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Drinking more water reduces bladder infections in women

Women who drank an additional 1.5 liters of water daily reduced repeat bladder infections by 48 percent

In the controlled trial, women who drank an additional 1.5 liters of water daily experienced 48 percent fewer repeat bladder infections than those who drank their usual volume of fluids, said senior author Dr. Yair Lotan, Professor of Urology and with the Simmons Cancer Center at UT Southwestern.

The participants self-reported their usual volume as less than 1.5 liters of fluid daily, which is about six 8-ounce glasses.

"That's a significant difference," said Dr. Lotan, Chief of Urologic Oncology at UT Southwestern Medical Center. "These findings are important because more than half of all women report having bladder infections, which are one of the most common infections in women."

More than a quarter of women experience a secondary infection within six months of an initial infection and 44 to 77 percent will have a recurrence within a year, said Dr. Lotan, holder of the Helen J. and Robert S. Strauss Professorship in Urology at UT Southwestern and Medical Director of the Urology Clinic at Parkland Health & Hospital System.

Physicians suspect more fluids help to reduce bacteria and limit the ability of bacteria to attach to the bladder.

Symptoms for acute uncomplicated cystitis, a type of urinary tract infection (UTI), include painful or difficulty in urination, a feeling of a full bladder, an urgency or frequency of urination, tenderness in the lower abdominal area, and possibly blood in the urine.

Because these infections are typically treated with antibiotics, the increased fluid could help reduce use of antibiotics and thereby help control antibiotic resistance, the researchers said.

The findings appear in *JAMA Internal Medicine*. Among the highlights over the 12-month study period:

- ***93 percent of women in the Water Group had two or fewer episodes of cystitis compared with 88 percent of women in the Control Group who had three or more episodes.***
- ***The number of cystitis episodes was about half in the Water Group compared with the Control Group.***
- ***Overall, there were 327 cystitis episodes: 111 in the Water Group and 216 in the Control Group.***
- ***The estimated mean annual number of antimicrobial regimens used to treat cystitis episodes was 1.9 in the Water Group compared with 3.6 in the Control Group.***
- ***The mean number of antimicrobial regimens used to treat cystitis episodes was 1.8 in the Water Group compared with 3.5 in the Control Group.***
- ***The mean time interval between cystitis events was 142.9 days in the Water Group compared with 85.2 days in the Control Group.***
- ***The median time to the first cystitis episode was 148 days in the Water Group compared with 93.5 days in the Control Group.***

Dr. Lotan, a member of UT Southwestern's Harold C. Simmons Comprehensive Cancer Center, uses minimally invasive, robotic, and open surgical techniques to treat bladder, prostate, kidney, ureteral, and testicular cancer.

He is nationally recognized for his research on urine markers in bladder cancer and molecular markers in other urologic cancers and was the first in North Texas to perform a robotic cystectomy, or removal of the bladder.

UT Southwestern's Urology Department developed the Snodgrass repair, a surgical procedure used around the world for hypospadias, a congenital condition in which the opening of the urethra develops abnormally; conducted the first large bladder cancer screening study in the U.S.; and was among the first in the world to offer continent urinary diversion for bladder cancer patients.

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Irreversible damage to color vision linked to popular erectile dysfunction drug

Color vision problems caused by retinal damage on a cellular level can result from a high dose of sildenafil

In a first-of-its-kind study, Mount Sinai researchers have shown that color vision problems caused by retinal damage on a cellular level can result from a high dose of sildenafil citrate, the popular erectile-dysfunction medication sold under the brand name Viagra. The results demonstrate that excessive use of the drug could lead to long-term vision problems, including possible irreversible damage. The findings have been published in the fall issue of *Retinal Cases*.

"People live by the philosophy that if a little bit is good, a lot is better. This study shows how dangerous a large dose of a commonly used medication can be," said lead investigator Richard Rosen, MD, Director of Retina Services at New York Eye and Ear Infirmary of Mount Sinai (NYEE). "People who depend on colored vision for their livelihood need to realize there could be a long-lasting impact of overindulging on this drug."

Rosen and a team of investigators from NYEE based their study on a 31-year-old patient who arrived at an urgent care clinic complaining of red-tinted vision in both eyes that hadn't gone away in two days. He reported that his symptoms began shortly after taking a dose of liquid sildenafil citrate that he purchased over the internet (sildenafil citrate can cause visual disturbances with normal dosage, but symptoms typically resolve within 24 hours). The patient told doctors he had consumed much more than the recommended 50mg dose, and that symptoms began shortly after ingestion. The patient was then diagnosed with persistent retinal toxicity linked to the high dose of medication damaging the outer retina. His tinted vision has not improved more than a year after his initial diagnosis, despite various treatments.

Mount Sinai researchers used state-of-the-art technology, including adaptive optics (AO) and optimal coherence tomography (OCT), to examine his retina for evidence of structural damage at the cellular level, something that had never been done before. AO is a sophisticated technology that allows clinicians to examine microscopic structures of the eye in living patients with extreme detail in real time. OCT is an advanced imaging system that reveals the cross-sectional details of the retina layer by layer.

The high-tech imaging allowed investigators to see microscopic injury to the cones of the retina, the cells which are responsible for color vision. The damage was similar to that seen in animal models of hereditary retinal disease such as retinitis pigmentosa or cone-rod dystrophy.

"To actually see these types of structural changes was unexpected, but it explained the symptoms that the patient suffered from. While we know colored vision disturbance is a well-described side effect of this medication, we have never been able to visualize the structural effect of the drug on the retina until now," said Dr. Rosen. "Our findings should help doctors become aware of potential cellular changes in patients who might use the drug excessively, so they can better educate patients about the risks of using too much."

http://bit.ly/2RqZGwJ

New study reveals association between diuretic drug use in type 2 diabetes and risk of lower limb amputation

Diuretic drug use in individuals with type 2 diabetes (T2D) associated with significantly increased risk of serious lower limbs problems

New research presented at this year's annual meeting of the European Association for the Study of Diabetes (EASD) in Berlin, Germany, reveals that the use of diuretic drugs in individuals with

type 2 diabetes (T2D) is associated with a significantly increased risk of serious problems in their lower limbs which can lead to amputation.

The research was conducted by Dr Louis Potier, Department of Diabetology, Endocrinology and Nutrition, Bichat Hospital, Assistance Publique - Hôpitaux de Paris, Paris, France, and colleagues. The aim of the study was to analyse the association between diuretic use and the risk of what are known as lower limb events (LLE) in patients with T2D. These events include lower extremity amputations (LEA), and lower limb revascularisations (LLR) such as angioplasty or the bypassing of blocked or damaged blood vessels to prevent amputations.

Recently, it has been observed that individuals with T2D who take canagliflozin, a member of a relatively new type of diabetes drug called an SGLT2 inhibitor, to reduce their blood glucose are at an increased risk of undergoing limb amputations. The authors suggest that this side effect may be caused by drug-induced hypovolaemia (decreased blood volume), and that if this is the case, then diuretics should also increase amputation risk as they have a similar effect.

The team drew their data from SURDIAGENE; a French observational cohort which includes T2D patients enrolled from 2002 until 2012. Participating subjects were followed up until whichever came first out of the onset of LLE, death, or 31 December 2015. There were 1459 studied participants of whom 670 were taking diuretics. During a follow-up period which averaged 7 years, LLE occurred in 85 (13%) of diuretic users and 57 (7%) of non-users.

To better account for difference in characteristics of patients taking or not diuretics, the authors used a propensity score matching approach by matching each patient using diuretics to a comparable non-user patient. Among the 1074 patients included in the matched cohort, those using diuretics had an almost doubled risk (75% higher) of LLE than non-users. These data were analysed further and revealed that there was a large increase in the risk of LEA (2.3 times greater in diuretic users than non-users), and while LLR showed a small increase (1.3 times greater in users), this result was not statistically significant.

The authors conclude: "Among patients with type 2 diabetes treated with diuretics, there was a significant and independent increase in the risk of lower limb events, coming predominantly from a rise in lower extremity amputations. Diuretics should be used cautiously in patients with type 2 diabetes at risk of amputations."

They add: "Further studies are needed to explore the role of drug-induced hypovolaemia in the association between the use of diuretics and LLE. The hypovolaemia hypothesis could provide an explanation for the increased risk of LEA observed with SGLT2 inhibitors."

http://bit.ly/2Oy06jC

Dog intelligence 'not exceptional'

People who think dogs are exceptionally intelligent are barking up the wrong tree, new research shows.

Scientists reviewed evidence that compared the brain power of dogs with other domestic animals, other social hunters and other carnivorans (an order including animals such as dogs, wolves, bears, lions and hyenas).

The researchers, from the University of Exeter and Canterbury Christ Church University, found the cognitive abilities of dogs were at least matched by several species in each of these groups.

The study examined more than 300 papers on the intelligence of dogs and other animals, and found several cases of "over interpretation" in favour of dogs' abilities.

"During our work it seemed to us that many studies in dog cognition research set out to 'prove' how clever dogs are," said Professor Stephen Lea, of the University of Exeter.

"They are often compared to chimpanzees and whenever dogs 'win', this gets added to their reputation as something exceptional.

"Yet in each and every case we found other valid comparison species that do at least as well as dogs do in those tasks."

The review focussed on sensory cognition, physical cognition, spatial cognition, social cognition and self-awareness.

"Taking all three groups (domestic animals, social hunters and carnivorans) into account, dog cognition does not look exceptional," said Dr Britta Osthaus, of Canterbury Christ Church University.

"We are doing dogs no favour by expecting too much of them. Dogs are dogs, and we need to take their needs and true abilities into account when considering how we treat them."

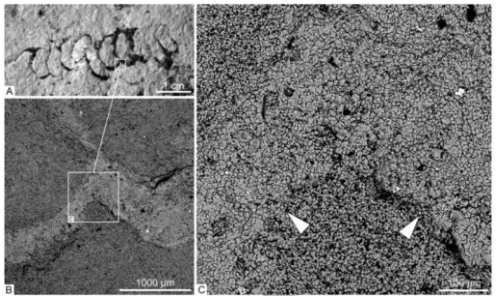
The paper, published in the journal Learning & Behavior, *is entitled: "In what sense are dogs special? Canine cognition in comparative context."*

http://bit.ly/2DRtq0r

Siberian paleontologists discovered the oldest macro-skeleton remains

Oldest skeletal remains on Earth belonged to microorganisms that lived 700-650 million years ago

The oldest skeleton remains known to fossil chronicle of the Earth belonged to the microorganisms that lived 700-650 million years ago. International research team proved that a larger organisms of the same period, such as *Palaeopascichnus linearis* up to 20 centimeters long, also had a skeleton. The research is published in *Precambrian Research*.



These are agglutinated walls in Palaeopascichnus linearis from the khatyspyt formation under the scanning electron microscope. (B, C) are magnified images showing the wall, the internal filling and the surrounding rock. White arrowheads mark the outer limit of the rim. **Anton Kolesnikov**

Palaeopascichnus resembles a series of spheres or ellipsoids, which are placed one by one and called chambers. They have been known for a long time and can be found all across the world since for that time period they were one of the most widespread living organisms. *Palaeopascichnus* was considered as fossil traces of life activity for a while: someone described them as traces on the surface of a substrate or sediment left by animal migration in search of food, someone - as petrified chains of feces, someone - as the algae remains.

Researchers from Institute of Petroleum Geology and Geophysics SB RAS and Novosibirsk State University together with their colleagues from Great Britain and France for the first time managed to prove that in fact *Palaeopascichnus* was a skeletal organism. The scientists found out that *Palaeopascichnus* has much in common with modern giant protozoa: deep-sea single-cell xenophyphores. For example, *Palaeopascichnus* agglutinated exoskeleton by staying motionless at the bottom and gluing around itself particles of rocks and sediment from the surrounding space. As a modern example of the agglutination caddisflies can be named, even though they are moving.

"The material was collected in the Arctic at the Olenek uplift of the northeast of the Siberian platform, where a very large accumulation of organisms was found," says one of the researchers Anton Kolesnikov, member of Institute of Petroleum Geology and Geophysics SB RAS and Doctor of the University of Lille. "When we made a thin cut through the *Palaeopascichnus* across the chamber, we saw that there is a certain wall composed of a material that is more coarse in comparison to the host rocks."

A set of diverse methods was used in this research: the scientists made thin saw cuts, or slides, studied them under microscope, conducted tomography studies, used scanning electron microscope and so for. Afterwards the researchers started to look at additional

materials from the White Sea, Ukraine, Australia, Canada, and all these samples confirmed the existence of a skeleton.

Through statistical calculations of rock grains size in the *Palaeopascichnus* wall and the surrounding space, the scientists also found that these organisms preferred to collect large particles to construct the skeleton rather than everything around them.

Palaeopascichnus turned out to be more lucky than other creatures of that time, such as Ediacaran biota, which almost disappeared approximately ten million years before the Cambrian. *Palaeopascichnus* lived up to the beginning of the Cambrian, and theoretically modern xenophyphores might be their distant descendants.

Apart from *Palaeopascichnus*' potential descendants, the paleontologists discovered their ancient relatives. "The thing is that there are plenty organisms like *Palaeopascichnus*," Anton Kolesnikov notes. "For instance, genus Orbesiana, which was discovered in the well drilled near Moscow by a famous scientist, founder of the Ediacaran biota study, Boris Sokolov. He described the fossils that he found as the ancient macroscopic algae, and after that this material got lost for a while. Recently, the family of Boris Sokolov offered us his archives and we found the original material with detailed explanatory note."

The researchers managed to use the most advanced equipment, and with the help of British and French colleagues they showed that Orbesiana was far from being an algae. More likely, they were close to *Palaeopascichnus* and might be placed in one group of the oldest macro-skeletal organisms. "*Palaeopascichnus* preferred to build their skeleton of single row chambers, while Orbesiana used multiple raw building as they either created spirals and foam-like clusters of irregular shape or simply were two- and multi-row," explains Anton Kolesnilov.

For the next step of the research the paleontologists plan to further examine organisms, that could be attributed to this group. In other words, the researchers have to deeply understand the taxonomy of these first macro-skeletal creatures of the Ediacaran biota.

Reference:
https://www.sciencedirect.com/science/article/pii/S0301926817307052?via%3Dihub#!

http://bit.ly/2IDCTY3

Free thinking: researchers identify origins of free will in the brain

Combination of two cognitive processes creates the perception of free will

Long the domain of philosophy and religion, free will has also been defined by scientists as a combination of two cognitive processes - the desire to act (or volition) and the sense of responsibility for our actions (or agency.) Together, these processes create the perception of free will, and damage to volition or agency can leave patients without the desire to move or speak or the sensation that their movements are not their own, respectively.

Neuroscientists led by Michael Fox, MD, PhD, of Beth Israel Deaconess Medical Center (BIDMC) used brain lesion network mapping - a technique pioneered by Fox at BIDMC - to find the anatomical origins of the perception of free will. Their findings were published today in the Proceedings of the National Academy of Sciences.

"Lesion network mapping is a recently validated technique that allows scientists to map symptoms caused by brain injury to specific brain networks," said Fox, Director of the Laboratory for Brain Network Imaging and Modulation at BIDMC and an Associate Professor of Neurology at Harvard Medical School. "In this study, we used this network localization approach to determine the neuroanatomical basis for disordered free will perception."

Fox and colleagues, including lead author, R. Ryan Darby, MD, PhD, formerly a fellow in Fox's lab at BIDMC and now of Vanderbilt University Medical Center, identified 28 cases in the medical literature in which brain injury disrupted volition, leaving patients with akinetic mutism - a lack of motivation to move or speak. They also identified 50 cases in which brain injury disrupted agency and caused patients to feel their movements were not their own, a syndrome known as alien limb syndrome.

Network mapping revealed that, while the brain injuries were quite diverse in their locations, the lesions fell within one of two distinct brain networks. All of the injuries disrupting volition were functionally connected to the anterior cingulate cortex, a region of the brain associated with motivation and planning. Ninety percent of lesions causing alien limb fell within a brain network functionally connected to the precuneus cortex, part of the brain associated with agency.

Finally, the authors showed that their findings were relevant beyond patients with brain injury. Brain stimulation to these same sites altered free will perception in healthy research participants, and neuroimaging of psychiatric patients with altered free will perception revealed abnormalities fell with these same brain networks.

"Our study was focused on patients with disorders of free will for movements; however, free will is commonly discussed as it relates to social, legal and moral responsibility for decisions, not just movement," said Fox. "It remains unknown whether the network of brain regions we identify as related to free will for movements is the same as those important for moral decision-making."

In addition to Fox and Darby, the research team also included Juho Joutsa and Matthew Burke of BIDMC.

Investigators were supported by funding from the Sidney R. Baer, Jr. Foundation, the NIH (R01MH113929 and K23NS083741), the Nancy Lurie Marks Foundation, the Dystonia Medical Research Foundation, the Alzheimer's Association, the BrightFocus Foundation, Academy of Finland, and the Finnish Medical Foundation.

http://bit.ly/2IAOAi5

A Woman Was Hit By a Wave at the Beach. It Ruptured One of Her Arteries.

A woman's beach vacation took an unexpected turn when she was hit so hard in the neck by a wave that it ruptured one of her arteries, according to a recent report of her case.

By Rachael Rettner, Senior Writer | October 2, 2018 07:31am ET

The 60-year-old woman, who lives in Ireland, was vacationing at the beach when an ocean wave struck her in the neck.

Soon, she began to experience intermittent headaches and neck pain, according to the report, published Sept. 12 in the journal BMJ Case Reports. After two weeks, she was still having these symptoms, and one of her eyelids began to droop, prompting her to seek medical care. When doctors examined the woman, they noticed that one of her pupils was smaller than the other.

The woman was initially diagnosed with Horner syndrome, which refers to a combination of symptoms caused by a disruption in a nerve pathway from the brain to the face, according to the Mayo Clinic.

Many things can cause Horner syndrome. In the woman's case, further imaging tests revealed that she had "carotid artery dissection" (CAD) in her right carotid artery. This occurs when blood leaks into a tear within the wall of the carotid artery, and as the blood pools, it separates the layers of the blood vessel wall. The right carotid artery is one of four arteries in the neck that delivers blood to the brain.

The dissection likely happened because the wave's impact led to a rupture of the "vasa vasorum," or the small blood vessels within the wall of the carotid artery, the authors wrote in the report.

Dr. Etimbuk Umana, an emergency medicine doctor at Galway University Hospitals in Ireland, who treated the patient, said that, prior to the woman's case, he had never seen or read any reports of a beach wave causing CAD. But unusual neck movements or blunt trauma to the neck (such as trauma experienced in a car crash) are known causes of CAD, he told Live Science. It's estimated that trauma causes up to 40 percent of cases of CAD, the authors wrote.

One concern for patients with CAD is the risk of stroke; indeed, the condition is a common cause of stroke for people under 50, according to the Cedars-Sinai medical centerin Los Angeles. A stroke can occur if a blood clot forms at the site of the blood vessel dissection and that clot blocks the flow of blood to the brain.

For this reason, patients with CAD may be treated with anti-clotting drugs (such as blood thinners) to prevent stroke. But for patients who have a rupture of the vasa vasorum, anti-clotting drugs might actually pose a risk of increased bleeding, the report said.

The woman was initially treated with anti-clotting drugs, but the treatment was stopped, in part due to concerns about bleeding risk. Also, the woman didn't have any signs of stroke or other brain problems.

The woman was monitored closely and took Lyrica (pregabalin), a medicine used to treat nerve pain, to help with her pain. Six months later, tests showed that the artery injury had completely healed. The authors said that more studies are needed to weigh the risks and benefits of anti-clotting drugs for patients like the one in this report.

http://bit.ly/2yeMLCR

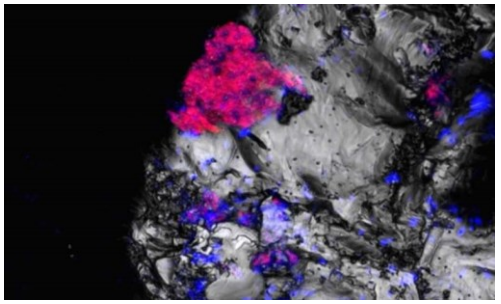
Cyanobacteria found living 600 meters underground without sunlight

October 2, 2018 by Bob Yirka, Phys.org report

A team of researchers from Spain, Germany and the U.S. has found a type of cyanobacteria that is capable of living more than 600 meters underground—in the absence of sunlight. In their paper published in *Proceedings of the National Academy of Sciences*, the group describes their study of the cyanobacteria and what they found.

The Rio Tinto region in Spain has long been a stand-in for Mars—the landscape there is red due to an abundance of iron and sulphur minerals. Because of its similarities to Mars, researchers have studied rock samples taken from above and underground, looking to better understand what sorts of life can exist in such a barren place. In this new effort, the researchers drilled a 613-meter borehole to study rock samples far below the surface. The team found cyanobacteria living in cracks and crevices within samples. Other bacteria have been found living far below the surface in the area, but cyanobacteria are different. Up until now, scientists believed they needed sunlight to survive.

Cyanobacteria derive energy through photosynthesis—hence the need for sunlight. They are also some of the oldest forms of life on the planet. Prior research has suggested that they were responsible for adding oxygen to the atmosphere, making it possible for other forms of life to evolve.



Viable cyanobacterial cells (red fluorescent signals) attached to rock fragments **PNAS**

Surprised by their find, the researchers went back for more samples using more stringent protocols to ensure that they were not contaminated. They found groups of cyanobacteria living in air pockets in rocks.

To learn how the cyanobacteria are able to survive without sunlight, the team examined them under a microscope. They found that in most respects, the cyanobacteria were the same as their cousins

living on the surface in the surrounding area. When testing the air in the pockets, they discovered that the tiny creatures were consuming hydrogen gas as evidenced by lower hydrogen levels where the cyanobacteria were found. They also found evidence that the subsurface cyanobacteria had one small adaptation to their photosynthetic system that allowed them to use a "safety valve" to produce energy. In other cyanobacteria, the valve is used to release excess energy to prevent overheating when sunlight is abundant.

More information: *Fernando Puente-Sánchez et al. Viable cyanobacteria in the deep continental subsurface, Proceedings of the National Academy of Sciences (2018). DOI: 10.1073/pnas.1808176115*

http://bit.ly/2Rwm3hU

Research Shows Wind Farms Could Divert Hurricane Rains

With enough wind turbines, the rainfall from Hurricane Harvey could have been reduced by 20 percent, according to a new modeling study.

by Richard Kemeny

Nature's strength was laid bare again last week as two tropical storms marauded through Southeast Asia and the southeastern United States. Super Typhoon Mangkhut, thought to be one of the most powerful cyclones to hit the Philippines in decades, uprooted homes and turned roads into violent rivers. It killed at least 81 people before twisting its way over the South China Sea and careering into the Chinese mainland where the death toll rose further. On the US east coast, Hurricane Florence caused widespread flooding, killed at least 37 people, and left millions without power. And as with Hurricane Harvey in 2017, Florence stalled over the continent, dropping ever more rain long after making landfall.

In the face of such a raw display of nature's fury, it may seem like little can be done to lessen the blow of a hurricane. But according to new research, help in tempering the power of hurricanes could one day come from an unexpected source: offshore wind farms.

The idea of deliberately modifying the weather with wind turbines has been around for decades, but little work has been done to calculate whether or not it could really work. In 2014, a group of researchers including Cristina Archer, a civil and environmental engineer from the University of Delaware, showed how using an army of wind turbines to extract kinetic energy from the air could potentially pacify hurricanes. The team calculated that a massive array of 78,000 turbines could reduce coastal storm surges—such as the one Hurricane Katrina shoved onto New Orleans in 2005—by up to 79 percent.

In new follow-up work, Archer and her colleagues have shown the potential for wind turbines to sap the rain from hurricanes, too.

Archer's calculations were done using a weather forecasting model into which she plugged atmospheric data from Hurricane Harvey, which drowned the southeastern United States with 100 trillion liters of water in August 2017. She also included calculations reflecting how wind turbines affect the local atmosphere by increasing turbulence and drag. The results reveal how an array of wind turbines would affect the wind speed and direction of the oncoming hurricane, potentially reducing the downstream rainfall.

Archer's team tested the interaction for wind farms of different sizes with varying densities of turbines. According to their calculations, a platoon of around 59,000 turbines spaced 900 meters apart would have cut the rainfall Houston experienced from Harvey by more than 20 percent.

"You're not going to eliminate hurricane damage but reduce it," Archer explains. "It's one thing to have some puddles on the street and another when you have water on the first floor of people's homes."

The surprising result stems from the fact that hurricane winds generally slow down when the storm reaches land. The land surface is less uniform than the sea, and this increase in roughness causes the wind to slow down, converge, and be forced upward. As the moist air rises, it cools, releasing the moisture as rain. Wind turbines have a similar effect on the wind, increasing the amount of rain in and around the turbine array. "You kind of squeeze out the moisture from the hurricane," says Archer.

Mike Biggerstaff, a meteorologist at the University of Oklahoma, says the idea seems to work on paper, but he would want to see much more detailed simulations than Archer and her colleagues used in their tests. He also believes the turbines would have to be extremely tightly spaced to have this effect on the wind.

"The results should not cause political leaders to think that hurricane impacts can so easily be mitigated," he says. "But it should motivate more sophisticated studies."

Ronald Smith, a meteorologist from Yale University in Connecticut, wonders whether turbines could even survive hurricane-force winds. "They have good braking systems, but probably not for Category 5 hurricanes," he says.

Archer admits that the idea of creating a 60,000-turbine offshore wind farm is far-fetched—the world's largest wind farm, on the edge of the Gobi Desert in China, has roughly 7,000 turbines. The largest offshore wind farm, in the Irish Sea, has just 87 turbines spread over 145 square kilometers. Instead, Archer hopes this research will inspire further studies. "It's just the beginning of a potentially interesting new research area," she says.

Yet given that large arrays of wind turbines may potentially slow down winds and mitigate downstream rainfall from a hurricane, might existing wind farms already be altering local weather patterns? According to Lee Miller, an environmental engineer at Harvard University in Massachusetts, they are. "Observational studies around wind farms have now quantified differences in not only wind speed, but also surface temperature, turbulence, evaporation, and carbon dioxide concentration," Miller says.

In a sense, these meteorological alterations could be considered a mild form of geoengineering. Right now the effects are small, but as wind farms grow in size, the impact on local weather patterns might rise commensurately.

Miller supports Archer's efforts. "Given the expectation that the solution to reducing future climate change is the widespread deployment of low-carbon energy sources like wind and solar power, a deeper understanding of the climatic impacts seems both critical and timely."

This year's hurricane season is already devastating, but it is far from over. What's more, extreme weather is expected to intensify in coming decades. "In the shadow of future climate change," says Miller, "this proactive type of research should be actively encouraged."

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

Japan set to allow gene editing in human embryos

Draft guidelines permit gene-editing tools for research into early human development.

David Cyranoski

Japan has issued draft guidelines that allow the use of gene-editing tools in human embryos. The proposal was released by an expert panel representing the country's health and science ministries on 28 September. Although the country regulates the use of human embryos for research, there have been no specific guidelines on using tools such as CRISPR–Cas9 to make precise modifications in their DNA until now.

Tetsuya Ishii, a bioethicist at Hokkaido University in Sapporo, says that before the draft guidelines were issued, Japan's position on gene editing in human embryos was neutral. The proposal now encourages this kind of research, he says. But if adopted, the guidelines would restrict the manipulation of human embryos for reproduction, although this would not be legally binding.

Manipulating DNA in embryos could reveal insights into early human development. Researchers also hope that in the long term, these tools could be used to fix genetic mutations that cause diseases, before they are passed on.

But the editing of genes in human embryos, even for research, has been controversial. Ethicists and many researchers worry that the technique could be used to alter DNA in embryos for non-medical reasons. Many countries ban the practice, allowing gene-editing tools to be used only in non-reproductive adult cells.

Researchers around the world have published at least eight studies on gene editing in human embryos. Some of the work was done in China and the United States, where using the technique does not break any laws if done with private funding; some was done in the United Kingdom, where permission must be granted by a national regulatory body.

Japan's draft guidelines will be open for public comment from next month and are likely to be implemented in the first half of next year.

doi: 10.1038/d41586-018-06847-7

http://bit.ly/2IDsM5j

3,500-year-old pumpkin spice? Archaeologists find the earliest use of nutmeg as a food

Earliest-known use of nutmeg as a food ingredient

As all things pumpkin spice arrive in grocery store aisles and on restaurant menus, a new study published in the journal Asian Perspectives describes the earliest-known use of nutmeg as a food ingredient.

Found at an archaeological site on Pulau Ay, a small island in the Banda Islands, central Maluku, Indonesia, the nutmeg was found as residue on ceramic potsherds and is estimated to be 3,500 years old -- about 2,000 years older than the previously known use of the spice.

The study and two excavations in 2007 and 2009 were led by Peter Lape, professor of anthropology at the University of Washington and curator of archaeology at the Burke Museum, in collaboration with colleagues from Universitas Gadjah Mada in Indonesia, the University of New South Wales in Australia and others.

The Pulau Ay archaeological site was occupied from 2,300 to 3,500 years ago, with animal bones, earthenware pottery, stone tools, and post molds of possible housing structures found. The variety of artifacts discovered provides evidence of changes in how people utilized marine food resources, pottery and domestic animals over time.

Over the first 500 years at the site, people shifted from a predominately fish-based diet to primarily eating domesticated pigs. In addition, pottery was initially thin-walled vessels adapted for storage of liquids that may have allowed people to survive on this water-poor island. A few hundred years later, thicker-walled pottery better adapted for cooking appears along with pig bones.

"This site shows us how people adapted to living on these small tropical islands in stages, from occasional use as fishing camps to permanent occupation," Lape said. "It's also fascinating to see such early use of nutmeg, a spice that changed the world a few thousand years later."

It was on the pottery where Lape's co-authors Judith Field and Adelle Coster found not only the nutmeg, but also residue from six other plants including sago and purple yam. These plants could have been collected from wild plants, or possibly cultivated through farming.

Pulau Ay is a small island lacking both indigenous land mammals and surface water. It likely would not have supported a permanent human population that did not have the technological advantages of domestic animals and water storage.

However, by surveying additional archaeological sites, the study's authors suggest that the island was regularly visited by people targeting its rich marine reef resources for several thousand years before more permanent populations were established in the early Neolithic, the later part of the Stone Age. The most likely homeland for these visitors is the nearest large island of Seram, 100 kilometers to the east. People who possessed sufficient knowledge of Pulau Ay and the seafaring skills to make regular return trips there would seem to be likely candidates for the first Neolithic settlers as well.

Sometime around 2,300 years ago, the site was largely or totally abandoned, and no other sites in the Banda Islands have so far been found that date to the period between 2,300 and 1,500 years ago. Future work aims to answer why these remote islands, which attracted the settlement of people who were quite connected to other places before and after this period, would have been abandoned for 800 years.

Studies of sites like this one can help illuminate the complex cultural processes at work during the Neolithic period, which saw the introduction of many new plants, animals and technologies to the islands of Southeast Asia. The results from this site show that these changes did not happen all at once, but rather were gradually adopted and adapted to allow people to utilize these tropical island seascapes in new ways.

As for the nutmeg, understanding its earliest origins of human use helps connect the dots to later international trades. By the 14th century (and possibly earlier), long-distance traders were traveling to Banda to obtain nutmeg; this valuable spice brought the Banda Islands international renown during the early modern era.

The find provides a new perspective on a key ingredient that is still a valuable commodity today--especially in a multi-billion dollar industry of fall-themed foods and beverages.

The fieldwork was supported by the residents and government officials of Pulau Ay and Banda Naira. The 2007 fieldwork was conducted with the support of the National Geographic Society, with permission from Lembaga Ilmu Pengetahuan Indonesia (LIPI), as well as Maluku provincial and local governments, and was a collaborative effort between the Universitas Gadjah Mada, the University of Washington, and Balai Arkeologi Ambon. The 2009 fieldwork included the same partners and was conducted with support of the Henry Luce Foundation, with permission from Kementarian Riset dan Teknologi.

https://bbc.in/2OI1wsd

Cervical cancer: Australia 'to be first to eliminate disease'

Australia will become the first country to effectively eliminate cervical cancer if vaccination and screening rates are maintained, researchers say.

The disease could be eradicated as a public health issue nationally within 20 years, according to new modelling.

It is predicted to be classified as a "rare cancer" in Australia by 2022, when it should drop to less than six cases per 100,000 people.

Scientists attribute the progress to national prevention programmes.

In 2007, Australia became one of the first countries to introduce a Human Papilloma Virus (HPV) vaccination scheme for girls. The programme was later extended to boys. It complemented a national screening programme that began in 1991.

The new modelling was published by the Cancer Council New South Wales (NSW), a charity, in The Lancet Public Health Journal on Wednesday.

Elimination efforts

Cervical cancer is caused by "high-risk" types of HPV, a sexually transmitted infection. It is the fourth-most frequent cancer in

women and has a high mortality rate globally, according to the World Health Organization (WHO).

Australia's current annual cervical cancer rate stands at seven cases per 100,000 people, about half the global average.

The study predicted that annual cases in Australia would drop to four in 100,000 by 2035 - a potential elimination threshold, the researchers suggested.

The WHO has not yet established such a standard for when cervical cancer becomes so uncommon it is deemed eliminated.

"Regardless of what the [elimination] threshold is, it is likely Australia would be the first country to reach it given our current low rate of cervical cancer, and our strong prevention programmes," Dr Megan Smith, a researcher from Cancer Council NSW told the BBC.

Last year, Australia replaced its routine screening standards for the cancer - a pap smear examination - with more sensitive HPV cervical screening tests. Researchers have estimated that the switch to the new test, conducted only every five years, will reduce cancer rates by at least 20%.

According to the WHO, about nine in 10 deaths from cervical cancer happen in low and middle-income countries.

What is the Human Papilloma Virus (HPV)?

•HPV is the name given to a common group of viruses; there are more than 100 types of HPV

•Many women will be with infected with HPV over the course of their lifetime without any ill-effect

•In the vast majority of cases, there will be no symptoms and the infection will clear on its own, but in some cases persistent infection can lead to cervical disease

•Some types of HPV are high risk because they are linked to the development of some cancers

•Other lower risk HPV types can lead to genital warts

•Nearly all cervical cancers (99.7%) are caused by infection from a high risk HPV

•The HPV vaccine protects against four types of HPV which cause around 80% of cervical cancer and the vast majority of genital warts

Source: NHS Choices

http://bit.ly/2pCPulB

Neanderthal healthcare practices crucial to survival

New research has suggested that Neanderthals embraced healthcare practices, such as assisting in cases of serious injury and the challenges of childbirth.

October 3, 2018 by Samantha Martin

Healthcare practices in this period of human evolution have often been studied alongside complex cultural behaviour, mostly based around research into rituals and symbols associated with death. This new study, however, sets out, for the first time, that healthcare could have had a more strategic role in Neanderthal survival.

Previous research at the University had already suggested that compassion and caring for the injured and dying could have been a factor in the development of healthcare practices, but further investigation has now shown that there was evolutionary drivers behind it too.

Researchers investigated the skeletal remains of more than 30 individuals where minor and serious injuries were evident, but did not lead to loss of life. The samples displayed several episodes of injury and recovery, suggesting that Neanderthals must have had a well-developed system of care in order to survive.

Animal attacks

Dr. Penny Spikins, from the University of York's Department of Archaeology, said: "Neanderthals faced multiple threats to their lives, particularly from large and dangerous animals, but in popular culture Neanderthals have such a brutish and strong image that we

haven't really thought too deeply about their vulnerabilities before now.

"We have evidence of healthcare dating back 1.6 million years ago, but we think it probably goes further back than this. We wanted to investigate whether healthcare in Neanderthals was more than a cultural practice; was it something they just did or was it more fundamental to their strategies for survival?

"The high level of injury and recovery from serious conditions, such as a broken leg, suggests that others must have collaborated in their care and helped not only to ease pain, but to fight for their survival in such a way that they could regain health and actively participate in the group again."

Serious risk

It is generally accepted that more than 80% of the skeletal remains known to archaeologists display several injuries, some of which may have required simple remedies, such as food and rest, and others that would have required serious levels of care due to a high risk to life.

Neanderthals lived in small groups, so any one loss of life was particularly significant to the survival of the whole community. Injury, over disease, was the most common threat, as Neanderthals didn't live in the type of environment, or in large enough communities, to be at high risk from pathogens.

Neanderthal women, however, were at risk from difficulties in childbirth. The shape of their pelvis and the size and shape of a child's head was similar to that of modern-day humans, so it is assumed that they would also have encountered some common issues in childbirth.

Neanderthal 'midwives'

Dr. Spikins said: "It is likely that they would have had assisted childbirth; the role that we now attribute to midwives. Without support, they probably could not have survived the toll that the death rate of mothers and babies could have taken on their communities.

"When we look at the daily risks and dangers involved in hunting and finding food, as well as in childbirth in respect to their small hunting communities, it is not surprising that they would develop practices to improve health and reduce mortality risk.

"We can start to see healthcare as a pattern of evolutionary significant collaborative behaviour, alongside hunting together, food sharing and parenting. In this we can see why providing healthcare to those in need today is such an important part of human life."

Researchers now aim to expand this work to look at potential methods of healthcare and how far back healthcare practices can be traced.

More information: *Penny Spikins et al, Living to fight another day: The ecological and evolutionary significance of Neanderthal healthcare, Quaternary Science Reviews (2018). DOI: 10.1016/j.quascirev.2018.08.011 , dx.doi.org/10.1016/j.quascirev.2018.08.011*

http://bit.ly/2C18jGE

‘Honeygate’ deepens as new tests reveal 27% of brands are adulterated

The new discovery significantly deepens the ‘fake honey’ scandal.

Mark Patrick Taylor * **Xiaoteng Zhou** **

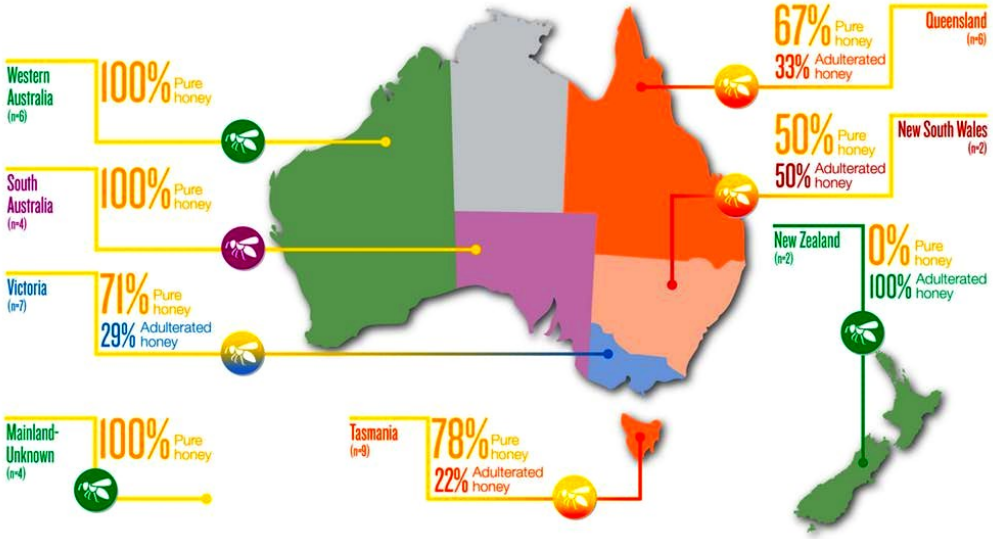
More than a quarter of commercial honey brands have potentially been watered down with sugar cane, corn syrup or other products, according to our new analysis of 95 products from local food markets and supermarket shelves.

Our discovery is set to deepen the concern over the authenticity of honey for sale in Australia, in the wake of last month’s “fake honey” scandal, which revealed the widespread adulteration of honey with cheaper substances. Australia is the world’s fourth-largest honey exporter, and the revelations pose a threat to its reputation as a leading producer and supplier of honey.

Our study, published in Nature's Scientific Reports, analysed 100 honeys from 19 countries, including Australia. The study included five raw honey samples (that is, honey direct from the hive) and 95 commercial samples, 38 of them from Australian-based producers.

Analysis of the 95 commercial honeys showed that 27% of them were of "questionable authenticity", meaning they had potentially been adulterated with cane and/or corn syrups. This means they should not be classified as genuine pure honey.

Of the Australian-sourced commercial honeys we analysed, 18% were identified as likely to have been adulterated in a similar way.



Results of pure and adulterated Australasian honeys analysed in this study.
Monique Chilton/Copperplate Design

Our study used the only internationally accepted method for determining honey adulteration. This method detects the presence of sugars from a type of plants known as C4 plants – the group that includes corn and sugar cane – as opposed to pure honey, which is made from the nectar of flowers from a different group, called C3 plants.

C4 and C3 plants each have unique isotopic signatures, which allows us to ascertain whether a honey sample is pure (containing only compounds from C3 plants) or whether it has been adulterated with sugars from C4 plants.

An old problem

Honey adulteration is nothing new. It has been on the rise since the 1970s, when cheap high-fructose corn syrup became widely available. Because both corn syrup and sugar cane are cheaper than honey, they are an easy way to increase honey volume and boost profits.

Some operators adulterate honey with rice sugars that enable them to circumvent the C4 test. Some rice syrup producers openly advertise the fact that their products will not cause adulterated honeys to fail the C4 test.

Honey can be adulterated either during or after production. Inadvertent adulteration might happen through overfeeding of sucrose to bees during periods when food sources are limited, or at harvest time. This practice, if done occasionally, can protect colonies at times of low food availability. But if used injudiciously it can also filter through into the finished product.

Of course, our study also comes hot on the heels of recent revelations that 12 of 28 Australian honeys were adulterated with rice and other syrups. That discovery was made using a new proprietary method that can reportedly detect adulteration with a wider range of compounds and also identify the geographic origins of the honey. However, this method does not currently meet the provisions of the Codex Alimentarius Commission, the international body that sets food standards.

Our research group has previously shown that honey can indeed be traced back to its point of origin, by comparing trace chemicals in bees and their honey with those in the dusts and soils where it was produced.

In our latest research, we therefore also investigated whether the commercial honey samples can indeed be tracked back to where they supposedly came from. We found that honey from different continents and regions do indeed have different chemical signatures, which paves the way for detecting mislabelled or geographically fraudulent honey.

There is no evidence that adulterated honeys cause any significant health risk (beyond those posed by eating sugary foods anyway). However, in many cases consumers are not getting the supposedly genuine pure honey they have paid for.

But our research, along with previous studies, reveals the scale of the problem.

For Australian honey to retain its premium position in the global market, there needs to be a better framework around the chain of custody and certification of honey. Only then will customers have a guarantee that their "pure" honey is exactly what it says on the label.

* ***Professor of Environmental Science, Macquarie University***
** ***PhD candidate, Macquarie University***

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Common herbicide compound may save millions of lives

Chemical compound found in common herbicides could fight hospital-acquired human fungal pathogenic infections

A chemical compound found in common herbicides could help fight hospital-acquired human fungal pathogenic infections, which claim an estimated two million lives per year.

A team of international researchers led by The University of Queensland has discovered that the chemical chlorimuron ethyl also targets a range of fungal infections that are potentially fatal to humans, particularly people undergoing treatments which place the immune system under stress.

Dr Luke Guddat, from UQ's School of Chemistry and Molecular Biosciences, said the finding was very timely, given the growth in drug-resistant infections.

"There are more drug-resistant fungal diseases than ever - posing a major threat to global human health - and new drugs are urgently required to combat these diseases," he said.

"Through this research we wanted to see if a specific class of commercial herbicide has the ability to stop the growth of these infections. "We thought this was a good idea, since plants and fungi have a similar enzyme that these chemicals inhibit, and it turns out we were correct."

The researchers tested five different families of compounds, to see if they could inhibit a key enzyme from the fungal species, *Candida albicans* and *Cryptococcus neoformans*.

One of the five, chlorimurion ethyl, was a stand-out candidate.

"In studies in the petri dish and with mice, it was highly effective at preventing proliferation of growth," Dr Guddat said. "By inhibiting this enzyme you're removing a key metabolic step that makes three types of amino acids, which these infections need to grow.

"And most importantly, humans don't have this enzyme - we obtain these amino acids from our food - so there's very little chance that these compounds will be toxic to humans, a factor which limits the use of many of the other currently prescribed antifungal drugs."

Dr Guddat said while there's a bright future for the development of compounds to treat this type of infection, more research is necessary. "We're only at the early stage of this journey, but we're excited to see the prospects for new treatments in the future."

The study was published in Proceedings of the National Academy of Sciences (DOI: 10.1073/pnas.1809422115).

http://bit.ly/2y6Bl4C

Mass. General-led study supports aspirin's ability to reduce liver cancer risk

Supports evidence from previous studies suggesting regular use of aspirin can reduce risk of developing primary liver cancer

The results of a study led by Massachusetts General Hospital (MGH) investigators support evidence from previous studies suggesting the regular use of aspirin can reduce the risk of developing primary liver cancer - also called hepatocellular carcinoma (HCC). Their report analyzing data from two long-term epidemiologic studies appears in JAMA Oncology and finds that regular aspirin use - taking two or more 325 mg tablets a week for five years or more - led to a significantly reduced risk of developing HCC, which is the second leading cause of cancer death worldwide.

"Regular use of aspirin led to significantly lower risk of developing HCC, compared to infrequent or no aspirin use, and we also found that the risk declined progressively with increasing aspirin dose and duration of use," says Tracey Simon, MD, a research fellow in the MGH Division of Gastroenterology, lead author of the report. "Since regular aspirin use carries the risk of increased bleeding, the next step should be to study its impact in populations with established liver disease, since that group is already at risk for primary liver cancer."

While HCC is relatively rare, its incidence in the U.S. has increased over the past 40 years and mortality rates have accelerated faster than those of any other cancer. The primary risk factor for HCC is cirrhosis - which can be caused by Hepatitis B or C infection, alcohol use disorder or nonalcoholic fatty liver disease. HCC usually is diagnosed at a late stage, leading to an average survival time of less than a year. Aspirin is known to block the production of inflammatory lipids that can lead to liver injury, and while some previous studies have suggested that regular use could help prevent HCC, information on the optimal dosage and required duration of treatment has not been available.

The research team examined more than three decades of data collected as part of the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS), which have compiled comprehensive health data on more than 170,000 participants since the 1980s. As part of the biennial questionnaires, participants were asked whether they took aspirin on a regular basis, how many standard-dose (325 mg) tablets they took a week and for how long. Information on HCC diagnosis was also compiled from the questionnaires and from the National Death Index of the National Center for Health Statistics.

Among the more than 133,300 participants whose data was analyzed - more than 45,800 women and 87,500 men - regular aspirin use, defined as two or more standard-dose tablets a week, led to a 49 percent reduction in the relative risk of developing HCC. Among those taking aspirin for five years or more, the relative risk was reduced by 59 percent. Just as the risk reduction increased with longer duration of aspirin use, it also decreased if aspirin was discontinued, disappearing by eight years after aspirin use was halted. Regular use of acetaminophen or nonsteroidal anti-inflammatory drugs like ibuprofen had no impact on HCC risk.

"The long duration of aspirin use could be necessary because primary liver cancer takes many years to grow. Aspirin may act at the earliest stages of cancer development, or even at precancerous stages, by delaying or preventing inflammation or liver fibrosis," says Simon. "While it's still too early know whether starting aspirin therapy might be an effective strategy to prevent HCC, efforts to understand the mechanisms behind these beneficial effects could help identify urgently-needed prevention strategies or biomarkers for a cancer that is a growing public health problem."

Senior author Andrew Chan, MD, MPH, chief of the MGH Clinical and Translational Epidemiology Unit in the Department of Medicine and the Division of Gastroenterology, adds, "Aspirin use is already recommended for prevention of heart disease and colorectal cancer in certain U.S. adults. These data also add to a growing list of cancers for which aspirin appears to have anti-cancer activity, which could be a rationale for more patients to discuss an aspirin regimen with their physicians." Chan is a professor of Medicine at Harvard Medical School.

Additional co-authors of the JAMA Oncology *report are Kathleen Corey, MD, MPH, MMSc, and Raymond Chung, MD, MGH Gastroenterology; Yanan Ma, PhD, Edward Giovannucci, MD, and Xuehong Zhang, MD, ScD, Brigham and Women's Hospital; Jeffrey Meyerhardt, MD, MPH, Dana-Farber Cancer Institute; Charles Fuchs, MD, MPH, Yale University Cancer Center; Jonas Ludvigsson, MD, PhD, Karolinska University Hospital, Stockholm, and Dawn Chong, MD, National Cancer Center, Singapore. Support for the study includes National Cancer Institute grants UM1 CA186107, UM1 CA167552 and K07 CA188126; and National Institute of Diabetes and Digestive and Kidney Diseases grants K24 DK078772, K23 DK099422 and K24 DK098311. Andrew Chan is a Stuart and Suzanne Steele MGH Research Scholar.*

http://bit.ly/2zUlq3w

Evidence mounts linking aspirin to lower risk of ovarian cancer

New JAMA Oncology study shows daily use can reduce risk by 23 percent

TAMPA, Fla. -- Taking a low-dose aspirin daily may help women lower their risk of developing ovarian cancer. A new study co-led by Moffitt Cancer Center found that women who reported taking a low-dose aspirin every day had a 23 percent lower risk of ovarian cancer compared to nonaspirin users. The research also found that women who were heavy users of nonaspirin nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen (Advil) or naproxen (Aleve), over a long period of time had a higher risk of developing ovarian cancer.

The findings were published online today by JAMA Oncology.

Ovarian cancer is the most fatal gynecological cancer, largely due to lack of early detection strategies. It is believed that inflammation that occurs during ovulation plays a role in the development of this cancer. But anti-inflammatory medications, such as aspirin, have been shown to lower the risk of certain types of cancers.

For this study, Shelley Tworoger, Ph.D., associate center director for Population Science at Moffitt, worked with researchers at Huntsman Cancer Institute and the Harvard T.H. Chan School of Public Health to analyze data from more than 200,000 women who took part in the Nurses' Health Studies based at Brigham and Women's Hospital in Boston. Of the participants, 1,054 developed ovarian cancer. Researchers looked at the participants' use of aspirin (325 milligrams), low-dose aspirin (100 milligrams or less), non-aspirin NSAIDs and acetaminophen.

Their analysis found that low-dose aspirin use was associated with a lower risk of ovarian cancer while standard-dose aspirin use was not. Conversely, the data showed that women who took non-aspirin NSAIDs often, defined by at least 10 tablets per week for many years, had an increased risk of developing the disease.

The findings help confirm research published earlier this year by Tworoger in the Journal of the National Cancer Institute. The study, which used data pooled from 13 studies in the Ovarian Cancer Cohort Consortium, included more than 750,000 women, of which 3,500 were diagnosed with ovarian cancer. It found that daily use of aspirin reduced ovarian cancer risk by 10 percent.

"We're not quite at the stage where we could make the recommendation that daily aspirin use lowers ovarian cancer risk. We need to do more research. But it is definitely something women should discuss with their physician," said Tworoger.

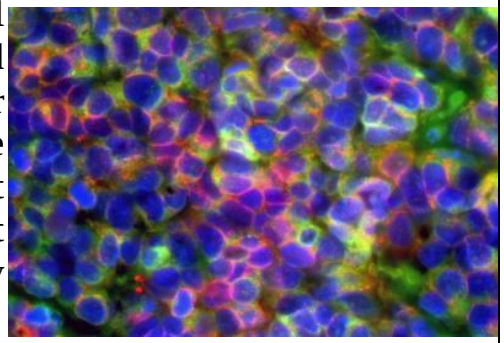
http://bit.ly/2ILSDZf

UCLA researchers discover aggressive prostate and lung cancers are driven by common mechanisms

Discovery of a common process in development of late-stage, small cell cancers of the prostate and lung

Alice Walton

UCLA researchers have discovered a common process in the development of late-stage, small cell cancers of the prostate and lung. These shared molecular mechanisms could lead to the development of drugs to treat not just prostate and lung cancers, but small cell cancers of almost any organ.



Microscopic image of small cell neuroendocrine prostate cancer: cancer cells are seen expressing diagnostic prostate cancer markers in green and red (blue color indicates the cell nucleus) **Jung Wook Park & Owen Witte**

The key finding: Prostate and lung cells have very different patterns of gene expression when they're healthy, but almost identical patterns when they transform into small cell cancers. The research suggests that different types of small cell tumors evolve similarly, even when they come from different organs.

The study, led by Dr. Owen Witte, founding director of the UCLA Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research and professor of microbiology, immunology and molecular genetics, was published in the journal Science. Witte collaborated with scientists from UCLA's Crump Institute for Molecular Imaging and the UCLA Jonsson Comprehensive Cancer Center.

Cancers that become resistant to treatment often develop into small cell cancers -- also known as small cell neuroendocrine carcinomas, or SCNCs -- which generally have extremely poor prognoses. Certain cancers can evade treatment in part by changing cell types - from aggressive adenocarcinoma to small cell carcinoma, for example.

Previous research hinted that small cell cancers from different organs may be driven by common mechanisms, but the UCLA study is the first to so clearly describe the steps in their evolution.

"Small cell cancers of the lung, prostate, bladder, and other tissues were long thought to be similar in name alone -- and they were treated by oncologists as different entities," Witte said. "Over the past few years, though, researchers have increasingly begun to realize that there are similarities in the cancers, and that's what our work confirms."

Dr. Jung Wook Park, the study's first author, and UCLA collaborators explored the potential parallels between the cancer types by transplanting human prostate cells with five genes, known collectively as PARCB, into mice. When those cells grew in the mice, they displayed unique features of human small cell neuroendocrine carcinomas.

The team also identified that for small cell neuroendocrine carcinomas to develop in the prostate, two tumor suppressor genes, TP53 and RB1, which are known for protecting normal cells from transforming into cancer cells, had to be simultaneously inactivated when PARCB was introduced.

Additional tests confirmed striking similarities between the PARCB-SCNC cells and small cell prostate cancer cells from humans. In particular, RNA expression and the turning on and off of certain genes were nearly identical.

"The similarities between the PARCB-SCNC cancers and human small cell prostate cancer samples were extraordinary," Witte said. "If you blindly gave the data sets to any statistician, they would think they were the same cells."

The team also looked at large databases of gene expression, to compare the patterns of gene expression in their PARCB-SCNC

cells to cancers of other organs. They found that the pattern of gene expression in PARCB-SCNC cells was extremely similar to those of both prostate and lung small cell cancers.

Next, they tested whether PARCB genes could alter healthy cells from human lungs into small cell lung cancers, and the scientists found that they could.

The team now is working on mapping which genes control the entire cascade of events that underlies the transition to small cell cancer.

"Our study revealed shared 'master gene regulators' -- the key proteins that control expression of multiple genes in small cell cancer cells," Witte said. "Studying the network of the master gene regulators could lead to a new way of combating deadly cancers."

The research was supported by the Broad Stem Cell Research Center Stem Cell Training Program and Hal Gaba Fund for Prostate Cancer Research, the UCLA Medical Scientist Training Program, the UCLA Specialized Program of Research Excellence in Prostate Cancer, the National Institutes of Health, the National Cancer Institute, the Prostate Cancer Foundation, the Department of Defense, the American Cancer Society and the W.M. Keck Foundation.

https://wb.md/2CtnJnN

Fines, Payouts Near $1B for 'Adulterated' Cancer Drugs

Whistleblowers Get $93M in New Settlement

Nick Mulcahy

AmerisourceBergen Corporation, a major US drug wholesaler, agreed this week to pay $625 million to resolve federal civil liability stemming from its "repackaging and sale of adulterated and unapproved new drugs" as well as from double billing and paying kickbacks to physicians, according to the US Department of Justice.

The settlement comes more than a year after AmerisourceBergen pleaded guilty to introducing these same adulterated and "misbranded" drugs into interstate commerce, which is a federal offense, and agreed to pay $260 million to settle the criminal charge.

"AmerisourceBergen Corporation placed corporate profits over patients' needs, endangering the health of vulnerable cancer patients," Richard P. Donoghue, US Attorney for the Eastern District of New York, said in a press statement this week.

The civil and criminal charges — and the $885 million in total fines and payouts — are all connected to a 13-year-long scheme perpetrated by a division of AmerisourceBergen.

Between 2001 and 2014, workers at the company's division Medical Initiatives, in Dothan, Alabama, created and shipped millions of prefilled syringes containing oncology drugs.

The drug-containing syringes were sent to oncology centers, medical practices, and physicians in all 50 states for use in the supportive care of patients with cancer undergoing chemotherapy.

The drugs included *Procrit* (epoetin alfa), *Aloxi* (palonosetron), *Kytril* (granisetron) and its generic form granisetron, *Anzemet* (dolasetron), and *Neupogen* (filgrastim).

Glass vials of the drugs were purchased by Medical Initiatives and then illegally repackaged into plastic syringes at the Alabama facility.

The repackaging took advantage of the vials' "overfill," or an extra 10% of drug. That amount is added into glass vials ensure that a full dose is available when drug is pulled in cancer clinics (because some might get stuck on the glass).

A clever exploitation of that overfill was the profit source for Medical Initiatives and its parent company, AmerisourceBergen, and their prefilled syringe product line. The company profited because it needed only 10 vials of drug to create 11 prefilled syringes thanks to the 10% overfill in each vial.

The US Department of Justice estimated a minimum profit of $99 million from the scheme from 2001-2014.

Medical Initiatives workers extracted the drugs — including the overfill — from the glass vials and "pooled" the drugs into

intravenous bags or larger containers. From those containers, which were reportedly sometimes left out overnight uncovered, the syringes would be filled.

Sanitary conditions at Medical Initiatives were allegedly substandard, with a packaging "cleanroom" that, at times, contained open adhesive bandages, iPods and exposed earbuds, skin lotion, aloe gel, chewing gum, and nonsterile mops, as reported by *Medscape Medical News* last year.

Also, according to company logs, the facility had on average more than 100 syringes each week that contained "floaters"; employees would not destroy these syringes but instead filtered out the debris. In the case of Procrit, this was a clear violation of US Food and Drug Administration (FDA) labeling, which calls for destruction of any such compromised product.

How They Avoided FDA Scrutiny

Notably, AmerisourceBergen did not register Medical Initiatives with the FDA as a repackager.

By avoiding registration, the company evaded FDA inspection and important safety and sterility safeguards, including current good manufacturing practices, according to the US Department of Justice. The prefilled syringe manufacturing process at Medical Initiatives was illegal; what they did to drugs and biologics (that is, altering them) requires that a company file a new drug application or biologic license application. It did neither. Instead the company claimed to be a pharmacy, which the federal authorities called a "sham."

Last year, an expert not involved with the United States' case commented on the safety of the prefilled syringes.

"There are always risks (low) — even from the original manufacturers' vials. But those risks rise significantly when that sterile product is transferred to a prefilled syringe, especially if appropriate sterile procedures and validations are not uniformly followed," said Dwight Kloth, PharmD, director of pharmacy at Fox Chase Cancer Center in Philadelphia, Pennsylvania, in an email to *Medscape Medical News*.

However, last year in a statement AmerisourceBergen said that "neither the government nor AmerisourceBergen are aware of any adverse events [among patients] associated with the use of Medical Initiatives Inc syringes."

In the civil charges settled this week, AmerisourceBergen was also accused of billing multiple physicians for individual vials, causing those physicians to bill the government more than once, and paying kickbacks to get physicians to purchase their cancer supportive-care drugs through the pre-filled syringe program.

In a statement reported by Reuters, AmerisourceBergen said that the recent settlement is indicative that some practices at the now disbanded Medical Initiatives unit "were not consistent with AmerisourceBergen's approach to corporate compliance."

The federal charges against AmerisourceBergen stem from three whistleblower suits filed by former Amerisource employee Michael Mullen, a Florida oncology practice Omni Healthcare, and Michigan pharmacy workers Daniel Sypula and Kelly Hodge, according to the legal news website *Law360*. The group will share $93 million in whistleblower reward money, but the terms were not disclosed.

http://bit.ly/2IGCSCA

Daytime naps help us acquire information not consciously perceived, study finds

'I'll sleep on it' proves scientifically sound advice

The age-old adage "I'll sleep on it" has proven to be scientifically sound advice, according to a new study which measured changes in people's brain activity and responses before and after a nap. The findings, published in the *Journal of Sleep Research*, support the

advice which suggests that a period of sleep may help weighing up pros and cons or gain insight before making a challenging decision.

The Medical Research Council-funded study, led by University of Bristol researchers, aimed to understand whether a short period of sleep can help us process unconscious information and how this might affect behaviour and reaction time.

The findings further reveal the benefits of a short bout of sleep on cognitive brain function and found that even during short bouts of sleep we process information that we are not consciously aware of.

While previous evidence demonstrates that sleep helps problem solving, resulting in enhanced cognition upon awaking; it was not clear whether some form of conscious mental process was required before or during sleep to aid problem solving. In this study, researchers hid information by presenting it very briefly and "masking" it - so it was never consciously perceived - the masked prime task. The hidden information, however, was processed at a subliminal level within the brain and the extent to which it interferes with responses to consciously perceived information was measured.

Sixteen healthy participants across a range of ages were recruited to take part in an experiment. Participants carried out two tasks - the masked prime task and a control task where participants simply responded when they saw a red or blue square on a screen. Participants practiced the tasks and then either stayed awake or took a 90-minute nap before doing the tasks again.

Using an EEG, which records the electrical activity naturally produced in the brain, researchers measured the change in brain activity and response pre-and-post nap.

Sleep (but not wake) improved processing speed in the masked prime task - but not in the control task - suggesting sleep-specific improvements in processing of subconsciously presented primes.

The findings suggest that even a short bout of sleep may help improve our responses and process information. Therefore, the results here suggest a potentially sleep-dependent, task-specific enhancement of brain processing that could optimise human goal-directed behaviour.

Importantly, while it is already known that the process of acquiring knowledge and information recall, memory, is strengthened during sleep. This study suggests that information acquired during wakefulness may potentially be processed in some deeper, qualitative way during sleep

Dr Liz Coulthard, Consultant Senior Lecturer in Dementia Neurology at the University of Bristol Medical School: Translational Health Sciences, said: "The findings are remarkable in that they can occur in the absence of initial intentional, conscious awareness, by processing of implicitly presented cues beneath participants' conscious awareness.

"Further research in a larger sample size is needed to compare if and how the findings differ between ages, and investigation of underlying neural mechanisms."

Paper: 'Nap-Mediated Benefit to Implicit Information Processing Across Age Using an Affective Priming Paradigm' by E Coulthard et al in the Journal of Sleep Research *[open access]*

http://bit.ly/2OKJnJY

European badgers' gut bacteria may be a powerful ally in the fight against tuberculosis

What do cattle, European badgers, and gut bacteria have in common?

They are all central players in a complex web surrounding a disease that affects multiple species, often with devastating results—tuberculosis. Now, new research funded by Morris Animal Foundation is shedding light on how one player, gut bacteria, may

help protect both badgers and cattle from this common, pervasive and deadly illness.

A major outbreak of bovine tuberculosis is significantly impacting agriculture in the United Kingdom. Badgers are known carriers of Mycobacterium bovis (the bacteria that causes tuberculosis in cattle) and are suspected to be a source of disease spread. The use of the human tuberculosis vaccine, Bacillus Calmette-Guerin, in badgers was considered to be a humane and long-term solution to reduce TB spillover from badgers but was falling short on effectiveness.

Dr. Jorge Gutierrez, University of Surrey researcher and lead author of the paper, wanted to know why and wondered if both the reason for this shortfall and its solution could be found in the gut bacteria of badgers.

The team, along with collaborators at the UK's Animal and Plant Health Agency, found gut bacteria from badgers may be decreasing the effectiveness of the BCG vaccine, but at the same time may be killing off *M. bovis*. It's a bad news/good news scenario that may help improve tuberculosis prevention. The team's findings recently were published in *BMC Microbiology*.

Some natural gut bacteria produce substances that can kill off their competitors or make the gut a hostile place for them. Dr. Gutierrez wondered if this might be going on in the badger gut too. His team isolated several types of natural gut bacteria, specifically lactic acid bacteria, from the feces of badgers. They found some of these bacteria kill off the BCG vaccine, which could reduce its effectiveness in this species. But with this finding, there is good news, too.

"As *M. bovis* is often excreted from infected badgers in their feces, we might find a way to use these gut bacteria to kill *M. bovis* instead; a way of naturally reducing contamination of the badgers' environment with the bacteria that cause TB," said Dr. Gutierrez. "We also found the lactic acid from badgers was good at stimulating the badger's immune system, which could be good news for improving the effectiveness of the vaccine."

Current TB intervention measures in the United Kingdom includes controlling cattle movement, limiting cattle contact with wildlife in pastures as well as culling badgers. Keeping cattle away from wildlife is challenging for livestock managers. Also, badgers live locally within a social structure that can be disrupted by culling, leading badgers to travel further, taking the disease with them. An effective vaccine strategy would be optimal for all animals affected by this disease, as well as being an environmentally sound solution

"New long-term, environmentally friendly and sustainable solutions are needed both for the badgers and other animals affected by this disease," said Dr. Gutierrez. "Our findings might explain in part why the BCG vaccine has variable results in badgers but also points to a possible future solution. There's still a lot to learn about the bacteria that make up the natural flora of the badger gut."

"All animals, including humans, contain both beneficial and harmful bacteria," said Dr. Kelly Diehl, Interim Vice President of Scientific Programs at Morris Animal Foundation. "Unfortunately, harmful bacteria get all the press as these microbes can make us sick or trigger large-scale disease outbreaks. Dr. Gutierrez's work is a superb example of how we might be able to use the beneficial bacteria already living in our bodies in novel ways to help combat diseases such as bovine TB."

More recently, Dr. Gutierrez and his wildlife management collaborator, the Spanish company Ingulados, isolated beneficial gut bacteria from wild boars, another TB reservoir species in parts of mainland Europe. They are exploring its use to naturally and safely help mitigate bovine TB spillover in Spain.

More information: *Anna Stedman et al, Lactic acid Bacteria isolated from European badgers (Meles meles) reduce the viability and survival of Bacillus Calmette-Guerin*

(BCG) vaccine and influence the immune response to BCG in a human macrophage model, BMC Microbiology (2018). DOI: 10.1186/s12866-018-1210-z

https://nyti.ms/2NtOWrH

Deep in Human DNA, a Gift From the Neanderthals

Long ago, Neanderthals probably infected modern humans with viruses, perhaps even an ancient form of H.I.V. But our extinct relatives also gave us genetic defenses.

By Carl Zimmer

People of Asian and European descent — almost anyone with origins outside of Africa — have inherited a sliver of DNA from some unusual ancestors: the Neanderthals.

These genes are the result of repeated interbreeding long ago between Neanderthals and modern humans. But why are those genes still there 40,000 years after Neanderthals became extinct?

A 45,000-year-old Neanderthal skeleton found in La Chapelle-aux-Saints, France. Many modern humans carry Neanderthal genes. **Pascal Goetgheluck/Science Source**

As it turns out, some of them may protect humans against infections.

In a study published on Thursday, scientists reported new evidence that modern humans encountered new viruses — including some related to influenza, herpes and H.I.V. — as they expanded out of Africa roughly 70,000 years ago.

Some of those infections may have been picked up directly from Neanderthals. Without immunity to pathogens they had never encountered, modern humans were particularly vulnerable.

"We were actually able to not only say, 'Yes, modern humans and Neanderthals exchanged viruses,'" said David Enard, an evolutionary biologist at the University of Arizona and co-author of the new paper, published in the journal Cell. "We are able to start saying something about which types of viruses were involved."

But if Neanderthals made us sick, they also helped keep us well. Some of the genes inherited from them through interbreeding also protected our ancestors from these infections, just as they protected the Neanderthals.

Lluis Quintana-Murci, a geneticist at the Pasteur Institute in Paris who was not involved in the new research, said that until now, scientists had not dreamed of getting such a glimpse at the distant medical history of our species.

"Five years ago, we would never have imagined that," he said.

Our immune cells kill off viruses with an arsenal of weapons, such as antibodies and signals that cause infected cells to commit suicide. But Dr. Enard began his research by wondering if humans have evolved other ways to avoid getting infected.

Viruses can't replicate on their own. They appropriate proteins inside our cells to do the heavy lifting, copying viral genes and building new shells to put them in. If those proteins were to change shape, however, it should become harder for viruses to use them to multiply. "Instead of a strategy where you attack the virus, you run away from it," said Dr. Enard.

To learn whether this is really a defense the body uses, Dr. Enard needed to find all the human proteins known to interact with at least one virus. But no such list existed. So he plowed through the scientific literature, looking for every example.

Once he had built a catalog of 1,300 proteins — it took four months — he studied their evolutionary history. By comparing these proteins across different species, he discovered that many have changed over the course of evolution.

In the several million years since our ancestors split from other primates, one-third of the adaptive changes in our proteins have occurred among those that interact with viruses. And this

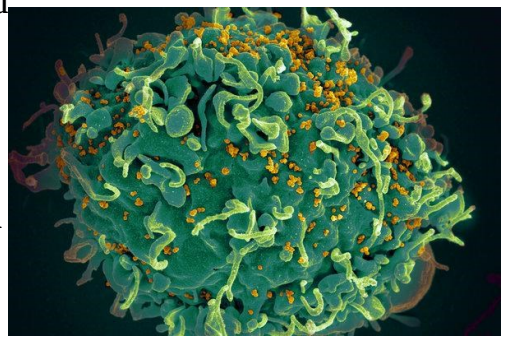
remarkable discovery led Dr. Enard and Dr. Dmitri Petrov, an evolutionary biologist at Stanford University, to wonder about Neanderthals.

The common ancestor both of modern humans and Neanderthals lived roughly 600,000 years ago, probably in Africa. Neanderthals left the continent long before modern humans and spread across a huge range, from the coast of Spain to Siberia, before becoming extinct.

From fossils, scientists have been able to reconstruct entire genomes of Neanderthals. And they've found that living people with non-African ancestry carry 1 percent or 2 percent Neanderthal DNA. That remnant DNA got into our gene pool through repeated interbreeding. But after Neanderthals became extinct, their DNA gradually declined in our genomes.

It's likely that most Neanderthal genes were bad for our health or reduced our fertility, and therefore were lost in modern humans. But certain Neanderthal genes became more common, probably because they provided some kind of evolutionary advantage.

In recent years, researchers have found that some of those genes encode proteins made by immune cells. They speculated that modern humans benefited by borrowing Neanderthal genes to fight infections.



A human T-cell, green, which helps the immune system fight viruses, under attack by H.I.V., in yellow. Neanderthal genes may have protected modern humans from an ancestor to the virus. **Science Source**

Dr. Enard and Dr. Petrov had a more specific question: Did modern humans acquire genes that helped cells evade specific viruses by altering the shapes of cellular proteins?

The researchers pored through the genomes of living Asians and Europeans, and discovered a large fraction of those Neanderthal genes make proteins that interact with viruses.

The viruses that infected Neanderthals must have posed a major threat to modern humans as they left Africa.

They had no immunity to these infections. But Neanderthals did, and through interbreeding, Neanderthals provided modern humans with genetic defenses. "It's like they brought the knife, but they also brought the shield," Dr. Petrov said.

Dr. Enard and Dr. Petrov also found clues about exactly what kinds of viruses these Neanderthal genes protect against.

In living humans, many of the proteins made by those genes interact only with influenza viruses, for example. Others interact only with H.I.V. "We are not saying that viruses that infect the human population now come from Neanderthals," said Dr. Enard. It's clear, for example, that H.I.V. jumped into humans just a century ago from chimpanzees.

Instead, it's likely that modern humans got infected with an ancient relative of H.I.V. Dr. Enard couldn't say how they were exposed to the new pathogen — perhaps directly through sex with Neanderthals, or by eating animals that both modern humans and Neanderthals hunted. But it's clear that, for billions of people alive today, Neanderthal genes likely play an important role in defending against such viruses. "We are not anything but the result of our past," said Dr. Quintana-Murci.

https://wb.md/2NrEDV5

Paying Physicians, Patients to Lower LDL-C Is Cost-effective

Financially incentivizing patients and physicians to control low-density-lipoprotein cholesterol (LDL-C) is cost-effective, a new model-based economic evaluation suggests.

Debra L Beck

"Our model allowed us to take a clinical trial scenario, which offered behavioral and financial incentives for only 12 months, and look at it over the lifetime because patients and payers aren't interested in just what happens during a trial, they want to avert events for a lifetime," explained senior author Thomas A. Gaziano, MD, MSc, Harvard T.H. Chan School of Public Health, Boston, in an interview.

"What we found is that it is cost-effective to offer these financial incentives even for just one year."

Their findings were published online September 14 in *JAMA Network Open*.

The analysis was a planned follow-on to a 4-group randomized clinical trial published in 2015 that showed financial incentives shared between physicians and patients were better at reducing LDL-C compared with no financial incentives, or incentives aimed at either physicians or patients alone.

Strategies for physician- or patient-only incentives were associated with greater costs and lower quality-adjusted life years (QALYs), compared with the shared-incentives strategy, which had an incremental cost-effectiveness ratio (ICER) of $60,000/QALY.

QALYs are the standard measure of effect in cost-effectiveness analysis and account for both the quantity and quality of life, whereas ICERs measure the difference in cost divided by the difference in health for an intervention compared with its alternative. A lower ICER suggests better value for money than a higher one.

"Even if we say the benefits trail off after 10 years and people don't remain vigilant about taking their medications, it was still cost-effective to invest in that year of incentives with a cost per QALY of about $60,000," said Gaziano.

When the duration of LDL-C level reduction was assumed to last only 5 years with linear waning, the ICER went up to $130,000 per QALY. But on the flip side, if no waning of effect was assumed, the shared-incentives strategy had a very affordable ICER of just $5900 per QALY.

Mean age, LDL-C levels, and 10-year coronary heart disease risk were similar in the modeled population (n = 1,000,000) and the observed trial population. To this, the investigators added a "virtual usual-care" control group that received no intervention at all.

This virtual usual-care strategy was associated with higher lifetime costs and lower QALYs compared to all other strategies, even assuming a 10-year waning in effect from the trial's interventions.

"Even the control group in the trial, who only used the electronic pill bottle but weren't given any financial incentives whatsoever, they still saw significant cholesterol lowering," Gaziano said. "So, just knowing that someone knew every time you didn't twist open your pill bottle helped people change their behaviour, and was cost-effective compared to usual care."

Gaziano is a cardiologist at Brigham & Women's Hospital and a health policy researcher involved in the development of decision analytic models to assess the cost-effectiveness of various screening, prevention and management decisions. Ankur Pandya, PhD, also from Harvard T.H. Chan School of Public Health, was the first author on the study.

A Wellness Initiative With Data

Commenting on these findings for *theheart.org | Medscape Cardiology*, Lauren G. Gilstrap, MD, MPH, also a cardiologist and health policy researcher, Dartmouth University, Lebanon, New Hampshire, called the analysis "sophisticated" and "rigorous."

"This study was very thoughtfully performed with an eye toward providing something relevant to insurers, payers, and employers — the entities we see who are looking for out-of-the-box ways to help individuals improve their overall health and who are taking up a number of these wellness initiatives," said Gilstrap.

"This is much more than most wellness initiatives have prior to implementation," she added. "With this analysis, they have some real empirical data on which to base a decision of whether or not they want to invest in something similar to this, rather than just saying, 'oh, that sounds good, it should probably work.'"

She felt the base-case assumption of a 10-year waning in effect on LDL-C was "on the conservative end of the spectrum."

"It's patient specific, but I think that by and large when people tolerate their medicines well and don't have a lot of side effects, and the vast majority of people do really well on statins, and the drugs are generically priced, I think the vast majority of patients will keep taking them," said Gilstrap.

Pay-4-Performance Initiative That Worked

In the original 2015 randomized trial on which this cost-effectiveness analysis was based, 344 primary care physicians and 1503 patients cared for by those physicians were enrolled. Patients were eligible if they had a 10-year Framingham Risk Score (FRS) of 20% or greater, had coronary artery disease equivalents with LDL-C levels of 120 mg/dL or greater, or had an FRS of 10% to 20% with LDL-C levels of 140 mg/dL or greater.

Patients in all four groups of the trial were given electronic pill bottles (Vitality GlowCap) that, when opened, wirelessly transmitted a signal to a web platform accessible by study staff.

Physicians in the physician-incentive group and patients in the patient-incentive group could "earn" just over $1000 annually in incentive payouts. In the shared-incentives intervention, that amount was split between the physician and patient.

Physicians and patients in the control group received no incentives tied to outcomes, but all patient participants received up to $355 each for trial participation and the electronic pill bottle.

The trial made innovative use of principles of behaviour economics, including leveraging loss aversion — the tendency to strongly prefer avoiding losses over acquiring similarly sized gains.

At 1 year, patients in the shared incentives group had achieved a mean reduction in LDL-C of 33.6 mg/dL, significantly greater than the 25.1 mg/dL reduction seen in the control group (P = .002).

Mean reductions in LDL-C in the physician incentives group (27.9 mg/dL) and patient incentives group (25.1 mg/dL) did not differ significantly from those seen in the control group.

"The effect seen with just the electronic pill bottle is consistent with prior literature," said Gilstrap. "We know from a whole host of prior studies...that directly observed therapy, pill counts, and things like that, dramatically improve adherence, so it would make sense that some form of accountability would have an impact."

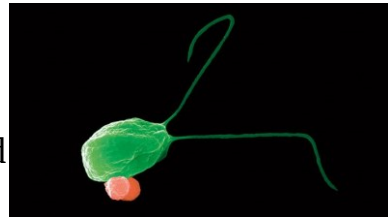
This study was funded by grants from the National Institute on Aging and the National Heart, Lung, and Blood Institute. Gaziano reported receiving funds through a grant from Novartis, multiple grants from the National Institute of Health, and advisory board with Takeda and Teva. Gilstrap disclosed no relevant financial relationships.

JAMA Network Open. Published online September 14, 2018. Abstract

https://go.nature.com/2y5hP8W

Bionic algae barrel through blood to deliver drugs

Plant cells pressed into service as swift and biodegradable couriers.



A swimming algal cell (green) is bedecked with spherical cargo carriers (red) that can be loaded with drugs. **O. Yasa et al./Adv. Mater.**

Swimming algae have been enlisted to carry drugs to individual cells, raising the prospect that such 'microswimmers' could deliver targeted therapies.

Miniscule devices propelled by living organisms can 'swim' through the body to deliver cargo such as doses of drugs. A variety of organisms have been joined with artificial structures to treat

some tumours, but the most commonly used organisms — bacteria — can be toxic and multiply rapidly, limiting their use.

As an alternative, Metin Sitti and his colleagues at the Max Planck Institute for Intelligent Systems in Stuttgart, Germany, tested the freshwater alga *Chlamydomonas reinhardtii*. Nontoxic and biodegradable, it moves by lashing a propeller-like tail. The researchers outfitted individual algal cells with magnetic polymer beads that could hold drugs in small amounts and allowed the researchers to steer the algae by applying a magnetic field to them.

In the lab, these microswimmers darted through bodily fluids such as blood at more than 100 micrometres per second and successfully deposited payloads onto mammalian cells. The authors plan future *in vivo* tests to determine the microswimmers' compatibility with the human immune system. *Adv. Mater.* (2018)

http://bit.ly/2y8J56f

The Pentagon Wants to Make an Army of Virus-Spreading Insects. Scientists Are Concerned.

Can a task force of insects carrying genetically modified viruses save America's farms — or are they an uncontrollable bioweapon in the making?

By Brandon Specktor, Senior Writer

This is the debate swirling around a controversial new Pentagon research project called "Insect Allies." Funded by the Defense Advanced Research Projects Agency (DARPA), the project involves using gene-editing techniques like CRISPR to infect insects with modified viruses that could help make America's crops more resilient. If a cornfield were hit by an unexpected drought or suddenly exposed to a pathogen, for example, Insect Allies might deploy an army of aphids carrying a genetically modified virus to slow the corn plant's growth rate.

According to the DARPA website, these "targeted therapies" could take effect in a single growing season, potentially protecting the American crop system from food security threats like disease, flooding, frost and even "threats introduced by state or non-state actors."

Members of the scientific community are skeptical. In a letter published today (Oct. 5) in the journal Science, a team of five scientists voiced concerns that the project could be easily exploited as a biological weapon — or at least be perceived as one by the international community.

"In our opinion the justifications are not clear enough. For example, why do they use insects? They could use spraying systems," Silja Voeneky, a co-author of the letter and professor of international law at the University of Freiburg in Germany, told The Washington Post."To use insects as a vector to spread diseases is a classical bioweapon."

Blake Bextine, program manager for Insect Allies, is less concerned. "Anytime you're developing a new and revolutionary technology, there is that potential for [both offensive and defensive] capability," Bextine told The Washington Post. "But that is not what we are doing. We are delivering positive traits to plants… We want to make sure we ensure food security, because food security is national security in our eyes."

Insect Allies is still in the early stages of development, and at least four U.S. colleges (Boyce Thompson Institute, Penn State University, The Ohio State University and the University of Texas at Austin)have received funding to carry out research. Bextine told The Washington Post that the project recently achieved its first milestone — testing whether an aphid could infect a stalk of corn with a designer virus that caused fluorescence. According to the Washington Post, "the corn glowed."

https://wb.md/2OJX0t1

PRAC Recommends Restrictions on Fluoroquinolone, Quinolones

EMA recommends restricting the use of systemic and inhaled fluoroquinolone and quinolone

Megan Brooks

The European Medicine Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) has recommended restricting the use of systemic and inhaled fluoroquinolone and quinolone antibiotics following a safety review.

"Very rarely, patients treated with fluoroquinolone or quinolone antibiotics have suffered long-lasting and disabling side effects, mainly involving muscles, tendons, and bones, and the nervous system," the EMA said in a news release.

The PRAC also advised that some medicines, including all those that contain a quinolone antibiotic, be removed from the market.

The PRAC recommended that the remaining fluoroquinolone antibiotics should not be used to treat infections that might improve without treatment or are not severe (such as throat infections); to treat patients who have previously had serious side effects with a fluoroquinolone or quinolone antibiotic; or to treat mild or moderately severe infections unless other antibacterial medicines commonly recommended for these infections cannot be used.

They should also not be used to prevent traveler's diarrhea or recurring lower urinary tract infections.

The PRAC further recommended that fluoroquinolone antibiotics be used with caution in the elderly, patients with kidney problems, patients who have had an organ transplantation, or those who are being treated with a systemic corticosteroid, as these patients are at higher risk of tendon injury caused by fluoroquinolone and quinolone antibiotics.

The PRAC recommends that healthcare providers advise patients to stop taking a fluoroquinolone antibiotic at the first sign of a side effect involving muscles, tendons, or bones (such as inflamed or torn tendon, muscle pain or weakness, and joint pain or swelling) or the nervous system (such as feeling pins and needles, tiredness, depression, confusion, suicidal thoughts, sleep disorders, vision and hearing problems, and altered taste and smell).

The PRAC safety review was announced in early 2017, as reported by *Medscape Medical News*, and covered the fluoroquinolone antibiotics ciprofloxacin, flumequine, levofloxacin, lomefloxacin, moxifloxacin, norfloxacin, ofloxacin, pefloxacin, prulifloxacin, and rufloxacin; and the quinolone antibiotics cinoxacin, nalidixic acid, and pipemidic acid.

In 2016, the US Food and Drug Administration (FDA) enhanced warnings about the link between fluoroquinolones and disabling and potentially permanent side effects involving tendons, muscles, joints, nerves, and the central nervous system.

In July, the FDA ordered label changes for fluoroquinolones to strengthen warnings about the antibiotics' risks for mental health side effects and serious blood sugar disturbances, as reported by *Medscape Medical News*.

The PRAC recommendations will now be sent to EMA's Committee for Medicinal Products for Human Use (CHMP), which will adopt the Agency's final opinion.

The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU member states. The new restrictions on the use of fluoroquinolones and quinolones will become applicable after a Commission decision is issued.

https://wb.md/2zVKDSj

Most Physicians Disenchanted With Their Profession: Survey

70% of physicians would not recommend their profession, 50% considering quitting within 5 years

Megan Brooks

Seven out of 10 physicians would not recommend their profession to their children or other family members, and more than half are thinking about retiring within the next 5 years, including one-third of those under the age of 50, according to a new national survey by The Doctors Company, a physician-owned medical malpractice insurer.

The survey of more than 3400 US physicians uncovered a "complex picture" of the attitudes of physicians nationwide toward the important issues facing the industry, with physicians reporting feeling disenchanted with the practice of medicine, the authors note in their report.

While the rate of change within practice models may have slowed in recent years, many physicians view the adoption of electronic health records (EHRs) and new reimbursement models as compromising the traditional doctor-patient relationship and the ability to provide quality patient care, the authors say.

Yet the survey also shows that physicians have not wavered in their advocacy for preserving the doctor-patient relationship and providing high-quality care.

Among the key findings from the Future of Healthcare survey:

* More than half of physicians (54%) plan to retire within the next 5 years because of pressure from declining reimbursement, increased administrative burden, and industry consolidation. The average age of men who took the survey was 62; for women, it was 55. Male physicians are more likely to retire than female physicians. Women are more likely to report that they are primary care physicians (PCPs) and men are much more likely to report being surgical specialists, so the burdens leading doctors to retire may be felt less on the PCP level, the authors say.

* More than half of physicians (54%) believe EHRs have had a negative impact on physician-patient relationships. "Doctors are concerned that EHRs are burdensome and distracting during patient interaction. One doctor suggested that the software causes major frustration to patients and physicians alike," the authors report.

* Nearly two-thirds (61%) of physicians believe EHRs are having a negative impact on efficiency and productivity. "Many comments suggest that doctors are frustrated with the functionality, reliability, and lack of interoperability within their EHRs," the authors note.

* More than 40% of doctors think value-based care will have a negative impact on the physician-patient relationship. "Many doctors worry that pay-for-performance reimbursement doesn't take into account the nuances of the doctor-patient relationship and puts a focus on population-level data instead of individual outcomes," the authors say. Along this same line, 63% of the physicians surveyed said they believe value-based care and reimbursement will have a negative impact on their earnings.

* Almost two-thirds (62%) of doctors say they don't plan to change practice models, perhaps indicating that the pace of practice change seen in recent years may have run its course, the authors say.

* Three quarters (75%) of solo practitioners plan to stay independent. "Private practices are increasingly being acquired by health systems that want to better control the continuum of care, and some medical groups are merging to create larger practices to drive efficiency, cost savings, and better technology," the authors note. "Nonetheless, three quarters of the solo practitioners who took this survey told us they don't expect to be a part of that industry shift, but rather expect to remain independent. While many are staying put in their current practice model, physicians expressed concern about how industry changes will impact the future of individual and small group practices."

* Physicians have mixed views on accountable care organizations, with 43% saying they do not plan to participate and 57% saying they plan to participate, are undecided, or need more information.

* Physicians also have mixed feelings about clinically integrated networks (CINs): 38% do not plan to participate in a CIN and 37% are either undecided or need more information about participating in a CIN.
* Physicians are also split on independent physician associations: 30% plan to participate, 36% do not plan to participate, and 34% are either undecided or need more information.
* More than half (56%) of physicians don't plan to participate in patient-centered medical homes, 15% plan to participate, and 29% are undecided or need more information.

The survey included physicians in a range of medical specialties from 49 states and the District of Columbia who are insured by The Doctors Company. The report was created in partnership with Modern Healthcare Custom Media and is available online.

http://bit.ly/2QtKuv0

Puppy Cuteness Is Perfectly Timed to Manipulate Humans

Dogs become most irresistible to people just when they need us most.

Sarah Elizabeth Adler

"All puppies are cute," explains Clive Wynne, the head of Arizona State University's canine-science laboratory. "But not all puppies are equally cute." Indeed, breeders have long found that puppies become their cutest selves at the eight-week mark; any older, and some breeders offer a discount to bolster would-be owners' weakened desire. Such fine-tuned preferences might seem arbitrary, even cruel. But recent research indicates that peak puppy cuteness serves important purposes—and might play a fundamental role in binding dog and owner together.

In a study published this spring, Wynne and his colleagues sought to pin down, scientifically, the timeline of puppy cuteness. Their finding largely matched that of breeders: People consistently rated dogs most attractive when they were six to eight weeks old. This age, Wynne says, coincides with a crucial developmental milestone: Mother dogs stop nursing their young around the eighth week, after which pups rely on humans for survival. (Puppies without human caretakers face mortality rates of up to 95 percent in their first year of life.) Peak cuteness, then, is no accident—at exactly the moment when our intervention matters most, puppies become irresistible to us.

to be especially vulnerable to cute things. Research dating back to the 1940s shows that virtually any creature with babylike features—large eyes, a bulging forehead, short limbs—is capable of drawing our affection, from the unsurprising (seals, koalas) to the odd (axolotls, a type of salamander) to the inanimate (Mickey Mouse). But canine cuteness is uniquely human-directed, and its strategic deployment is not confined to puppies. In a 2017 study of dogs ages one to 12, psychologists in the United Kingdom showed that people's pets were significantly more likely to raise their brows and stick out their tongue when humans were looking at them, visual cues that lend grown canines a puppyish air. Other research makes clear just why dogs seek to command our attention in this way. Oxytocin, the so-called love hormone, has been found to surge in dogs and their owners after they look in each other's eyes—initiating the same feedback loop that exists between human mothers and their babies. In other words, the more dogs get us to look at them, the more tightly bonded to them we grow.

Born blind and basically deaf, puppies aren't interactive in their first weeks of life, and Wynne notes that many people find animals in this stage alien and unappealing. A recent study focused on humans showed that, similar to six-week-old puppies, six-month-old babies are seen as significantly cuter than newborns.

Which brings us to the final purpose of peak cuteness: to make up for newborn ugliness. As the psychologists Gary Sherman and

Jonathan Haidt have proposed, the delayed onset of cuteness in human babies offers benefits far beyond kicking our caretaking instinct into overdrive—it also prompts a flood of social interactions, such as petting, playing, and baby-talking. These acts are developmentally crucial to puppies as well, but they can't be carried out very effectively with the extremely young. And so "one is not born cute," Sherman and Haidt conclude. "One becomes cute."

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A Man Took Antibiotics Before Going to the Dentist. He Developed An Ultra-Rare Brain Side Effect

For one 60-year-old man, a root canal turned life threatening

By Rachael Rettner, Senior Writer

SAN FRANCISCO — As scary as it may sound, a root canal is a fairly routine dental procedure. But for one 60-year-old man, the procedure turned life threatening when he developed meningitis, a swelling of the tissue surrounding his brain and spinal cord. Even more surprising, though, was that this dangerous outcome wasn't due to some ghastly slip of the dentist's drill or a germ-coated dental instrument. Indeed, the procedure went off without a hitch.

But several days after the procedure, the man arrived at an emergency room in New Jersey with a fever, headaches and neck pain. He informed doctors of his recent root canal and also mentioned that his dentist had instructed him to take amoxicillin — a common antibiotic — several days before the procedure.

Because of his symptoms, doctors suspected he had meningitis, which is almost always caused by an infection of some kind. So, they started him on antibiotics, but he only got worse.

That's when the doctors treating him suspected he might have drug-induced meningitis, or symptoms of meningitis that are triggered not by an infection, but by a specific drug. And in this case, the drug was amoxicillin.

Such a side effect is very rare, said Dr. Maria Nagori, an infectious-disease doctor at Geisinger Community Medical Center in Scranton, Pennsylvania, who treated the patient in 2017. "It's such an uncommon thing; I'd never heard of it before," said Nagori, who was completing a fellowship at Cooper University Hospital in Camden, New Jersey, at the time of the case.

Indeed, upon further research, Nagori found that only about a dozen cases of amoxicillin-induced meningitis had ever been reported.

Nagori presented the man's case report here on Oct. 4 at IDWeek, a meeting of several organizations focused on infectious diseases. The report has not yet been published in a peer-reviewed journal.

When tests for various infections came back negative, doctors stopped the man's antibiotic treatment, and he started getting better. At a follow-up visit, he was doing well, Nagori told Live Science.

After further questioning, doctors learned that the man had developed meningitis twice before: in 2011 and 2015. Each time, his meningitis symptoms occurred after he took amoxicillin before a dental procedure. But because the man had been treated at several different hospitals, and this is a rare side effect, no one made the connection with amoxicillin until his 2017 treatment.

What's more, the man didn't have any medical condition or risk factors that would have caused him to need antibiotics before a dental procedure like a root canal, Nagori said, meaning the antibiotics were unnecessary.

Nagori and colleagues advised the patient not to take amoxicillin again. Instead, he could take the antibiotic clindamycin.