodstream infections.

In 2015, *N. meningitidis* began to appear in heterosexual men coming to the Sexual Health Clinic in Columbus as the cause of urethritis: inflammation leading to painful urination. These infections were

initially presumed to be gonorrhea, caused by *N. gonorrhoeae*. More than 100 cases have been reported in Columbus, and the same type of *N. meningitidis* infection has appeared in Michigan, Indiana and Georgia.

Jose Bazan, DO, the Clinic's medical director and assistant professor of medicine (infectious diseases) at Ohio State University and Abby Norris Turner PhD, assistant professor of medicine (infectious diseases) teamed up with Tzeng and David Stephens, MD, professor of medicine of Emory University School of Medicine, and colleagues from Indiana University School of Medicine and the Centers for Disease Control and Prevention (CDC) to investigate.

The Columbus clinic is part of the CDC's nationwide Gonococcal Isolate Surveillance Project (GISP), which monitors antibiotic resistance. Emory co-authors include Carlos del Rio, MD, professor of medicine and global health and director of the Atlanta GISP laboratory, and Timothy Read, PhD, associate professor of medicine and human genetics.

The scientists looked at the genomes of 52 *N. meningitidis* samples from Columbus, and two from Indianapolis and two from Atlanta. All 56 genomes had many common features, so they're closely related, but they are continuing to evolve.

N. meningitidis is usually classified by serogroups, based on the structure of the capsule. Vaccines against the A, C, Y, and W serogroups have been available in the US for years, and vaccines against serogroup B were introduced in 2014.

Outbreaks of *N. meningitidis* serogroup C meningitis and sepsis have been observed in several countries among men who have sex with men. In contrast, the bacteria described in the PNAS paper could not be assigned to any serogroup based on initial screening tests.

The loss of several genes for synthesizing components of the capsule explains the blank result, Tzeng says. However, clues in the DNA of the capsule-less bacteria make them look like they were originally derived from a serogroup C ancestor.

It is possible that vaccines that were approved in the last few years against the B serogroup might still be effective against this meningococcal clade, because the capsule-less bacteria continue to produce other proteins targeted by those vaccines, the scientists found. A vaccine against gonorrhea has been a challenge, because repeat infections are common.

N. meningitidis doesn't usually encounter low-oxygen conditions, but this clade, linked to urethritis, has picked up genes that help them to grow in the environment of the urogenital tract. Based on their sequences, the genes appear to have come directly from *N. gonorrhoeae*, suggesting that on at least one occasion, the two types of bacteria were in the same place and exchanged DNA.

"All the urethritis patients responded to standard treatments for gonorrhea and there were no alarming resistance markers," Tzeng says. "However, as the gene conversion demonstrates, this clade can readily take up DNA from gonococci and it is not unthinkable that gonococcal antibiotic resistance genes could jump into this clade by gene transfer, if it is to its advantage."

The research was supported by the National Institute of Allergy and Infectious Diseases (R01AI107116, R21AI128313, R21AI121860 and R01AI116706).

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Monkey business produces rare preserved blood in amber fossils

First fossilized red blood cells from a mammal, preserved so perfectly they appear to have been prepared for display

CORVALLIS, Ore. - Two monkeys grooming each other about 20-30 million years ago may have helped produce a remarkable new find - the first fossilized red blood cells from a mammal, preserved so perfectly in amber that they appear to have been prepared for display in a laboratory. The discovery, published in the *Journal of Medical Entomology*, also describes the only known fossils of a type of parasite that still exists today, *Babesia microti*, which infects the blood cells of humans and other animals.

Two small holes in the back of a blood-engorged tick, which allowed blood to ooze out just as the tick became stuck in tree sap that later fossilized into amber, provide a brief glimpse of life in a tropical jungle millions of years ago in what is now the Dominican Republic.

"These two tiny holes indicate that something picked a tick off the mammal it was feeding on, puncturing it in the process and dropping it immediately into tree sap," said George Poinar, Jr., professor emeritus in the College of Science at Oregon State University, author of the study and an international expert on plant and animal life forms found preserved in amber.



This tick found as a fossil in amber shows two small holes in its back, as if it were just picked off the animal it was feeding on. George Poinar, Jr., courtesy of Oregon State University

"This would be consistent with the grooming behavior of monkeys that we know lived at that time in this region. The fossilized blood cells, infected with these parasites, are simply amazing in their detail. This discovery provides the only known fossils of Babesia-type pathogens."

The fossil parasites add to the history of the Order Piroplasmida, of which the Babesiidae is one family. In humans, the parasite *B. microti* can cause babesiosis, a disease with symptoms that resemble malaria and can be fatal. A related parasite in cattle can cause Texas cattle fever, which has been a historic problem in the plains states, and just this spring is causing another outbreak that has led to quarantines on more than 500,000 acres of land in Texas.

"The life forms we find in amber can reveal so much about the history and evolution of diseases we still struggle with today," Poinar said.

"This parasite, for instance, was clearly around millions of years before humans, and appears to have evolved alongside primates, among other hosts."

Part of what makes these fossils unique, Poinar said, is the clarity by which the parasites and blood cells are preserved, almost as if they had been stained and otherwise treated in a laboratory for inspection. The parasites were different enough in texture and density to stand out clearly within the red blood cells during the natural embalming process for which amber is famous.

<http://bit.ly/2niLA2B>

Gallbladder removal is common -- but is it necessary? Seventy percent of patients who kept their gallbladders despite biliary pancreatitis had no recurrence 4 years later

Johns Hopkins researchers say that the findings they published in the current edition of *The American Journal of Gastroenterology* could have important implications for the field of personalized medicine.

The study determined that while most patients who were hospitalized with acute biliary pancreatitis had their gallbladders removed, many patients who did not fared well over a four-year follow-up period.

Cholecystectomy, or surgical gallbladder removal, is the standard medical treatment for patients hospitalized for acute biliary pancreatitis, which typically is a result of gallstones. Because the risk of organ failure, sepsis and other dangerous complications increases with recurrent attacks of biliary pancreatitis, the procedure is recommended within four weeks of the initial diagnosis.

But what about patients with that condition who, for whatever reason, do not have their gallbladders removed? Seventy percent of the patients in the study who declined the surgery were not hospitalized again for pancreatitis.

"These findings tell us that there may be a way to avoid gallbladder removal surgery," says Susan Hutfless, Ph.D., assistant professor of medicine at the Johns Hopkins University School of Medicine and principal investigator of the study.

The study was designed as the largest-ever look at adherence to the accepted medical guidelines around pancreatitis hospitalizations. The finding about patients who do not adhere was incidental.

Hutfless and the study's lead author, Ayesha Kamal, M.B.B.S., postdoctoral fellow in the Department of Medicine at the Johns Hopkins University School of Medicine, examined a database containing information on more than 17,000 cases across the United States between 2010 and 2013. Patients in the study had private insurance and were under the age of 65. Seventy-eight percent of those patients had their gallbladders removed within 30 days of their initial hospitalization, in keeping with accepted medical guidelines. Less than 10 percent of those patients returned to the hospital with pancreatitis.

Of the 3,705 patients who did not adhere to the guidelines, 1,213 had a cholecystectomy within six months. But the nearly 2,500 patients who did not have the surgery within 30 days had still not had it four years later.

Acute pancreatitis is the nation's third-leading gastrointestinal cause of hospitalization, resulting in more than 275,000 admissions and over \$2 billion in total costs in 2012. Numerous studies have found that, in most cases, cholecystectomy prevents additional pancreatitis-related hospitalizations.

The authors list a number of barriers that could prevent people suffering from the condition to comply with physician recommendations of gallbladder removal. Lack of resources, surgeon or patient preference, and inaccurate billing coding each could be a reason why a patient with biliary pancreatitis would not undergo cholecystectomy.

But with nearly 80 percent of those patients undergoing the procedure, Kamal says the compliance numbers were unexpectedly high.

It is not clear why some noncompliant patients had recurrences and some did not. Hutfless cautions that more research is necessary before drawing any conclusions from the findings related to patients noncompliant with medical guidelines.

"This paper shows that as medicine evolves, it is important to reflect on opportunities to refine care further," Hutfless says. "The

personalization of cholecystectomy timing is still a hypothesis and would need to be tested in rigorous studies. For now, there is clear evidence that the guidelines are beneficial to patients and should be followed."

Additional authors on the study were Eboselume Akhuemonkhan, Vikesh Singh and Anthony N. Kalloo of The Johns Hopkins University School of Medicine and Venkata S. Akshintala of the University of Pittsburgh Medical Center.

<http://bit.ly/2nQF3Zb>

Hormones are behind hernias of the groin in elderly men, study suggests

Altered sex hormone levels that weaken and scar muscle tissue in the lower abdomen

ORLANDO--Researchers have identified an apparent cause of inguinal hernia, or groin hernia, in older men: altered sex hormone levels that weaken and scar muscle tissue in the lower abdomen. Results of their study using an animal model will be presented Monday at ENDO 2017, the Endocrine Society's 99th annual meeting in Orlando, Fla.

"We have discovered that both increased estrogen action and decreased testosterone action leads to inguinal hernia formation," said Hong Zhao, M.D., Ph.D., the study's lead author and a research associate professor at Northwestern University Feinberg School of Medicine in Chicago, Ill.

She and the other researchers found the link between hormones and hernias accidentally while using a mouse model for breast cancer research, said senior investigator Serdar Bulun, M.D., professor and chair of obstetrics and gynecology at Northwestern Medicine. They had created humanized transgenic mice by genetically modifying them to carry the human gene for aromatase, which is the key enzyme for the conversion of testosterone into estrogen. The mice expressed human aromatase and had thus higher levels of muscle tissue estrogen compared with control mice.

One day the investigators noticed that the male mice, used for breeding, could not walk and had a swollen lower abdomen. They

initially thought the swelling was a tumor but later realized it was an extremely large groin hernia.

The cause of inguinal hernia is unknown, although risk factors include being male and older age. One in four men in the United States over their lifetime will develop an inguinal hernia, Bulun said.

This type of hernia, in which fatty or intestinal tissue bulges out of the abdominal wall, can cause pain, pressure, burning and swelling of the scrotum or groin area. A hernia repair operation is the only treatment but has potential postoperative complications, including pain, nerve injury and infection. Furthermore, he said, "There is a very high recurrence rate of hernia after hernia repair."

As men age, their estrogen levels increase and their testosterone levels drop. The researchers found that their mouse model mimics the increased estrogen formation in the tissue and the decreasing blood testosterone levels seen in elderly men.

Furthermore, when they looked at the rodents' muscle tissue from the lower abdomen, they found tissue atrophy (weakening) and fibrosis (scarring), comparable to that observed in human muscle tissue specimens from patients who had undergone inguinal hernia operations.

Then, in a different group of these mice that express aromatase, the investigators treated the animals with an aromatase inhibitor medication. Bulun said, "Treatment entirely prevented muscle cell atrophy, fibrosis and hernia formation, further supporting a central role of estrogen in inguinal hernia in aging men."

They plan to continue their study. "We hope to shed light on the mechanism behind inguinal hernia and help develop less invasive and more curative treatments for inguinal hernia," Zhao said. "This knowledge may allow treatment or prevention with novel nonsurgical approaches."

For instance, Bulun suggested, therapy with aromatase inhibitors might prevent recurrence after hernia repair or even help men avoid surgery in the first place.

<http://bit.ly/2oGx5Ws>

New archaeological evidence throws light on efforts to resist 'the living dead'

Villagers believed it would stop the corpses rising from their graves

A new scientific study of medieval human bones, excavated from a deserted English village, suggests the corpses they came from were burnt and mutilated. Researchers from the University of Southampton and Historic England believe this was carried out by villagers who believed that it would stop the corpses rising from their graves and menacing the living.

The team found that many of the bones from Wharram Percy in North Yorkshire showed knife-marks -- suggesting the bodies had been decapitated and dismembered. There was also evidence of the burning of body parts and deliberate breaking of some bones after death.

The findings are published in an article in the Journal of Archaeological Science Reports. The research was led by Simon Mays, Human Skeletal Biologist at Historic England, working in collaboration with Alistair Pike, Professor of Archaeological Sciences at the University of Southampton.

In medieval times, there was a folk-belief that corpses could rise from their graves and roam the local area, spreading disease and violently assaulting those unlucky enough to encounter them. Restless corpses were usually thought to be caused by a lingering malevolent life-force in individuals who had committed evil deeds or created animosity when living.

Medieval writers describe a number of ways of dealing with revenants, one of which was to dig up the offending corpse, decapitate and dismember it, and burn the pieces in a fire. Perhaps the bones from Wharram Percy were parts of bodies that were mutilated and burnt because of medieval fears of corpses rising from their graves.

The researchers considered other theories, but this explanation appears to be the most consistent with the alterations observed on the bones.

In some societies, people may be treated in unusual ways after death because they are viewed as outsiders. However, analysis of strontium isotopes in the teeth showed this was not the reason in this case. Professor Alistair Pike, who directed the isotopic analysis, explains: "Strontium isotopes in teeth reflect the geology on which an individual was living as their teeth formed in childhood. A match between the isotopes in the teeth and the geology around Wharram Percy suggests they grew up in an area close to where they were buried, possibly in the village. This was surprising to us, as we first wondered if the unusual treatment of the bodies might relate to their being from further afield, rather than local."

Famines were quite common in medieval times, so another possibility might be that the remains were of corpses that had been cannibalised by starving villagers. However, the evidence did not seem to fit. For example, in cannibalism, knife marks on bone tend to cluster around major muscle attachments or large joints, but at Wharram Percy the knife marks were not at these locations but mainly in the head and neck area.

Simon Mays concludes: "The idea that the Wharram Percy bones are the remains of corpses burnt and dismembered to stop them walking from their graves seems to fit the evidence best. If we are right, then this is the first good archaeological evidence we have for this practice. It shows us a dark side of medieval beliefs and provides a graphic reminder of how different the medieval view of the world was from our own."

The bones come from the deserted medieval village of Wharram Percy, North Yorkshire, a site managed by English Heritage. There was a total of 137 bones representing the mixed remains of at least ten individuals. They were buried in a pit in the settlement part of the site. They date from the 11th-14th centuries AD.

The article can be read at

<http://www.sciencedirect.com/science/article/pii/S2352409X1630791X>

<http://bit.ly/2o94F61>

Chemicals that cure malaria can kill weeds too

Many antimalarial drugs are effective herbicides

April 3, 2017 by David Stacey

Plant biologists at The University of Western Australia have revealed the relationship between plants and the parasite that causes malaria is close enough to mean many antimalarial drugs are effective herbicides. The work offers a new take on an evolutionary connection made in the 1990s when herbicides were shown to interfere with processes in the malarial parasite.

The research, published in Scientific Reports, shows that the extensive knowledge of antimalarial drugs could be applied to creating much-needed new herbicides.

This line of thinking began in 2008 when Dr Joshua Mylne, a plant geneticist, enlisted in the Army Reserve and was assigned to the Australian Army Malaria Institute in Brisbane. Dr Mylne said almost 20 years ago, researchers used herbicides to prove that the malarial parasite Plasmodium contained an organelle that was essential and did many of the same things plant chloroplasts did.

"Subsequently, herbicides were used as starting points to develop new antimalarial drugs, but thinking seems not to have extended in the opposite direction," Dr Mylne said. "There is an urgent need for new herbicides and in particular ones that work differently or have different targets; a feature called the mode of action."

Dr Mylne, now a principal investigator with UWA's School of Molecular Sciences, affiliated with the national ARC Centre of Excellence in Plant Energy Biology, said herbicides were integral for modern day agriculture, but the success of glyphosate and spiralling costs to develop new herbicides had stymied progress. "In the past 30 years no new herbicide mode of action has been brought to market during a time that over 500 new cases of herbicide resistance have appeared," he said.

Co-author and organic chemist Associate Professor Keith Stubbs said antimalarial drugs were ideal as starting points because they were non-toxic to humans and often had the right chemical properties to also affect plants.

Lead author and PhD student Maxime Corral said the finding would enable researchers to use knowledge about antimalarial drugs and even the drugs themselves to develop new herbicides against weeds. "By working with the tiny seeds of the model plant *Arabidopsis* we can test thousands of compounds at the same time," he said. "Making this connection doesn't just mean working with antimalarials such as herbicides, it also means you can think about what antimalarial modes of action are not being exploited by herbicides and whether they could be."

Dr Mylne also sees a more ambitious use for this connection. "Despite decades of use, the way some antimalarial drugs work remains unknown," Dr Mylne said. "Plants are easy to work with so we might be able to use plant genetics to reveal how antimalarial drugs work".

The study 'Herbicidal properties of antimalarial drugs' was supported by the Australian Research Council.

More information: Maxime G. Corral et al. Herbicidal properties of antimalarial drugs, Scientific Reports (2017). DOI: 10.1038/srep45871

<http://bit.ly/2nKmODZ>

Brain cancer patients live longer wearing electric cap designed to zap tumors

After decade of stalled treatment improvements, cap is a modest, pricey step forward.

Beth Mole - 4/4/2017, 1:16 AM

An electric skull cap designed to zap cancer cells trying to grow in the brains of wearers proved useful at improving patient survival in a five-year clinical trial.

When combined with standard chemotherapy, the cap more than doubled five-year survival rates of brain cancer patients—from 5 percent to 13 percent—researchers reported Sunday at the annual

meeting of the American Association for Cancer Research being held in Washington, DC. The trial involved 695 patients newly diagnosed with an aggressive form of brain cancer called glioblastoma multiforme.

The modest survival improvement is exciting for such a nasty form of cancer, researchers said. "Glioblastoma is the deadliest primary malignancy of the central nervous system for adults," Dr. Roger Stupp, professor of neurological surgery at Northwestern, said in a press release. "The last time any form of treatment was shown to improve survival for patients with this disease was more than 10 years ago." But it comes with a steep price—around \$700 a day, the AP reports. Most US insurers are covering the caps, which have already gained FDA approval. The company behind the trial and the device, Novocure, is covering those on Medicare, Novocure CEO Bill Doyle said.

Charged treatment

The cap, called the Optune, works by sending alternating, intermediate-frequency (200kHz) electrical fields into the brains of cancer patients. The idea is that the electrical fields disrupt cell division, preventing cells from properly lining up their chromosomes during a cellular split. This disruption, the company says, is fatal to cells. But because cancer cells make up the majority of the cells dividing in the brains of adult cancer patients, the treatment is more harmful to tumors than the brain.



Novocure

Patients are supposed to wear the cap for at least 18 hours every day, as well as stay on a standard chemotherapy, called temozolomide. The Optune has strips of electrodes connected to a small generator that patients can carry around in a bag. The electrical fields cause mild

warming, but otherwise they don't disrupt normal daily life. And patients can wear a hat over their futuristic-looking medical caps.

In the five-year, phase III clinical trial—from July 2009 to November 2014—466 glioblastoma patients were randomly assigned to try out the Optune with their temozolomide treatment, while 229 others took just temozolomide.

The median overall survival jumped from 16 months among patients on the standard chemotherapy to 21 months for those also using the Optune, researchers found. In the first two years, the Optune seemed to boost patient survival rates from 31 percent to 43 percent. At three years, survival went from 16 percent to 26 percent. And at four years, standard treatment patients had an 8 percent survival rate, while cap-wearers had a 20 percent rate. At five years, survival rates jumped from 5 to 13 percent.

"You cannot argue with them—they're great results," Antonio Chiocca, neurosurgery chief at Brigham and Women's Hospital in Boston, told the AP. (Chiocca was not involved with Novocure or the Optune.) He added that the effects were unlikely to be due to placebo effect.

Novocure is working on treating other forms of cancer with the electrical fields, including advanced pancreatic cancer.

<http://bit.ly/2o4jyVz>

Quickly assessing brain bleeding in head injuries using new device

Commercially available hand-held EEG device and accurately rules out whether a person with a head injury likely has brain bleeding

In a clinical trial conducted among adults in 11 hospitals, researchers have shown that a hand-held EEG device approved in 2016 by the U.S. Food and Drug Administration that is commercially available can quickly and with 97 percent accuracy rule out whether a person with a head injury likely has brain bleeding and needs further evaluation and treatment.

According to the Centers for Disease Control and Prevention, about 2.5 million Americans each year show up to the emergency room with suspected head injuries. Most of these people receive a CT scan, and more than 90 percent of the scans show no structural brain injury, creating needless radiation exposure and medical costs estimated at about \$1,200 per scan.

In a report on their clinical trial, described online March 31 in *Academic Emergency Medicine*, the researchers say the new device -- which measures electrical activity in the brain and then uses an algorithm to decide if a patient is likely to have brain bleeding -- can help with clinical decision-making and triage of patients, and could reduce the need for CT scans.

"Before our study, there were no objective, quantitative measures of mild head injury other than imaging," says lead investigator Daniel Hanley Jr., M.D., the Legum Professor of Neurological Medicine and director of the Brain Injury Outcomes Program at the Johns Hopkins University School of Medicine. "This work opens up the possibility of diagnosing head injury in a very early and precise way.

"This technology is not meant to replace the CT scan in patients with mild head injury, but it provides the clinician with additional information to facilitate routine clinical decision-making," says Hanley. "If someone with a mild head injury was evaluated on the sports or battlefield, then this test could assist in the decision of whether or not he or she needs rapid transport to the hospital. Alternatively, if there is an accident with many people injured, medical personnel could use the device to triage which patients would need to have CT scans and who should go first. Those showing a 'positive' for brain injury would go first."

The study only looked at adults and didn't assess how well the device could predict traumatic brain injuries in children or teens.

The study, Hanley says, was designed to test the accuracy and effectiveness of AHEAD 300, a device developed by BrainScope

Company Inc. of Bethesda, Maryland, that is now available to a limited audience through a centers of excellence program.

Throughout its eight years of development, the company has tested this and prior generations of the device in multiple human trials. The point of the device is to assess the likelihood that a patient has more than 1 milliliter of bleeding in the brain and needs immediate evaluation by medical personnel.

To begin, the researchers recruited 720 adults who came to 11 Emergency Departments across the nation between February and December 2015 with a closed head injury, meaning the skull was intact.

Participants were between 18 and 85 years old, and 60 percent were men. Upon entry to the Emergency Department, each physician performed standard clinical assessments for head injuries used at their site. A trained technician then administered the Standardized Assessment of Concussion and the Concussion Symptom Inventory to characterize the patient's symptoms, and then used the AHEAD 300 device to measure electroencephalogram (EEG) data -- essentially tracking and recording brain wave patterns -- from patients while they reclined quietly for five to 10 minutes.

The device includes a disposable headset that records the EEG data from five regions on the forehead and feeds the signals back to the hand-held AHEAD 300 device in real time. In addition, the technician entered certain clinical/demographic information into the device, including age; the Glasgow Coma Scale score, which rates how conscious a person is; and if there was a loss of consciousness related to the injury.

The device was programmed to read approximately 30 specific features of brain electrical activity, which it uses an algorithm to analyze, and how the patient's pattern of brain activity compared to the same pattern of brain activity considered normal. For example, it looked for how fast or slow information traveled from one side of the

brain to the other, or whether electrical activity in both sides of the brain was coordinated or if one side was lagging.

The accuracy of the device was tested using CT scans from the participants. The presence of any blood within the intracranial cavity was considered a positive finding, indicating brain bleeding. After 72 to 96 hours, the researchers followed up with phone calls to the patients and/or looked at medical records after 30 days to further confirm the accuracy of each participant's injury status.

Of the 720 patients, 564 turned out not to have traumatic brain injuries, and 156 did have them, as determined by independently measured and judged CT scan assessments.

On the basis of AHEAD 300 classification, the researchers sorted patients into "yes" or "no" categories, indicating likely traumatic brain injury with over 1 millimeter of bleeding or not. Of 564 patients without brain bleeding, as confirmed with CT scans, 291 patients were scored on the AHEAD 300 as likely not having a brain injury. Of the 156 patients with confirmed brain bleeding, 144, or 92 percent, were assessed as likely to have an injury by the AHEAD 300 classification. Of those confirmed with brain bleeding via CT scan, 12 participants, or 8 percent, had some intracranial bleeding, and five participants, or 3 percent, had more than 1 milliliter of blood in the brain.

Because many of the incorrect yes/no classifications don't contain information about how close a patient is to the cutoff, the researchers then created three categories to sort patients by -- "yes," "no" and "maybe" -- to see if this boosted the accuracy of the device. The maybe category included a small number of patients with greater-than-usual abnormal EEG activity that was not statistically high enough to be definitely positive.

When the results were recalculated on the three-tier system, the sensitivity of detecting someone with a traumatic brain injury increased to 97 percent, with 152 of 156 traumatic head injuries detected, and 99 percent of those had more than or equal to 1 milliliter of bleeding in the brain. None of the four false negatives required

surgery, returned to the hospital due to their injury or needed additional brain imaging.

The trial results also show the device predicted the absence of potentially dangerous brain bleeding 52 percent of the time in the participants tested with the yes/no classification. Using the yes/no/maybe classification, the device classified 281 patients as having a brain injury, correctly predicting whether someone didn't have a head injury 39 percent of the time.

The researchers say these predictive capabilities improve on the clinical criteria currently used to assess whether to do a CT scan -- known as the New Orleans Criteria and the Canadian Head CT rules -- and predicted the absence of brain bleeding more than 70 percent of the time in those people with no more than one symptom of brain injury, such as disorientation, headache or amnesia.

As with a typical EEG, the test doesn't cause any type of sensation or risk. There is a small chance of skin irritation from the discs that read the electrical activity.

Although an exact cost hasn't been set by BrainScope, the maker of the device, the company says it will be a fraction of the cost of a CT scanner, which starts at \$90,000 and goes up to \$2.5 million depending on the capabilities, and it will be cheaper and significantly faster to administer. In September 2016, the device was cleared by the Food and Drug Administration for use in a clinical setting.

Additional authors on the study included Leslie S. Prichep of New York University School of Medicine and BrainScope Company; Jeffrey Bazarian of the University of Rochester Medical Center; J. Stephen Huff of University of Virginia Health System; Rosanne Naunheim of Washington University Barnes-Jewish Hospital; John Garrett of Baylor University Medical Center; Elizabeth Jones of Memorial Hermann-Texas Medical Center; David Wright of Emory University's Grady Memorial Hospital; John O'Neill of Allegheny General Hospital; Neeraj Badjatia of R Adams Cowley Shock Trauma Center; Dheeraj Gandhi of the University of Maryland, Baltimore; Kenneth Curley of the Uniformed Services University of the Health Sciences; Richard Chiacchierini of R.P. Chiacchierini Consulting LLC; Brian O'Neil of Detroit Receiving Hospital; and Dallas Hack of Brain Health.

This study was funded in part by the U.S Army (contract #W81XWH-14-C-1405).

COI: All principal investigators at each university site received funds from BrainScope Company Inc. to support subject recruitment, consenting and data acquisition.

<http://bit.ly/2oLzqb6>

Skeletons developed as chemistry of oceans changed, study shows

Skeletons and shells first came into being 550 million years ago as the chemical make-up of seawater changed, a study suggests.

Ancient marine life may have developed from soft-bodied animals into creatures with hard body parts as oxygen levels rose and calcium and magnesium levels in prehistoric oceans changed, researchers say.

Until now, little was known about how skeletons and shells -- which are made of calcium carbonate -- first evolved, the team says.

Previous theories suggested that soft-bodied organisms had undergone a mass extinction, which allowed organisms with skeletons and shells to flourish.

However, researchers at the University of Edinburgh have found that the earliest lifeforms with hard body parts co-existed with closely related soft-bodied species.

The team examined a range of fossils unearthed from limestone rocks in Siberia, which formed millions of years ago from seawater with high levels of calcium carbonate.

They concluded that hard-bodied lifeforms were first present only in such environments where high levels of calcium carbonate allowed organisms to develop primitive hard parts.

Around 10m years later, the diversity of life of Earth increased rapidly -- a period known as the Cambrian explosion -- and hard-bodied life began to thrive. An increased threat from predators led lifeforms to develop new, more complex hard parts in environments that were less carbonate-rich, the team says.

The development of hard body parts -- through a process called biomineralisation -- marked a significant evolutionary advance from the previous world of soft-bodied life, the team says.

The study is published in the journal *Proceedings of the Royal Society B*. The research was carried out in collaboration with Lomonosov Moscow State University.

Professor Rachel Wood, of the University of Edinburgh's School of GeoSciences, who led the study, said: "How animals produced shells and skeletons is one of the major events in the evolution of life. We are only now starting to understand the processes underlying this revolution."

<http://bit.ly/2oL0ufZ>

Google uses neural networks to translate without transcribing

Google's latest take on machine translation could make it easier for people to communicate with those speaking a different language, by translating speech directly into text in a language they understand.

By Matt Reynolds

Machine translation of speech normally works by first converting it into text, then translating that into text in another language. But any error in speech recognition will lead to an error in transcription and a mistake in the translation.

Researchers at Google Brain, the tech giant's deep learning research arm, have turned to neural networks to cut out the middle step. By skipping transcription, the approach could potentially allow for more accurate and quicker translations.

The team trained its system on hundreds of hours of Spanish audio with corresponding English text. In each case, it used several layers of neural networks – computer systems loosely modelled on the human brain – to match sections of the spoken Spanish with the written translation. To do this, it analysed the waveform of the Spanish audio to learn which parts seemed to correspond with which chunks of written English. When it was then asked to translate, each neural layer used this knowledge to manipulate the audio waveform until it was turned into the corresponding section of written English.

Corresponding patterns

"It learns to find patterns of correspondence between the waveforms in the source language and the written text," says Dzmitry Bahdanau

at the University of Montreal in Canada, who wasn't involved with the work.

After a learning period, Google's system produced a better-quality English translation of Spanish speech than one that transcribed the speech into written Spanish first. It was evaluated using the BLEU score, which is designed to judge machine translations based on how close they are to that by a professional human.

The system could be particularly useful for translating speech in languages that are spoken by very few people, says Sharon Goldwater at the University of Edinburgh in the UK.

International disaster relief teams, for instance, could use it to quickly put together a translation system to communicate with people they are trying to assist. When an earthquake hit Haiti in 2010, says Goldwater, there was no translation software available for Haitian Creole.

Goldwater's team is using a similar method to translate speech from Arapaho, a language spoken by only 1000 or so people in the Native American tribe of the same name, and Ainu, a language spoken by a handful of people in Japan.

Rare languages

The system could also be used to translate languages that are rarely written down, since it doesn't require a written version of the source language to produce successful translations.

Until it is tested on a much larger dataset, it's hard to tell how the new approach really compares with more conventional translation systems, says Goldwater. But she thinks it could set the standard for future machine translation.

Some services already use machine translation to let people who speak different languages have conversations in real time. Skype introduced a live speech-to-text translation feature in 2014 and now supports nine languages, including Mandarin and Arabic as well as the most common European languages. But like other existing translation methods, Skype's transcribes speech into text before translating that text into a different language.

And text translation service Google Translate already uses neural networks on its most popular language pairs, which lets it analyse entire sentences at once to figure out the best written translation. Intriguingly, this system appears to use an “interlingua” – a common representation of sentences that have the same meaning in different languages – to translate from one language to another, meaning it could translate between a language pair it hasn’t explicitly been trained on. The Google Brain researchers suggest the new speech-to-text approach may also be able to produce a system that can translate multiple languages.

But while machine translation keeps improving, it’s difficult to tell how neural networks are coming to their solutions, says Bahdanau. “It’s very hard to understand what’s happening inside.”

Journal reference: arXiv, DOI: arxiv.org/abs/1703.08581

<http://bit.ly/2o9Dw37>

MERS-like coronavirus identified in Ugandan bat

Novel coronavirus in a bat from Uganda that is similar to the one causing Middle East Respiratory Syndrome (MERS) in humans

WASHINGTON, DC - A team of researchers in the United States and Uganda has identified a novel coronavirus in a bat from Uganda that is similar to the one causing Middle East Respiratory Syndrome (MERS) in people, giving further credence to the theory that such viruses originate in bats. The work, part of the United States Agency for International Development's (USAID's) Emerging Pandemic Threats PREDICT project, was described this week in mBio®, an online open-access journal of the American Society for Microbiology.

Laboratory experiments with the virus, named PREDICT/PDF-2180, indicate that while its overall genetics appear similar to MERS-coronavirus (MERS-CoV), there are significant differences in part of its spike gene - the segment of the virus responsible for invading cells. Therefore, in its current state it is unlikely to pose a threat to humans, said lead study author Simon J. Anthony, Ph.D., an assistant professor of epidemiology at Columbia University's Mailman School of Public

Health and its Center for Infection and Immunity. By contrast, MERS-CoV itself has been shown to spread from animals such as camels to humans and between humans.

MERS, first reported in Saudi Arabia in 2012, is an illness marked by severe acute respiratory disease with symptoms of fever, cough and shortness of breath. About 4 of every 10 patients with the condition have died, according to the Centers for Disease Control and Prevention. The PREDICT project, led by the University of California, Davis (UCD), is a multicenter global initiative for surveillance and discovery of viruses that could pose a pandemic threat through animal-human transmission of pathogens.

For the study, Anthony and colleagues at the UCD One Health Institute and with the non-profit organization Gorilla Doctors sequenced the genome of the PDF-2180 virus found in a rectal swab taken from a bat trapped in February 2013 in southwestern Uganda. Overall, the virus was 87 percent identical to MERS-CoV and 91 percent identical to NeoCoV, another coronavirus found in a bat from South Africa. However, part of the spike gene was only 46 percent identical to the one belonging to MERS-CoV.

Next, to test the ability of the virus to spread to humans, researchers at the University of North Carolina constructed an infectious MERS-CoV clone expressing the PDF-2180 spike protein. Viruses derived from the clone could reproduce themselves but could not enter cells expressing DPP4, the receptor normally used by MERS-CoV, or establish new infections either in Vero cells derived from monkeys or in human airway cells from healthy lung donors.

"In its current form, evolution notwithstanding, this virus is probably not going to be a threat to human health," Anthony said. The team plans to repeat the experiments with other viral samples to get a better grasp of what animal-borne viruses pose a risk to human health.

The discovery of the virus adds to the growing number of coronaviruses identified in bats, Anthony said, including NeoCoV from South Africa; Mex_CoV-9 from Mexico; BatCoV/KW2E from

Thailand; P.pipi/VM314 from the Netherlands; H.sav/206645-40 from Italy; and BetaCoV/SC2013, HKU4 and HKU5, from China.

"Collectively, these examples demonstrate that the MERS-related coronaviruses are highly associated with bats and are geographically widespread," Anthony said.

The study was supported by the USAID Emerging Pandemic Threats PREDICT project and by the National Institute of Allergy and Infectious Disease.

<http://bit.ly/2oI8sbX>

Discovery of 'mini-brains' could change understanding of pain medication

The human body's peripheral nervous system could be capable of interpreting its environment and modulating pain, neuroscientists have established, after successfully studying how rodents reacted to stimulation.

Until now, accepted scientific theory has held that only the central nervous system - the brain and spinal cord - could actually interpret and analyse sensations like pain or heat.

The peripheral system that runs throughout the body was seen to be a mainly wiring network, relaying information to and from the central nervous system by delivering messages to the 'control centre' (the brain), which then tells the body how to react.

In recent years there has been some evidence of a more complex role for the peripheral nervous system, but this study by the Hebei Medical University in China and the University of Leeds highlights a crucial new role for the ganglia, a collection of 'nodules'. Previously these were believed to act only as an energy source for messages being carried through the nervous system. In addition, researchers now believe they also have the ability to act as 'mini brains', modifying how much information is sent to the central nervous system.

The five year study found that nerve cells within the ganglia can exchange information between each other with the help of a signalling molecule called GABA, a process that previously believed to be restricted to the central nervous system. The findings are published

today in the *Journal of Clinical Investigation* and have potential future implications for the development of new painkillers, including drugs to target backache and arthritis pain.

Pain relief drugs

Current pain relief drugs are targeted at the central nervous system and often have side effects including addiction and tolerance issues.

The new research opens up the possibility of a route for developing non-addictive and non-drowsy drugs, targeted at the peripheral nervous system. Safe therapeutic dosage of these new drugs can also be much higher, potentially resulting in higher efficacy.

Whilst the study showed a rodent's peripheral nervous system was able to interpret the type of stimulation it was sensing, further research is still needed to understand how sensations are interpreted and whether these results apply to humans.

In addition, the theory would need to be adopted by drug development companies and extensively tested before laboratory and clinical trials of a drug could be carried out. Should the findings be adopted, a timescale of at least 15-20 years might be required to produce a working drug.

Nerve arrangements

Neuroscientist Professor Nikita Gamper, who led the research at both universities, said: "We found the peripheral nervous system has the ability to alter the information sent to the brain, rather than blindly passing everything on to the central nervous system.

"We don't yet know how the system works, but the machinery is definitely in place to allow the peripheral system to interpret and modify the tactile information perceived by the brain in terms of interpreting pain, warmth or the solidity of objects. "Further research is needed to understand exactly how it operates, but we have no reason to believe that the same nerve arrangements would not exist in humans.

"When our research team looked more closely at the peripheral system, we found the machinery for neuronal communication did exist in the

peripheral nervous system's structure. It is as if each sensory nerve has its own 'mini-brain', which to an extent, can interpret incoming information."

Co-author of the study, Professor Xiaona Du from Hebei Medical University, added: "This dramatically changes our understanding of pain medication because in theory it is now possible to target drugs at the peripheral nervous system which could widen the type of treatments available."

Professor Gamper believes the findings may present a challenge to the accepted 'Gate Control Theory of Pain'. The theory holds that a primary 'gate' exists between the peripheral and central nervous systems, controlling what information is sent to the central system.

The study now suggests the transmission of information to the central nervous system must go through another set of gates, or more accurately a process similar to a volume control, where the flow of information can be controlled by the peripheral nervous system.

"Peripheral nerves have the ability to dial up or down the signal which goes through these gates to the brain", said Professor Gamper. "Importantly, we believe that these gates can be exploited for therapeutic control of pain."

Research Council support

Dr Kathryn Adcock, Head of Neurosciences and Mental Health at the Medical Research Council, which part funded the work, said: "These findings are an interesting step in advancing scientists' understanding of the mechanisms underpinning pain perception. We are committed to supporting work such as this to aid the continued search for new and better pain treatments."

A view from industry

Lishuang Cao, head of Membrane Physiology at GlaxoSmithKline R&D in Shanghai commented on this research: "This interesting finding could pave the way for developing novel pain medicines by targeting the peripheral GABA signaling pathway and at the same time avoiding or reducing the side effects of many existing pain killers.

"Further work is needed to understand the physiological role of GABA in painful situations like inflammatory, neuropathic and chronic pain. More importantly we need to know if the same mechanism is present in human beings' peripheral nervous systems."

Further information

The full research paper, Local GABAergic Signaling within Sensory Ganglia Controls Peripheral Nociceptive Transmission, is published in the Journal of Clinical Investigation at 9pm UK time (BST) / 4pm EST 4 April 2017.

<http://bit.ly/2oLRclV>

Pre-existing immunity to dengue and West Nile may cause increased risk in Zika-infected

Zika may pose a particular risk to people previously infected with two related viruses

As the Zika virus continues to spread rapidly across the globe, it might pose a particular risk to people previously infected with two related viruses, dengue and West Nile, researchers at the Icahn School of Medicine at Mount Sinai have found. Their study, published in the journal *Science*, may help explain the severe manifestations of Zika virus infection observed in specific populations, including those in South America.

The Zika virus is a member of the flavivirus family, as are dengue and West Nile. It was discovered in 1947 but remained relatively obscure until 2015, when a large outbreak occurred in Brazil and rapidly spread to other South and Central American countries. Today, the Zika virus is endemic to several U.S. territories, especially Puerto Rico, and active transmission has been reported in Florida and Texas. It is a significant public health concern because of the widespread outbreaks, the virus's association with microcephaly and other neurological disorders, and its long-term persistence in human tissues—it can be sexually transmitted for months after the initial infection.

This study is the first to report a large-scale analysis of Zika virus enhancement by antibodies of individuals previously infected with the dengue and West Nile viruses. These findings raise urgent concern

since the dengue and West Nile viruses are often endemic in Zika affected regions.

"Recent studies have shown that the Zika virus protein is structured similarly to that of dengue and West Nile," said the study's co-author, Adolfo García-Sastre, PhD, Irene and Dr. Arthur M. Fishberg Professor of Medicine, Professor of Microbiology and Infectious Diseases, and Director of the Global Health and Emerging Pathogens Institute, Icahn School of Medicine at Mount Sinai. "Our study is the first large-scale analysis of Zika virus enhancement in individuals infected with dengue and West Nile."

Using blood samples from individuals infected with dengue and West Nile, researchers identified enhancement of Zika virus growth in cell cultures. The dengue- and West Nile-infected plasma was then administered to mice engineered to be susceptible to the Zika virus, resulting in increased mortality and morbidity, including fever and viral loads in the spinal cords and testes of the mice upon virus infection.

"We believe the antibody-dependent enhancement may explain the severe disease manifestations associated with recent Zika virus outbreaks, and highlights the need for great caution when designing vaccines for Zika and other flaviviruses," said co-author Jean Lim, PhD, Assistant Professor of Microbiology, Icahn School of Medicine at Mount Sinai. "Further understanding of pre-existing immunity is a high priority in the development of a vaccine that works."

"We found that the antibody-dependent enhancement effect was dependent on the dose of plasma administered," said co-author Florian Krammer, PhD, Associate Professor of Microbiology, Icahn School of Medicine at Mount Sinai. "Low concentrations of cross-reactive antibodies clearly enhanced disease."

The studies showed that high concentrations of dengue immune plasma resulted in protection against Zika infection, with 100 percent survival, no weight loss, and decreased symptoms. It was the lower concentrations that resulted in enhanced morbidity and mortality,

highlighting that antibody-dependent enhancement is a particular worry in individuals with waning antibody levels.

The American Red Cross collaborated with the Mount Sinai team on this study.

<http://bit.ly/2p8F76I>

About 10% of Pregnant Women with Zika Had Babies with Birth Defects

5-10% of pregnant women in the U.S. contracting Zika had babies with birth defects related to the virus

By Rachael Rettner, Senior Writer | April 4, 2017 02:50pm ET

About 5 to 10 percent of pregnant women in the U.S. who contracted the Zika virus in 2016 - typically after traveling abroad - had babies with birth defects related to the virus, according to a new report. The report, from the Centers for Disease Control and Prevention, is the largest study to look at outcomes among pregnant women with Zika infections.

The report also found that the risk of birth defects was slightly higher for women who contracted a Zika infection during their first trimester. Among these women, 15 percent had babies with birth defects tied to the virus, the report said.

What's more, the percentage of infants with certain birth defects born to women who had contracted Zika was 30 times higher than the overall percentage of infants who had similar birth defects seen in the years before Zika, the researchers said.

"Zika continues to be a threat to pregnant women in the United States," Dr. Anne Schuchat, acting director of the CDC, said at a news conference today (April 4). "We do know this devastating outbreak is far from over, and the consequences of this outbreak are heartbreaking. With warm weather and a new mosquito season approaching, prevention is crucial to protect the health of mothers and babies."

For the report, the researchers analyzed information from about 1,300 U.S. pregnant women in 44 states who had a possible Zika virus infection in 2016. These women had tested positive for either the Zika

virus or an "unspecified flavivirus," which could include Zika or another virus in that family, such as the dengue virus.

Of these women, 972 (about 75 percent) had completed their pregnancies by the time of the analysis. Most had a live birth, but about 8 percent had a pregnancy loss. Overall, 51 of the 972 women, or about 5 percent, had a baby with birth defects related to the virus. Among the 250 women with a confirmed Zika virus infection, about 10 percent had a baby with Zika-related birth defects, the report said.

These birth defects included brain abnormalities or microcephaly (a condition in which the baby's head is abnormally small), eye abnormalities or other conditions that result from problems with the central nervous system. However, the report "might significantly underestimate the impact of Zika," said Margaret Honein, a co-author of the report and chief of the CDC's Birth Defects Branch.

One reason for the possible underestimation is that although the CDC recommends that all infants born to mothers who may have been infected with Zika undergo brain imaging, just 25 percent of the babies in the study underwent such brain imaging. Imaging such as a CT scan or an MRI can detect brain abnormalities that can otherwise go unnoticed, the researchers said.

In addition, the researchers did not follow up with the babies after birth, and some Zika-related anomalies may show up months later, Schuchat said. "These findings underscore the serious risk for birth defects posed by Zika virus infection during pregnancy and highlight why pregnant women should avoid Zika virus exposure," the report said.

The CDC recommends that pregnant women avoid traveling to areas where the local mosquitoes may carry Zika. Men and women who do travel to areas with Zika, or who live in those areas, can also lower their risk of infection by using mosquito repellent to prevent mosquito bites (the primary way Zika is transmitted) and by using condoms during sex (because the virus can also be transmitted sexually). Doctors should also screen all pregnant women for exposure to the

Zika virus. The report is published today (April 4) in the CDC journal Morbidity and Mortality Weekly Report.

<http://bit.ly/2o50zKr>

A new idea connects the synthesis of clays and the origin of metabolism

Connection between ZnS prebiotic photosynthesis and [clay replication has now been established](#)

The question of how life has begun has fascinated scientists from many disciplines and it was the organic chemist Graham Cairns-Smith who proposed the theory for the origin of life starting from clays instead of polymers such as RNA.

The source of the monomers such as nucleotides, amino acids and dicarboxylic acids were relegated by Cairns-Smith to the evolution of metabolism, which is the [synthesis](#) of [amino acids](#) and nucleotides from the citric acid cycle.

This problem of the evolution of metabolism has recently been advanced by the behavior of simple semiconductor minerals such as zinc sulfide (ZnS), which are capable of harvesting sunlight energy and converting this energy into the formation of chemical bonds of dicarboxylic acids from CO₂ thus providing the core reactions of universal metabolism before the existence of enzymes.

A connection between ZnS prebiotic photosynthesis and [clay replication](#) has now been established in a paper published by a team of scientists from the University of Kentucky and the Massachusetts Institute of Technology (MIT) in the United States, and McGill University in Canada. The paper has related how prebiotic metabolites available from simple sunlight promoted reactions can catalyze the synthesis of [clay minerals](#) (i.e., a zinc clay called sauconite). The work shows that central metabolites such as succinate and malate can enable the nucleation process for clay formation. These prebiotic metabolites have been generated by photocatalysis with ZnS, and this work demonstrates how they can catalyze the synthesis of clays.

The study published in the open access journal *Scientific Reports* shows how a clay synthesis can proceed catalyzed by prebiotic metabolites in only 20 hours at 90 °C and 1 atm. Clay formation generally requires much longer times as well as higher temperature and pressure. The cryogenic transmission electron microscopy clearly shows that clay nanoparticles can be observed after only 6 hours of synthesis, as verified by the incorporation of aluminum into the tetrahedral layer.

The team noted that the synthesis of clay can proceed at even lower temperatures, i.e., at just 70 °C, with the addition of a single seed particle. The work presents an excellent example of the reproductive power of clay minerals and the mechanism by which prebiotic metabolites catalyze their formation. Clay minerals acting as chemical sponges can retain water and polar organic molecules, and should have played a key role in the origin of life; 1) protecting against ultraviolet radiation, and 2) concentrating and catalyzing the polymerization of organic molecules such as RNA. The outcome of this work has direct implications to understand the origin of life on the early Earth and other rocky planets.

Ruixin Zhou, Kaustuv Basu, Hyman Hartman, Christopher J. Matocha, S. Kelly Sears, Hojatollah Vali & Marcelo I. Guzman. *Catalyzed Synthesis of Zinc Clays by Prebiotic Central Metabolites*, *Scientific Reports*, 7, 522, 2017. DOI: [10.1038/s41598-017-00558-1](https://doi.org/10.1038/s41598-017-00558-1)

<http://bbc.in/2nScE4R>

Vaccine credited with HPV virus reduction in Scotland

A campaign to vaccinate girls against a cancer-causing sexually transmitted infection has led to a dramatic drop in reported cases.

Researchers have found a 90% fall in levels of the human papilloma virus (HPV) in Scottish women since the vaccine was made available in 2008. HPV virus types are thought to account for about 90% of cervical cancers. Scientists hope the drop in HPV cases will lead to a significant drop in future cervical cancer cases.

The researchers, led by senior epidemiologist Dr Kevin Pollock at Health Protection Scotland, said they hoped to see a decrease in new diagnoses within a year.

He told BBC Radio Scotland: "The two HPV types we were vaccinating against - HPV 16 and HPV 18 - cause about 70% to 80% of cervical cancers within Scotland but the vaccine has exceeded our expectations because it appears to have knocked out another three high-risk HPV types which cause about 10% of cervical cancers.

"So we do forecast within the next few years a 90% reduction in cervical cancer within Scotland."

Researchers compared the cervical screening and vaccination records of women born in 1995, who had been vaccinated as teenagers, with those from unvaccinated women born between 1989 and 1990.

They found just 0.5% of women from the 1995 group tested positive for the virus, compared with 21.4% of women born before 1990.

The study also showed evidence that the vaccine protected against three other high-risk HPV genotypes involved in the development of cervical cancer.

'Significant impact'

The research will be presented to the Microbiology Society's annual conference in Edinburgh on Wednesday by Dr Kate Cuschieri, director of the Scottish HPV Reference Lab.

She said: "These new findings indicate that the positive impact of the HPV vaccine may be even greater than we initially thought.

"Collectively, these data demonstrate the significant and continued benefits of the HPV vaccination programme in Scotland, which has achieved a consistent and high uptake of around 90% in 12 to 13-year-old girls."

Dr Pollock added: "The very high uptake of the HPV vaccine is strongly associated with these massive reductions in high-risk HPV types that are known to cause approximately 90% of cervical cancer in Scottish women."

He said the virus was also known to cause a number of other cancers, including vulvovaginal, anal and a subset of head and neck cancers.

"These results suggest that this vaccine will also have a significant impact on these cancers in the years ahead", he said.

The research, which was funded by the Scottish government, looked at samples from more than 20,000 women, making it one of the largest population-based studies on the impact of the vaccine.

There were 388 new cases of cervical cancer in Scotland in 2014.

<http://bit.ly/2nluHV6>

Raccoon dog is a more acute risk than raccoon as vector for local parasites

Compared to the raccoon, the raccoon dogs are more closely related to foxes and thus the more emerging threat as an additional vector

Raccoons and raccoon dogs are non-native species in Europe, being endemic to North America and the Far East, respectively. Both were introduced to northern Europe and have extended their range to the south. In some places, they are even the most common carnivore species. And they are additional carriers for disease. Both are potential hosts for a number of different parasites, such as the fox tapeworm, which can also infest humans.

Raccoon still relatively harmless as disease carrier

Raccoons and raccoon dogs are often confused, but they are actually quite easy to distinguish by the differences in their face masks. Despite their similar appearance, the two species are not as closely related as the raccoon dog is with the fox. This also makes the raccoon dog a risk as an additional vector of disease, such as the fox tapeworm, a proven parasite of local foxes. But the raccoon can also transmit human-relevant parasites, such as the raccoon roundworm. Researchers from Vetmeduni Vienna for the first time studied samples from Austrian animals in the laboratory looking for parasitic pathogens. "Important was above all the question whether the animals can contribute or are already contributing to an increased spread of local parasites," explains Georg Duscher of the Institute of Parasitology. The study revealed that the raccoon currently represents a lower risk than the raccoon dog. "We have so far not discovered any parasites in the raccoon samples," the senior author explains. This

finding coincides with studies conducted in other European countries that have also found few relevant pathogens.

Raccoon dog: Relationship to fox a greater risk

The raccoon dog, on the other hand, represents a greater risk than the raccoon. In addition to parasites that cannot be transmitted to humans, the researchers also found the fox tapeworm as well as the trematode *Alaria alata*, or Duncker's muscle fluke, in individual samples. These were taken from raccoon dogs in different habitats across Austria. The infections with the fox tapeworm were restricted to western Austria, those with *A. alata* to the East. In both areas, the parasites were also shown to infest local foxes. Infections with the parasite *B. cf. microti*, in comparison, were found in samples regardless of their location. This parasite can also be transmitted by foxes. The researchers thus produced the first evidence of a parallel infection of the two animals in Europe. "The raccoon dog therefore clearly is an additional vector of fox-type parasites and should be controlled regularly," says Duscher.

Species distribution model could make studies easier

The abundance of the two carnivores in Austria remains relatively low in comparison to Germany and northern Europe, says first author Tanja Duscher from the Research Institute of Wildlife Ecology. This also has to do with the geographic conditions. She has created a so-called species distribution model for the two animals. The model calculates the probability of presence of the species in Austria. "The species distribution model allows us to predict where the two carnivores are most likely to spread in Austria. Such a model could help to support epidemiological monitoring." The raccoon dog, being more closely related with foxes, represents a greater risk as a host, says Georg Duscher. This non-native animal should therefore be controlled regularly -- although the raccoon should not be excluded either. The latter has so far been given a clean bill of health with few parasitic infestations. "Most raccoons in Europe originate from fur farms and are still largely parasite-free, probably because of the

veterinary examinations," explains Georg Duscher. The mixing of the founder populations, however, leads to parasitic transmission and could make raccoons more relevant in the future.

The article "Der Artikel „The raccoon dog (Nyctereutes procyonoides) and the raccoon (Procyon lotor)-their role and impact of maintaining and transmitting zoonotic diseases in Austria" by Tanja Duscher, Adnan Hodžić, Walter Glawischnig and Georg Duscher was published in Parasitology Research.

<http://link.springer.com/article/10.1007%2Fs00436-017-5405-2>

<http://bit.ly/2nShRd7>

New study sheds light on 'lung sparing effect'

'Lung sparing effect' may protect lung function at the expense of other growth in malnourished children

A new study suggests that in cases of severe malnutrition, the body may prioritise lung development at the expense of other less vital growth.

The findings, published in the *European Respiratory Journal* today (6 April 2017), found that children who are affected by severe acute malnutrition (SAM) in early childhood did not have significantly poorer lung function than unaffected children, but had shorter leg lengths than children not affected by malnutrition. The authors surmise that this could provide new evidence for the theory of 'lung sparing growth', whereby the body prioritises an important vital organ: the lungs.

Severe acute malnutrition is defined by a very low weight for height and affects more than 19 million children under 5 years of age worldwide. The authors sought to explore the long-term effects of early-life malnutrition on lung function.

Researchers carried out spirometry (lung function) and pulse oximetry (oxygen saturation of the blood) tests on 237 Malawian children who were malnutrition survivors, and compared their results with randomly selected children from the same community that were matched for sex and age, but who had never been treated for malnutrition.

Participant weight, chest depth and circumference, sitting height and leg length, HIV status, socioeconomic circumstances, sex, history of

pneumonia, history of tuberculosis, exposure to cooking smoke and body composition (lean/fat mass) was also compared.

The results of lung function and oxygen saturation tests showed no significant difference between formerly malnourished children and children who had never been treated for malnutrition, suggesting that malnutrition in early childhood does not impact lung function later in childhood. However, further key findings indicated that:

- **malnutrition survivors had shorter leg lengths; leg length was on average 1.9 cm shorter than children in their community of the same age**
- **malnutrition survivors were 73% more likely to be severely short for their age than children in their community of the same age**

Lead author Dr Natasha Lelijveld, who completed research while studying at University College London and is now based at the London School of Hygiene & Tropical Medicine, said: "As far as we know, this is the first paper to hypothesise that severe acute malnutrition may result in lung sparing, in a similar fashion to studies that have found evidence of brain-sparing. The findings are very significant because, although it is great to see that lung function was apparently unaffected by malnutrition in these survivors, the process of preserving the lungs in infancy, at the expense of other growth, might mean that malnutrition survivors are at greater risk of other complications later in life."

The research team hopes that the findings will lead to more research in to severe acute malnutrition survivors, to enable such children to lead long and healthy lives. Dr Lelijveld continued: "We hope that adolescence, as a time of rapid growth and development, might be a second window to steer the health of these children back on track. This might be influenced by providing good nutrition to encourage limb growth, or through instilling healthy lifestyles to reduce the heightened risk of adult diseases; more research must be done in this area to determine what will be most effective."

The study identified girls and HIV positive children as the most at-risk of poor lung function among this particular group, and advised they

should be especially considered in intervention packages that seek to improve lung function in survivors of severe acute malnutrition.

An accompanying [editorial on lung-sparing growth](#), also featured in the *ERJ*, highlights the quality of the new research and discusses the hypothesis of lung-sparing theory in more detail.

<http://bit.ly/2oPWcG4>

Cannibal Calories: Early Humans Likely Didn't Eat Each Other for Nutrition

Unlikely ancient hominins cannibalized each other as an easy alternative to going out and hunting

By Knvul Sheikh, Live Science Contributor | April 6, 2017 02:43pm

Prehistoric humans were known to feast on horses and reindeer, but occasionally, these early humans would also chow down on each other. Scientists have uncovered grisly evidence of this ancient cannibalism in butchered bones of children and adults found in caves across Europe. But the gnawing question has always been what motivated the urge to supplement the prehistoric diet with human flesh.

Now, a new study suggests that it is unlikely ancient hominins cannibalized each other as an easy alternative to going out and hunting. The human body simply does not provide enough calories to be a good source of nutrition, the researchers found.

"For an animal of our size and body weight, our calorie values are as expected, but if you compare it to say a horse or a wild cow or a bison, we really don't have much calorific value at all," said study author James Cole, a Paleolithic archaeologist at the University of Brighton in the United Kingdom.

Using published research on the average body weight and composition of a modern male human, Cole calculated the number of calories provided by fat and protein. He then created a detailed template for the calorie values of various body parts, such as the thighs, liver and lungs.

These calorie values may vary for some non-Homo sapiens species, according to Cole. In Neanderthals, for example, the values may be

higher because they had greater muscle mass, he said. But the template provides a good proxy for minimum calories of prehistoric hominins, such as Homo erectus, Homo antecessor and even Neanderthals.

Cole compared these calorie estimates to those for animal species that prehistoric hominins are known to have consumed — mammoths, woolly rhinos, bison, horses, birds and various species of deer. He found that human tissue provided significantly fewer calories than most of the larger animals that could have been hunted easily. A horse, for example, would have provided around 200,000 calories from its muscle alone, whereas human tissue would have given only 32,000 calories, according to the study.

The results, published online today (April 6) in the journal *Scientific Reports*, suggest that hunting and consuming hominins wouldn't have been a reliable source of food for prehistoric humans, as many archeologists previously thought, Cole said. Rather, it's more likely that cannibalism was socially driven, he added. For example, Neanderthals or other hominins may have cannibalized each other when having to defend their territory, or as a way of resolving competition within a group.

This hypothesis is also supported by the scarcity of fossil records of Paleolithic cannibalism. Bones of adults, children and teenagers carrying teeth marks and other signs of cannibalism have been found deep inside caves in large groups, indicating that the whole group was likely consumed in one go, instead of as part of regular diet, Cole said. In the future, archaeologists can use the template as a tool for evaluating human fossil sites and interpreting the motivations behind the acts of cannibalism at each site, he said. Scientists can look at the calorie values of various animal remains found next to human bones and analyze whether that particular prehistoric group was struggling for survival and was therefore driven to cannibalism due to a lack of other food options, or if they were cannibalizing as ritual or to defend their territory.

"The stereotype of the Neanderthal is not true," Cole said. Accepting that our Neanderthal cousins ate their own kind doesn't mean that they were brutes. Their motivations could have been just as varied as our motivations for various behaviors are. "We should expect that the reason they engaged in cannibalism could be complex, and different for each episode, rather than trying to limit them to one label."

<http://bit.ly/2oj9UjV>

Salk scientists expand ability of stem cells to regrow any tissue type

Chemical cocktail enables cultured mouse and human stem cells to generate both embryonic and extra-embryonic tissues

LA JOLLA - When scientists talk about laboratory stem cells being totipotent or pluripotent, they mean that the cells have the potential, like an embryo, to develop into any type of tissue in the body. What totipotent stem cells can do that pluripotent ones can't do, however, is develop into tissues that support the embryo, like the placenta. These are called extra-embryonic tissues, and are vital in development and healthy growth.

Now, scientists at the Salk Institute, in collaboration with researchers from Peking University, in China, are reporting their discovery of a chemical cocktail that enables cultured mouse and human stem cells to do just that: generate both embryonic and extra-embryonic tissues. Their technique, described in the journal *Cell* on April 6, 2017, could yield new insights into mammalian development that lead to better disease modeling, drug discovery and even tissue regeneration. This new technique is expected to be particularly useful for modeling early developmental processes and diseases affecting embryo implantation and placental function, possibly paving the way for improved in vitro fertilization techniques.

"During embryonic development, both the fertilized egg and its initial cells are considered totipotent, as they can give rise to all embryonic and extra-embryonic lineages. However, the capture of stem cells with such developmental potential in vitro has been a major challenge in

stem cell biology," says Salk Professor Juan Carlos Izpisua Belmonte, co-senior author of the paper and holder of Salk's Roger Guillemin Chair. "This is the first study reporting the derivation of a stable stem cell type that shows totipotent-like bi-developmental potential towards both embryonic and extra-embryonic lineages."

Once a mammalian egg is fertilized and begins dividing, the new cells segregate into two groups: those that will develop into the embryo and those that will develop into supportive tissues like the placenta and amniotic sac. Because this division of labor happens relatively early, researchers often can't maintain cultured cell lines stably until cells have already passed the point where they could still become either type. The newly discovered cocktail gives stem cells the ability to stably become either type, leading the Salk team to dub them extended pluripotent stem (EPS) cells.

"The discovery of EPS cells provides a potential opportunity for developing a universal method to establish stem cells that have extended developmental potency in mammals," says Jun Wu, a senior scientist at Salk and one of the paper's first authors. "Importantly, the superior interspecies chimeric competency of EPS cells makes them especially valuable for studying development, evolution and human organ generation using a host animal species."

To develop their cocktail, the Salk team, together with the team from Peking University, first screened for chemical compounds that support pluripotency. They discovered that a simple combination of four chemicals and a growth factor could stabilize the human pluripotent stem cells at a developmentally less mature state, thereby allowing them to more efficiently contribute to chimera (a mix of cells from two different species) formation in a developing mouse embryo. They also applied the same factors to mouse cells and found, surprisingly, that the newly derived mouse stem cells could not only give rise to embryonic tissue types but also differentiate into cells from the extra-embryonic lineages. Moreover, the team found that the new mouse stem cells have a superior ability to form chimeras and a single cell

could give rise to an entire adult mouse, which is unprecedented in the field, according to the team.

"The superior chimeric competency of both human and mouse EPS cells is advantageous in applications such as the generation of transgenic animal models and the production of replacement organs," adds Wu. "We are now testing to see whether human EPS cells are more efficient in chimeric contribution to pigs, whose organ size and physiology are closer to humans." Human EPS cells, combined with the interspecies blastocyst complementation platform as reported by the same Salk team in [Cell in January 2017](#), hold great potential for the generation of human organs in pigs to meet the rising demand for donor organs.

"We believe that the derivation of a stable stem cell line with totipotent-like features will have a broad and resounding impact on the stem cell field," says Izpisua Belmonte.

Other authors included: Takayoshi Yamauchi, Atsushi Sugawara and Zhongwei Li of Salk; Yang Yang, Bei Liu, Jun Xu, Jinlin Wang, Cheng Shi, Yaxing Xu, Jiebin Dong, Chengyan Wang, Weifeng Lai, Jialiang Zhu, Liang Xiong, Dicong Zhu, Xiang Li, Chen Li, Aibin He, Yaqin Du, Ting Wang, Chaoran Zhao, Haibo Li, Hongquan Zhang, Xiaochun Chi, and Huan Shen of Peking University; Weifeng Yang and Ming Yin of Beijing Vitalstar Biotechnology; Fangyuan Sun and Xiangyun Li of Hebei University; Yifang Liu of Tsinghua University; Cheng Li of Peking-Tsinghua Center for Life Sciences; Shuguang Duo of the Chinese Academy of Sciences.

<http://bit.ly/2oPWuWD>

Low ammonium levels in urine may indicate serious risks for kidney disease patients

In patients with chronic kidney disease, low urine ammonium excretion identified individuals at high risk of kidney disease progression or death.

Washington, DC -- New research indicates that measuring ammonium excretion in the urine may help identify patients with chronic kidney disease (CKD) who face serious health risks. The findings appear in an upcoming issue of the *Journal of the American Society of Nephrology* (JASN).

Keeping the body's pH level in balance is important for normal organ function. Doctors commonly assess whether a patient's body fluids contain too much acid, a condition called acidosis, by measuring bicarbonate levels in the blood. This can indicate whether the body is having trouble maintaining its acid-base balance, but it may reveal only part of the picture because the kidneys are important for eliminating acid in the urine.

Kalani Raphael, MD (University of Utah) and his colleagues looked to see if urine levels of ammonium may be a better indicator of acid accumulation in the body. Their analysis included 1044 individuals with CKD in the African American Study of Kidney Diseases and Hypertension.

The researchers found that low urine ammonium excretion predicted kidney failure or death in CKD patients irrespective of serum bicarbonate concentration. Compared with participants with the highest levels of daily ammonium excretion, those with the lowest levels had a 46% higher risk of dying or needing dialysis, and those with intermediate levels had a 14% higher risk. Low ammonium excretion predicted these outcomes even in patients who had normal serum bicarbonate. In addition, those with low ammonium excretion had a 2.6-fold higher risk of developing acidosis within one year.

"These results suggest that low urine ammonium excretion identifies individuals at high risk of CKD progression or death irrespective of the serum bicarbonate concentration," said Dr. Raphael. "Overall, acid levels in the urine provide important information about kidney health above and beyond acid measurements obtained from the blood." The findings also suggest that CKD patients with low urine ammonium excretion might benefit from alkali before overt acidosis develops. Additional research is needed to test this.

Study co-authors include David Carroll, Jennifer Murray, Tom Greene, PhD, and Srinivasan Beddhu, MD. Disclosures: The authors reported no financial disclosures.

The article, entitled "Urine ammonium predicts clinical outcomes in hypertensive kidney disease," will appear online at <http://jasn.asnjournals.org/> on April 6, 2017, doi: 10.1681/ASN.2016101151.

<http://bit.ly/2ojbbaQ>

How a Fitness Tracker Spotted a Woman's Life-Threatening Condition

A Connecticut woman is crediting her Fitbit with saving her life, after the device detected signs of life-threatening blood clots.

By Rachael Rettner, Senior Writer | April 7, 2017 02:38pm ET

The woman, 73-year-old Patricia Lauder, had recently retired and bought a Fitbit to help her get in shape, according to a statement from the University of Connecticut, where Lauder was treated. But then, she began to feel ill, even though doctors' tests for health problems came back negative.

She also noticed that her heart-rate reading on her Fitbit was gradually increasing, until one day, it spiked to 140 beats per minute. She called 911 and was taken to the hospital, where tests showed that she had a condition called pulmonary embolisms, or blood clots in her lungs. Doctors gave her anti-clotting medication, which got rid of the clots.

"If I didn't have a Fitbit on my wrist, I would never have known that my heart rate was getting dangerously high," Lauder told UConn Today, the news website for the university. "And I might not be here to tell my story."

Experts say that, because some fitness trackers include heart rate monitors, the devices can potentially alert people to certain health problems that cause changes in heart rate.

"Heart rate is a general signal for how much stress your body's under," Dr. Allen Taylor, a cardiologist and professor of medicine at Georgetown University School of Medicine in Washington, D.C., told Live Science in a 2015 interview. Like a fever, a high heart rate could be a symptom of many conditions, so it cannot be used by itself to make a diagnosis, Taylor said. But "for certain conditions, [if] patients find their heart rates running faster, it could alert them to say 'something's not right here,' Taylor said.

A rapid or irregular heartbeat can be a sign of a pulmonary embolism, according to the Mayo Clinic. The blockage caused by the clots can

require the heart to start working harder to pump blood through vessels, and this can also lead to an increase in blood pressure inside the lungs, the Mayo Clinic says.

Other conditions that a fitness tracker might detect include atrial fibrillation (an erratic heartbeat), anemia (a low red blood cell count) and an overactive thyroid. All of these conditions can lead to a faster-than-normal heart rate. A normal resting heart rate is between 60 and 100 beats per minute, according to the Mayo Clinic.

In September 2015, a high school senior credited his Apple Watch with saving his life, when the device showed he had a heart rate of 145 beats per minute. An exam revealed that he had rhabdomyolysis, a condition in which muscles release a protein that damages the kidneys and other organs.

And last year, doctors in New Jersey used data from a man's Fitbit to determine how to treat him when he arrived at the ER with a rapid and irregular heart rate.

Still, it's important to note that having a normal heart rate doesn't necessarily mean you're healthy, Taylor said.

And fitness trackers like the Fitbit aren't approved medical devices, so they cannot be used to diagnose cardiovascular conditions. A study published last year found that wrist-worn heart rate monitors, which are typically used on fitness trackers, are not as accurate as chest strap monitors. The researchers advised fitness-tracker users to be aware that the devices' heart-rate readings aren't always accurate.

<http://bit.ly/2nsRVIM>

Why did we see 'the dress' differently? The answer lies in the shadows, new research finds

When "the dress" went viral in 2015, millions were divided on its true colors: gold and white or black and blue?

In a new study, New York University neuroscientist Pascal Wallisch concludes that these differences in perception are due to our assumptions about how the dress was illuminated.

Those who thought that the dress, worn by the mother of a bride at a wedding in Scotland, was photographed in a shadow likely saw the garment as gold and white; by contrast, those who thought it was illuminated by artificial light were more likely to see it as black and blue.

"The original image was overexposed, rendering the illumination source uncertain," explains Wallisch, who serves as a clinical assistant professor in NYU's Department of Psychology.

"As a result, we make assumptions about how the dress was illuminated, which affects the colors we see."

"Shadows are blue, so we mentally subtract the blue light in order to view the image, which then appears in bright colors--gold and white," Wallisch continues. "However, artificial light tends to be yellowish, so if we see it brightened in this fashion, we factor out this color, leaving us with a dress that we see as black and blue.

"This is a basic cognitive function: to appreciate the color on an object, the illumination source has to be taken into account, which the brain does continuously." The findings, based on an online study with more than 13,000 participants, appear in the *Journal of Vision*.

The study's participants, who had previously seen the dress, were asked whether or not they believed it was in a shadow.

These beliefs -- about whether or not the dress was in a shadow--strongly affected the perceptual experience of the dress. Among those who saw it in a shadow, four out of five participants believed it to be white and gold; by contrast, only about half of participants who did not see it in a shadow saw the garment bearing these colors.

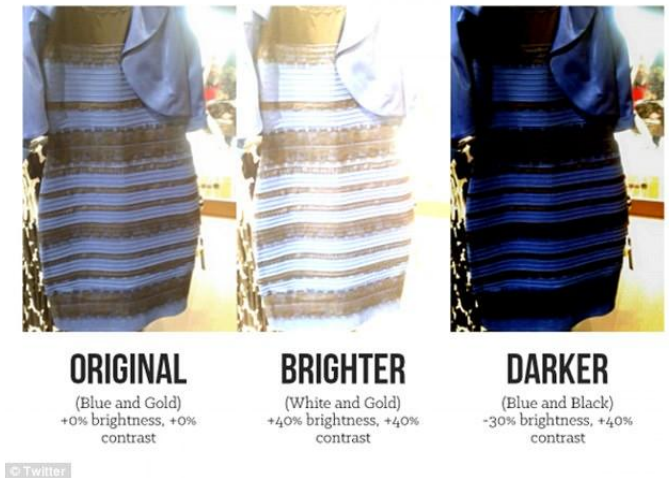
Wallisch then considered what could explain these findings. He hypothesized that differing perceptions could be linked to one's exposure to daylight--quite simply, people who rise and go to bed early, and spend many of their waking hours in sunlight (i.e., under a blue sky), are more likely to see the dress as white and gold than are night owls, whose world is illuminated not by the sun, but, rather, by long-wavelength artificial light.

To test this, he asked participants if they go to bed early and feel best in the morning (i.e., "larks") or if they like to sleep in and feel best at night ("owls"), then matched this self-identified circadian type with how they saw the dress.

Consistent with the hypothesis, larks were significantly more likely to see the dress as white and gold--relative to owls--underscoring the relative effects of exposure to daylight.

"This suggests that whatever kind of light one is typically exposed to influences how one perceives color," Wallisch says.

Conversely, demographic factors such as gender and age had comparatively small effects on the perception of the dress image.



People who spend more time in sunlight are more likely to assume 'warm' illumination and see the dress as white and gold. A number of people in 2015 turned to photo editing software to highlight the role of illumination in the illusion (pictured)

The findings broaden our understanding of how a bistable stimulus--i.e., one that is fundamentally ambiguous and open to subjective interpretation--works in color perception and, more specifically, offer new insights into a long-standing question about color perception: Is the color you see the same color I see?

"The answer -- based on this research - is 'not necessarily'," Wallisch observes. "If illumination conditions are unclear, your assumptions about the illumination source will matter, and those might depend on lifestyle choices, such as when you go to sleep."

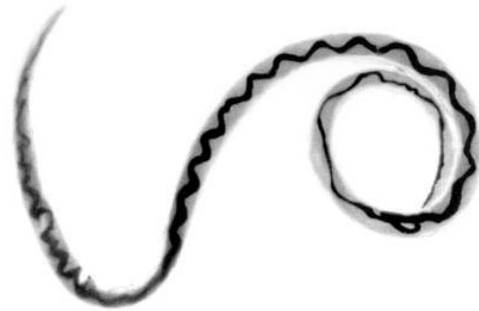
<http://bit.ly/2obTyYz>

Concern growing for brain-invading worms, spread by slugs and rats

Rat lungworm has been around for decades, but uptick has health officials worried.

Beth Mole - 4/9/2017, 1:00 AM

There have been six cases of a rare parasitic infection called “rat lungworm” in Maui in the last three months, health officials reported this week. The number is small, but it’s a dramatic jump from the normal number of cases. In the decade before this period, the island had only seen two other cases.



*Adult female worm of *Angiostrongylus cantonensis* recovered from rat lungs with characteristic barber-pole appearance (anterior end of worm is to the top).*

Scale bar = 1 mm. [Lindo et al.](#)

The surprising uptick has health officials and residents alike worried about the rise of the worm, which can invade the human brain. In infected people, the infection may be symptomless and resolve on its own. But for others, rat lungworm moves into the brain and can cause inflammation, pain, and other neurological problems such as tremors. In those cases, it can be fatal. In all cases, rat lungworm is very difficult to diagnose, and there is no treatment.

So far, at least three of the six cases have been confirmed by the state. There’s also a seventh possible case.

In April, one of the patients with a confirmed infection, 47-year-old Tricia Mynar, told [Honolulu Civil Beat](#): “The parasites are in the lining of my brain, moving around.” She described the feeling as if “every once in a while somebody opens the top of my head, sets a hot iron inside my brain, then pushes the steam button.”

As the name suggests, rat lungworm is a parasitic roundworm (*Angiostrongylus cantonensis*) that infects rats’ lungs as well as their blood and brains. Infected rats poop out worm larvae, which can be picked up by snails, slugs, lizards, land crabs, and freshwater shrimp. These are intermediate hosts that shed the worm. Humans can pick up the infection by handling or eating any infected critter or by eating produce that has been contaminated by roaming infected snails and slugs.

In Maui, the current uptick appears to be linked to a boom in the population of an invasive “semi-slug” that is a particularly good carrier of the worm. While native slugs and snails may be carriers around 25 percent of the time, the invasive semi-slug has a carriage rate of around 70 to 80 percent of the time, [The Maui News reported](#). Once alerted to the problem, residents reported seeing the semi-slugs in their yards and gardens. They’re taking steps to knock back the population, as well as rein in the rats.

But, [as The Atlantic noted](#), the rise of the rat lungworm has been a long time coming. Researchers have noted that with climate change and increasing global travel, the parasite has been spreading to new places and causing more cases.

The first human case was recorded in 1944 in Taiwan, and it was thought to be spread around during World War II. Since then, rat lungworm has been prevalent in parts of Southeast Asia and Western Pacific Islands, including Australia. In the past few decades, the parasite made its way to the US, reaching Hawaii, California, [Oklahoma](#), Alabama, Louisiana, Florida, and other parts of the Gulf Coast.

In Hawaii at least, rat lungworm seems to be there to stay. “The problem isn’t going to go away,” Maui Invasive Species Committee Manager Adam Radford told [The Maui News](#). “Our focus is on educating the public and determining the extent through social media and potentially [a] survey.”

<http://bbc.in/2nPpiRp>

Rules of memory 'beautifully' rewritten

What really happens when we make and store memories has been unravelled in a discovery that surprised even the scientists who made it.

By James Gallagher Health and science reporter, BBC News website

The US and Japanese team found that the brain "doubles up" by simultaneously making two memories of events. One is for the here-and-now and the other for a lifetime, they found.

It had been thought that all memories start as a short-term memory and are then slowly converted into a long-term one. Experts said the findings were surprising, but also beautiful and convincing.

'Significant advance'

Two parts of the brain are heavily involved in remembering our personal experiences. The hippocampus is the place for short-term memories while the cortex is home to long-term memories.

This idea became famous after the case of Henry Molaison in the 1950s. His hippocampus was damaged during epilepsy surgery and he was no longer able to make new memories, but his ones from before the operation were still there.

So the prevailing idea was that memories are formed in the hippocampus and then moved to the cortex where they are "banked".

The team at the Riken-MIT Center for Neural Circuit Genetics have done something mind-bogglingly advanced to show this is not the case. The experiments had to be performed on mice, but are thought to apply to human brains too.

They involved watching specific memories form as a cluster of connected brain cells in reaction to a shock. Researchers then used light beamed into the brain to control the activity of individual neurons - they could literally switch memories on or off.

The results, published in the journal Science, showed that memories were formed simultaneously in the hippocampus and the cortex.

Prof Susumu Tonegawa, the director of the research centre, said: "This was surprising." He told the BBC News website: "This is contrary to the popular hypothesis that has been held for decades. "This is a significant advance compared to previous knowledge, it's a big shift."

The mice do not seem to use the cortex's long-term memory in the first few days after it is formed. They forgot the shock event when scientists turned off the short-term memory in the hippocampus.

However, they could then make the mice remember by manually switching the long-term memory on (so it was definitely there).

"It is immature or silent for the first several days after formation," Prof Tonegawa said.

'Strong case'

The researchers also showed the long-term memory never matured if the connection between the hippocampus and the cortex was blocked. So there is still a link between the two parts of the brain, with the balance of power shifting from the hippocampus to the cortex over time.

Dr Amy Milton, who researches memory at Cambridge University, described the study as "beautiful, elegant and extremely impressive". She told the BBC News website: "I'm quite surprised.

"The idea you need the cortex for memories I'm comfortable with, but the fact it's so early is a surprise. "This is [just] one study, but I think they've got a strong case, I think it's convincing and I think this will tell us about how memories are stored in humans as well."

For now, this is simply a piece of fundamental science that explains how our bodies work. But Prof Tonegawa says it may illuminate what goes on in some diseases of memory including dementia.

One of his previous studies showed mice with Alzheimer's were still forming memories but were not able to retrieve them. "Understanding how this happens may be relevant in brain disease patients," he said.

<http://bit.ly/2nPBq4H>

Mars is so small because Jupiter shook up its formation

Mars can blame Jupiter for its small stature.

By Abigail Beall

The Red Planet may be much smaller than we expect because Jupiter's gravity beat it up as it was forming.

Models of our solar system's formation suggest that Mars should be between 1.5 and two times Earth's mass. Instead, it weighs in at a mere one-tenth the mass of our world.

Now an old theory that might explain why is resurfacing: gas left over from the formation of Jupiter meddled with the rocks that ultimately built Mars, making them fall apart rather than clump together.

The gas giants formed by accreting gas from the protoplanetary disc that surrounded the sun. As they grew, their gravity started to have more impact than the remaining disc on the still-forming rocky planets. The disc's gravity pulled the protoplanets' axes of rotation in one direction, but the gravity from Jupiter came from the opposite direction, tugging them that way. When those competing forces balanced in a certain way, the protoplanets felt a kick from Jupiter's gravity at the same point in their orbit around the sun, an effect known as sweeping resonance.

"Before the kicks, collisions between solids occurred at low velocity, so they merged," says Scott Kenyon at the Harvard-Smithsonian Center for Astrophysics. "After the kicks, the collisions are at high velocity, so colliding objects fragment."

Revived theory

A trio of researchers led by Douglas Lin at the University of California at Santa Cruz first proposed this general scenario over a decade ago. Now Kenyon and Ben Bromley at the University of Utah have revived it specifically to explain Mars's diminutive size.

"Recent studies of meteorites suggest Mars formed much more rapidly than [Lin's team] assumed, so we worked out the consequences for a disc that evolves more rapidly," Kenyon says.

Lin and his colleagues also published a paper in February in The Astrophysical Journal suggesting Jupiter's sweeping resonance could have been responsible for clearing the asteroid belt of rocks smaller than 50 kilometres wide. The theory might also hold for other solar systems, suggesting asteroid belts could be common wherever there are massive planets. "It is a rich subject," Lin says.

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<http://bit.ly/2nt6NH5>

Grey hair linked with increased heart disease risk in men

Grey hair has been linked with an increased risk of heart disease in men, in research presented today at EuroPrevent 2017.1

Malaga, Spain - "Ageing is an unavoidable coronary risk factor and is associated with dermatological signs that could signal increased risk," said Dr Irini Samuel, a cardiologist at Cairo University, Egypt. "More research is needed on cutaneous signs of risk that would enable us to intervene earlier in the cardiovascular disease process."

Atherosclerosis and hair greying share similar mechanisms such as impaired DNA repair, oxidative stress, inflammation, hormonal changes and senescence of functional cells. This study assessed the prevalence of grey hair in patients with coronary artery disease and whether it was an independent risk marker of disease.

This was a prospective, observational study which included 545 adult men who underwent multi-slice computed tomography (CT) coronary angiography for suspected coronary artery disease. Patients were divided into subgroups according to the presence or absence of coronary artery disease, and the amount of grey/white hair.

The amount of grey hair was graded using the hair whitening score: 1 = pure black hair, 2 = black more than white, 3 = black equals white, 4 = white more than black, and 5 = pure white. Each patients' grade was determined by two independent observers.

Data was collected on traditional cardiovascular risk factors including hypertension, diabetes, smoking, dyslipidaemia, and family history of coronary artery disease.

The researchers found that a high hair whitening score (grade 3 or more) was associated with increased risk of coronary artery disease independent of chronological age and established cardiovascular risk factors. Patients with coronary artery disease had a statistically significant higher hair whitening score and higher coronary artery calcification than those without coronary artery disease.

In multivariate regression analysis, age, hair whitening score, hypertension and dyslipidaemia were independent predictors of the presence of atherosclerotic coronary artery disease. Only age was an independent predictor of hair whitening.

"Atherosclerosis and hair greying occur through similar biological pathways and the incidence of both increases with age," said Dr Samuel. "Our findings suggest that, irrespective of chronological age, hair greying indicates biological age and could be a warning sign of increased cardiovascular risk."

Dr Samuel said asymptomatic patients at high risk of coronary artery disease should have regular check-ups to avoid early cardiac events by initiating preventive therapy.

"Further research is needed, in coordination with dermatologists, to learn more about the causative genetic and possible avoidable environmental factors that determine hair whitening," she added. "A larger study including men and women is required to confirm the association between hair greying and cardiovascular disease in patients without other known cardiovascular risk factors."

She concluded: "If our findings are confirmed, standardisation of the scoring system for evaluation of hair greying could be used as a predictor for coronary artery disease."