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Taking antidepressants during pregnancy increases risk of autism by 87 percent

Ground breaking study published in JAMA Pediatrics looks at outcomes of 145,456 pregnancies after antidepressant use

Using antidepressants during pregnancy greatly increases the risk of autism, Professor Anick Bérard of the University of Montreal and its affiliated CHU Sainte-Justine children's hospital revealed today. Prof. Bérard, an internationally renowned expert in the fields of pharmaceutical safety during pregnancy, came to her conclusions after reviewing data covering 145,456 pregnancies.

"The variety of causes of autism remain unclear, but studies have shown that both genetics and environment can play a role," she explained. "Our study has established that taking antidepressants during the second or third trimester of pregnancy almost doubles the risk that the child will be diagnosed with autism by age 7, especially if the mother takes selective serotonin reuptake inhibitors, often known by its acronym SSRIs." Her findings were published today in JAMA Pediatrics.

Bérard and her colleagues worked with data from the Quebec Pregnancy Cohort and studied 145,456 children between the time of their conception up to age ten. In addition to information about the mother's use of antidepressants and the child's eventual diagnosis of autism, the data included a wealth of details that enabled the team to tease out the specific impact of the antidepressant drugs. For example, some people are genetically predisposed to autism (i.e., a family history of it.) Maternal age, and depression are known to be associated with the development of autism, as are certain socio-economic factors such as being exposed to poverty, and the team was able to take all of these into consideration.

"We defined exposure to antidepressants as the mother having had one or more prescription for antidepressants filled during the second or third trimester of the pregnancy. This period was chosen as the infant's critical brain development occurs during this time," Prof. Bérard said.

"Amongst all the children in the study, we then identified which children had been diagnosed with a form of autism by looking at hospital records indicating diagnosed childhood autism, atypical autism, Asperger's syndrome, or a pervasive developmental disorder. Finally, we looked for a statistical association between the two groups, and found a very significant one: an 87% increased risk." The results remained unchanged when only considering children who had been diagnosed by specialists such as psychiatrists and neurologists.

The findings are hugely important as six to ten percent of pregnant women are currently being treated for depression with antidepressants. In the current study, 1,054 children were diagnosed with autism (0.72% of the children in the study), on average at 4.5 years of age. Moreover, the prevalence of autism amongst children has increased from 4 in 10,000 children in 1966 to 100 in 10,000 today. While that increase can be attributed to both better detection and widening criteria for diagnosis, researchers believe that environmental factors are also playing a part. "It is biologically plausible that anti-depressants are causing autism if used at the time of brain development in the womb, as serotonin is involved in numerous pre- and postnatal developmental processes, including cell division, the migration of neuros, cell differentiation and synaptogenesis - the creation of links between brain cells," Prof. Bérard explained.

"Some classes of anti-depressants work by inhibiting serotonin (SSRIs and some other antidepressant classes), which will have a negative impact on the ability of the brain to fully develop and adapt in-utero"

The World Health Organization indicates that depression will be the second leading cause of death by 2020, which leads the researchers to believe that antidepressants will likely to remain widely prescribed, including during pregnancy. "Our work contributes to a better understanding of the long-term neurodevelopmental effects of anti-depressants on children when they are used during gestation. Uncovering the outcomes of these drugs is a public health priority, given their widespread use," Prof. Bérard said.

About this study: Takoua Boukhris, Odile Sheehy, Laurent Mottron, MD, PhD, and Anick Bérard, PhD, published "Antidepressant use during pregnancy and the risk of autism spectrum disorder in children" in JAMA Pediatrics on December 14, 2015.

http://www.eurekalert.org/pub_releases/2015-12/du-het121415.php

Humans evolved to get better sleep in less time

Humans sleep shorter, deeper than our closest animal relatives

Insomniacs take heart: Humans get by on significantly less sleep than our closest animal relatives. The secret, according to a new study, is that our sleep is more efficient.

Researchers from Duke University scoured the scientific literature and compiled a database of slumber patterns across hundreds of mammals including 21 species of primates -- from baboons and lemurs to orangutans, chimpanzees and people. They then used statistical techniques to account for each species' position in the primate family tree.

They found that humans are exceptionally short sleepers -- getting by on an average of seven hours of sleep a night, whereas other primate species, such as

southern pig-tailed macaques and gray mouse lemurs, need as many as 14 to 17 hours.

What's more, our sleep tends to be more efficient, meaning we spend a smaller proportion of time in light stages of sleep, and more of our sleep time in deeper stages of sleep. A dream state called rapid eye movement sleep, or REM, for example, makes up nearly 25 percent of our overall sleep. But in primates such as mouse lemurs, mongoose lemurs and African green monkeys, REM sleep barely climbs above five percent.

"Humans are unique in having shorter, higher quality sleep," said anthropologist and study co-author David Samson of Duke, who logged nearly 2,000 hours watching orangutans in REM and non-REM sleep as part of his dissertation research prior to coming to Duke.

The human sleep gap isn't merely the result of round-the-clock access to artificial light from streetlamps and computer screens, the researchers say. A separate study of the sleep habits of people living in three hunter-gatherer societies without electricity in Tanzania, Namibia and Bolivia found they get slightly less shut-eye than those of us with electronic gadgets.

If artificial light and other aspects of modern life were solely responsible for shortening our sleep, we'd expect hunter-gatherer societies without access to electricity to sleep more, Samson said.

Rather, the study by Samson and Duke anthropologist Charlie Nunn suggests that humans replaced sleep quantity with sleep quality long before the glare of smartphones came to be.

The researchers attribute the shift towards shorter, more efficient sleep in part to the transition from sleeping in "beds" in the trees, as our early human ancestors probably did, to sleeping on the ground as we do today.

Once on the ground, Samson said, early humans likely started sleeping near fire and in larger groups in order to keep warm and ward off predators such as leopards and hyenas -- habits which could have enabled our ancestors to get the most out of their sleep in the shortest time possible.

Shorter sleep also freed up time that could be devoted to other things, like learning new skills and forging social bonds, while deeper sleep helped to cement *those skills, sharpen memory and boost brainpower, Samson said.*

The findings appear in the journal Evolutionary Anthropology.

This research was supported by grants from the National Science Foundation (BCS-1355902) and Duke University.

A digital version of this story is available at http://today.duke.edu/2015/12/humansleep.

CITATION: "Sleep intensity and the evolution of human cognition," Samson, D. and C. Nunn. Evolutionary Anthropology, December 2015. DOI: 10.1002/evan.21464

http://www.eurekalert.org/pub_releases/2015-12/epfd-tcc121115.php

Treating colon cancer with vitamin A

Scientists identify a biological mechanism that can be exploited to counteract colon cancer relapses

A leading cause of cancer deaths worldwide, colon cancer is famously resistant to treatment. There are many reasons for this, but one has to do with a group of persisting cancer cells in the colon that cause relapses. Conventional therapies against them are mostly ineffective. EPFL scientists have now identified a biological mechanism that can be exploited to counteract colon cancer relapses. The approach activates a protein that is lost in the persisting cancer cells. The researchers were able to reactivate it using vitamin A, thus eliminating the cancer cells and preventing metastasis. The study is published in Cancer Cell, and introduces a new way to treat colon cancer.

When a colon-cancer patient receives treatment, e.g. chemotherapy, most of the cancer cells die off. But the genetic mutations that caused the cancer in the first place can survive in a specific group of cells of the colon. These are actually stem cells, meaning that they are premature cells waiting to grow into full-blown, normal cells of the colon. After cancer treatment ends, the surviving stem cells, still containing the cancerous mutations, can reappear and cause a relapse.

The lab of Joerg Huelsken at EPFL studied how differentiated colon cells come from stem cells in the gut. Using an array of different techniques, the team looked at cells, mouse models and samples from human patients.

Proteins and signaling pathways

The study focused on a protein called HOXA5, which belongs to a family of proteins that regulate the development of the fetus. These proteins are made during early development and work together to make sure that every tissue is correctly identified and that the fetus's body and limbs are patterned properly. In the adult body, proteins like HOXA5 regulate the body's stem cells to maintain both the identity and function of different tissues. Huelsken's team found that in the gut, HOXA5 plays a major role in restricting the number of stem cells, as well as the cells that make them.

Like all proteins, HOXA5 originates from a specific gene. The study showed that the cancerous stem cells of the colon use a biological mechanism that blocks it. This mechanism is called a "signaling pathway" because it involves a domino of molecules, each activating the next one down the line. The purpose of a signaling pathway is to transmit biological information from one part of the cell to another, e.g. from the outer membrane all the way to the nucleus. By blocking the HOXA5 gene, the cancerous stem cells of the colon can grow uncontrollably and spread, causing relapses and metastasis.

Retinoids: a way to fight back

The researchers looked for ways to reverse the blocking of HOXA5. The answer came from vitamin A. This small chemical structure is called a retinoid, and it has been known to induce differentiation of stem cells in the skin. The EPFL scientists found that retinoids can re-activate HOXA5. In mice that had colon cancer, the treatment with retinoids blocked tumor progression and normalized the tissue. By turning the gene for HOXA5 back on, this treatment eliminated cancer stem cells and prevented metastasis in the live animals. The researchers got similar results with samples from actual patients.

The new study suggests that patients that may profit from this well-tolerated treatment can be identified based on their expression pattern for the HOXA5 gene. Retinoid differentiation therapy could be significantly effective against colon cancer, not only for treatment of existing disease but also as a preventive measure in high-risk patients.

This study included contributions from EPFL's core facilities, Kyoto University, and the Japan Science and Technology Agency. It was funded by EMBO, the Swiss League against Cancer, the Swiss National Science Foundation and the NCCR in Molecular Oncology.

Ordóñez-Morán P, Dafflon C, Imajo M, Nishida E, Huelsken J. HOXA5 Counteracts Stem Cell Traits by Inhibiting Wnt Signaling in Colorectal Cancer. Cancer Cell Dec. 14, 2015. DOI: 10.1016/j.ccell.2015.11.001

http://www.eurekalert.org/pub_releases/2015-12/b-bda121015.php

Bob Dylan: A source of inspiration for medical scientists

Lyrics in the biomedical literature have increased exponentially since 1990

The number of articles citing the lyrics of Bob Dylan in the biomedical literature has increased exponentially since 1990, according to a study in the Christmas issue of The BMJ. In 2014, it was revealed that a group of scientists at the Karolinska Institutet in Sweden had been sneaking the lyrics of Bob Dylan into their papers as part of a long-running bet.

So, another group of Karolinska researchers decided to investigate how the lyrics of Bob Dylan are cited in the titles of published biomedical papers. A search of all his song and album titles was conducted in May 2015. A selection of the most popular Dylan songs were also searched to find modified titles. In all, 213 of 727 references were classified as unequivocally citing Bob Dylan and were included in the subsequent analysis.

According to the search, the first Dylan-citing article appeared in 1970 in Journal of Practical Nursing, eight years after his debut album was released. Interestingly, the researchers note that, after a handful of citations during Bob Dylan's heyday in the first half of the 1970s, very few articles in the biomedical sciences cited Bob Dylan until 1990. However, since then, the number of articles has increased exponentially.

The two most cited Dylan songs are The Times They Are A-Changin' (135 articles) and Blowin' In The Wind (36 articles). The search also revealed the use of other popular titles such as All Along The Watchtower, Knockin' On Heaven's Door, and Like A Rolling Stone.

Some journals have a greater preponderance of Dylan-citing articles than others; for instance, no less than six articles citing Dylan songs were found in Nature. However, citing Bob Dylan in a paper doesn't appear to generate more attention in the research community, say the authors.

Recent evidence suggests that Bob Dylan has a great deal of respect for the medical profession, they add, as shown in the song Don't Fall Apart On Me Tonight, in which Dylan laments:

"I wish I'd have been a doctor / Maybe I'd have saved some life that had been lost / Maybe I'd have done some good in the world / 'Stead of burning every bridge I crossed."

Based on this present survey, the researchers suggest that the medical profession shows the same respect for Bob Dylan. They point to several possible explanations but conclude, "it is clear that Bob Dylan's rich song catalogue has provided a source of inspiration for medical scientists."

http://www.eurekalert.org/pub_releases/2015-12/bu-bup121415.php

Binghamton University professor launches web tool to track impact of drugs worldwide

Billions of dollars have been spent on developing drugs and supplying them around the world, but which companies' drugs are actually making an impact?

BINGHAMTON, NY - Billions of dollars have been spent on developing drugs and supplying them around the world, but which companies' drugs are actually making an impact?

The Global Health Impact Index, headed by Binghamton University Associate Professor Nicole Hassoun and highlighted in a new article published Friday in PLOS ONE, addresses this issue by ranking pharmaceutical companies based on their drugs' impact on global health. ***VIDEO:*** ***http://youtu.be/2rn5nRmyhOI***

The Global Health Impact Index considers how companies drugs measure up on the basis of their impact on the "big three" infectious diseases: malaria, HIV/AIDS and tuberculosis.

While previous indexes have measured the need for different drugs worldwide, the Global Health Impact Index is the first to measure the actual impact of these drugs.

"People have focused on measuring the need for different drugs...but we're looking at the impact that they're actually having," said Hassoun.

"This is important for setting goals, evaluating performance -- trying to have a bigger impact on global health and saving millions of lives."

The index looks at three things: the need for several important drugs for tuberculosis, HIV/AIDS, and malaria; the drugs' effectiveness; and the number of people who can access the drugs.

Each company's score is the sum of its drugs' impacts.

According to the index, the companies whose drugs having the most impact on the "big three" diseases are:

Sanofi
Novartis
Pfizer

The following companies' drugs had the lowest drug impact scores on the index:

Eli Lilly
Kyorin Pharmaceutical Co.
Bayer Healthcare

"We are looking at the outcomes of the drugs that the companies hold, so the actual impact on death and disability," said Hassoun.

"We're looking at the amount of death and disability that the company's drugs are alleviating."

Hassoun hopes to motivate pharmaceutical companies to meet the health needs of impoverished people around the world through an initiative supported by Academics Stand Against Poverty (ASAP), an international professional association focused on helping poverty researchers and teachers enhance their positive impact on severe poverty.

According to Hassoun and ASAP, one third of all deaths globally, about 18 million per year, are linked to poverty, because people living in poverty cannot afford medicines and pharmaceutical companies do not have the financial incentive to develop treatments for diseases that primarily affect impoverished people.

By better understanding the impacts of companies' products on the burden of disease, said Hassoun, researchers can have a tool for measuring impact; governments, donors, etc. can better target their efforts; and companies can be incentivized to focus on impact.

Hassoun's manuscript, "The Global Health Impact Index: Promoting Global Health" was published Dec. 11 in PLOS ONE.

http://www.eurekalert.org/pub_releases/2015-12/vcu-msu121415.php

Massey scientists uncover process that could drive the majority of cancers

The gene p53 has been described as the "guardian of the genome" due to its prominent role in preventing genetic mutations.

More than half of all cancers are thought to originate from p53 mutations or loss of function, and now a recent study by VCU Massey Cancer Center scientist Richard Moran, Ph.D., explains why.

Published in Molecular Cancer Therapeutics, Moran's research results describe how mutations and or loss of function of the p53 gene activate a protein complex known as mammalian target of rapamycin complex 1 (mTORC1), which helps regulate the energy resources needed for cell proliferation. mTORC1 is made up of several dozen proteins, and cells use the intracellular membranes of their lysosome as a scaffold to bring all of these proteins together. In response to the need of a normal cell, the p53 gene helps maintain proper levels of a protein known as tuberous sclerosis complex 2 (TSC2) in the lysosome. When p53 is not functioning properly, Moran's team found that TCS2 levels in the lysosome drop, and a small protein known as RHEB takes its place. It is this accumulation of RHEB that activates mTORC1 and leads to the abnormal control of cell proliferation.

"We have uncovered for the first time the signaling process that leads to excessive growth of cancer when p53 is lost. These protein interactions are like individual links in the chain of events leading to the development of cancer," says Moran, Paul M. Corman, M.D., Chair in Cancer Research, associate director for basic research and co-leader and member of the Developmental Therapeutics research program at VCU Massey Cancer Center as well as professor of pharmacology and toxicology at the VCU School of Medicine.

In a related study, Moran's team focused on pemetrexed, an existing drug he co-developed that is now used as a first-line treatment for the majority of lung cancers.

In the Journal of Biological Chemistry, Moran and his colleagues demonstrate that pemetrexed works by shutting down the mTORC1 protein complex through the inhibition of one of its controlling components, a protein known as raptor. The researchers found that pemetrexed works regardless of whether or not there are p53 mutations or loss of function. Additionally, they found that it works even if the key regulator of mTORC1, TSC2, is no longer functioning.

"Our findings suggest that pemetrexed may have much greater clinical utility than previously imagined," says Moran. "This research lays the foundation for its use

against other cancers in which p53 is not functioning properly, as well as tuberous sclerosis complex, a syndrome driven by loss of TSC2 function that causes disastrous growth of benign but progressive tumors in major organs."

Moran collaborated on these studies with Shirley Taylor, Ph.D., director of the Biological Macromolecule Core Facility and member of the Cancer Molecular Genetics research program at Massey and associate professor of microbiology and immunology at the VCU School of Medicine; Stuti Agarwal and Catherine Bell, both Ph.D. students in Moran's lab; and Scott Rothbart, from the Center for Epigenetics at Van Andel Research Institute in Grand Rapids, Michigan.

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http://nyti.ms/1TXIIxH

120 Multistate Outbreaks: Tip of Iceberg in Food-borne Infection

The E. coli infections linked to the Chipotle Mexican Grill restaurant chain are only the latest cluster of illnesses caused by contaminated food.

By NICHOLAS BAKALAR DEC. 14, 2015

To be sure, the Chipotle outbreak was large. As of Dec. 2, according to the Centers for Disease Control and Prevention, 52 people had been infected in nine states and 20 had been hospitalized. But there was nothing unusual about such incidents.

As of Nov. 23, an outbreak of E. coli traced to a sample of diced celery and onions sold at Costco had infected 19 people in seven states. Five people had been hospitalized, and two had developed kidney failure. By Dec. 2, Salmonella from nut butter spread had infected people in nine states.

According to an analysis published in Morbidity and Mortality Weekly Report last month, there were 120 multi-state outbreaks of food-borne infection from 2010-14 — an average of one every two weeks.

Every state in the country has been affected, along with Washington, D.C., and Puerto Rico, and the outbreaks led to 7,929 illnesses, 1,460 hospitalizations and 66 deaths.

Fruits, vegetable row crops like lettuce, beef and sprouts were the main sources. But seeded vegetables, dairy products, chicken, fish, eggs and turkey have all been contaminated.

Imported foods accounted for only 18 of the outbreaks, so experts did not blame poor hygiene in foreign countries. Widespread food-borne outbreaks are being identified more often, partly because of better surveillance and reporting, and because of the greater centralization of food processing and distribution practices.

Although they accounted for disproportionate numbers of serious illness and deaths, the 120 multi-state outbreaks were in a sense the tip of the iceberg. Over the five-year period, the C.D.C. reported 4,163 cases of food-borne disease outbreaks, or an average of more than two a day. More than 71,000 people were sickened, 4,247 were hospitalized, and 118 died.

“These outbreaks are a big problem and our goal is to prevent them,” said the lead author of the report, Samuel J. Crowe, an epidemiologist at the C.D.C. “We want to detect quickly, trace the food back to its source, and learn where the food was contaminated.”

Video: Chasing Outbreaks: How Safe Is Our Food?

A 1993 E. coli outbreak linked to Jack in the Box hamburgers sickened 700 people and drew new attention to the dangers of food-borne illness. More than 20 years later, how far have we come? By Retro Report on Publish Date May 10, 2015. Watch in Times Video »

http://bit.ly/1TXJlHw

Your Hair Mites Are So Loyal Their DNA Reflects Your Ancestry

Mite DNA could hold clues to ancient human migrations and future skin health

By Brian Handwerk

Most people would probably prefer to forget that their eyebrows are also shaggy ecosystems, home to scores of microscopic hair mites. But a DNA analysis reveals that your mites are incredibly loyal to you—and that could help scientists trace ancient human migrations and perhaps find new ways to treat common skin ailments.

Demodex folliculorum is a species of mite that lives in and around the hair follicles of humans and other mammals. Bowdoin College evolutionary geneticist Michael Palopoli and his colleagues sampled the DNA of these mites living on a diverse group of 70 human hosts.

Sequencing the mites' mitochondrial DNA revealed different lineages that closely match the ancestral geography of their human hosts. One mite lineage is common among people of European ancestry, no matter where they live in the world now, and is persistent even after generations in new locations. Other mite lineages are more common among people of Asian, African or Latin American ancestry.

There are a few possible reasons for this unusual mite fidelity, says Palopoli. His group favors the co-called skin traits model: “There may be something about the skin of people from different geographic origins that may be selecting for mites from different mitochondrial lineages,” he explains. “But we don't know what it might be about the skin that may be selecting for one lineage of mites over another.”

Following this line of inquiry could help researchers solve mysteries of how and why otherwise benign mites have been previously linked to skin disorders such as rosacea and blepharitis, or eyelid inflammation.

“One logical question that these results raise is whether one of these different, diverging mitochondrial lineages of mites might tend to be more or less likely than another in causing skin disorders," says Palopoli. "Maybe a mite from one mitochondrial lineage is particularly likely to cause rosacea. That could be really important, but we just don't know at this point.”

Mining the DNA sequences of our faithful mite pals could also provide a new tool for scientists to trace ancient human migrations.

George Perry, who heads an anthropological genomics lab at Pennsylvania State University, notes that some interesting findings have emerged from research on the various species that live with us, whether we like them or not.

“Probably the most widely studied is the stomach bacteria Helicobacter pylori,” he notes. “It's nearly ubiquitous in developing countries, and it closely tracks a lot of human migration movements.” Interesting theories of human history have also emerged from studies of head lice, he adds.

“There's a hypothesis that one ancient lineage of Pediculus humanus is the result of an archaic hominin speciation event, and then was transmitted by direct physical contact between those hominins and modern humans," Perry says. "So this theory suggests that although those hominins are now extinct, we still have their lice.”

The study by Palopoli and his colleagues, published this week in the Proceedings of the National Academy of Sciences, may add hair mites to the mix of species that can help track our species' history.

“We've got these genetically diverse mite lineages existing on all of us, and that provides a wealth of information, potentially, for unraveling different human migration patterns,” Palopoli said.

So far, the early exploration of mite lineages appears to tell a story consistent with the favored "out of Africa" model for human migration, which says that all humans alive today come from a group that left Africa about two million years ago.

“All four of the diverging clades appear in the mites on people of African ancestry, while only subsets appear on Europeans or Asians," says Palopoli. "So our hypothesis is that all four clades were present on us when we lived in Africa, but since we've come out, different subsets have migrated along with Asians and Europeans.”

Sampling mites from a wider variety of human ancestries, including more people now living in Africa, could help reveal how the mites and humans co-evolved.

“It looks like the mites are fairly faithful to people from a particular region, at least at this broad scale we've looked at so far, and the signal still remains that mites vary substantially in people from across different geographic areas, so it provides promise as a system to test where people are from,” Palopoli adds.

Using the mites for evidence of our origins may also spur more interest in understanding the habits of our largely unknown life partners. But breeding more familiarity with our hair mites could take some getting used to. Human test subjects typically had two reactions to seeing the minute beasties who've been living in their hair, Palopoli reports. “One reaction is that they were sort of fascinated with them. The other reaction is that they were pretty grossed out.”

http://www.eurekalert.org/pub_releases/2015-12/p-hzi121015.php

Herpes zoster is linked to increased rates of both stroke and myocardial infarction

Shingles is linked to a transient increased risk of stroke and myocardial infarction

Herpes zoster (also called "shingles") is linked to a transient increased risk of stroke and myocardial infarction (MI) in the months following initial zoster diagnosis, according to a study published by Caroline Minassian and colleagues from the London School of Hygiene and Tropical Medicine, UK, published in this week's PLOS Medicine.

The researchers identified 42,954 Medicare beneficiaries aged ?65 years who had had a herpes zoster diagnosis and an ischemic stroke and 24,237 beneficiaries who had had a herpes zoster diagnosis and an MI during a 5-year period. They then calculated age-adjusted incidence ratios for stroke and MI during pre-defined periods up to 12 months after a diagnosis of zoster relative to time periods when the patient did not have recent zoster (the baseline period). Compared to the baseline period, there was a 2.4-fold increased rate of ischemic stroke and a 1.7-fold increased rate of MI in the first week after herpes zoster. The increased rate of acute cardiovascular events reduced gradually over the 6 months following herpes zoster. There was no evidence that MI or ischemic stroke incidence ratios varied between individuals who had been vaccinated against zoster and those who had not been vaccinated.

While the researchers used a self-controlled case series design that controls for fixed confounders, residual confounding by time-varying factors such as major life events or stress may limit the accuracy of the findings. Furthermore, only a few participants in the study were vaccinated, which limits the study's power to detect an effect of vaccination.

The authors say "These findings enhance our understanding of the temporality and magnitude of the association between zoster and acute cardiovascular events."

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Competing Interests:

I have read the journal's policy and the authors of this manuscript have the following competing interests: LS has undertaken consultancy for GlaxoSmithKline (GSK). ID has consulted for Gilead and GSK and holds stock in GSK. GSK does not currently market a zoster vaccine. The authors declare no other competing interests.

Citation:

Minassian C, Thomas SL, Smeeth L, Douglas I, Brauer R, Langan SM (2015) Acute Cardiovascular Events after Herpes Zoster: A Self-Controlled Case Series Analysis in Vaccinated and Unvaccinated Older Residents of the United States. PLoS Med 12(12): e1001919. doi:10.1371/journal.pmed.1001919

http://www.eurekalert.org/pub_releases/2015-12/rumc-noq121515.php

Not ordinary growing pains

Study finds acupuncture effective treatment for chronic pain in children

It is upsetting to see anyone in pain, but it's especially heartbreaking to watch a child endure chronic pain.

In addition to the suffering itself, chronic pain can cause traumatic effects on a child's quality of life, and it can have significant physical, psychological and social consequences. Making matters worse, chronic pain greatly can affect the child's parents or caregivers by causing feelings of helplessness and inadequacy.

Treating children with chronic pain can be complex, due to kids' vulnerability while they're growing and fear of causing long-term effects. Data about the safety and efficacy of therapeutic options for children is limited.

"Effective treatment of pain can be particularly difficult because it's subjective; but with children, it is increasingly difficult because a child may not be able to communicate effectively depending on the age and accurate recognition of pain," says Angela Johnson, MSTOM, MPH, practitioner of Chinese medicine of Rush's Cancer Integrative Medicine Program.

Johnson led a recent study at Rush that found that acupuncture may be a safe and effective adjunctive integrative medicine treatment for chronic pain in pediatric patients. Results of the study were published in the December 2015 issue of Alternative and Complementary Therapies.

"While acupuncture has been shown to reduce pain in adults, there is very little data on whether it's effective in children." Johnson says. "This study looked at the effect of acupuncture in children directly, rather than examining data collected from adults. This focus is especially important, since children experience pain in different ways than adults."

Not stuck with pain

Chronic pain is pain that lasts weeks, months, or even years, and is estimated to affect 20 to 35 percent of children under age 18 worldwide. Conditions that can cause chronic pain in children include headaches, abdominal pain, back pain, musculoskeletal pain, scoliosis, leukemia, sports injuries and Crohn's disease.

The Rush study included 55 children and adolescents between age 7 and 20 who experienced chronic pain conditions. Each patient received up to eight individually tailored acupuncture treatments at Rush lasting 30 minutes.

All patients reported significant and progressive declines across all levels of pain throughout the eight-session treatment, with stronger pain reductions during early treatment. Participants also reported substantial pain reductions from the start to the end of each session. Additionally, patients reported significant reductions in health, emotional, social, and educational problems. These findings were corroborated by similar reductions in parent-reported observations of the same issues.

"Acupuncture provides an amazing alternative to chronic pain medication. This is especially true for patients who may have to cope with pain for most of their life, including those who have sickle cell anemia and aftereffects of cancer. In addition it helps with anxiety and depression," says Paul Kent, MD, co-principal investigator of the study and pediatric oncologist at Rush.

I've had patients completely weaned off all their pain medications when receiving acupuncture therapy. It is also benefited patients who struggle with chronic nausea."

To measure self-reported intensity, location and quality of pain, the study used the Adolescent Pediatric Pain Tool, which assesses pain using the following criteria:

A body outline diagram to identify pain areas.

A pain-intensity score measured on a 10-centimeter line anchored by the words "no pain," "little," "medium," "large" and "worst possible pain."

A number of pain-quality descriptors, yielding both a tallied score indicating number of words circled (circle scores), and tallied scores for sensory, affective, temporal and evaluative pain quality subscales. Higher circle scores indicate a greater subjective experience of pain, higher measurement scores indicate higher levels of pain intensity, and pain-quality descriptors (sensory, affective, temporal and evaluative) help describe the pain experience.

This study contributes to the sparse literature on the use of acupuncture in a pediatric population, and supports acupuncture's feasibility as an effective strategy for managing chronic pain.

"The results of this study suggest that acupuncture can have a profound positive impact on the health and well-being of children who experience the disabling effects of chronic pain," Johnson says. She hopes to expand her research to larger groups of children in order to understand more about how acupuncture can help relieve their chronic pain.

"Like any good doctors, we want to reduce children's suffering," she says, "and we hope that this study will be a first step in our being able to do more for these kids."

http://www.eurekalert.org/pub_releases/2015-12/kp-svh121515.php

Shingles vaccine helps protect older patients with end-stage renal disease

Kaiser Permanente study advances knowledge about safety and effectiveness of vaccine commonly given to older adults

PASADENA, Calif - Elderly patients with end-stage renal disease (ESRD) who received the shingles vaccine were half as likely to develop shingles compared to those who were not vaccinated. The new study from Kaiser Permanente, published in Clinical Infectious Diseases, also found the best protection against shingles was achieved when patients received the vaccination shortly after beginning dialysis.

Shingles (also known as herpes zoster) is a painful skin rash that affects one in three adults and is caused by the varicella zoster virus, the same virus that causes chickenpox. The shingles vaccine is recommended for adults 60 and older. With ESRD, the kidneys stop working, requiring patients to undergo either dialysis or an organ transplant. Patients with ESRD are at greater risk than the general population for a variety of infections, including a 72 percent increased risk of developing shingles.

"Previously the shingles vaccine was not widely given to patients on dialysis due to concerns of possible side effects and questions regarding its efficacy. Our study offers new real-world data to support the Centers for Disease Control's recommendation that elderly patients with chronic renal failure receive the shingles vaccine, if medically eligible," said Hung Fu Tseng, PhD, MPH, study lead author, Kaiser Permanente Southern California Department of Research & Evaluation.

This study is part of Kaiser Permanente's ongoing efforts to better understand the safety and effectiveness of shingles vaccines. In a study published earlier this year, Kaiser Permanente researchers found that people who received a vaccination for shingles but still contracted shingles had a lower risk of developing post-herpetic neuralgia (or PHN), a potentially long lasting and painful complication of the condition. In addition, in research published last year, Kaiser Permanente researchers found the shingles vaccine continues to be effective in protecting older adults against shingles, even after they undergo chemotherapy.

The ESRD study population consisted of patients 60 years and older on chronic dialysis who were members of Kaiser Permanente in Southern California. Researchers followed 582 patients who received the shingles vaccine from January 2007 through December 2013 and compared them with 2,910 ESRD patients during the same period who never received the vaccine. Researchers found:

The shingles vaccine was associated with a 50 percent lower incidence rate of shingles among ESRD patients

The three-year risk of shingles was 4.1 percent for those who were vaccinated and 6.6 percent for those who were not

If the vaccine was given within two years of beginning dialysis, the shingles incidence rate was less than one-third of the rate in unvaccinated individuals

Other authors of the study include Yi Luo, MS, Jiaxiao Shi, PhD, Lina S. Sy, MPH, Sara Tartof, MPH, PhD, John J. Sim, MD, Rulin Hechter MD, PhD and Steven J. Jacobsen, MD, PhD. All authors are with the Kaiser Permanente Southern California Department of Research & Evaluation, except for Dr. Sim, who is with the Division of Nephrology and Hypertension, Kaiser Permanente Los Angeles Medical Center.

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http://bit.ly/1QB1Q6Q

How Fermentation Gives Us Beer, Wine, Cheese—and Cancer?

Even in the presence of oxygen, cancer cells and some bacteria prefer fermentation, a new study finds

By Bret Stetka on December 15, 2015

In 1931 German physician, physiologist and biochemist Otto Heinrich Warburg won the Nobel Prize for his discovery that cancerous cells—unlike most healthy human cells, which produce energy using oxygen via respiration—favor the anaerobic process of fermentation, or the conversion of sugar into acids, gases or alcohol, even in the presence of oxygen. This has perplexed scientists ever since because fermentation is a far less efficient means of generating energy than aerobic metabolism, hence its pejorative tag as a “wasteful metabolism.”

But a team of scientists from the University of California, San Diego, has discovered that although oxygen-based metabolism is a more efficient means of energy production, the costs required to produce the molecular machinery that

drives respiration are twice those needed to ferment the sugar glucose. Their work could have implications in identifying potential targets in treating cancer.

The team measured what is called proteome allocation—or the fraction of all cellular proteins devoted to various tasks—to determine the metabolic costs of generating energy and cell growth in Escherichia coli bacteria. The enzymes that facilitate respiration—the raw machinery that normally supports human cellular life—are large and lumbering and need to be produced prolifically to keep us, and our steadily growing cells, going. Put another way, a higher percentage of a fast-growing cell's proteome is dedicated to growth whereas a smaller fraction is available for other cellular processes, including energy production.

University of California, San Diego, physics and biology professor Terry Hwa, who led the study, likens his findings, recently published in Nature, to coal versus nuclear energy. "Coal factories produce energy less efficiently than nuclear power plants on a per-carbon basis, but they are a lot cheaper to build," he said in a statement. So the decision of which route to generate energy depends on the availability of coal and the available budget for building power plants." Fast-growing cells find fermentation the cheaper path. In this sense it is coal energy for cells. (Scientific American is part of Nature Publishing Group.)

The idea that cellular metabolism and growth might be based on the cost-benefit balance of producing the proteins necessary to generate energy and grow was first proposed by a team of Dutch theoretical biologists in 2009. Hwa's findings confirm those findings. And although prevailing dogma views cancer as a genetic disorder—or really a complex of disorders caused by countless possible mutations—some researchers are coming around to the idea that the ultimate pathologic insult might be impaired or altered energy production.

Thomas Seyfried, a biologist at Boston College who was not part of this study, feels that cancer is a metabolic disorder, citing the large body of evidence implicating mitochondrial dysfunction in cancer. Mitochondria—or the "powerhouses" of our cells—are where cellular energy production takes place. "There is now substantial evidence from a broad range of disciplines showing some degree of defect in the number, structure or function of mitochondria in all types of tumor cells. These mitochondrial defects cause the enhanced glucose uptake and the fermentation seen in tumor cells," Seyfried explains.

In a 2014 paper by Seyfried and colleagues published in Carcinogenesis he cites ample evidence to support his claim, including showing that a cell's tumor potential is suppressed if it is transplanted with normal mitochondria; and conversely that transferring mitochondria from tumor cells into the cytoplasm of normal cells increases the chances that those once normal cells will become cancerous. He also points out the large body of work connecting the etiological dots: Many of the mutated genes associated with cancer seem to exert their effects by impairing cellular respiration. It is also possible, Seyfried strongly feels, that transitioning from respiration to fermentation produces free radicals that cause genetic mutations associated with cancer.

Seyfried also suggests a possible evolutionary explanation for fermentation in cancer cells, citing work by Carlos Sonnenschein and Ana Soto at Tufts University showing that the default state for cells is to proliferate, like cancer cells do, and that aerobic respiration in the mitochondria normally helps keep this growth in check. "Unbridled proliferation driven by fermentation metabolism was the state of existence for most cells before oxygen entered the atmosphere some two billion years ago," he explains. "A gradual loss of respiratory control together with a compensatory fermentation underlies the origin of cancer."

The association between energy production and cancer is likely far from being completely understood, and although Hwa cautions that he is not a cancer biologist, he feels there is definite promise in pursuing treatments that tinker with metabolism. "I can see that interfering with fermentation could be an effective strategy to slow down tumor growth," he explains, "since slow-growing cells rely more on respiration to generate energy—then, in principle, this treatment strategy is naturally more disruptive to fast-growing cancer cells than normal cells."

Current cancer treatment emphasizes interfering with cell signaling pathways that could lead to runaway cellular growth. "But from this study," Hwa says, "[we found] that maybe we don't need to be so concerned with signaling and could instead work to slow down the efficiency of fermentative processes. We can then count on cancer cells' growth to slow down as they shift to respiration."

As more and more mutations associated with varying cancers are uncovered, developing oncology therapies could seem a Sisyphean undertaking. But a single pathology—one that perhaps results in the mutations associated with cancer—could make developing effective cancer therapies a whole lot easier.

As Otto Warburg's work alluded to nearly a century ago, perhaps this entails simply encouraging cancer to take a breath of fresh air.

http://www.eurekalert.org/pub_releases/2015-12/uosf-ugf121515.php

USF geologists focus on mineral for clues to beginning of biological life on earth

In Earth's beginning, meteorites striking the planet to provide light may have carried an extraterrestrial mineral that, as it corroded in water, could have provided the essential chemical spark for the birth of biological life

On the early Earth, light came not only from the sun but also from the incessant bombardment of fireball meteorites continually striking the planet. Now, the

recent work of University of South Florida (USF) associate professor of geology Matthew Pasek, USF researcher Maheen Gull, and colleagues at Georgia Institute of Technology, has demonstrated that these meteorites may have carried within them an extraterrestrial mineral that, as it corroded in water on Earth, could have provided the essential chemical spark leading to the birth of biological life on the planet.

In previous work, Pasek and colleagues suggested that the ancient meteorites contained the iron-nickel phosphide mineral "schreibersite," and that when schreibersite came into contact with Earth's watery environment a phosphate, a salt, was released that scientists believe could have played a role in the development of "prebiotic" molecules.

This is a fragment of the Seymchan meteorite from Russia. The majority of this 6 inch meteorite consists of iron-nickel metal, and the darker-colored structure in the center is schreibersite. **University of South Florida**

In a recent study appearing in Nature Publishing Group's Scientific Reports, the researchers focused on the properties of schreibersite and conducted experiments with the mineral to better understand how - in a chemical reaction with the corrosive effects of water called "phosphorylation" - schreibersite could have provided the phosphate important to the emergence of early biological life.

"Up to ten percent of the Earth's crustal phosphate may have originated from schreibersite, so the mineral was abundant and readily available to engage in early chemical reactions," said Pasek. "This ready and abundant source of reactive phosphorous may have been an important part of the prebiotic Earth and possibly the planet Mars," said Pasek.

What needed to be determined, however, was just how schreibersite reacted chemically with the early Earth's watery environment and what resulted from the chemical reaction.

To test their hypothesis, they built an early Earth model environment, an organic-rich aqueous solution in which schreibersite might react and corrode in a way similar to how events may have unfolded in prebiotic chemistry. The model they constructed provided an opportunity to observe the thermodynamics of phosphorylation reactions of a phosphorus-containing synthetic schreibersite, which they created to be structurally identical to its meteorite counterpart.

"A thorough exploration of the extent of phosphorylation of nucleosides (made of a base and a five carbon sugar) by schreibersite was necessary to evaluate its potential prebiotic importance," explained Gull, a post-doctoral fellow and visiting researcher at USF. "All of our experiments indicated that a basic pH, rather than acidic pH, was required for the production of phosphorylated products. Although phosphorylation can take place using a variety of phosphate minerals in non-aqueous solution, prebiotic oxidation in water is more likely given the dominance of water across the solar system."

The prebiotic reaction they duplicated in the laboratory may have been similar to the reactions that ultimately led to the emergence of metabolic molecules, such as adenosine triphosphate (ATP), which is called the 'molecule of life' because it is central to energy metabolism in all life.

Pasek and Gull also explained that even life today builds from activated nucleotides and that phosphates are still an important part of metabolic processes in biological life, so it is likely that a phosphorylated biomolecule played an important part in creating the prebiotic chemical context from which biological life emerged. Prior work on nucleoside phosphorylation has shown that inorganic phosphate can serve as both a catalyst and a reactant in nucleoside synthesis, they said.

"The reactions we observed in our experiments have shown that the necessary prebiotic molecules were likely present on the early Earth and that the Earth was predisposed to phosphorylated biomolecules," the researchers concluded. "Our results suggest a potential role for meteoritic phosphorus in the development and origin of early life."

The researchers also concluded that the mechanism of phosphorylation was still unknown and actively being investigated. "It is possible that the process occurs in solution or on the surface of the schreibersite," they explained.

http://www.eurekalert.org/pub_releases/2015-12/nch-aac121415.php

Antibiotics alone can be a safe, effective treatment for children with appendicitis

Using antibiotics alone to treat children with uncomplicated acute appendicitis is a reasonable alternative to surgery when chosen by the family.

A study led by researchers at Nationwide Children's Hospital found that three out of four children with uncomplicated appendicitis have been successfully treated with antibiotics alone at one year follow-up. Compared to urgent appendectomy, non-operative management was associated with less recovery time, lower health costs and no difference in the rate of complications at one year.

"Families who choose to treat their child's appendicitis with antibiotics, even those who ended up with an appendectomy because the antibiotics didn't work, have expressed that for them it was worth it to try antibiotics to avoid surgery," said Peter C. Minneci, MD who led the study published online Dec. 16 in JAMA

Surgery with Katherine J. Deans, MD. The pair are co-directors of the Center for Surgical Outcomes Research and principal investigators in the Center for Innovation in Pediatric Practice in The Research Institute at Nationwide Children's. "These patients avoided the risks of surgery and anesthesia, and they quickly went back to their activities."

"Surgery has long been the 'gold standard' of care for treating appendicitis because by removing the appendix we eliminate the chance that the appendicitis will ever come back," said Dr. Deans. "However, early in our careers we noticed that patients with appendicitis who were placed on antibiotics overnight until their surgery the following morning felt better the next day. So, Pete and I asked ourselves: do they really need to have surgery?"

In the first study conducted and published in the United States examining non-operative management for appendicitis, they enrolled 102 patients age 7 to 17 who were diagnosed with uncomplicated acute appendicitis at Nationwide Children's between October 2012 and October 2013. Participants had early/mild appendicitis, meaning that they experienced abdominal pain for no more than 48 hours; had a white blood cell count below 18,000; underwent an ultrasound or CT scan to rule out rupture and to verify that their appendix was 1.1 centimeter thick or smaller; and had no evidence of an abscess or fecalith, which is hard stone-like piece of stool.

Thirty-seven families chose antibiotics alone and 65 opted for surgery. Those patients in the non-operative group were admitted to the hospital and received IV antibiotics for at least 24 hours, followed by oral antibiotics after discharge for a total of 10 days. Among those patients, 95% showed improvement within 24 hours and were discharged without undergoing surgery. Rates of appendicitis-related medical care within 30 days were similar between the groups with two patients in the non-operative group readmitted within 30 days for an appendectomy. At one year after discharge, three out of four patients in the non-operative group did not have appendicitis again and have not undergone surgery.

Appendicitis, caused by a bacterial infection in the appendix, is the most common reason for emergency abdominal surgery in children, sending more than 70,000 young people to the operating room each year. Although many of these cases are severe and require surgery, there are a good number that would be candidates for treatment with antibiotics alone, Dr. Minneci said.

"We believe that the results of our study reflect the effectiveness of offering non-operative management to patients and their families in clinical practice. The patient choice design allows the patient and family's preference to be aligned with their choice of therapy," said Dr. Deans. "Most parents are concerned about having surgery, in general. They're also very concerned about anesthesia. Some parents are very concerned about appendicitis coming back. It's really a matter of aligning your preferences, your values, what you think is most important to you, with the treatment that is best for you and your family."

For example, explained Dr. Minneci, if the family is so afraid of a recurrence that they visit the Emergency Department every time their child has abdominal pain, then their child will likely undergo increased imaging and eventually undergo an appendectomy. In that case, letting them choose an appendectomy upfront may be better for the child.

According to the study results, patients who were transferred to Nationwide Children's from other institutions expressed concerns about the distance and time necessary to come back if the appendicitis recurred. These families opted for surgery more often. Patients whose families spoke primary languages other than English were more likely to choose antibiotics as a course of treatment due to cultural values to avoid surgery if at all possible.

Both researchers, who are also Assistant Professors of Surgery and Pediatrics in The Ohio State University College of Medicine, say further studies are needed to see if the results they saw in this study apply in other health systems, and emphasize that the perceptions of both patient-families and surgeons can impact the study results. Their intention is to follow all the children in this study as long as possible to see if those treated with non-operative management continue to thrive.

Minneci PC, Mahida JB, Lodwick, DL, Sulkowski JP, Nacion KM, Cooper JN, Ambeba, EJ, Moss RL, Deans KJ. The effectiveness of patient choice in non-operative versus surgical management of uncomplicated acute appendicitis. JAMA Surgery. 2015 Dec 16 [Epub ahead of print].

http://www.eurekalert.org/pub_releases/2015-12/uosc-urd121115.php

USC researchers discover way to improve image sharpness for blind people with retinal implants

Longer pulses of electrical current allow patients to see focused spots of light

LOS ANGELES -- Retinal implants that deliver longer pulses of electrical current may noticeably improve image sharpness for individuals who have lost their sight due to retinitis pigmentosa, according to a new study by researchers from the USC Eye Institute and USC Viterbi School of Engineering.

The research will be published in the peer-reviewed journal Science Translational Medicine online on Dec. 16, 2015.

Retinitis pigmentosa (RP) is an inherited disease of the eye that causes blindness through gradual degeneration of photoreceptors, the light-sensing cells in the retina. The disease affects about one in 4,000 people.

Retinal implants (artificial retinas) give people with RP the ability to perceive light, using a system that includes a video camera mounted on a pair of eyeglasses, a video processing unit that transforms images from the camera into wirelessly transmitted electronic signals, and an implanted array of electrodes to stimulate visual neurons.

Retinal implants have enabled blind individuals to detect motion and locate large objects. However, because the implants may unintentionally stimulate axons in the retina, patients sometimes see large oblong shapes of light that reduce the quality of their vision. In order for patients to see more clearly, the images created by the implant should be composed of focal spots of light.

Current implant technology stimulates the retina with brief pulses of electrical current roughly 0.5 millisecond (ms) in duration. The researchers found that increasing the duration of the stimulus pulses allows visualization of distinct focal spots of light.

"This is a huge step forward in helping restore sight for people with retinitis pigmentosa," said Andrew Weitz, PhD, assistant professor of research ophthalmology. "Being able to create focused spots of light is important. Think of each light spot as a pixel in an image. By arranging many light spots into the shape of an object, we can generate sharp images of that object. For those of us who wear glasses, imagine the difference between trying to read a distant neon sign with and without your glasses on. For people with retinal implants, being able to see more clearly should have a big impact on their ability to recognize objects and navigate their environments. These improvements in vision can really boost a person's sense of independence and confidence."

The researchers tested various stimulus pulse durations in an animal model and validated their findings in a patient with an early version of the Argus retinal implant (Second Sight Medical Products, Inc.). The results indicated that longer pulse durations allowed the retina to be stimulated more precisely. In the animal model, all pulses 8 ms and shorter activated axons, obscuring the ability to generate a focal spot of light. Sixteen-millisecond pulses also stimulated axons but to a much lesser extent. Pulses 25 ms and longer produced no evidence of axonal stimulation, instead resulting in focal spots of light.

"Our findings further support that it is possible for patients with RP to see forms using artificial vision," said James Weiland, PhD, professor of ophthalmology and biomedical engineering. "This makes a strong case for developing high-resolution retinal implants."

This research was conducted through a partnership between the USC Eye Institute and USC's schools of medicine and engineering: the Viterbi School of Engineering Department of Biomedical Engineering and Ming Hsieh Department of Electrical Engineering; Keck School of Medicine's Departments of Ophthalmology, and of Physiology and Biophysics; and device manufacturer Second Sight Medical Products Inc., in Sylmar, CA.

Researchers who contributed to the study include: Andrew C. Weitz (Department of Ophthalmology, Department of Biomedical Engineering); Devyani Nanduri (Department of Biomedical Engineering); Matthew R. Behrend (Ming Hsieh Department of Electrical Engineering); Alejandra Gonzalez-Calle (Department of Biomedical Engineering); Robert J. Greenberg (Second Sight Medical Products Inc.,); Mark S. Humayun (Department of Ophthalmology, Department of Biomedical Engineering); Robert H. Chow (Department of Physiology and Biophysics, Department of Biomedical Engineering); and James D. Weiland (Department of Ophthalmology, Department of Biomedical Engineering).

http://bit.ly/1UV6tHO

Toxic Algae Causing Brain Damage in Sea Lions along California Coast

Brain scans reveal damage that leads to neurological and behavioral changes, including beach strandings

Reporting by Will Dunham; Editing by Peter Cooney

A toxin produced by marine algae is inflicting brain damage on sea lions along California's coast, causing neurological and behavioral changes that can impair their ability to navigate in the sea and survive in the wild, scientists said on Monday. Brain scans on 30 California sea lions detected damage in the hippocampus, a brain structure associated with memory and spatial navigation, in animals naturally exposed to the toxin known as domoic acid, the researchers said.

Domoic acid mimics glutamate, a chemical that transmits nerve impulses in the brain, and leads to over-activation of hippocampus nerve cells and chronic epilepsy, according to Emory University cognitive psychologist Peter Cook, who worked on the study while at the University of California-Santa Cruz. "The behavioral deficits accompanying brain damage with domoic acid are severe, and may negatively impact foraging and navigation in sea lions, driving strandings and mortality," Cook said.

Hundreds of sea lions annually are found stranded on California beaches with signs of domoic acid poisoning such as disorientation and seizures. Thousands are thought to be exposed to the toxin.

The microscopic algae, called Pseudo-nitzschia, responsible for the toxin occur naturally in coastal waters. Their blooms have become more frequent and severe in recent years. This year's bloom was the largest on record, reaching from Santa Barbara, California to Alaska.

Ocean pollution from chemicals like fertilizers and warming ocean temperatures associated with global climate change are believed to contribute to bloom size and frequency. The toxin accumulates in shellfish and small fish that consume algae.

Sea lions, other marine mammals and seabirds are exposed to it after eating those shellfish and fish.

"Domoic acid-producing blooms have been in the environment for a very long time, but the current pattern of much larger and more frequent blooms causing more visible damage to marine animals has been going on since the 1980s," Cook said.

Sea lions exposed to the toxin had greatly reduced connectivity between the hippocampus and the thalamus, a brain structure associated with sensory perception and regulation of motor functions. Those with hippocampus damage also performed worse on memory tasks such as one involving finding a food reward.

"Hundreds of sea lions end up in stranding facilities each year. A great many of them do die although some can be rehabilitated and survive for some time in the wild," Cook said.

http://bit.ly/1NxMyfe

Humans Caused a Major Shift in Earth's Ecosystems 6,000 Years Ago

We upended a pattern held for 300 million years, and that may mean we are causing a new phase in global evolution

By Kimbra Cutlip

It's hard to imagine a global force strong enough to change natural patterns that have persisted on Earth for more than 300 million years, but a new study shows that human beings have been doing exactly that for about 6,000 years.

The increase in human activity, perhaps tied to population growth and the spread of agriculture, seems to have upended the way plants and animals distribute themselves across the land, so that species today are far more segregated than they've been at any other time.

That's the conclusion of a study appearing this week in the journal Nature, and the ramifications could be huge, heralding a new stage in global evolution as dramatic as the shift from single-celled microbes to complex organisms.

A team of researchers led by S. Kathleen Lyons, a paleobiologist at the Evolution of Terrestrial Ecosystems (ETE) program in the Smithsonian's National Museum of Natural History, examined the distribution of plants and animals across landscapes in the present and back through the fossil record in search of patterns.

Mostly they found randomness, but throughout time, there was always a small subset of plants and animals that showed up in relationship to one another more often than can be attributed to chance. That relationship either meant that pairs of species occur together, so when you find one, you usually find the other. Or it meant the opposite: when you find one, the other is usually not present, in which case they're considered segregated.

An example would be that where there are cheetahs, you often find giraffes, because they prefer the same habitat. Predator-prey relationships can also cause animals to co-exist on the landscape, as in the case of dire wolves and giant ground sloths in the late Pleistocene. It's believed that dire wolves may have preyed on baby giant ground sloths.

On the flip side, segregated animals are those that appear together less often than they would by chance alone. Today, Grevy's zebra and colobus monkeys are rarely found together because they have evolved to exploit different landscapes.

The surprise discovery was that for 300 million years, it was more common for species pairs to occur together—to aggregate on a landscape—than it was for them to segregate. Then the pattern flipped around 6,000 years ago in North America. Around the same time the human population was expanding and becoming dependent on agriculture, plant and animal communities shifted to a pattern dominated by segregation.

Lyons and her colleagues looked at nearly 360,000 pairs of organisms from 80 communities on different continents, but the best data available to them around the time period in question came predominantly from North America. Lyons expects the pattern shift will be evident around the globe if other researchers look for it.

"It's striking that there's a community structure that is changing in ways it hasn't changed before and that appears to be associated with humans," says Erle Ellis, a professor of geography and environmental systems at the University of Maryland and a member of the International Union of Geological Sciences Anthropocene Working Group. "I would say it's one of the most interesting indicators I've ever seen of a shift in the biosphere associated with humans."

The scientists can't say exactly why the shift occurs at this distinct moment in human history, but they've gone to great lengths to rule out other possible connections, including examining ice cores to get at past climate conditions. There have been many periods of natural climate variability over those 300 million years, and still the pattern held steady, with an average of 64 percent of species pairs with significant relationships being aggregated.

After the shift 6,000 years ago, the average dropped to 37 percent. Today, a significant relationship between a pair of species is more likely to mean where you find one, you don't find the other. In other words, species are more segregated than they've ever been.

Though there's no smoking gun, Lyons has thoughts on the role humans played in this change. "We're living in a lot of areas where species used to overlap their

distributions," she says. "They don't overlap anymore because they can't get through the areas where we're living now."

Gregory Dietl, a paleoecologist and Curator of Cenozoic Invertebrates at the Paleontological Research Institution in Ithaca, New York, says that this break in a 300-million-year-old pattern signals that we're living in a new world, and that makes it more challenging to use the past to predict what may happen in the future. "For me that was the big piece," he says. "What does this more segregated pattern mean then, ultimately, for how species may adapt or just respond to climate change in the future?"

Dietl wrote a review of the study that also appears in the same issue of Nature. Like many of his colleagues who have seen the paper, he believes it's reasonable that increased segregation may make species more vulnerable to changes in their environment.

"It probably means species are more vulnerable to extinction because there are fewer connections between them," Lyons says. Humans have broken up plant and animal populations by destroying and fragmenting habitats. Their ranges are smaller, and no longer overlap in the way they once did.

"And because their geographic ranges are smaller, their abundances are almost certainly smaller." But understanding how environmental changes will impact species is far more difficult in a world without clear examples from the past to rely on.

Whether more plants and animals adapt or go extinct in the future, this dramatic shift in the past highlights the extent of human influences that have prompted the official naming of a new age: the Anthropocene.

"There's a tendency to think humans did not become a transformative force until fairly recently," says Ellis. "But this effect can be placed at the very beginnings of agriculture. So it's a very early indicator. The process of humans becoming distinct from other species and the way they transformed the Earth is really the cause of the Anthropocene. So this [study] is interesting in terms of asking where and when did this train leave the station?"

Discover why scientists think we are in a new geologic age and what it means for our future.

However, this study is not likely to help set the date scientists will use to mark the start of the Anthropocene. The Anthropocene Working Group is due to make that decision in 2016, and they're more likely to rely on the accepted practice of identifying a well-defined line in the sand—or in most cases, the rock—that represents the sum of environmental changes denoting the shift from one time period to the next.

Chair of the working group and professor of paleobiology at the University of Leicester, Jan Zalasiewicz, says that line is likely to have been drawn in 1952, when fallout from thermonuclear weapons tests deposited a distinct radioactive signature in sediment around the world.

"Radionuclides do not represent as big a change to the Earth system as do the changes in population dynamics described in the paper, but they do provide a sharper time marker," he wrote in an e-mail. And that's what the working group is looking for. What the current paper contributes to the discussion, however, may be something even bigger on Zalasiewicz's radar.

"This adds weight to the increasing impression that the Anthropocene is not simply different from the Holocene, but differs in some important respects also from all previous historical episodes on this planet," he wrote.

Zalasiewicz was one of the coauthors on a recent paper in The Anthropocene Review proposing that the significant impacts humans are making to life on the planet could be the start of a long transition to something completely new—a third stage in evolution.

The previous transition from single-celled organisms to complex life took roughly 100 million years, so it's not unreasonable to suggest that we're initiating a (very long-term) change in course for the biosphere.

Proponents of such a transition point to the global homogenization of plants and animals, the introduction of vast amounts of new energy into Earth's system from the burning of fossil fuels, the increasing integration of technology into a global network of human interactions and the dominance of a single species, Homo sapiens, directing the evolution of other species.

If Lyons's results can be replicated in the fossil record in other parts of the world, it would prove that our global influence on the evolution of life on Earth began thousands of years ago.

"I have to say that this result is so striking that I think it's going to keep a lot of scientists busy trying to decipher this," Ellis says. "They're opening up a door to a whole new way of looking at changes in the Earth system, changes in the biosphere, changes induced by humans. This isn't the final word, but it's the opening salvo to a discussion on it."

UPDATE 12/17/2015: A previous version of this article stated that elephants and giraffes form a "significant pair," when it should be giraffes and cheetahs, and that significant pairs of animals that are aggregated "always" are found together, and segregated animals are "never" seen together.

http://www.eurekalert.org/pub_releases/2015-12/oup-ivg121715.php

In vitro gametogenes: Just another way to have a baby?

How in vitro gametogenesis could create the possibility of same-sex couples having children biologically related to both partners

New analysis by a George Washington University academic examines the possibility of using in vitro gametogenesis (IVG) for human reproduction and its ethical and practical implications. The paper is published today (Friday) in the Journal of Law and the Biosciences.

IVG is the method, most advanced in mice, by which gametes are derived from pluripotent stem cells (capable of giving rise to several different cell types) or embryonic stem cells. IVG in humans could potentially allow for never-before used methods of procreation. Research suggests that whilst not yet advanced enough on human cells, IVG for reproduction may one day be possible in humans.

Using a relational autonomy framework, Professor Sonia Suter analyses the potential benefits and harms of IVG, which depend on the social, scientific, and legal contexts in which it is used. As enormous developments are necessary before IVG could be used in humans, Professor Suter comments that: "the ethical dilemmas about when and how such research should be done will be enormously challenging."

Several groups of people could potentially use IVG for reproduction: those who cannot conceive for physical reasons, same-sex couples, postmenopausal women or premenarche girls, and groups of more than two - multiplex parenting.

Same-sex couples must currently rely on gamete donors when using assisted reproductive technologies (ART) such as artificial insemination or IVF with a surrogate. What distinguishes IVG from current ART is that it would allow such couples to have biologically related children without using gamete donors. For example, a gamete of the opposite sex could be derived from an individual's cells. This in combination with a naturally derived gamete from the other member of the couple could be used to produce an embryo.

Professor Suter also discusses the implications of 'perfecting reproduction' with IVG. She explains: "IVG could play a role in efforts to have a healthy or enhanced child" by making prenatal selection "much easier and more robust." It could, for example, be used to create many more embryos for preimplantation genetic diagnosis than we can today, vastly refining the ability to select embryos.

Perhaps most crucial to the future use of IVG, as she also points out, are the potential risks of the procedure. "We have minimal knowledge," Suter says, "about the implications of switching cell types from differentiated to undifferentiated states and the implications of erasing and resetting imprinting patterns to facilitate reproduction. The only way to demonstrate the effectiveness and safety of these techniques in humans is to use in vitro gametes to try to produce viable offspring in controlled settings - when and if we deem it sufficiently safe to do so."

Despite concerns over the risks and the fact that the technology is still a way off, Professor Suter concludes that, given that we support ART as a society, in many ways, IVG may be just another way to have a baby.

http://www.eurekalert.org/pub_releases/2015-12/uons-dc121415.php

'Red Deer Cave people' bone points to mysterious species of pre-modern human

A thigh bone found in China suggests an ancient species of human thought to be long extinct may have survived until as recently as the end of the last Ice Age.

Sydney -- The 14,000 year old bone -- found among the remains of China's enigmatic 'Red Deer Cave people' -- has been shown to have features that resemble those of some of the most ancient members of the human genus, (Homo), despite its young age.

The discovery was made by a joint team led by Associate Professor Darren Curnoe from UNSW Australia (The University of New South Wales) and Professor Ji Xueping from the Yunnan Institute of Cultural Relics and Archaeology (YICRA, China). Their study is published today in the journal PLOS ONE.

The findings result from a detailed study of the partial femur, which had lain unstudied for more than a quarter of a century in a museum in southeastern Yunnan, following its excavation along with other fossilised remains from Maludong ('Red Deer Cave') in 1989.

The investigators found that the thigh bone matched those from species like Homo habilis and early Homo erectus that lived more than 1.5 million years ago but are cautious about its identity. "Its young age suggests the possibility that primitive-looking humans could have survived until very late in our evolution, but we need to careful as it is just one bone," Professor Ji said.

The discovery is expected to be controversial because, until now, it had been thought that the youngest pre-modern humans on mainland Eurasia -- the Neanderthals of Europe and West Asia, and the 'Denisovans' of southern Siberia -- died out about 40,000 years ago, soon after modern humans entered the region.

"The new find hints at the possibility a pre-modern species may have overlapped in time with modern humans on mainland East Asia, but the case needs to be built up slowly with more bone discoveries," Associate Professor Curnoe said.

Like the primitive species Homo habilis, the Maludong thigh bone is very small; the shaft is narrow, with the outer layer of the shaft (or cortex) very thin; the walls

of the shaft are reinforced (or buttressed) in areas of high strain; the femur neck is long; and the place of muscle attachment for the primary flexor muscle of the hip (the lesser trochanter) is very large and faces strongly backwards.

Surprisingly, with a reconstructed body mass of about 50 kilograms, the individual was very small by pre-modern and Ice Age human standards.

When the team first announced the discovery of the remains of the Red Deer Cave people from Maludong (Red Deer Cave) in Yunnan Province and Longlin Cave in nearby Guangxi Zhuang Autonomous Region in 2012, it divided the scientific community. At the time, the UNSW-YICRA team speculated the bones could represent an unknown new species, or perhaps a very early and primitive-looking population of modern humans, which had migrated to the region more than a hundred thousand years ago.

"We published our findings on the skull bones first because we thought they'd be the most revealing, but we were amazed by our studies of the thigh bone, which showed it to be much more primitive than the skulls seem to be," Professor Ji said.

The new discovery once again points towards at least some of the bones from Maludong representing a mysterious pre-modern species. The team has suggested in another recent publication that the skull from Longlin Cave is probably a hybrid between modern humans and an unknown archaic group -- perhaps even the one represented by the Maludong thigh bone.

"The unique environment and climate of southwest China resulting from the uplift of the Tibetan Plateau may have provided a refuge for human diversity, perhaps with pre-modern groups surviving very late," Professor Ji said.

Associate Professor Curnoe said: "This is exciting because it shows the bones from Maludong, after 25 years of neglect, still have an incredible story to tell. There may have been a diversity of different kinds of human living until very recently in southwest China. "The riddle of the Red Deer Cave people gets even more challenging now: Just who were these mysterious Stone Age people? Why did they survive so late? And why only in tropical southwest China?"

http://www.eurekalert.org/pub_releases/2015-12/eic-taf121615.php

The awakened force of a star

Perfectly timed for the release of "Star Wars Episode VII: The Force Awakens", this NASA/ESA Hubble Space Telescope has imaged a cosmic double-bladed lightsabre.

In the centre of the image, partially obscured by a dark Jedi-like cloak of dust, an adolescent star shoots twin jets out into space, demonstrating the fearsome forces of the Universe. This celestial lightsabre lies not in a galaxy far, far away, but within our home galaxy, the Milky Way. More precisely, it resides within a turbulent patch of space known as the Orion B molecular cloud complex, which is located just over 1350 light-years away in the constellation of Orion (The Hunter).

Bearing a striking resemblance to Darth Maul's double-bladed lightsabre in Star Wars Episode One, the spectacular twin jets of material slicing across this incredible image are spewing out from a newly formed star that is obscured from view, cloaked by swirling dust and gas.

When stars form within giant, gaseous clouds, some of the surrounding material collapses down to form a rotating, flattened disc encircling the nascent stars, which are known as protostars. This disc is where a potential planetary system might form. However, at this early stage, the star is mostly concerned with feeding its Jabba-like appetite. Gas from the disc rains down onto the protostar and, once nourished, the star awakens and jets of energised gas from its poles whirl out in opposite directions.

The two lightsaber-like streams crossing the image are jets of energized gas, ejected from the poles of a young star. If the jets collide with the surrounding gas and dust they can clear vast spaces, and create curved shock waves, seen as knotted clumps called Herbig-Haro objects. **ESA/Hubble & NASA, D. Padgett (GSFC), T. Megeath (University of Toledo), and B. Reipurth (University of Hawaii)**

The Force is strong with these twin jets; their effect on their environment demonstrates the true power of the Dark Side with a blast stronger than one from a fully armed and operational Death Star battle station. As they stream away from one another at high speeds, supersonic shock fronts develop along the jets and heat the surrounding gas to thousands of degrees.

Furthermore, as the jets collide with the surrounding gas and dust and clear vast spaces, they create curved shock waves. These shockwaves are the hallmarks of Herbig-Haro (HH) objects -- tangled, knotted clumps of nebulosity. The prominent Herbig-Haro object shown in this image is HH 24.

Just to the right of the cloaked star, a couple of bright points of light can be seen. These are young stars peeking through and showing off their own faint lightsabres. One hidden, cloaked source, only detectable in the radio part of the spectrum, has

blasted a tunnel through the dark cloud in the upper left of the image with a wider outflow resembling "force lightning".

All these jets make HH 24 the densest concentration of HH jets known in such a small region. Half of the HH jets have been spotted in this region in visible light, and about the same number in the infrared. Hubble's observations for this image were performed in infrared light, which enabled the telescope to pierce through the gas and dust cocooning the newly-forming stars and capture a clear view of the HH objects that astronomers are looking for. *The Hubble Space Telescope is a project of international cooperation between ESA and NASA.*