http://www.eurekalert.org/pub_releases/2015-03/quot-rtc032215.php

Rush to crush risks medicine effectiveness

People who take more than four doses of medicine a day appear more likely to crush tablets or open capsules potentially reducing their effectiveness, QUT research has found.

Also most of those who modified medication dosage forms didn't seek advice from healthcare professionals, instead turning to family and friends.

The study, by researchers from QUT and the University of Queensland, was published in the Journal of Pharmacy Practice and Research.

Dr Esther Lau, one of the researchers from QUT's School of Clinical Sciences, said almost half (44.2 per cent) of the 369 respondents did not think there would be issues with crushing or modifying tablets or capsules.

"It is concerning that this many of the people surveyed did not seem aware of the potential dangers associated with modifying dosage forms," she said.

"Depending on the tablet or capsule, and the type of medicine, modifying the dosage forms can lead to reduced effectiveness of the medication, and increased risk of adverse effects. "The research found more than 14 per cent of people have trouble swallowing tablets or capsules, and some people modified their medication even when they had no trouble swallowing them."

Overall, one in ten people reported modifying medication dosage forms, regardless of how many doses they were taking.

"Many participants said they would not seek advice before modifying medication dosage forms, nor tell a health professional if they experienced difficulty swallowing," Dr Lau said.

"But what is equally concerning is that none of the participants were advised by a pharmacist on what to do to make it easier for them to swallow their tablets, but past research has already identified that healthcare professionals are not asking patients often enough about swallowing difficulties.

"Health professionals need to be more assertive in providing consumer education, to ensure the general public is aware of the potential issues associated with swallowing difficulties and modifying medication dosage forms.

"Pharmacists are the medication experts, and ideally a pharmacist should be involved in advising and providing suitable options for administering medications to patients at risk of swallowing difficulties. However, managing swallowing difficulties should take an interdisciplinary approach and healthcare professionals need to care for these patients as a team."

Dr Lau and colleague Dr Manuel Serrano Santos are working with a group of international experts to advocate for an interdisciplinary approach for caring for patients with, or at risk of, swallowing troubles.

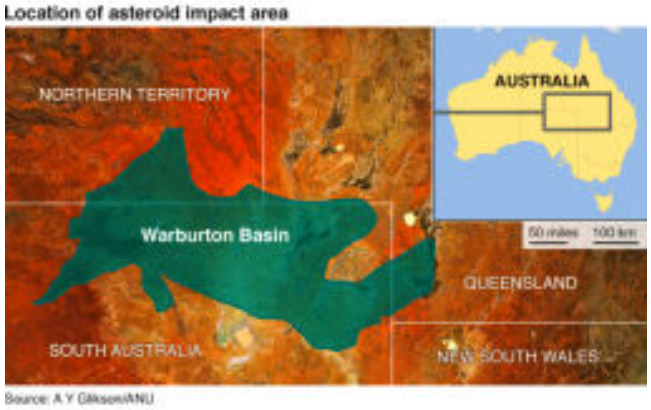
http://www.bbc.com/news/world-australia-32028173

'Largest ever asteroid impact' found in Australia

Scientists in Australia have discovered what they say is the largest asteroid impact area ever found.

The 400-kilometre (250-mile) wide area is buried deep in the earth's crust and consists of two separate impact scars. The team behind the discovery, from the Australian National University (ANU), said the asteroid broke into two before it hit, with each fragment more than 10km across. The impact is thought to have occurred at least 300 million years ago. Imaging of the rock in the Warburton Basin revealed deformation consistent with a huge impact

The surface crater has long since disappeared from central Australia's Warburton Basin but geophysical modelling below the surface found evidence of two massive impacts, said Dr Andrew Glikson, who led the ANU team. "It would have been curtains for many life species on the planet at the time," said Dr Glikson.



But the team, which published its findings in the geology journal Tectonophysics, has not been able to connect the impact to any known extinction.

"It's a mystery - we can't find an extinction event that matches these collisions," said Dr Glikson. "I have a suspicion the impact could be older than 300 million years."

Dr Andrew Glikson examines a sample of suevite - a rock with partially melted material formed during an impact. The rocks around the impact zone are roughly 300 to 600 million years old, but a layer of ash that would have been thrown up by the impact has not been detected as sediment in rock layers from the same period.

The large meteorite believed to have killed the dinosaurs 66 million years ago corresponds to a layer of sediment in rocks around the world.

"Large impacts like these may have had a far more significant role in the Earth's evolution than previously thought," Dr Glikson said.

The apparent impact zone in the Warburton Basin was discovered by accident while scientists were drilling 2km under the Earth's surface for a geothermal research project. The dig returned traces of rock that had been turned to glass by extreme temperature and pressure, consistent with a massive impact.

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Study shows association between migraine and carpal tunnel syndrome, reports PRS Global Open

Link may inform debate over nerve decompression surgery for migraine

Patients with carpal tunnel syndrome are more than twice as likely to have migraine headaches, reports a study in Plastic and Reconstructive Surgery - Global Open®, the official open-access medical journal of the American Society of Plastic Surgeons (ASPS).

The association also runs in the other direction, with migraine patients having higher odds of carpal tunnel syndrome, according to research by Dr. Huay-Zong Law and colleagues of University of Texas Southwestern Medical Center at Dallas. The findings add a new piece of evidence in the ongoing debate over the use of nerve decompression surgery as a treatment for migraine headaches.

Association between Carpal Tunnel Syndrome and Migraine

The researchers analyzed data from nearly 26,000 Americans responding to a national health survey. Among other questions, participants were asked whether they had had carpal tunnel syndrome during the past year or "severe headache or migraine" during the past three months. Patients with carpal tunnel syndrome have symptoms such as hand numbness and weakness, resulting from pressure on the median nerve in the wrist.

Based on these definitions, 3.7 percent of respondents had carpal tunnel syndrome and 16.3 percent had migraine headache. Associations between these two conditions were analyzed, with adjustment for patient- and health-related risk factors.

The results suggested that people with migraine were more likely to have carpal tunnel syndrome, and vice versa. Migraine was present in 34 percent of respondents with CTS, compared to 16 percent of those without CTS. After adjustment for other factors, the odds of having migraine were 2.6 times higher for those with CTS.

Carpal tunnel syndrome was present in eight percent of participants with migraine versus three percent of those without migraine. On adjusted analysis, the odds of having CTS were about 2.7 times higher for those with migraine.

The two conditions had some shared risk factors - especially female sex, obesity, diabetes, and smoking. Carpal tunnel syndrome was associated with older age and migraine with younger age. Both conditions were less common in Asians, and CTS was less common in Hispanics. The associations between CTS and migraine were independent of all of these factors.

Could Migraine Indicate Higher Future Risk of CTS?

Both CTS and migraines are common conditions with high costs and disability. The contributing causes of both conditions are "poorly understood." Carpal tunnel syndrome is the most common of a group of related conditions called compression neuropathies, with symptoms related to pressure on nerves.

Historically, migraine has not been considered to be a compression neuropathy. Dr. Law and colleagues write, "Recently, however, there is some evidence that migraine headache may be triggered by nerve compression in the head and neck, with some patients responding to nerve decompression by surgical release."

Some studies have reported improvement in migraine headaches after surgery to relieve pressure on nerves at specific migraine "trigger points." However, this concept remains "controversial" and "heavily debated," according to the authors.

The new study is the first to show an association between CTS and migraine. The nature of the connection remains unclear - the two conditions may share some "common systemic or neurologic risk factor," the researchers write.

Noting that migraine tends to occur at younger ages and CTS at older ages, Dr. Law and coauthors call for further studies to determine whether migraine headache may be an "early indicator" of patients who are more likely to develop CTS in the future. If so, such a connection "would allow for earlier diagnosis and treatment, or even prevention, of CTS by modification of risk factors," they conclude.

To hear more from the authors on their findings, visit:
https://www.youtube.com/watch?v=nrGFotX9oxM
Click here to read "An Association between Carpal Tunnel Syndrome and Migraine Headaches-National Health Interview Survey, 2010."
Article: "An Association between Carpal Tunnel Syndrome and Migraine Headaches-National Health Interview Survey, 2010." (doi: 10.1097/GOX.0000000000000257)

http://www.eurekalert.org/pub_releases/2015-03/njh-pvs032015.php

Promising vaccine strategy for type 1 diabetes extended to humans

Molecule that prevents Type 1 diabetes in mice has provoked an immune response in human cells

A molecule that prevents Type 1 diabetes in mice has provoked an immune response in human cells, according to researchers at National Jewish Health and the University of Colorado.The findings, published online in the Proceedings of the National Academy of Sciences, suggest that a mutated insulin fragment could be used to prevent Type 1 diabetes in humans.

"The incidence of Type 1 diabetes is increasing dramatically," said John Kappler, PhD, professor of Biomedical Research at National Jewish Health. "Our findings

provide an important proof of concept in humans for a promising vaccination strategy."

Type 1 diabetes is an autoimmune disease in which the immune system destroys the body's ability to produce insulin, a hormone essential for sugar metabolism. Researchers have tried administering insulin to people at risk for the disease as a form of immunotherapy similar to allergy shots. None of the trials has provoked an effective response.

The most recent findings suggest that an insulin fragment with a change to a single amino acid could provoke that elusive immune response. The idea for the substitution comes from more than a decade of work in Dr. Kappler's lab detailing the molecular minutiae of the immune system's response to insulin.

This work suggests that insulin is presented to the immune system in an unconventional manner, and that mutating one amino acid in an insulin fragment might provoke better recognition by the immune system.

In 2011, a team from Harvard University and the Dana Farber Cancer Institute reported that the strategy suggested by Dr. Kappler and his colleagues did indeed prevent type 1 diabetes in mice. Mice and humans, however, differ in many ways, and strategies that work in mice often fail to produce any response in humans.

In their current paper, Dr. Kappler, Aaron Michels, MD, at the Barbara Davis Center for Childhood Diabetes, and their colleagues mixed the naturally occurring insulin fragment and the mutated insulin fragment with separate cultures of human cells.

They found that human T cells responded minimally to the naturally occurring insulin fragment but quite strongly on the mutated one. The human T cells produced both pro-inflammatory and anti-inflammatory chemicals known as cytokines.

Researchers believe healthy immune responses balance pro- and anti-inflammatory factors. Autoimmune disease occurs when the pro-inflammatory response dominates.

While the current results do not prove that the mutated insulin fragment will work as a vaccine in humans, they do demonstrate a response in humans consistent with the vaccination response in mice. Some of the signals seen in human cells are associated T regulatory cells, which can dampen the immune response and hold it in check.

"The new findings confirm that the painstaking work we have done to understand the unconventional interaction of insulin and the immune system has relevance in humans and could lead to a vaccine and a treatment for diabetes," said Dr. Kappler. "We are eager to push this promising line of inquiry forward."

http://www.eurekalert.org/pub_releases/2015-03/uocd-dsf032015.php

Discontinuing statins for patients with life limiting illness

Discontinuing statin use in patients with late-stage cancer may help improve patients' quality of life without causing other adverse health effects

AURORA, Colo. - Discontinuing statin use in patients with late-stage cancer and other terminal illnesses may help improve patients' quality of life without causing other adverse health effects, according to a new study by led by researchers at the University of Colorado Anschutz Medical Campus and Duke University and funded by the National Institute of Nursing Research (NINR).

The finding, to be published in JAMA Internal Medicine on March 23, indicates that care for patients with advanced illness can be improved by discontinuing some therapies that are primarily preventive for other health concerns.

"There is an increasing evidence base that discontinuation of some therapies may be beneficial for selected patient populations," the authors write. Jean Kutner, MD, MSPH, professor of medicine at the University of Colorado School of Medicine, is the first author of the research study and Amy Abernethy, MD, PHD, of the Center for Learning Health Care at the Duke Clinical Research Institute, is the corresponding author.

Statins are among the most commonly prescribed medications in the United States with more than 25 percent of the nation's Medicare beneficiaries receiving statin therapy. These medications are usually taken to lower cholesterol and reduce the risk of heart attack or stroke. The benefits of statins typically take two years to accrue.

The study evaluated 381 patients. About half of them discontinued statins, while the other half continued the therapy. The average age of the patients was 74 years old and 48.8 percent of them had cancer. The median survival time for the entire study population was 219 days and the proportion of participants who died within 60 days was not significantly different between the groups that continued or discontinued statin therapy.

"If the results we report - improved quality of life, no significant differences in mortality, and modest cost savings - had been produced by a randomized clinical trial of a new drug in patients with advanced life-limiting illness, the trial would be heralded as a breakthrough and there would be discussion of how to speed access to this new drug," the authors write. "The same energy needs to be applied to determining when it is appropriate for physicians to discuss discontinuing statin therapy with their patients."

The study's results address significant concerns related to end-of-life health care. In the last year of life, the number of medicines increases by 50 percent, so reducing the number of medications may relieve the pill burden on some patients.

Also, more than 80 percent of Americans are expected to die of chronic illnesses, primarily cardiovascular disease, cancer, dementia and chronic lung disease.
Because statins are effective in primary prevention of cardiovascular disease, the number of patients on the therapy is expanding and it is frequently continued until the end of patients' life.
The authors say that their study should prompt physicians to discuss the uncertain benefit and possible harm of continuing statin therapy for people with life-liming illness and functional decline.
"For patients with shorter life expectancy, greater concern about pill burden, and more comfort-oriented goals of care," the authors conclude, "physicians may endorse discontinuing statins as a means to reduce the number of medications without apparent harmful effects on survival or quality of life."

http://www.eurekalert.org/pub_releases/2015-03/cwru-mav032315.php

Metformin and vitamin D3 show impressive promise in preventing colorectal cancer

Case Western Reserve scientists collaborate with China's Lanzhou University investigators in exploring the dual compound strategy

The concept was simple: If two compounds each individually show promise in preventing colon cancer, surely it's worth trying the two together to see if even greater impact is possible. In this instance, Case Western Reserve cancer researcher Li Li, MD, PhD, could not have been more prescient.
Not only did the combination of the two improve outcomes in animal studies, but the dual-compound effect was dramatically better than either option alone. Even better, these impressive results required only modest amounts of metformin and Vitamin D3, making concerns about side effects from mega-dosing entirely moot. Their piece served as the cover feature February's edition of Cancer Prevention Research.
The results are so promising, in fact, that Li, the Case Comprehensive Cancer Center's associate director for prevention research, already has three options in mind for clinical trials - outright primary prevention, prevention of colon adenoma recurrence, and enhancement of chances for survival for those who have colorectal cancers. In addition, compounds already are commercially available, which means they have proceeded successfully through several rounds of safety testing. As a result, the path to tests on humans will be somewhat smoother.
"In the two animal models, we showed that metformin and vitamin D3 did indeed work together," Li said. "Clearly, if we put the two together, they are much more potent in preventing colon neoplasia than by taking just either one of them alone. The medium dose also tells us that it is not necessary to take huge doses of the drugs to have a cancer-prevention effect. If the results in the animal models translate to humans, that will be a highly significant finding in colorectal cancer prevention."
Vitamin D3 is synthesized in the skin through diet or ultra violet irradiation. Among other things, the nutrient regulates cell proliferation, differentiation and apoptosis, all key components in preventing runaway cell growth characteristic of cancer. Importantly, vitamin D3 inhibits activation of the Wnt/β-catenin pathway, which triggers the genes responsible for proliferation of colon cancer cells.
Metformin inhibits abnormal cell growth by stimulating the AMP-activated protein kinase (AMPK) pathway. AMPK leads to weakened mTOR signaling and protein synthesis necessary for cancer cells to grow. Metformin has also been shown to suppress proliferation of colon epithelial cells and aberrant crypt foci (ACF). ACF are clusters of abnormal tube-like glands in the colon and rectum that lead to the development of colorectal polyps, often the precursors to colorectal cancer.
The metformin-vitamin D3 research in the mice and rats grew out of a collaboration formed between Case Western Reserve and researchers in China as part of what had been the Case Western Reserve Center of Transdisciplinary Research on Energetics and Cancer (TREC) program led by Nathan A. Berger, MD, (2005-2011) and the Case-China Health Initiative that Li directs. The National Institutes of Health-funded Case TREC targeted research toward reducing cancer linked with obesity, poor diet and low levels of physical activity. Li was principal investigator in one of the three main projects in the TREC program and has since engaged in active collaboration with investigators in China. Therefore, it was a natural for him to turn to colleagues in China to collaborate in the metformin-vitamin D3 research in lab animals. Essentially, Li conceived the hypothesis and participated in the study's design, while Lanzhou University scientists performed the extensive study in 110 rats and 125 mice.
For the investigation in China, the rats were induced chemically for a predisposition to develop neoplasia (precancerous cells) of the colon. The mice were induced chemically to develop colitis, an inflammation of the colon that often leads to neoplasia. In both the rats and the mice, some groups of the animals received varying doses of both vitamin D3 and metformin, and other groups received either vitamin D3 alone or metformin alone. The control groups either received no drug or Celebrex (celecoxib), a powerful non-steroidal anti-inflammatory drug as a positive control. The rats received treatment for 18 weeks and the mice for 20 weeks.
"Few colon neoplasias developed in the animals receiving moderate doses of metformin-vitamin D combination," said Li, also director of Swetland Center for

Environmental Health and Mary Ann Swetland Professor of Environmental Health Sciences and professor of Family Medicine at Case Western Reserve University School of Medicine. "On average, there was also a 40 percent decrease in the development of polyps in all animals receiving both drugs in combination compared to the control groups."

Overall, rats treated with metformin and vitamin D3 or with each compound singly experienced decreased numbers of tumors compared to the control groups, but the moderate dose metformin-vitamin D3 combo resulted in the most significant tumor-inhibiting effect. Tumor numbers in the colons of the rats were substantially less in the moderate-dose combo group. As for the mice, numbers of colorectal tumors were significantly fewer in the metformin-vitamin D3 combo group and noticeably fewer in mice treated with vitamin D3 alone.

Clinical trial options in humans include:

Testing dual metformin-vitamin D3 as an ongoing therapy for individuals who have had colorectal cancer as neo-adjuvant therapy. The goal would be increasing their chances for survival. Data has shown that vitamin D levels alone have been associated with better survival for people diagnosed with the illness;

Testing the metformin-vitamin D3 combination as a prevention measure in individuals with familial adenomatous polyposis (FAP). FAP causes affected individuals to acquire thousands of colon polyps when they are in their 20s, and by the time they are age 30 or 40, they are diagnosed with colon cancer;

Administering both compounds in individuals diagnosed with colon cancer one to four weeks before their surgery. The idea would be to compare their initial cancer biopsy tissue with the removed colon cancer tumor for changes in gene expression levels. The findings would reveal mechanisms for the progression of the disease, and then therapeutics could be developed to interrupt those.

"Persons with a 10 millimeter or larger adenoma polyp or high-grade neoplasia have a 50 percent chance for recurrence within four years," Li said. "We can screen them for colon cancer with colonoscopy every few years, but we don't have much to offer them in terms of prevention. This metformin-vitamin D3 combo may provide an opportunity to prevent recurrence."

The incidence of colon cancer is unlikely to recede any time soon. The illness is linked to obesity, metabolic syndrome, insulin resistance and diabetes, and these conditions are on the rise in the Western world and encroaching on Asia, particularly China. If proven effective, the metformin-vitamin D3 combo could eventually be prescribed in individuals with a strong family history of colon cancer and with leading risk factors.

"There is a lot of talk now about drug repurposing today where one drug developed for one condition can be used for an entirely different one," Li said. "Here we have two well-proven medicines that if you put them together, they appear prevent cancer, and they are safe."

Also weighing on this latest research by Li and fellow investigators was Stanton Gerson, MD, Asa & Patricia Shiverick and Jane Shiverick (Tripp) Professor of Hematological Oncology, and Director of the Case Comprehensive Cancer Center at Case Western Reserve University. "Millions of individuals with diabetes, even those who are pregnant, are taking metformin, and individuals with vitamin D deficiency are taking vitamin D3 medications," he said. "So metformin and vitamin D3 may already be providing a colorectal cancer prevention benefit to a significant number of people."

Joining Li in this research effort were senior coauthor Yong-Jie Wu, lead author Wan Li and contributing authors Qi Long Wang, Xia Liu, Shu Hong-Don, Hong-Xia Li, Chun-Yang Li, Li-Shu Guo, Jing-Miao Gao, and Lan Ma, all of the Key Laboratory of Preclinical Study for New Drugs of Gansu Province, Department of Pharmacology, School of Basic Medicine, Lanzhou University, and Nathan A. Berger, Case Comprehensive Cancer Center.

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http://www.eurekalert.org/pub_releases/2015-03/ciot-oss032315.php

Our solar system may have once harbored super-earths

Caltech and UC Santa Cruz researchers say Earth belongs to a second generation of planets

Long before Mercury, Venus, Earth, and Mars formed, it seems that the inner solar system may have harbored a number of super-Earths - planets larger than Earth but smaller than Neptune. If so, those planets are long gone - broken up and fallen into the sun billions of years ago largely due to a great inward-and-then-outward journey that Jupiter made early in the solar system's history.

This possible scenario has been suggested by Konstantin Batygin, a Caltech planetary scientist, and Gregory Laughlin of UC Santa Cruz in a paper that appears the week of March 23 in the online edition of the Proceedings of the National Academy of Sciences (PNAS). The results of their calculations and simulations suggest the possibility of a new picture of the early solar system that would help to answer a number of outstanding questions about the current makeup of the solar system and of Earth itself. For example, the new work addresses why the terrestrial planets in our solar system have such relatively low masses compared to the planets orbiting other sun-like stars.

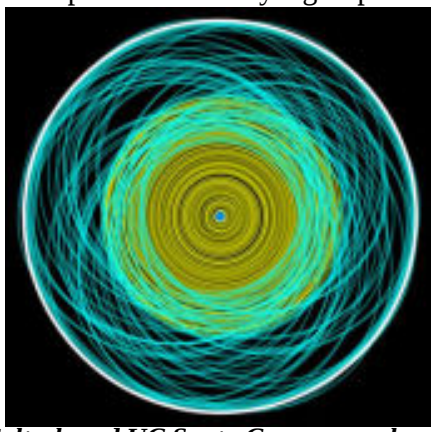
"Our work suggests that Jupiter's inward-outward migration could have destroyed a first generation of planets and set the stage for the formation of the mass-depleted terrestrial planets that our solar system has today," says Batygin, an assistant professor of planetary science. "All of this fits beautifully with other

recent developments in understanding how the solar system evolved, while filling in some gaps."

Thanks to recent surveys of exoplanets - planets in solar systems other than our own - we know that about half of sun-like stars in our galactic neighborhood have orbiting planets. Yet those systems look nothing like our own. In our solar system, very little lies within Mercury's orbit; there is only a little debris - probably near-Earth asteroids that moved further inward - but certainly no planets. That is in sharp contrast with what astronomers see in most planetary systems. These systems typically have one or more planets that are substantially more massive than Earth orbiting closer to their suns than Mercury does, but very few objects at distances beyond.

"Indeed, it appears that the solar system today is not the common representative of the galactic planetary census. Instead we are something of an outlier," says Batygin. "But there is no reason to think that the dominant mode of planet formation throughout the galaxy should not have occurred here. It is more likely that subsequent changes have altered its original makeup."

According to Batygin and Laughlin, Jupiter is critical to understanding how the solar system came to be the way it is today. Their model incorporates something known as the Grand Tack scenario, which was first posed in 2001 by a group at Queen Mary University of London and subsequently revisited in 2011 by a team at the Nice Observatory. That scenario says that during the first few million years of the solar system's lifetime, when planetary bodies were still embedded in a disk of gas and dust around a relatively young sun, Jupiter became so massive and gravitationally influential that it was able to clear a gap in the disk. And as the sun pulled the disk's gas in toward itself, Jupiter also began drifting inward, as though carried on a giant conveyor belt.



This snapshot from a new simulation by Caltech and UC Santa Cruz researchers depicts a time early in the solar system's history when Jupiter likely made a grand inward migration (here, Jupiter's orbit is represented by the thick white circle at about 2.5 AU). As it moved inward, Jupiter picked up primitive planetary building blocks, or planetesimals, and drove them into eccentric orbits (turquoise) that overlapped the unperturbed part of the planetary disk (yellow), setting off a cascade of collisions that would have ushered any interior planets into the sun. K. Batygin/Caltech

"Jupiter would have continued on that belt, eventually being dumped onto the sun if not for Saturn," explains Batygin. Saturn formed after Jupiter but got pulled toward the sun at a faster rate, allowing it to catch up. Once the two massive planets got close enough, they locked into a special kind of relationship called an orbital resonance, where their orbital periods were rational - that is, expressible as a ratio of whole numbers. In a 2:1 orbital resonance, for example, Saturn would complete two orbits around the sun in the same amount of time that it took Jupiter to make a single orbit. In such a relationship, the two bodies would begin to exert a gravitational influence on one another.

"That resonance allowed the two planets to open up a mutual gap in the disk, and they started playing this game where they traded angular momentum and energy with one another, almost to a beat," says Batygin. Eventually, that back and forth would have caused all of the gas between the two worlds to be pushed out, a situation that would have reversed the planets' migration direction and sent them back outward in the solar system. (Hence, the "tack" part of the Grand Tack scenario: the planets migrate inward and then change course dramatically, something like a boat tacking around a buoy.)

In an earlier model developed by Bradley Hansen at UCLA, the terrestrial planets conveniently end up in their current orbits with their current masses under a particular set of circumstances - one in which all of the inner solar system's planetary building blocks, or planetesimals, happen to populate a narrow ring stretching from 0.7 to 1 astronomical unit (1 astronomical unit is the average distance from the sun to Earth), 10 million years after the sun's formation. According to the Grand Tack scenario, the outer edge of that ring would have been delineated by Jupiter as it moved toward the sun on its conveyor belt and cleared a gap in the disk all the way to Earth's current orbit.

But what about the inner edge? Why should the planetesimals be limited to the ring on the inside? "That point had not been addressed," says Batygin.

He says the answer could lie in primordial super-Earths. The empty hole of the inner solar system corresponds almost exactly to the orbital neighborhood where super-Earths are typically found around other stars. It is therefore reasonable to speculate that this region was cleared out in the primordial solar system by a group of first-generation planets that did not survive.

Batygin and Laughlin's calculations and simulations show that as Jupiter moved inward, it pulled all the planetesimals it encountered along the way into orbital resonances and carried them toward the sun. But as those planetesimals got closer to the sun, their orbits also became elliptical. "You cannot reduce the size of your orbit without paying a price, and that turns out to be increased ellipticity,"

explains Batygin. Those new, more elongated orbits caused the planetesimals, mostly on the order of 100 kilometers in radius, to sweep through previously unpenetrated regions of the disk, setting off a cascade of collisions among the debris. In fact, Batygin's calculations show that during this period, every planetesimal would have collided with another object at least once every 200 years, violently breaking them apart and sending them decaying into the sun at an increased rate.

The researchers did one final simulation to see what would happen to a population of super-Earths in the inner solar system if they were around when this cascade of collisions started. They ran the simulation on a well-known extrasolar system known as Kepler-11, which features six super-Earths with a combined mass 40 times that of Earth, orbiting a sun-like star. The result? The model predicts that the super-Earths would be shepherded into the sun by a decaying avalanche of planetesimals over a period of 20,000 years.

"It's a very effective physical process," says Batygin. "You only need a few Earth masses worth of material to drive tens of Earth masses worth of planets into the sun."

Batygin notes that when Jupiter tacked around, some fraction of the planetesimals it was carrying with it would have calmed back down into circular orbits. Only about 10 percent of the material Jupiter swept up would need to be left behind to account for the mass that now makes up Mercury, Venus, Earth, and Mars.

From that point, it would take millions of years for those planetesimals to clump together and eventually form the terrestrial planets - a scenario that fits nicely with measurements that suggest that Earth formed 100-200 million years after the birth of the sun. Since the primordial disk of hydrogen and helium gas would have been long gone by that time, this could also explain why Earth lacks a hydrogen atmosphere. "We formed from this volatile-depleted debris," says Batygin.

And that sets us apart in another way from the majority of exoplanets. Batygin expects that most exoplanets - which are mostly super-Earths - have substantial hydrogen atmospheres, because they formed at a point in the evolution of their planetary disk when the gas would have still been abundant. "Ultimately, what this means is that planets truly like Earth are intrinsically not very common," he says.

The paper also suggests that the formation of gas giant planets such as Jupiter and Saturn - a process that planetary scientists believe is relatively rare - plays a major role in determining whether a planetary system winds up looking something like our own or like the more typical systems with close-in super-Earths. As planet hunters identify additional systems that harbor gas giants, Batygin and Laughlin will have more data against which they can check their hypothesis - to see just how often other migrating giant planets set off collisional cascades in their planetary systems, sending primordial super-Earths into their host stars.

The researchers describe their work in a paper titled "Jupiter's Decisive Role in the Inner Solar System's Early Evolution."

http://www.eurekalert.org/pub_releases/2015-03/osu-szd032315.php

Study: Zinc deficiency linked to immune system response, particularly in older adults

Zinc, an important mineral in human health, appears to affect how the immune system responds to stimulation, especially inflammation, new research from Oregon State University shows.

CORVALLIS, Ore. - Zinc deficiency could play a role in chronic diseases such as cardiovascular disease, cancer and diabetes that involve inflammation. Such diseases often show up in older adults, who are more at risk for zinc deficiency.

"When you take away zinc, the cells that control inflammation appear to activate and respond differently; this causes the cells to promote more inflammation," said Emily Ho, a professor and director of the Moore Family Center for Whole Grain Foods, Nutrition and Preventive Health in the OSU College of Public Health and Human Sciences, and lead author of the study.

Zinc is an essential micronutrient required for many biological processes, including growth and development, neurological function and immunity. It is naturally found in protein-rich foods such as meat and shellfish, with oysters among the highest in zinc content.

Approximately 12 percent of people in the U.S. do not consume enough zinc in their diets. Of those 65 and older, closer to 40 percent do not consume enough zinc, Ho said. Older adults tend to eat fewer zinc-rich foods and their bodies do not appear to use or absorb zinc as well, making them highly susceptible to zinc deficiency.

"It's a double-whammy for older individuals," said Ho, who also is a principal investigator with the Linus Pauling Institute.

In the study, researchers set out to better understand the relationship between zinc deficiency and inflammation. They conducted experiments that indicated zinc deficiency induced an increase in inflammatory response in cells. The researchers were able to show, for the first time, that reducing zinc caused improper immune cell activation and dysregulation of a cytokine IL-6, a protein that affects inflammation in the cell, Ho said.

Researchers also compared zinc levels in living mice, young and old. The older mice had low zinc levels that corresponded with increased chronic inflammation and decreased IL-6 methylation, which is an epigenetic mechanism that cells use

to control gene expression. Decreased IL-6 methylation also was found in human immune cells from elderly people, Ho said.

Together, the studies suggest a potential link between zinc deficiency and increased inflammation that can occur with age, she said.

The findings were published recently in the journal Molecular Nutrition & Food Research. Co-authors are Carmen P. Wong and Nicole A. Rinaldi of the College of Public Health. The research was supported by the Oregon Agricultural Experiment Station, Bayer Consumer Care AG of Switzerland, and OSU.

Understanding the role of zinc in the body is important to determining whether dietary guidelines for zinc need to be adjusted. The recommended daily intake of zinc for adults is 8 milligrams for women and 11 milligrams for men, regardless of age. The guidelines may need to be adjusted for older adults to ensure they are getting enough zinc, Ho said.

There is no good clinical biomarker test to determine if people are getting enough zinc, so identifying zinc deficiency can be difficult. In addition, the body does not have much ability to store zinc, so regular intake is important, Ho said. Getting too much zinc can cause other problems, including interfering with other minerals. The current upper limit for zinc is 40 milligrams per day.

"We think zinc deficiency is probably a bigger problem than most people realize," she said. "Preventing that deficiency is important."

Understanding why older adults do not take in zinc as well is an important area for future research, Ho said. Additional research also is needed to better understand how zinc works in the body, she said.

http://www.eurekalert.org/pub_releases/2015-03/uovh-spc032015.php

Sweeping prostate cancer review upends widely held belief on radiation after surgery

Findings shed light on side effects of radiation after prostate removal

Important news for men receiving treatment for prostate cancer: Two new studies from the University of Virginia School of Medicine have upended the widely held view that it's best to delay radiation treatment as long as possible after the removal of the prostate in order to prevent unwanted side effects.

"The common teaching has been, without clear evidence, that urinary incontinence and erectile function are worse when radiation is delivered earlier rather than later, but we didn't see any protective effect of delayed radiation compared to earlier radiation," said radiation oncologist Timothy N. Showalter, MD, of the UVA Cancer Center."It contradicts the clinical principle of delaying radiation as long as possible for the sake of the patient's side effects. It really speaks against that, and that ought not to be used for a reason to delay radiation."

The findings inject hard facts into a debate that has long divided the medical community, with many radiation oncologists preferring adjuvant therapy - radiation given soon after prostate removal to kill off any remaining cancer cells - and many urologists preferring salvage therapy - radiation given later, when prostate-specific antigen tests suggest it's needed.

"Urologists tend to prefer to forgo adjuvant radiation therapy, because they fear the side effects, and radiation oncologists tend to prefer offering adjuvant radiation therapy because they fear the risk of metastasis [cancer spreading to other sites in the body]," Showalter said.

Showalter conducted his two studies to address the lack of facts, in hopes of providing doctors with the information they need to determine the best course of treatment.

"There's this commonly held belief that the longer you delay radiation therapy, the more opportunity a patient has for recovery from prostatectomy, and therefore the better long-term function in terms of urinary and bowel function - the longer you delay it, the better they'll function," he said.

"A lot of clinicians believe that if you wait six months, 12 months, 18 months, that each additional step gets you some benefit in terms of toxicity. That didn't make sense to me from a medical perspective, because I can't think of any other surgery where we think recovery requires a year or more. We often, for other cancers, deliver post-operative radiation very soon."

The findings, based on a review of approximately 16,000 patients' outcomes, shed light on the side effects of radiation treatment after prostate removal. "What we found is that the addition of radiation therapy after prostatectomy does lead to a noticeable increase in GI [gastrointestinal] and GU [genitourinary] side effects. However, delaying radiation therapy offers no protective benefit and in fact may increase the risk of GI complications," Showalter said. The research also found adjuvant therapy did not increase rates of erectile dysfunction.

The takeaway for men receiving prostate cancer treatment, Showalter said, is that they should discuss the best strategy with their physicians based on their particular case. "If someone's at generally low risk of prostate cancer recurrence and they have low-grade disease, it's probably still reasonable to take a delayed salvage radiation therapy approach," Showalter said.

"Once there's a real, compelling reason to deliver radiation, there doesn't seem to be a benefit to delaying their radiation in terms of avoiding complications. And we know from other studies, the earlier radiation is delivered, the more effective it is for these patients. The more likely it is to cure them."

http://bit.ly/18YFZT6

Sushi parasite inspires worm test for cancer

Roundworms can sniff out cancer in urine

by **Vijay Shankar**

Dogs do it. Rats do it. Even some people seem to be able to sniff out cancer and other diseases. Now we can add the humble roundworm to the list of super-smellers.

Japanese researchers have discovered that *Caenorhabditis elegans* worms can detect cancer in people's urine. They are working with technology companies Hitachi and Johnan to turn the finding into a diagnostic test that can be used to catch the disease in its early stages.

"In existing tests, people must have different examinations according to the type of cancer they have", says Takaaki Hirotsu from Kyushu University in Fukuoka, Japan, who co-led the work. "Our odour-based test detected all nine types of cancer we tested."

Scent of a tumour

Hirotsu and his colleague, Hideto Sonada, decided to investigate roundworms' cancer detecting abilities after Sonada encountered a 63-year-old man with *Anisakis* larvae in his digestive system. This roundworm can be picked up by eating infected raw fish.

The parasites had attached themselves to a small lesion in the man's stomach that turned out to be the early stages of gastric cancer. The case is one of 29 recorded since 1970 of roundworms attaching themselves to cancers, 62 per cent of which were when the cancer was still in its early stages.

Hirotsu and Sonada's team wondered if the odour of the cancer lesion was attracting the roundworms. To find out, they put droplets of culture medium that cancer cells had grown in on one side of petri dishes. On the other side they put drops of fresh culture medium. When they added *C. elegans* to the dishes, the worms moved towards the cancer medium.

They grew other kinds of cells in the medium, such as human skin cells, but these induced no such attraction in the worms. The researchers also knocked out the olfactory sense neurons in some of the worms. This stopped them moving towards the cancer side of the dish, suggesting that the worms are indeed attracted by smell.

Sensitive sniffers

To see if they could diagnose cancer, the worms were placed in the vicinity of spots of urine from people with and without cancer. Sure enough, the worms were attracted only to the samples of the people with cancer. With samples taken from 242 people, 24 of whom had a cancer diagnosis, the worms made the correct diagnosis 96 per cent of the time, a success rate that the researchers say is better than any blood test.

The participants had various different types of cancer, and Hirotsu says the worms successfully identified cancer in all nine they were exposed to - stomach, colorectal, colon, oesophageal, pancreas, bile duct, prostate, breast and lung cancer.

The team are now investigating whether different cancer types release different odours, and whether this has an effect on the worms. They hope to have a commercial product ready by 2019. The idea would be that users send a urine sample to the company and get the results back the next day, says Hirotsu.

"It's very surprising that the nematodes exhibited such a strong binary response to 'cancer' versus 'no cancer' urine," says Michael Phillips at Menssana Research, a New Jersey-based company developing diagnostic tests based on people's breath. He says the complexity of the tumours and the environment in which the samples are collected can contribute to confusing results. "We ought to suspend judgement on the test until it has been replicated in other labs using very careful controls," he says.

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http://www.eurekalert.org/pub_releases/2015-03/acs-mfh021915.php

More flavorful, healthful chocolate could be on its way

A way to make chocolate even more nutritious and sweeter

DENVER - Chocolate has many health benefits - it can potentially lower blood pressure and cholesterol and reduce stroke risk. But just as connoisseurs thought it couldn't get any better, there's this tasty new tidbit: Researchers have found a way to make the treat even more nutritious - and sweeter.

They will describe their research here today at the 249th National Meeting & Exposition of the American Chemical Society (ACS), the world's largest scientific society. The meeting features nearly 11,000 reports on new advances in science and other topics. It is being held here through Thursday.

Cocoa undergoes several steps before it takes shape as a candy bar. Workers cut down pods from cocoa trees, then split open the pods to remove the white or purple cocoa beans. They are fermented in banana-lined baskets for a few days and then set out to dry in the sun. Roasting, the next step, brings out the flavor. But some of the healthful polyphenols (antioxidants) are lost during the roasting process, so the researchers wanted to figure out a way to retain as much of the polyphenols and good flavors as possible.

"We decided to add a pod-storage step before the beans were even fermented to see whether that would have an effect on the polyphenol content," says Emmanuel Ohene Afoakwa, Ph.D., who is at the University of Ghana. "This is not

traditionally done, and this is what makes our research fundamentally different. It's also not known how roasting affects polyphenol content."

Afoakwa's team divided 300 pods into four groups that were either not stored at all or stored for three, seven or 10 days before processing. This technique is called "pulp preconditioning." After each storage period passed, fermentation and drying were done as usual. He reports that the seven-day storage resulted in the highest antioxidant activity after roasting.

To assess the effects of roasting, the researchers took samples from each of the storage groups and roasted them at the same temperature for different times. The current process is to roast the beans for 10-20 minutes at 248-266 degrees Fahrenheit, he explains. Afoakwa's team adjusted this to 45 minutes at 242 degrees Fahrenheit and discovered that this slower roasting at a lower temperature increased the antioxidant activity compared to beans roasted with the conventional method.

In addition, the beans that were stored and then roasted for 45 minutes had more polyphenols and higher antioxidant activity than beans whose pods were not stored prior to fermentation, says Afoakwa. He explains that pulp preconditioning likely allowed the sweet pulp surrounding the beans inside the pod to alter the biochemical and physical constituents of the beans before the fermentation. "This aided the fermentation processes and enhanced antioxidant capacity of the beans, as well as the flavor," he says. He adds that the new technique would be particularly useful for countries in Southeast Asia and Latin America where cocoa beans produce a chocolate with a less intense chocolate flavor and have reduced antioxidant activity.

Looking to the future, he says the team will be studying in more detail the effects of roasting on the flavor of freshly picked compared to stored cocoa beans. They will be testing different temperatures and roasting and storing times to determine if even higher amounts of antioxidants can be retained through the process.

The researchers acknowledge funding from the Belgium Government under the VLIR TEAM Cocoa Project between Ghent University, Ghent, Belgium, and the University of Ghana, Accra, Ghana.

http://www.eurekalert.org/pub_releases/2015-03/acs-ftf022015.php

Fat turns from diabetes foe to potential treatment

A new weapon in the war against type 2 diabetes is coming in an unexpected form: fat.

DENVER - Researchers have discovered a new class of potentially therapeutic lipids, called fatty-acid esters of hydroxy fatty acids (FAHFAs). These lipids are found at lower levels in people with insulin resistance, a risk factor for type 2 diabetes, compared with those who don't have the condition. Administering FAHFAs to diabetic mice improved their glucose metabolism and insulin secretion, opening a surprising avenue for the development of novel medications for the disease.

The team will describe their approach in one of nearly 11,000 presentations at the 249th National Meeting & Exposition of the American Chemical Society (ACS), the world's largest scientific society, taking place here through Thursday.

One in ten people in the United States has type 2 diabetes, which is the seventh leading cause of death. Excess weight and body fat increase disease risk. Genes also play a role, but much remains unknown.

"There are some drugs available for treating type 2 diabetes, but there are still gaps in our knowledge about what causes it," says Alan Saghatelian, Ph.D., who is at the Salk Institute for Biological Studies. He co-led the study with Barbara Kahn, M.D. "Our discovery came out of basic research to understand the mechanism underlying type 2 diabetes."

The researchers had been studying insulin resistance, a metabolic defect believed to contribute to the development and progression of type 2 diabetes. Insulin resistance occurs when the body does not respond to the insulin being produced, causing glucose to build up in the blood. It is typically associated with obesity. But Kahn's team at Beth Israel Medical Deaconess Center found that they could create obese mice that were unusually sensitive to insulin.

As it turned out, these mice had levels of a previously undiscovered family of fats, which they named FAHFAs, that was massively elevated - 16- to 18-fold. The researchers suspected that these lipids were behind the increased insulin sensitivity. They figured if that were the case, then research on these newly discovered fats could someday lead to a diabetes therapy. In total, the researchers identified 16 different types of FAHFAs in the mice using a technique called mass spectrometry.

To check that their findings weren't limited to rodents, the researchers measured FAHFA levels in the blood samples from human subjects, finding lower levels of these compounds in those with insulin resistance. They also checked various foods and detected FAHFAs in many common items, such as apples, broccoli, beef, chicken and eggs. "We've been eating them for a long time, and they aren't toxic," says Saghatelian, suggesting FAHFAs may be safe to use as a medication.

To test how well FAHFAs could work as a potential therapy, the researchers fed the lipids to insulin- resistant mice, and observed an improvement in inflammation, insulin sensitivity and glucose uptake. Although this experiment suggests that FAHFAs may make good type-2-diabetes drugs, Saghatelian says he's now looking beyond lipids. "These are very cool compounds, but lipids aren't typically used as drugs for several reasons, including that they might not be able to reach

effective doses in the relevant tissues," he says. "But the existence of FAHFAs means there is a metabolic pathway for making and breaking down these molecules. Identifying the enzymes involved in those processes may provide a lead toward even better drug targets."

The Saghatelian and Kahn laboratories are currently parsing human tissues for those that show increasing or decreasing levels of FAHFAs. Once identified, the scientists will search the tissue for enzymes involved in FAHFA metabolism. Drugs could potentially be developed that work by either increasing the activity of enzymes that produce FAHFAs or blocking those that destroy FAHFAs.

"As we learn more about type 2 diabetes," says Saghatelian, "we may be able to come up with better therapies that treat the disease with fewer side effects and that are effective in a larger number of people."

Kahn and Saghatelian acknowledge funding from the National Institutes of Health, Searle Scholars Award, Burroughs Welcome Fund, a Sloan Research Fellowship and JPB foundation.

http://www.eurekalert.org/pub_releases/2015-03/nooa-cwa031215.php

Child with autism improves with antibiotic; prompts new investigations into autism

Surprising observation leads parent to collaboration with researchers to organize first scientific conference and special issue of scientific journal on the role of gut bacteria in autism

Dallas, TX - John Rodakis, the parent of a child with autism was not looking to launch an international investigation into the microbiome (the collection of microorganisms that live on and in us) and autism, but, as he describes in his newly published article in the scientific journal Microbial Ecology in Health and Disease, when his young son's autism unexpectedly and dramatically improved while taking an antibiotic for strep throat, he began a quest to understand why. Following the surprise improvement, Mr. Rodakis, who in addition to being a parent is also a medical venture capitalist with a background in molecular biology and a Harvard MBA, began to examine the medical literature where he found a lone study from 1999 conducted at Chicago Rush Children's hospital that documented a similar phenomenon in autistic children. After speaking with other parents and clinicians he discovered that improvements on antibiotics such the one his son experienced were frequently observed, but not well studied. "I was determined to understand what was happening in the hope of helping both my son and millions of other children with autism."

The Father's quest led him to world-renowned autism researcher Dr. Richard Frye, head of the Autism Research Program at Arkansas Children's Hospital Research Institute and his team and together they began a collaboration that grew to include other researchers from many different medical disciplines from all parts of the world. As the parent/researcher collaboration intensified, two ideas emerged: that the group should design a research trial to try to understand this unusual phenomenon and to hold a scientific conference on autism and the microbiome. "Careful parental observations can be crucial. In science we take these observations, put them through the scientific method, and see what we find. This is what can lead to ground breaking scientific discoveries and breakthroughs in the field", said Dr. Frye.

This past June, the group held a first-of-its-kind conference: The First International Symposium on the Microbiome in Health and Disease with a Special Focus on Autism which was co-sponsored by Mr. Rodakis' newly formed non-profit N of One: Autism Research Foundation. As a result of that conference, a special issue on Autism and The Microbiome is being published in the peer-reviewed scientific journal, Microbial Ecology in Health and Disease. The issue features articles from conference presenters and others including an article by Mr. Rodakis, titled "An n=1 case report of a child with autism improving on antibiotics and a father's quest to understand what it may mean."

New evidence for the microbiome's involvement in autism spectrum disorder has been rapidly accelerating in recent years. Fifteen years ago, another autism parent, Ellen Bolte, had what at the time was a far-fetched hypothesis: that gut bacteria played a role in some cases of autism. Her efforts resulted in the 1999 small, but ground-breaking clinical trial conducted at Chicago Rush Children's hospital that Mr. Rodakis found while doing his research. Today, that hypothesis has grown into a large body of evidence demonstrating a link between the microbiome and autism, also called the "gut-brain" connection. Just this summer a team at Arizona State University led by Dr. Rosa Krajmalnik-Brown published findings repeating what others have documented that showed that children with autism exhibited less bacterial diversity in their guts than typically developing children. Dr. Krajmalnik-Brown, was also a speaker at the conference and also has a paper appearing in the special issue.

In the article out this month, Mr. Rodakis outlines the personal story of how his child's autism symptoms improved while taking a common antibiotic and then goes on to summarize recent human and animal-model research into possible biological mechanisms at work. Mr. Rodakis does not suggest that antibiotics are a treatment for autism, but rather may be useful as a research tool. Mr. Rodakis adds, "Current research is demonstrating that gut bacteria play previously undiscovered roles in health and disease throughout medicine. The evidence is very strong that they also play a role in autism. It's my hope that by studying these

antibiotic-responding children, we can learn more about the core biology of autism."

Mr. Rodakis argues that that the microbiome's role in autism is a promising area for further research, though under-funded by the current major public and private organizations that fund autism research. Mr. Rodakis' active efforts to shape and encourage research into promising areas is part of a broader trend of patients and affected families playing an increasing role in driving promising medical research.

Mr. Rodakis argues that the link between the microbiome and autism is not just plausible, but given recent research, likely.

The entire article may be read at:
http://www.microbecolhealthdis.net/index.php/mehd/article/view/26382

http://www.bbc.com/news/health-32030946

Preventive surgery for cancer genes

While most women in the UK have a one in 54 chance of developing ovarian cancer in their lifetime, for those who inherit faulty genes, like Angelina Jolie, the risk increases to one in two.

By Michelle Roberts Health editor, BBC News online

If women know they have BRCA gene mutations, they can choose to take action before cancer develops.

But weighing the risk of cancer that might never grow against the very real trauma of surgery to remove healthy tissue as a preventive measure is an incredibly difficult conundrum, as Angelina Jolie explains.

"I did not do this solely because I carry the BRCA1 gene mutation, and I want other women to hear this.

"A positive BRCA test does not mean a leap to surgery," she says in her diary in the New York Times.

"In my case, the Eastern and Western doctors I met agreed that surgery to remove my tubes and ovaries was the best option, because on top of the BRCA gene, three women in my family have died from cancer."

What is BRCA?

BRCA1 and BRCA2 are genes that help repair damage to the DNA in our cells. If people inherit a mutated version of either of these genes it puts them at greater risk of certain cancers.

Jolie learned some time ago that she had inherited a faulty BRCA1 gene from her mother.

She had already lost her mother, grandmother and aunt to cancer, which alerted doctors that she might also be at risk.

Who should get tested?

In the UK, around one in every 500 people will carry a BRCA mutation.

Generally, experts only recommend screening if a person has a strong family history of breast or ovarian cancer.

For example:

One first degree relative (mum, dad, sibling) and one second degree relative (aunt, uncle, grandparent) diagnosed before the age of 50

Two first degree relatives diagnosed before the age of 50

Three or more first or second degree relatives diagnosed at any age

If I have BRCA, what are my risks?

For women carriers of BRCA1, it means their lifetime risk of breast cancer will range from 65-85% and their risk of ovarian cancer from 40-50%.

Men with BRCA mutations also have a slightly elevated risk of breast cancer.

Jolie's doctors estimated that she had an 87% risk of breast cancer and a 50% risk of ovarian cancer in her lifetime unless she underwent surgery.

In 2013, award-winning actress decided to have both breasts removed. And now in 2015 she has had her next preventive surgery - the removal of her ovaries and fallopian tubes.

Her doctors advised that she should have this surgery about a decade before the earliest onset of cancer in her female relatives. Her mother's ovarian cancer was diagnosed when she was 49. Jolie is now 39.

Does surgery remove any risk of cancer?

No, but it does greatly reduce the risk.

Surgery does not completely guarantee that cancer will not develop - it is impossible to remove all of the at-risk tissue.

And there are side effects to consider - taking out the ovaries removes a woman's fertility and puts her into the menopause, for example.

Faulty BRCA genes are responsible for around 5% of all breast cancer cases and 10% of ovarian cancers, meaning the rest are caused by other factors.

What if I don't want surgery?

Although Jolie says surgery was the right choice for her, she says it may not be for others faced with the same dilemma.

"There is more than one way to deal with any health issue. The most important thing is to learn about the options and choose what is right for you personally."

Some people may opt instead for enhanced screening - frequent check-ups to make sure no cancer is growing.

Doctors may also prescribe drugs like tamoxifen to reduce the risk of cancer developing.

As Jolie says: "There is more than one way to deal with any health issue. The most important thing is to learn about the options and choose what is right for you personally."

http://www.eurekalert.org/pub_releases/2015-03/hfhs-2tj032015.php

Second Tommy John surgery linked to performance decline, shortened career

Major League Baseball pitchers who underwent a second Tommy John surgery saw their performance decline and their career shortened, according to researchers at Henry Ford Hospital.

VIDEO

DETROIT - In a retrospective, case-controlled study, researchers analyzed performance and longevity data of 33 pitchers who had a second surgery following the original elbow reconstruction between 1996 and 2012 and compared them with pitchers of similar age who had no prior Tommy John surgery. Key findings for pitchers after a second surgery:

- ***65 percent returned to pitching at MLB level.***
- ***On average they lasted three years or less at the MLB level.***
- ***Innings pitched dropped nearly in half.***
- ***Walks jumped to 4.79 from 4.02 for every nine innings.***
- ***Wins and losses dropped in half.***

The study is believed to the largest to date to evaluate pitching performance and career longevity after a second Tommy John surgery. It is being presented at the annual meeting of the American Academy of Orthopedic Surgeons March 23-31 in Las Vegas.

"Although a second surgery may not be career ending, it appears to be career-limiting by virtue of a decreased workload and pitching productivity," says Vasilios (Bill) Moutzouros, M.D., a Henry Ford orthopedic surgeon and the study's senior author.

"And for those who return to the major league level, they experience a mixed bag of performance levels. In several categories their performance declines significantly."

The findings come one year after a companion Henry Ford study showed for the first time a link between the surgery and declining pitching performance at the MLB level. It involved the largest cohort of MLB pitchers at the time to examine the issue.

An UCL injury is believed to be tied to the overuse and excessive stress on the inner elbow, coupled with pitching velocity and joint motion, says Robert Keller, M.D., a four-year Henry Ford orthopedic resident and study co-author whose father Phil was a teammate of pitcher Tommy John in the 1970s.

"It's possible that increased surveillance of pitch counts, a lesser pitching role or a lack of arm endurance after a second surgery may be contributing factor in performance and pitching workload," Dr. Keller says.

Tommy John surgery, named after the former Los Angeles Dodgers pitcher who underwent the pioneering surgery 40 years ago, has since been performed on legions of pitchers at the professional and collegiate levels. In medicine it is known as ulnar collateral ligament (UCL) reconstruction. During the two-hour outpatient procedures, the UCL in the medial elbow is replaced with a tendon from the same arm or from the hamstring area.

In a second, or revision, surgery, a new tendon is attached to the inner elbow where the UCL should be. It is made more delicate due to scar tissue from the original surgery and the subsequent injury.

The study was funded by Henry Ford Hospital.

http://www.eurekalert.org/pub_releases/2015-03/gumc-aln031815.php

After learning new words, brain sees them as pictures

The brain learns words quickly by tuning neurons to respond to the whole word

WASHINGTON - When we look at a known word, our brain sees it like a picture, not a group of letters needing to be processed. That's the finding from a Georgetown University Medical Center (GUMC) study published in the Journal of Neuroscience, which shows the brain learns words quickly by tuning neurons to respond to a complete word, not parts of it.

Neurons respond differently to real words, such as turf, than to nonsense words, such as turt, showing that a small area of the brain is "holistically tuned" to recognize complete words, says the study's senior author, Maximilian Riesenhuber, PhD, who leads the GUMC Laboratory for Computational Cognitive Neuroscience.

"We are not recognizing words by quickly spelling them out or identifying parts of words, as some researchers have suggested. Instead, neurons in a small brain area remember how the whole word looks - using what could be called a visual dictionary," he says.

This small area in the brain, called the visual word form area, is found in the left side of the visual cortex, opposite from the fusiform face area on the right side, which remembers how faces look. "One area is selective for a whole face, allowing us to quickly recognize people, and the other is selective for a whole word, which helps us read quickly," Riesenhuber says.

The study asked 25 adult participants to learn a set of 150 nonsense words. The brain plasticity associated with learning was investigated with functional magnetic resonance imaging (fMRI), both before and after training.

Using a specific fMRI technique known as fMRI-rapid adaptation, the investigators found that the visual word form area changed as the participants learned the nonsense words. Before training the neurons responded like the training words were nonsense words, but after training the neurons responded to

the learned words like they were real words. "This study is the first of its kind to show how neurons change their tuning with learning words, demonstrating the brain's plasticity," says the study's lead author, Laurie Glezer, PhD.

The findings not only help reveal how the brain processes words, but also provides insights into how to help people with reading disabilities, says Riesenhuber. "For people who cannot learn words by phonetically spelling them out - which is the usual method for teaching reading - learning the whole word as a visual object may be a good strategy."

In fact, after the team's first groundbreaking study on the visual dictionary was published in Neuron in 2009, Riesenhuber says they were contacted by a number of people who had experienced reading difficulties and teachers helping people with reading difficulties, reporting that learning word as visual objects helped a great deal. That study revealed the existence of a neural representation for whole written real words - also known as an orthographic lexicon - the current study now shows how novel words can become incorporated after learning in this lexicon.

"The visual word form area does not care how the word sounds, just how the letters of the word look together," he says. "The fact that this kind of learning only happens in one very small part of the brain is a nice example of selective plasticity in the brain,"

Study co-authors include Judy Kim, Josh Rule, and Xiong Jiang, PhD, from Georgetown University Medical Center.

The research was funded by a National Science Foundation grant (1026934), with additional support through the National Institutes of Health's Intellectual and Development Disorders Research Center (5P30HD040677-13).

http://www.eurekalert.org/pub_releases/2015-03/p-ncv032315.php

Norovirus candidate vaccine induces broad antibody responses in trial participants

Multivalent candidate vaccine elicits broad antibody responses to a range of norovirus strains

A multivalent candidate vaccine elicits broad antibody responses to a range of norovirus strains, including strains not included in the vaccine or previously encountered by participants, according to a new study published this week in PLOS Medicine. The results of the study, led by Lisa Lindesmith and Ralph Baric of the University of North Carolina at Chapel Hill, indicate that a vaccine to norovirus may be available in the future.

Worldwide, noroviruses cause one in five cases of viral gastroenteritis. An estimated annual 300 million cases of norovirus infection contribute to roughly 260,000 deaths, mostly in low-income countries. Over time, noroviruses evade natural immunity by antigenic drift, which allows them to escape from antibodies produced in response to earlier infections.

Recent efforts to develop a norovirus vaccine have focused on virus-like particles (VLPs), which are constructed from molecules of the virus's capsid (outer shell). In a phase I clinical trial, one multivalent VLP vaccine elicited antibody generation, but did not confer immunity to the tested strain of virus. In the current study, Lindesmith and colleagues characterized serum specimens from ten multivalent VLP vaccine clinical trial participants for antibodies to vaccine VLPs and also to VLPs representing viruses that were not contained in the vaccine.

The researchers found that VLP vaccine can rapidly elicit antibody responses to a broad range of vaccine and non-vaccine VLPs, including to two VLPs representing human noroviruses that they could not have previously encountered. Overall, antibodies to norovirus strains to which participants had previously been exposed dominated the immune response.

These findings provide evidence that, if achieved, VLP-vaccine-induced norovirus immunity may overcome the ability of noroviruses to evade immunity by antigenic drift. These results must be interpreted cautiously. The study is small, and the assays used may not replicate how the immune system of a vaccine recipient will respond to true norovirus infection. Additionally, the study participants were all adults aged 18 to 49 years, while a vaccine is most needed for young children (who account for the majority of severe infections) and the elderly (who are most likely to die from infection). Next steps include further development of VLP-based vaccines and additional clinical trials. The authors state: "These data reveal new information about complex norovirus immune responses to both natural exposure and to vaccination, and support the potential feasibility of an efficacious multivalent norovirus VLP vaccine for future use in human populations."

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Competing Interests: MTF, CWM, KD, and JS do not have any competing interests. LCL and RSB have received royalties from a licensing agreement with Ligocyte (now Takeda). FB is an employee of Takeda Pharmaceuticals International. CR, RRG, RFB, and PMM are employees of Takeda Vaccines. RRG has stock in Takeda Vaccines, Inc. CR holds stock or options in Takeda Pharmaceuticals. RFB holds patents on Takeda's norovirus vaccine drug substance, owns Takeda stock, is PI of a research contract from the Department of Defense for norovirus vaccine development, is a board member of the Montana BioScience Alliance, and is a registered lobbyist. JF is an employee of EMMES and is contracted through Takeda Vaccines.

Citation: Lindesmith LC, Ferris MT, Mullan CW, Ferreira J, Debbink K, Swanstrom J, et al. (2015) Broad Blockade Antibody Responses in Human Volunteers after Immunization with a Multivalent Norovirus VLP Candidate Vaccine: Immunological Analyses from a Phase I Clinical Trial. PLoS Med 12 (3): e1001807. doi:10.1371/journal.pmed.1001807

http://nyti.ms/1E2DSLw

Experts Back Angelina Jolie Pitt in Choices for Cancer Prevention

Ms. Jolie Pitt's frank discussion will encourage women in similar situations to consider their own options

By PAM BELLUCK

Cancer experts said Tuesday that the actress and filmmaker Angelina Jolie Pitt was wise to have had her ovaries and fallopian tubes removed last week because she carries a genetic mutation, BRCA1, that significantly increases the risk of ovarian cancer, a disease so difficult to detect that it is often found only at an advanced, untreatable stage.

They also said Ms. Jolie Pitt's decision to discuss her own choices so frankly will encourage women in similar situations to consider their own options. BRCA mutations cause about 5 to 10 percent of breast cancers and 10 to 15 percent of ovarian cancers among white women in the United States. It is unclear how common the mutations are in other racial and ethnic groups.

"Prophylactic removal of ovaries and fallopian tubes is strongly recommended in women before age 40 in BRCA1 and BRCA2 mutation carriers," said Dr. Susan Domchek, executive director of the University of Pennsylvania's Basser Research Center, which specializes in BRCA mutations. "There is no effective screening for ovarian cancer and too many women with advanced stage ovarian cancer die of their disease."

Writing for The New York Times's Op-Ed page, Ms. Jolie Pitt, 39, said she had expected to have her ovaries and fallopian tubes removed, a procedure called a laparoscopic bilateral salpingo-oophorectomy, but that a cancer scare made her decide to undergo the procedure sooner. Her mother, aunt and grandmother died of cancer. "To my relief, I still had the option of removing my ovaries and fallopian tubes and I chose to do it," she wrote.

Two years ago, she ignited a worldwide discussion about options for women at high risk for breast cancer when she wrote that she had had both breasts removed because BRCA1, the same genetic mutation that prompted her surgery last week, increased her risk of breast cancer.

Several doctors said that for women in similar situations, they generally recommend that ovaries be removed before breasts, but the cost is that women who do so go into early menopause and can no longer bear children. However, removing the ovaries substantially decreases a woman's risk of developing breast cancer. Also, breast cancer is generally more detectable and treatable than ovarian cancer. "We're really quite pushy about oophorectomy," Dr. Domchek said. "And we talk about mastectomy as an option."

Experts said that some details mentioned by Ms. Jolie Pitt might not apply to all women with such mutations or might be characterized differently by doctors. For example, Ms. Jolie Pitt wrote that she was advised to have the surgery about 10 years before the age at which her mother was first diagnosed, which was 49. But doctors said a better rule of thumb is between ages 35 and 40, ideally after a woman has finished having children but before her cancer risk rises sharply.

Ms. Jolie Pitt also said she had a yearly test for the CA-125 protein to monitor the possibility of ovarian cancer. She noted that her doctor said the test missed a high percentage of cancers. Some experts said they had stopped such tests because they miss so many cancers and have not been shown to improve survival rates.

"We've basically said there's no data to support it and we're recommending the surgery," said Dr. Kenneth Offit, chief of the clinical genetics service at Memorial Sloan Kettering Cancer Center. He added: "In the end what she did is fine. She got to the right place. She had ovarian surgery done within the window of time."

Ms. Jolie Pitt's decision not to remove her uterus was consistent with what experts recommended. "There is no research showing that having a BRCA mutation puts women at risk for uterine cancer," said Dr. Jamie Bakkum-Gamez, a gynecologic oncologist at the Mayo Clinic.

Dr. Jamie Bakkum-Gamez and other experts endorsed her decision to take hormone replacement therapy - an estrogen patch and a progesterone intrauterine device - to counteract symptoms of surgery-induced menopause.

Ms. Jolie Pitt, who has six children, three adopted, wrote that she knows these decisions are "far harder" for women who still want to get pregnant and that she had learned they might have options "to remove their fallopian tubes but keep their ovaries." Experts cautioned that the evidence is still slim on whether fallopian tube removal is effective at preventing ovarian cancer.

Shira Krance, 35, who has a BRCA2 mutation, had a double mastectomy two years ago and said she has considered whether to have the fallopian tubes removed before her ovaries.

"Doctors will give you a lot of options, but nobody will tell you what to do," said Ms. Krance, who lives in Valley Cottage, N.Y., and has two young children. "It's scary, the idea of not being around when your children grow up. That's the worst thing and I'm going to do everything I can to avoid that."

Ethel Zelenske, 62, a BRCA1 carrier who lives in Baltimore, had her tubes and ovaries removed in 2007. A few years later, she was diagnosed with peritoneal

cancer, a condition that Dr. Offit said each year occurs in about half of a percent of women who have had their ovaries removed. Ms. Zelenske was treated but had a recurrence of the peritoneal cancer two years ago.

"My doctors have told me that I will always be in treatment," said Ms. Zelenske, who like many other women welcomed Ms. Jolie Pitt's public disclosure. "I really love that she said knowledge is power because I say that all the time."

http://www.bbc.com/news/science-environment-32048273

Curiosity Mars rover detects 'useful nitrogen'

Nasa's Curiosity rover has made an interesting nitrogen discovery on the surface of Mars.

Its big internal lab has detected nitric oxide (NO) - oxidised nitrogen - as it analysed dust and rock samples.

The compound was very likely released from the breakdown of nitrates during the heating of the powders.

If nitrates are the source, it would add to the evidence that the planet had the conditions necessary to sustain life in its distant past.

Nitrogen is essential for all known forms of life, but it needs to be in the right form to be useful.

On Earth, specialist soil microbes "fix" the not-so-useful nitrogen in the atmosphere into nitrate (NO_3) - a nitrogen atom bound to three oxygen atoms - which can then be processed by other biological systems.

There is no evidence that the nitrates suggested in the Curiosity lab experiments were produced in this exact same way.

A more probable scenario, say rover scientists, is that the nitrates resulted from other conversion processes that involve lightning and meteorite strikes

The team saw the signs of the nitrates in scooped samples of surface dust and in samples drilled from mudstones.

These mudstones have already demonstrated that the ancient crater in which Curiosity sits had rivers and lakes, with water and a chemistry that would have been habitable.

Last week, rover scientists reported the possible detection of a fatty acid in the robot's drilled samples.

Fatty acids are key components of the cell membranes found in all life forms. But again - just as with the nitrates - there are non-biological routes to their production. Of itself, a detection proves nothing.

The nitric oxide result is reported by Jennifer Stern and colleagues in this week's edition of the journal Proceedings of the National Academy of Sciences.

http://www.eurekalert.org/pub_releases/2015-03/aaoo-mop032415.php

Majority of parents unaware of safe pitching practices

Sixty-four percent of parents said their child had suffered upper extremity pain due to pitching

A new study presented today at the 2015 Annual Meeting of the American Academy of Orthopaedic Surgeons (AAOS) found that 53 percent of the parents/caregivers of youth baseball pitchers are unaware of safe pitching practices designed to prevent overuse injuries--common tears or damage, most often to the elbow (ulnar collateral ligament) or shoulder--which can cause pain, lost play time and, if not treated appropriately, arthritis, deformity and disability. Between 2 and 8 percent of youth pitchers will suffer an overuse injury from throwing too hard, too often, too young, and/or without appropriate rest once pain begins in the shoulder or elbow. One recent study found that approximately 38 percent of pitchers will miss at least one game because of arm pain, with 34 percent experiencing pain severe enough to warrant a doctor's visit.

As the number of overuse injuries continues to rise in young baseball players, safe pitching guidelines--which focus on proper warm up exercises; maximum play time and pitch counts; recommended rest periods; appropriate ages for learning various types of pitches; and not playing on multiple teams, year round or on consecutive days--are being integrated into play at many of the nation's 200,000 youth baseball teams, ideally with a firm, cooperative commitment from coaches, parents/caregivers and players.

"Ensuring the safety of all athletes through injury prevention is absolutely necessary, especially when it comes to youth competitors," said University of Florida orthopaedic surgeon and lead study author Andrew Waligora, MD.

In the study, researchers distributed and analyzed results from a 22-question survey completed by the parents of 60 youth baseball players. The content of the survey was based on recommendations provided by the USA Baseball and Medical Safety Advisory, Little League Baseball and the American Sports Medicine Institute. Sixty-one percent of the respondents identified themselves as the child's mother. Ninety-three percent of the respondents were white, 41 percent were 41 to 50 years old, and 44 percent were the parent of a pitcher between the ages of 13 and 16.

Fifty-three percent of the parents or caregivers said they were unaware of the existence of safe pitching guidelines, 54 percent stated that they did not actively participate in monitoring their child's pitch count, and 20 percent were unaware of how many pitches their child threw in a typical game. Among the other findings:

49 percent of pitchers threw in more than one league at a time, and 25 percent pitched in a league more than nine months out of the year.

Sixteen percent of the parents or caregivers surveyed did not know what kind of pitches their children threw.

Seventy-five percent of parents or caregivers of 11- to 12-year-old players said their child threw "curveballs," and 17 percent, "sliders." Of those who were aware of their child throwing "breaking pitches" - curveballs, sliders, slurves or screwballs (all more advanced pitches) - 18 percent reported that they learned how to throw these pitches from a parent.

Sixty-four percent of parents or caregivers recalled their child having upper extremity pain as a direct result of pitching, 38 percent had to miss either a game or pitching because of discomfort, and 34 percent experienced pain concerning enough to be evaluated by a medical professional.

There were no significant correlations between the number of pitches typically thrown in a game, the child's position when not pitching, number of months pitched during the year, who keeps track of pitch count, and arm pain.

"This research emphasizes the importance of caregiver participation in ensuring compliance with youth safe pitching practices," said Dr. Waligora. "Despite the implementation and easy accessibility of safe pitching guidelines, a large portion of caregivers surveyed were unaware and/or noncompliant with these established recommendations. Given the results of this study, further measures need to be taken to improve both education and compliance. Injury prevention should be a multi-disciplinary approach that includes informing coaches, parents and youth pitchers about safe pitching practices. Future directions may include establishing outreach programs for the youth baseball community."

More information on youth baseball safety is available at STOP Sports Injuries and the American Orthopaedic Society for Sports Medicine (AOSSM).

http://www.eurekalert.org/pub_releases/2015-03/agu-eoj032515.php

Explosions of Jupiter's aurora linked to extraordinary planet-moon interaction

Jovian aurora sometimes flares up because of a process having nothing to do with the Sun

WASHINGTON, D.C. - On Earth, bursts of particles spewed by the Sun spark shimmering auroras, like the Northern Lights, that briefly dance at our planet's poles. But, on Jupiter, there's an auroral glow all the time, and new observations show that this Jovian display sometimes flares up because of a process having nothing to do with the Sun.

Jupiter watchers have long known that the giant planet's ever-present polar auroras - thousands of times brighter and many times bigger than Earth - are powered by both electrically charged particles from the Sun colliding with Jupiter's magnetic field and a separate interaction between Jupiter and one of its many moons, called Io. But there are also auroral explosions on Jupiter, or periods of dazzling brightening, similar to auroral storms on Earth, that no one could definitively trace back to either of those known causes.

In the aurora-making interaction of Jupiter and Io, volcanoes on the small moon blast clouds of electrically charged atoms (ions) and electrons into a region surrounding Jupiter that's permeated by the planet's powerful magnetic field, thousands of times stronger than Earth's.

Rotating along with its rapidly spinning planet, the magnetic field drags the material from Io around with it, causing strong electric fields at Jupiter's poles. The acceleration of the ions and electrons produce intense auroras that shine in almost all parts of the electromagnetic spectrum but most brightly in high-energy bands, like ultraviolet light and X-rays, that are invisible to unaided human eyes.

Now, new observations of the planet's extreme ultraviolet emissions show that bright explosions of Jupiter's aurora likely also get kicked off by the planet-moon interaction, not by solar activity.

A new scientific paper about these observations by Tomoki Kimura of the Japan Aerospace Exploration Agency (JAXA), in Sagamihara, Kanagawa, Japan, and his colleagues, was published online today in Geophysical Research Letters, a journal of the American Geophysical Union.

Starting in January 2014, a telescope aboard the JAXA's Hisaki satellite, which focused on Jupiter for two months, recorded intermittent brightening of the giant planet's aurora. The telescope detected sudden flare-ups on days when the usual flow of charged particles from the Sun, known as the solar wind, was relatively weak.

Additional space and ground-based telescopes, including the Hubble Space Telescope, also viewed Jupiter during these lulls in the solar wind. Both Hisaki and Hubble witnessed explosions of the planet's aurora despite the solar wind's calm, suggesting that it's the Jupiter-Io interaction driving these explosions, not charged particles from the Sun, according to the new study.

The new research does not address exactly what is happening in the Jovian magnetosphere to cause the temporary brightening of auroral explosions.

http://bbc.in/1bnaR0R

NASA's Curiosity rover finds fatty acids on Mars

IS there lard on Mars?

NASA's Curiosity Rover has detected what may be a fatty acid molecule in the soil of the Red Planet, although it is not clear whether it is biological in origin.

The find was presented by David Glavin, who works on the rover's SAM instrument, at the Lunar and Planetary Science Conference in The Woodlands, Texas, last week.

SAM analyses gases released by heating samples of rock, and the results are interpreted by matching the data to compounds analysed on Earth. One SAM reading seems to relate to a type of fatty acid molecule. These are important for life because organisms use them to build cell membranes, but they could have a non-biological origin.

Glavin also confirmed previous hints from SAM of an organic compound called chlorobenzene. Again, this might not be a sign of life, but it suggests that complex organic molecules can survive on the surface of Mars, upping the chances of future missions finding microbes if they are there.

http://www.eurekalert.org/pub_releases/2015-03/jhm-uom032315.php

Use of minimally invasive surgery could lower health care costs by hundreds of millions a year

More use of minimally invasive surgery for common procedures can dramatically reduce post-operative complications and cut the nation's health care bill by hundreds of millions

A new analysis of surgical outcomes nationwide concludes that more use of minimally invasive surgery for certain common procedures can dramatically reduce post-operative complications and shave hundreds of millions of dollars off the nation's health care bill.

Results of the research, conducted by Johns Hopkins investigators and published March 25 in JAMA-Surgery, indicate that American hospitals collectively could prevent thousands of post-surgical complications and save between $280 million and $340 million a year by using more minimally invasive procedures instead of traditional open surgery for routine operations of the appendix, colon and lungs.

"Minimally invasive surgery, done in the right patients, represents an under-recognized opportunity not only for cost savings, but also for making surgery safer, reducing the very real suffering associated with surgical complications," says lead investigator Marty Makary, M.D., M.P.H., professor of surgery at the Johns Hopkins University School of Medicine.

Minimally invasive surgery, also known as laparoscopic or keyhole surgery, involves making tiny surgical incisions, or "keyholes," to access organs and operate on them, in contrast with cutting into and through much larger areas of tissue. For the study, the research team analyzed more than 80,000 surgical cases from the National Inpatient Sample database, tracking seven common post-surgical complications and associated billing charges for certain common operations. The procedures tracked involved operations of the appendix, colon or lungs, selected because both the traditional open and the minimally invasive approaches are considered standard of care.

While not all patients are candidates for minimally invasive treatment, the researchers note, the study revealed great variation in its use among those who do qualify -- similar patients treated at similar hospitals.

To calculate the cost difference between traditional open and minimally invasive surgery, the investigators compared the actual cost for each patient who underwent traditional surgery against the estimated cost for the same patient undergoing minimally invasive treatment. In addition, the investigators calculated potential cost savings under two hypothetical scenarios: when all hospitals increased their use of minimally invasive surgery by 50 percent and when the hospitals performing the fewest such procedures, the so-called low utilizers, upped them to the level of hospitals performing in the upper one-third.

The tally showed that if all U.S. hospitals increased the number of minimally invasive procedures by 50 percent, they would avert 3,578 complications, reduce hospital stay by 144, 863 days and save $288 million a year. If hospitals performing the fewest minimally invasive operations boosted their levels to those of their higher-performing counterparts, the collective savings would be $337 million a year, 4,306 fewer complications and 169,819 fewer hospital days.

The research team says the findings should be heeded as a call to action by hospital leaders to increase capacity for minimally invasive treatment and create a more streamlined division of labor so that surgeons with expertise in minimally invasive treatment can operate on patients who qualify for this approach.

The authors caution that minimally invasive surgery is not always the optimal method of treatment, and some patients are not candidates for it.

"The decision to perform an open versus minimally invasive procedure should be made according to each patient's specific case and overall health, among other factors," Makary says. "But our results make a very strong case that minimally invasive surgery is grossly underutilized and, at a minimum, ought to be offered to patients more often."

Other Johns Hopkins investigators involved in the research included Tim Xu, Susan Hutfless, Michol A. Cooper, Mo Zhou, and Allan B. Massie.

http://bit.ly/1EGZxEf

Here's How Music Really Could Soothe Your Soul

A leading scholar theorizes that music developed as an evolutionary adaptation to help us deal with the contradictory nature of life

By Laura Clark smithsonian.com

Why does music impact us so deeply? There's never been a real answer. But Leonid Perlovsky, a research physicist and investigator of human cognitive functioning, has a new theory - music helps our brains integrate distasteful contradictions.

According to Perlovsky, writing at The Conversation, music's effect on the brain is connected to the theory of cognitive dissonance. "Cognitive dissonance is the idea that people experience unpleasant feelings when they either possess contradictory knowledge, or are confronted with new information that opposes existing beliefs," he writes. Say you think you're a great cook, but you catch your friends secretly spitting their dinner into their napkins. That shock and emotional pain you feel - that's cognitive dissonance.

In order to deal with the feelings that emerge from contradictory knowledge, we tend to alter our beliefs or feelings on the troubling subject. So perhaps, as you clear the still-full plates from the table, you tell yourself that you really can cook but your friends probably wouldn't know a good paella if it hit them in the mouth.

Yet, as Perlovsky points out, one "manifestation of cognitive dissonance is the rejection of new knowledge." So, "if people are willing to deceive themselves or ignore new information, how has human culture evolved?" Music may play a big part, he theorizes.

Perlovsky's research, he asserts, shows how music can help us move beyond the experience of cognitive dissonance and hold on to even unhappy new information. He cites one study performed on four-year-old boys who each individually played with five Pokemon toys and then were asked to rank the figures based on personal preference. The experimenter then told each boy not to play with their second-favorite choice and left the room.

When she came back, the boys still wouldn't play with that second-favorite toy. "When confronted with conflicting information ("I like this toy, but I shouldn't play with it"), each boy apparently rejected his initial preference for it," writes Perlovsky. But when the same experiment was performed, but this time with music playing in the experimenter's absence, the "toy retained its original value. The contradictory knowledge didn't lead the boys to simply discard the toy."

"The idea is that music - which can convey an array of nuanced emotions - helps us reconcile our own conflicted emotions when making choices," Perlovsky writes. And, he highlights, this is good for our entire species, since "the more diverse, differentiated emotions we possess, the more well-founded our decisions become."

http://www.eurekalert.org/pub_releases/2015-03/icl-hip032515.php

Head injury patients show signs of faster aging in the brain

People who have suffered serious head injuries show changes in brain structure resembling those seen in older people, according to a new study.

Researchers at Imperial College London analysed brain scans from over 1,500 healthy people to develop a computer program that could predict a person's age from their brain scan. Then they used the program to estimate the "brain age" of 113 more healthy people and 99 patients who had suffered traumatic brain injuries. The brain injury patients were estimated to be around five years older on average than their real age.

Head injuries are already known to increase the risk of age-related neurological conditions such as dementia later in life. The age prediction model may be useful as a screening tool to identify patients who are likely to develop problems and to target strategies that prevent or slow their decline.

"Your chronological age is not necessarily the best indicator of your health or how much longer you will live," said Dr James Cole, who led the study, from the Department of Medicine at Imperial College London. "There is a lot of interest in finding biomarkers of ageing that can be used to measure a certain aspect of your health and predict future problems."

The study, published in the April issue of Annals of Neurology, used magnetic resonance imaging (MRI) to study changes in brain structure. The researchers used a machine learning algorithm to develop a computer program that could recognise age-related differences in the volume of white matter and grey matter in different parts of the brain.

The model was then used to estimate subjects' ages based on their brain scans. The study included 99 patients with traumatic brain injuries (TBI) caused by road accidents, falls or assaults, who had persistent neurological problems. The scans were taken between one month and 46 years after their injuries.

In healthy controls, the average difference between predicted age and real age was zero. In TBI patients, the difference was significantly higher, with a bigger discrepancy in patients with more severe injuries. Bigger differences in predicted age were associated with cognitive impairments such as poor memory and slow reaction times.

There was also a correlation between time since injury and predicted age difference, suggesting that these changes in brain structure do not occur during the injury itself, but result from ongoing biological processes, potentially similar to those seen in normal ageing, that progress more quickly after an injury.

"Traumatic brain injury is not a static event," said Dr Cole. "It can set off secondary processes, possibly related to inflammation, that can cause more damage in the brain for years afterwards, and may contribute to the development of Alzheimer's or other forms of dementia."

The researchers believe the age prediction model could be applied not just to TBI patients, but might also be useful to screen outwardly healthy people.

"We want to do a study where we use the program to estimate brain age in healthy people, then see if the ones with 'old brains' are more likely to get

neurodegenerative diseases. If it works, we could use it to identify people at high risk, enrol them in trials and potentially prescribe treatments that might stave off disease," said Dr Cole.

The researchers received funding from the EU Seventh Framework Programme and a National Institute for Health Research (NIHR) professorship for Professor David Sharp. The research was also supported by the NIHR Imperial Biomedical Research Centre.

http://www.eurekalert.org/pub_releases/2015-03/cums-mia032515.php

Medicaid is a very good investment even if it does not lower cholesterol or blood pressure

Quality-life year gains average $62,000

Researchers at Columbia University's Mailman School of Public Health analyzed the results of the Oregon Health Experiment, where eligible uninsured individuals were randomly assigned Medicaid or to stay with their current care. Considered controversial because the experiment found no measurable gains for physical health it did reveal benefits for mental health, financial wellbeing, and preventive screening. In terms of quality-adjusted life years, the researchers showed that Medicaid is an excellent value--a $62,000 gain in quality-adjusted life years. Study findings are online in the American Journal of Public Health.

In 2008, the state of Oregon randomly provided Medicaid coverage to approximately 10,000 individuals out of 30,000 selected from all Medicaid-eligible residents. Of the 10,000 randomly receiving Medicaid there were 6,315 in the treated category and 5,769 in the control group. Using high performance computers and the resources of GRAPH, a Columbia Mailman School initiative that studies how to optimize population health policy, the researchers analyzed survey responses and biomarker data for both samples. Findings showed that Medicaid provided substantial financial protections, increased rates of preventive testing, reduced depression, and improved self-rated health. Alternately, Medicaid did not significantly lower blood pressure, serum cholesterol, or blood glucose levels.

In response to the findings, opponents of Medicaid called for its funding to be stopped, while proponents hailed the study as proof that Medicaid was a worthwhile investment because it showed some benefits. Representatives from both groups claimed that the sample size was too small to draw conclusions about physical benefits.

"Both ways of thinking are correct," said Peter Muennig, MD, MPH, associate professor of Health Policy and Management at Columbia University's Mailman School of Public Health and first author. "While the arguments of Medicaid proponents and opponents are plausible and the concerns about sample size are justified, we found that the benefits to mental health and fiscal protections are meaningful enough to justify further expansion of Medicaid."

The research team points to preventive measures like mammography and the estimates of the U.S. Task Force on Clinical Preventive Services that higher rates of screening for disease saves lives. But because there is no scientific evidence that proves this, these benefits were not included in the current analysis. "By excluding these potential benefits while including all of their costs, we can be even more certain that our estimate of $62,000 quality-adjusted life year gained is conservative," noted Muennig.

"Because none of the observed outcomes were harmful and because all costs were included, one can be much more certain that the combined effects of all benefits of Medicaid are cost-effective."

http://www.eurekalert.org/pub_releases/2015-03/slu-jso032515.php

Just slip out the back, Jack

We're wired to get over romantic break ups

ST. LOUIS - A Saint Louis University research review article suggests people are hardwired to fall out of love and move onto new romantic relationships.

"Our review of the literature suggests we have a mechanism in our brains designed by natural selection to pull us through a very tumultuous time in our lives," said Brian Boutwell, Ph.D., associate professor of criminology and criminal justice and associate professor of epidemiology at Saint Louis University. "It suggests people will recover; the pain will go away with time. There will be a light at the end of the tunnel."

Boutwell and his colleagues examined the process of falling out of love and breaking up, which they call primary mate ejection, and moving on to develop a new romantic relationship, which they call secondary mate ejection.

Drawing largely upon the field of evolutionary psychology, they say men and women might break up for different reasons. For instance, a man is more likely to end a relationship because a woman has had a sexual relationship with another man. For evolutionary reasons, men should be wired to try and avoid raising children that aren't genetically their own, the authors say.

"Men are particularly sensitive to sexual infidelity between their partner and someone else," Boutwell said. "That's not to say women don't get jealous, they certainly do, but it's especially acute for men regarding sexual infidelity."

On the other hand, a woman may be more likely to break up if her partner has been emotionally unfaithful partly because of evolutionary reasons. Over the deep time of evolution, natural selection has designed mate ejection in females to avoid the loss of resources, such as help in raising a child and physical protection, that their mates provide.

Sometimes both men and women end a relationship for the same reason. "For instance, neither gender tends to tolerate or value cruelty on the part of their partner," Boutwell said.

In addition, some people might be more likely than others to fall out of love or have problems moving. The ability to break up and find someone new to love lies along a continuum, influenced by environmental and genetic factors.

Brain imaging studies of men and women who claimed to be deeply in love also provided important clues about dealing with breakups. Functional MRIs showed an increase in neuronal activity in the parts of the brain - the pleasure areas - that also become active with cocaine use.

"Helen Fisher's work has revealed that this circuitry in the brain, which is deeply associated with addictive behaviors, also is implicated in the feelings associated with romantic attraction and may help explain the attachment that often follows the initial feelings of physical infatuation with a potential mate. Think of it as that initial feeling of falling in love, when you want to constantly be around the other person, almost in an addictive way," Boutwell said.

Falling out of love, Boutwell contends, might be compared to asking a cocaine addict to break his or her habit.

"To sever that bond and move on is a huge ask of a person," he said. "Ultimately, trying to move on from a former mate may be similar in some ways to an attempt at breaking a drug habit."

Building off the drug addiction analogy, Boutwell examined studies about the brains of former cocaine addicts to try to predict how the brains of those who are breaking a relationship habit might look.

Images of the brains of those no longer using cocaine showed a larger volume of gray matter in various brain regions, which were markedly different from images of brains of active cocaine users.

"We might argue that different regions of the brain act in a way that once that addiction has been severed, then help to facilitate a person moving on and finding a new partner," Boutwell extrapolated. "A person might initially pursue their old mate--in an attempt to win back their affection. However, if pursuit is indeed fruitless, then the brains of individuals may act to correct certain emotions and behaviors, paving the way for people to become attracted to new mates and form new relationships."

Conducting functional MRI studies that examine the brains of men and women who have rebounded from a relationship and fallen in love again would provide additional evidence to lend credibility to or dismiss the addiction hypothesis, he added.

In an additional attempt to understand what is going on inside the brain when a relationship ends, Boutwell examined research regarding the impact of a group of antidepressant medications called selective serotonin reuptake inhibitors (SSRIs) on romantic love. The use of SSRIs can potentially lower levels of dopamine, norepinephrine and testosterone, which might stifle romantic feelings and sexual interest.

"This is not to say that people should cease using their anti-depressants without consulting their doctors. That could be potentially tragic and a very bad decision," Boutwell said. "Rather, like any medication, it is important to fully understand the side effects. In this case, those side effects might impinge on the intimate feelings of one partner towards another."

Boutwell urged more research into lost love to better understand the difficulties that can creep into a romantic relationship.

"If we better understand mate ejection, it may offer direct and actionable insight into ways in which couples can save a relationship that might otherwise come to stultifying and abrupt halt," he said.

The review paper was published in the March 2 issue of the Review of General Psychology. Coauthors are J.C. Barnes, Ph.D., University of Cincinnati, and Kevin M. Beaver, Ph.D., Florida State University and King Abdulaziz University in Saudi Arabia.

http://www.eurekalert.org/pub_releases/2015-03/uoc--emp032515.php

Emergency medicine physicians urge colleagues to help prevent gun violence

Two practicing emergency medicine physicians urge their colleagues to take direct action to protect the health and safety of patients and communities

SACRAMENTO, Calif - In an editorial posted online today in the Annals of Emergency Medicine, two practicing emergency medicine physicians from the University of California, Davis, and Brown University -- both thought leaders at the forefront of finding solutions to the public health crisis of gun violence -- urge their colleagues to take direct action to protect the health and safety of patients and communities.

Their editorial follows the Feb. 24 call to action by eight health professional organizations, including the American College of Emergency Physicians, and the American Bar Association, to reduce firearm injuries and deaths in the U.S. -- unprecedented support that suggests mobilization to prevent firearm violence may be underway.

"Firearm violence causes nearly as many deaths as motor vehicle crashes," said Garen J. Wintemute, an emergency medicine professor at UC Davis and a national authority on evidence-based strategies to prevent firearm violence. "Firearms are

involved in most homicides and suicides, and the number of suicides by firearm is increasing -- especially among older white men.

"Emergency medicine physicians have limited opportunities to prevent a death once a shooting has occurred, because most people who die from their wounds do so where they are shot. Gun ownership or having a gun in the household is a well-documented risk factor for a violent death. For that reason, we believe physicians should also work to help prevent shootings," he said.

The authors describe how America successfully reduced motor-vehicle-related deaths by better vehicle and roadway design and public policies that make driving under the influence a crime. Yet no comparable public-health campaign focused on reducing gun violence has been launched.

The authors particularly emphasize the need for a national policy requiring background checks on all transfers of firearms to help prevent access to firearms by those who are prohibited from having them. They recommend adding two other high-risk groups to the list of individuals who are prohibited from purchasing firearms. These include persons with a history of violent misdemeanor convictions, such as assault and battery and domestic violence, as well as those with a documented history of addiction and alcohol abuse.

"Controlled studies of felons, those who have committed violent misdemeanors and persons prohibited for mental-health reasons have all shown reductions in risk for future violence of 25 percent or more when these individuals are denied firearm purchases," said Megan Ranney, an emergency medicine physician and director of the Emergency Digital Health Innovation program at Rhode Island Hospital and the Warren Alpert Medical School of Brown University.

The authors also address mental illness and gun violence. While they agree with recommendations that focus on behavior and expanded access to treatment, they emphasize that serious mental illness directly accounts for only 4 percent of interpersonal violence. In contrast, mental illness is associated with between 47 and 74 percent of suicides. The risk of firearm injury increases when mental illness coexists with alcohol abuse, drug abuse and a history of prior violence.

"Physicians need to include questions about firearms when assessing risk of violence in their patients, and need to act on the information, especially when patients are expressing thoughts of dangerousness to themselves or others, are intoxicated or are in the emergency department for a violence-related injury," Ranney said.

At a time when civilian fatalities from gunshot wounds for 2004 to 2013 have outnumbered combat fatalities from World War II, the authors welcome the unprecedented support from leading organizations of health and legal professionals for policy recommendations to reduce gun violence.

"Physicians can take direct action to protect the health and safety of patients and communities," Wintemute said. "While we may not all agree on all the specifics, enough of us will agree on enough of them to make a difference for the better."

http://www.eurekalert.org/pub_releases/2015-03/tl-tld032415.php

The Lancet Diabetes & Endocrinology: New score predicts heart disease and stroke risk for anyone in world aged over 40

For the first time, scientists have developed a new risk score that can predict the 10-year risk of developing heart disease or having a stroke in persons aged 40 years or older in any world country.

The research is published in The Lancet Diabetes & Endocrinology journal, and was led by Dr Goodarz Danaei, Assistant Professor of Global Health at the Harvard T. H. Chan School of Public Health in Boston, USA.

Danaei and colleagues developed, validated, and evaluated the new score, called Globorisk, using data from eight cohort studies [1], including more than 50 000 participants. Unlike previous risk scores, Globorisk can be updated to fit local conditions and risk factor levels in different countries using routinely available information.

Dr Danaei explains, "Globorisk is an important advance in the field of global cardiovascular disease prevention. Until now, most prediction scores were developed using a single cohort study and were never validated for accuracy in national populations for low- and middle-income countries. Therefore, clinicians and public health policy makers in these countries were left without a reliable tool to predict cardiovascular risk in their patients, community, or country."[2]

Globorisk measures cardiovascular risk in individuals aged 40 or older by factoring in the person's smoking status, blood pressure, diabetes status, and total cholesterol level, whilst adjusting for the effects of sex and age on cardiovascular disease between countries.

The researchers recalibrated and applied their risk score to 11 countries from different world regions [3], using data from recent national health surveys to replace the average age-and-sex risk factor levels in each country and incorporating cardiovascular disease death rates for each age-and-sex group. They developed country-specific risk charts for predicting individuals' risk of cardiovascular disease (see figure 4 pages 7-14), and country-specific assessments of the 10-year cardiovascular disease burden (see figure 5 page 15).

They estimate that the proportion of people at high risk (10% or higher) of having a fatal heart attack or stroke within 10 years is higher in low- and middle-income countries (eg, China and Mexico) compared with high-income countries (eg, South Korea, Spain, and Denmark). For example, in China around a third of men

and women (nearly 170 million aged between 40 and 84 years) have a high 10-year risk of dying from a cardiovascular event compared with only 5-10% of men and women in Spain and Denmark (see figure 5 page 15).

According to Dr Danaei, "Globorisk can be used to identify individuals at high risk of developing cardiovascular disease who are most likely to benefit from lifestyle changes or preventive drug treatment. Moreover, by estimating the number of people who have a high risk in any given country we have more chance of accurately measuring progress towards the WHO target of 50% coverage of multidrug treatment and counselling for people aged 40 years and older at high risk of cardiovascular disease." [2]

Karel Moons from the Utrecht University Medical Center in the Netherlands and Ewoud Schuit from the same centre and from Stanford University in the USA, both authors of a linked Comment, say, "A next step would be to quantify the effects, on a population level, of introducing in these countries the Globorisk model combined with subsequent risk-based preventative management. These quantifications might further help, and indeed convince, decision-makers across the world to decide on wide-scale introduction of prediction models and risk-based management for cardiovascular disease." [2]

This study was funded by the US National Institutes of Health, UK Medical Research Council, and the Wellcome Trust.

[1] Atherosclerosis Risk in Communities, Cardiovascular Health Study, Framingham Heart Study original cohort, Framingham Heart Study offspring cohort, Honolulu Heart Program, Multiple Risk Factor Intervention Trial, Puerto Rico Heart Health Program, and Women's Health Initiative Clinical Trial.

[2] Quotes direct from authors and cannot be found in text of Article / Comment

[3] China, Czech Republic, Denmark, England, Iran, Japan, Malawi, Mexico, South Korea, Spain, and the USA.

http://bit.ly/1E38ZGM

Want to Live Longer? Don't Sleep So Much

New research links longer sleep duration with a shorter life

If you're like most people, you'd kill for a longer night's sleep. But in turn, longer sleep might just kill you. New research shows that adults who sleep more than eight hours a night are at a higher risk of early death.

When Franco Cappuccio of the University of Warwick analyzed 16 sleep studies covering more than a million people, he found that 30 percent of people who slept more than eight hours a night died early, reports Ruth Alexander for the BBC. That's an 18 percent rise in mortality rate from sleepers who reported getting six hours a night or less in the sack.

Why the increased chance of death? Cappuccio, who corrected for depression and sleeping pill use in his review, thinks it has to do with underlying health issues that could be causing longer sleep. But Alexander reports that another researcher has seen increased inflammation and depression in study participants who got an extra two hours of sleep a night - results that could be related to "prolonged inactivity."

Cappuccio also co-authored a recent paper about the connection between sleep and strokes. Though his team admits that more research is needed, their findings suggest "a significant increase in stroke risk among long sleepers and a modest increase among short sleepers."

In the wake of another sleep study that suggests women who get an extra hour of sleep have higher libidos and better genital arousal, what's a confused sleep seeker to do?

"I think the take-home message should not be that more sleep is better, but that it is important to allow ourselves to obtain the sleep that our mind and body needs," the libido study's author told the *Sydney Morning Herald*. That's consistent with the mortality study - since it found that 12 percent of people who get less than six hours of sleep also died early, the answer could be a solid seven hours of shut-eye per night.

http://bit.ly/1HJQV5S

An Asteroid Boulder Will Be A Stepping Stone on the Journey to Mars

NASA announces details in its plan to capture an asteroid and bring it into lunar orbit

By Marissa Fessenden

NASA's plan to snag an asteroid and bring it into orbit around the moon for astronauts to explore just took another step toward reality. For a while now, the agency had been considering two options for its Asteroid Redirect Mission (ARM): One that would grab an entire small asteroid and tow it back and another that would land on a larger asteroid, scoop up a smaller, boulder-sized chunk and cart that back.

Today, NASA associate administrator Robert Lightfoot announced in a press briefing that the mission will go with the second option. After extensive review, so-called option B would be less expensive and offer a better chance for success. If the mission chose to grab a small asteroid, they would need to choose a final target one year before launch. Going for a boulder essentially offers several choices at once.

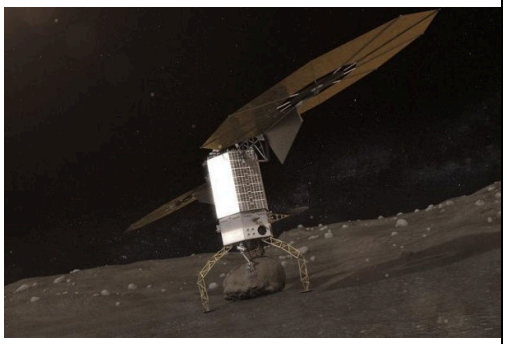
From past missions, NASA has learned that the surfaces of larger asteroids are strewn with boulders. With option B, the team can identify several likely targets

and send spacecraft with the ability to take measurements on all of them before grabbing one.

"We will make an educated choice on which to pull," Lightfoot said.

NASA also laid out a planned timeline for the mission. The ARM robotic spacecraft will launch in December 2020 and cruise on solar electric propulsion toward the chosen asteroid.

NASA has announced that it is eying three candidates: Itokawa, Bennu and 2008 EV5. In the press briefing, Lightfoot focused on 2008 EV5, "one we think we have fairly well characterized," though other candidates may present themselves in the coming years.



***The Asteroid Redirect Vehicle gets ready to push off from the asteroid after grabbing a boulder in this artist's interpretation* (NASA)**

After about two years flight, the ARM spacecraft will sidle up to the asteroid, make a soft landing and start sampling a few boulders. Once the selection is make, the spacecraft will take its bounty into a "halo orbit" around the large asteroid.

Spacecraft and boulder together will be a small mass compared to the asteroid, but it will be enough to gradually nudge the larger body's movement.

"We are talking about a small deflection," Lightfoot said, but one that can be measured from Earth.

This part of the mission will prove that NASA has the capability to move an asteroid - a vital part of the ARM mission is to test whether Earth would be able to avert an asteroid headed for impact.

The spacecraft will hang out in halo orbit for 215 to 400 days, depending on how successful that nudge is. Then with asteroid boulder secured, it will make its way back toward an orbit around the moon.

The plan is for the boulder and spacecraft to be in place, stably orbiting the Moon and ready for astronauts to visit and study by 2025.

The Orion spacecraft, carrying a two-man crew, will be able to dock with the ARM spacecraft. A NASA press statement offers more details:

This crewed mission will further test many capabilities needed to advance human spaceflight for deep space missions to Mars and elsewhere, including new sensor technologies and a docking system that will connect Orion to the robotic spacecraft carrying the asteroid mass. Astronauts will conduct spacewalks outside Orion to study and collect samples of the asteroid boulder wearing new spacesuits designed for deep space missions.

Collecting these samples will help astronauts and mission managers determine how best to secure and safely return samples from future Mars missions. And, because asteroids are made of remnants from the formation of the solar system, the returned samples could provide valuable data for scientific research or commercial entities interested in asteroid mining as a future resources.

The mission will also be a critical demonstration of the capabilities of the solar electric propulsion system, which converts the Sun's energy into power that then sends charged atoms streaming behind the spacecraft, propelling it forward.

"Future SEP-powered spacecraft could pre-position cargo or vehicles for future human missions into deep space, either awaiting crews at Mars or staged around the moon as a waypoint for expeditions to the Red Planet," NASA writes.

It might not be a whole asteroid, but the plan is no less impressive for the choice to retrieve a boulder.

NASA plans to keep the cost of the whole mission at $1.25 billon. Next, the agency will assess whether it will develop the propulsion system in-house or contract out.

Meanwhile, we all get a little closer to an exciting new era of human spaceflight and exploration.

http://www.eurekalert.org/pub_releases/2015-03/uops-rhs032615.php

Roseroot herb shows promise as potential depression treatment option, Penn team finds

Study is the first randomized, double-blind, placebo-controlled, comparison trial of oral R. rosea extract versus conventional antidepressant for mild to moderate major depressive disorder

PHILADELPHIA -- Rhodiola rosea (R. rosea), or roseroot, may be a beneficial treatment option for major depressive disorder (MDD), according to results of a study in the journal Phytomedicine led by Jun J. Mao, MD, MSCE, associate professor of Family Medicine, Community Health and Epidemiology and colleagues at the Perelman School of Medicine of University of Pennsylvania.

The proof of concept trial study is the first randomized, double-blind, placebo-controlled, comparison trial of oral R. rosea extract versus the conventional antidepressant therapy sertraline for mild to moderate major depressive disorder.

Depression is one of the most common and debilitating psychiatric conditions, afflicting more than 19 million Americans each year, 70 percent of whom do not fully respond to initial therapy. Costs of conventional antidepressants and their sometimes substantial side effects often result in a patient discontinuing use prematurely. Others opt to try natural products or supplements instead.

All of the study's 57 adult participants, enrolled from December 2010 and April 2013, had a DSM IV Axis 1 diagnosis of MDD, meaning they exhibited two or

more major depressive episodes, depressed mood and/or loss of interest or pleasure in life activities for at least 2 weeks, as well as symptoms including significant unintentional weight loss or gain, insomnia or sleeping too much, fatigue, and diminished ability to think or concentrate, and recurrent thoughts of death.

The participants received 12 weeks of standardized R. rosea extract, sertraline, or placebo. Changes over time in Hamilton Depression Rating (HAM-D), Beck Depression Inventory (BDI), and Clinical Global Impression (CGI) change scores were measured among groups.

Patients who took sertraline were somewhat more likely - as measured by Ham-D scores - to report improvement in their symptoms by week 12 of treatment than those who took R. rosea, although these differences were not found to be statistically significant. Patients taking R. rosea had 1.4 times the odds of improvement, and patients on sertraline had 1.9 times the odds of improvement versus those on a placebo. However, patients on sertraline experienced twice the side effects - most commonly nausea and sexual dysfunction -- than those on R. rosea: 63 percent versus 30 percent, respectively, reported side effects. These findings suggest that R. rosea may possess a more favorable risk to benefit ratio for individuals with mild to moderate major depressive disorder.

"These results are a bit preliminary but suggest that herbal therapy may have the potential to help patients with depression who cannot tolerate conventional antidepressants due to side effects," Mao said. "Larger studies will be needed to fully evaluate the benefit and harm of R. rosea as compared to conventional antidepressants."

This work was supported by the National Institutes of Health Center for Complementary and Integrative Health R21 AT005230, and the Jack Warsaw Fund for Research in Biological Psychiatry at the University of Pennsylvania. Mao was also supported by the National Institutes of Health Center for Complementary and Integrative Health K23 AT004112.

To access the abstract and full article, please visit:
http://authors.elsevier.com/a/1Qer83MpM~M8mB

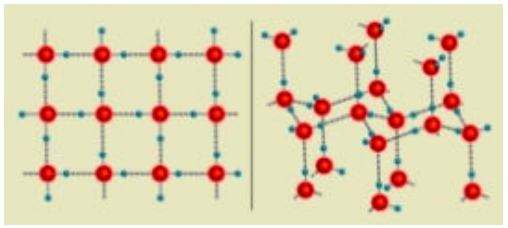
http://bit.ly/1D6aDro

New Form of Ice Forms in Graphene "Sandwich"

The ice's unusual square structure suggests why water can zip through stacks of the atom-thick sheets of carbon

March 26, 2015 |By Mark Peplow and Nature magazine

By flattening a droplet of water between two sheets of graphene, researchers have created a new form of ice. Just a few molecules thick, its atoms are locked in a square grid pattern. The discovery of 'square ice' highlights another remarkable property of graphene, which consists of flat, atom-thick sheets of carbon. Not only are graphene sheets remarkably stiff, strong and conductive, but they can also exert immense pressure on molecules trapped between them. This could explain why water seeps through stacks of graphene very quickly - a property that suggests the material could be used in desalination membranes to purify water.



In 'square ice', which has been seen between graphene sheets, water molecules lock flat in a right-angled formation. The structure is strikingly different from familiar hexagonal ice (right).

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Back in 2012, a team led by Andre Geim at the University of Manchester, UK - who shared the 2010 Nobel Prize in Physics for isolating and studying graphene - found that water vapor could pass through laminated sheets of graphene oxide, something that not even helium gas could manage. Two years later, they showed that liquid water performed the same trick through stacks of graphene oxide, even though those stacks filtered out other molecules.

Computer simulations suggested that water was forming layers of square ice between the graphene sheets. Pushing the ice from one end shunted all the molecules forward in concert, like carriages in a high-speed train. "But you never trust molecular-dynamics simulations," says Geim. Hence the latest experiment.

Ice to meet you

Geim's team dropped one microliter of water on to a sheet of graphene, and then placed a second graphene wafer on top, all at room temperature. As the water slowly evaporated, the graphene sheets were squeezed together until they were less than one nanometre apart, trapping pockets of water in the sandwich. Transmission electron microscopy revealed that these pockets contained square ice. "It's not totally unexpected," says Alan Soper, a physicist at the Rutherford Appleton Laboratory in Harwell, UK, who wrote a News & Views article that accompanies the report of the discovery, which is published in Nature. When water gathers into small clusters of just eight molecules, for example, it forms a cubic structure. "But it's never been observed in such an extended layer," he says. Soper reckons that square ice qualifies as a new crystalline phase of ice, joining 17 others that have already been observed.

Flat hunting

Square ice is strikingly different from normal ice. In a single, V-shaped water molecule (H_2O), an oxygen atom is connected to two hydrogen atoms by strong bonds. But it also forms weaker attractions to hydrogen atoms in two

neighbouring water molecules. In ice, these four bonds are usually arranged in a tetrahedral (pyramid) shape. But in a layer of square ice, all the atoms lie in a flat plane with a right angle between each oxygen–hydrogen bond. Geim's patches of square ice contained one, two or three of these layers, with oxygen atoms in adjacent layers sitting directly on top of one another.

The team calculated that the graphene sheets must be exerting more than 10,000 times atmospheric pressure to flatten water in this way. "It was a surprise the pressure was so high," says Geim. That pressure is generated when the graphene's carbon atoms get close enough to distort each other's electron clouds. This causes a mutual attraction, known as the van der Waals force, between carbon atoms in adjacent graphene layers. "It's like having millions of little springs holding them together," says Soper.

Geim thinks that square ice could turn up in other tight spaces, such as the interiors of nanotubes. And pinning down its properties should help the development of improved desalination filters based on graphene, he adds. "Finding out how the water behaves in a capillary is a big part of what we need to do to make a good filter," says Geim. "This is a very important step."

http://www.eurekalert.org/pub_releases/2015-03/uotm-cvm032615.php

Chikungunya virus may be coming to a city near you -- learn the facts

Painful and potentially debilitating disease is predicted to soon spread to the U.S.

The mosquito-borne chikungunya virus has been the subject of increasing attention as it spreads throughout South America, Central America, the Caribbean and Mexico. This painful and potentially debilitating disease is predicted to soon spread to the U.S. The University of Texas Medical Branch at Galveston's Scott Weaver, globally recognized for his expertise in mosquito-borne diseases, has been studying chikungunya for more than 15 years. Weaver and fellow infectious disease expert Marc Lecuit of the Institut Pasteur have summarized currently available information on this disease in the March 26 edition of the New England Journal of Medicine.

Since chikungunya was first identified in1952 in present-day Tanzania, the virus has been confirmed in other African countries, Asia, The South Pacific and Europe. In Dec. 2013, the first locally acquired case of chikungunya in the Americas was reported in the Caribbean. Since then, chikungunya has been identified in 44 countries or territories throughout the Americas with more than 1.3 million suspected cases reported to the Pan American Health Organization from affected areas.

Symptoms appear about three days after being bitten by an infected mosquito. The most common symptoms and signs are fever and severe joint pain and may include headache, arthritis, muscle pain, weakness and rash. Some patients will feel better within a week but others develop longer-term joint pain that can last weeks to years. Death is rare but can occur. People at increased risk for severe disease include young children, older adults and people with medical conditions such as diabetes or heart disease. Other than anti-inflammatory drugs to control symptoms and joint swelling, there are no specific therapies to treat infected persons and no licensed vaccines to prevent chikungunya fever.

"Chikungunya continues to be a major threat to public health around the world," said Weaver. "Until there is a treatment or vaccine, the control of chikungunya fever will rely on mosquito reduction and limiting the contact between humans and the two virus-carrying mosquitoes, Aedes aegypti and Aedes albopictus." These efforts generally focus on reducing or treating standing water and water storage containers where eggs are laid and larvae develop as well as wearing protective clothing and/or insect repellent.

Current research is focused on better understanding how exactly the virus enters and multiplies within the human and mosquito body. Researchers are also learning more about why some people develop long-term chronic joint pain after the initial chikungunya fever while others do not.

Several promising chikungunya vaccine candidates have reached late preclinical or phase one clinical testing, but final development will require major commercial investments. Another challenge to vaccine development lies in targeting locations where there will be many cases of chikungunya fever to set up and conduct clinical trials. Weaver is the director of the UTMB Institute for Human Infections and Immunity, scientific director of the Galveston National Laboratory and leads the Global Virus Network's Chikungunya Task Force.

http://www.eurekalert.org/pub_releases/2015-03/uonc-rit032515.php

Researchers identify timeline for HIV replication in the brain

A team of researchers has discovered HIV can begin replicating in the brain as early as four months after initial infection.

CHAPEL HILL, NC - The study followed 72 treatment naïve participants during the first two years of HIV infection. Through analysis of cerebral spinal fluid (CSF) and blood samples, 20 percent of subjects showed replication in the central nervous system (CNS) at four months. Additionally, 30 percent of participants showed evidence of a marked CSF inflammatory response in at least one time point and 16 percent of study volunteers showed a marked CSF inflammatory response at multiple time points, suggesting an ongoing infection in the CNS. The findings will be published in the scientific journal PLoS Pathogens.

"This shows that viral replication and inflammation can occur early in infection with the concern being that the damage caused could be irreversible," says study virologist Ronald Swanstrom, PhD, Director of the University of North Carolina's Center for AIDS Research (CFAR) and Professor of Biochemistry and Biophysics at UNC's School of Medicine. "HIV and inflammation have the potential to accelerate the aging process and cause neurocognitive impairment, in the extreme case resulting in HIV-associated dementia."

One-third of people not taking antiretroviral therapy (ART) to control their HIV will eventually develop HIV-associated dementia, Swanstrom says. For him, the study's results in these newly infected people stress the importance of routine HIV testing to catch the infection as early as possible to allow the prompt initiation antiretroviral therapy.

"This is yet another reason we want people on ART right away to limit the possibility of replication and inflammation in the brain," Swanstrom says.

Future studies could focus on whether or not damage to the brain caused by this early replication and inflammation is reversible. Swanstrom collaborated on the study with senior author and neurologist Serena Spudich, MD, Division Chief of Neurological Infections & Global Neurology and Associate Professor of Neurology at Yale School of Medicine, and neurologist Richard Price, MD, Professor of Neurology at the University of California San Francisco School of Medicine. The first author on the study was a UNC graduate student in the Department of Microbiology and Immunology, Christa Sturdevant, who is now a postdoctoral fellow at Duke University. The study was funded by the National Institute of Mental Health.

http://www.eurekalert.org/pub_releases/2015-03/uoc--ais032315.php

Antarctic ice shelves rapidly thinning

New study reveals accelerating losses over two decades

A new study led by Scripps Institution of Oceanography at UC San Diego researchers has revealed that the thickness of Antarctica's floating ice shelves has recently decreased by as much as 18 percent in certain areas over nearly two decades, providing new insights on how the Antarctic ice sheet is responding to climate change.

Data from nearly two decades of satellite missions have shown that the ice volume decline is accelerating, according to a study published on March 26, 2015, in the journal Science and supported by NASA. Scripps graduate student Fernando Paolo, Scripps glaciologist Helen Amanda Fricker, and oceanographer Laurie Padman of Earth & Space Research (a non-profit institute specializing in oceanography research) constructed a new high-resolution record of ice shelf thickness based on satellite radar altimetry missions of the European Space Agency from 1994 to 2012.

Merging data from three overlapping missions, the researchers identified changes in ice thickness that took place over more than a decade, an advancement over studying data from single missions that only provide snapshots of trends.

Total ice shelf volume (mean thickness multiplied by ice shelf area) across Antarctica changed very little from 1994 to 2003, then declined rapidly, the study shows. West Antarctic ice shelves lost ice throughout the entire observation period, with accelerated loss in the most recent decade. Earlier gains in East Antarctic ice shelf volume ceased after about 2003, the study showed. Some ice shelves lost up to 18 percent of their volume from 1994 to 2012.

"Eighteen percent over the course of 18 years is really a substantial change," said Paolo. "Overall, we show not only the total ice shelf volume is decreasing, but we see an acceleration in the last decade."

While melting ice shelves do not contribute directly to sea-level rise, the researchers indicate that there is an important indirect effect. "The ice shelves buttress the flow from grounded ice into the ocean, and that flow impacts sea-level rise, so that's a key concern from our new study," said Fricker.

Under current rates of thinning, the researchers estimate the ice shelves restraining the unstable sector of West Antarctica could lose half their volume within the next 200 years.

"This work demonstrates the power of satellite observations to understand change in the great polar ice sheets," said Thomas Wagner, Program Manager for Cryospheric Sciences at NASA Headquarters. "And with data spanning decades, we can understand some of the most important changes and their implications for sea-level rise."

Fricker said future studies will concentrate on the causes behind changes in ice shelf volume, including the effects of the atmosphere and ocean.

"We're looking into connections between El Niño events in the tropical Pacific and changes in the Antarctic ice sheet," said Paolo. "It's very far apart but we know that these teleconnections exist. That may ultimately allow us to improve our models for predicting future ice loss."

http://www.eurekalert.org/pub_releases/2015-03/uow-ewv032315.php

Ebola whole virus vaccine shown effective, safe in primates

An Ebola whole virus vaccine, constructed using a novel experimental platform, has been shown to effectively protect monkeys exposed to the often fatal virus.

MADISON, Wis. - The vaccine, described today (March 26, 2015) in the journal Science, was developed by a group led by Yoshihiro Kawaoka, a University of Wisconsin-Madison expert on avian influenza, Ebola and other viruses of medical

importance. It differs from other Ebola vaccines because as an inactivated whole virus vaccine, it primes the host immune system with the full complement of Ebola viral proteins and genes, potentially conferring greater protection.

"In terms of efficacy, this affords excellent protection," explains Kawaoka, a professor of pathobiological sciences in the UW-Madison School of Veterinary Medicine and who also holds a faculty appointment at the University of Tokyo. "It is also a very safe vaccine."

The vaccine was constructed on an experimental platform first devised in 2008 by Peter Halfmann, a research scientist in Kawaoka's lab. The system allows researchers to safely work with the virus thanks to the deletion of a key gene known as VP30, which the Ebola virus uses to make a protein required for it to reproduce in host cells. Ebola virus has only eight genes and, like most viruses, depends on the molecular machinery of host cells to grow and become infectious. By engineering monkey kidney cells to express the VP30 protein, the virus can be safely studied in the lab and be used as a basis for devising countermeasures like a whole virus vaccine. The vaccine reported by Kawaoka and his colleagues was additionally chemically inactivated using hydrogen peroxide, according to the new Science report.

Ebola first emerged in 1976 in Sudan and Zaire. The current outbreak in West Africa has so far claimed more than 10,000 lives. There are no proven treatments or vaccines, although several vaccine platforms have been devised in recent years, four of which recently advanced to the clinical trial stage in humans.

The new vaccine reported by Kawaoka has not been tested in people. However, the successful tests in nonhuman primates conducted at the National Institutes of Health (NIH) Rocky Mountain Laboratories, a biosafety level 4 facility in Hamilton, Montana, may prompt further tests and possibly clinical trials of the new vaccine. The work at Rocky Mountain Laboratories was conducted in collaboration with a group led by Heinz Feldmann of NIH.

Those studies were conducted with cynomolgus macaques, which are very susceptible to Ebola. "It's the best model," Kawaoka says. "If you get protection with this model, it's working."

Ebola vaccines currently in trials include:

A DNA-based plasmid vaccine that primes host cells with some of the Ebola proteins.

A vaccine based on a replication incompetent chimpanzee respiratory virus engineered to express a key Ebola protein.

A live attenuated virus from the same family of viruses that causes rabies, also engineered to express a critical Ebola protein.

A vaccine based on a vaccinia virus and engineered to express a critical Ebola protein.

Each of those strategies, Kawaoka notes, has drawbacks in terms of safety and delivery. Whole virus vaccines have long been used to successfully prevent serious human diseases, including polio, influenza, hepatitis and human papillomavirus-mediated cervical cancer.

The advantage conferred by inactivated whole virus vaccines such as the one devised by Halfmann, Kawaoka and their colleagues is that they present the complete range of proteins and genetic material to the host immune system, which is then more likely to trigger a broader and more robust immune response.

Early attempts to devise an inactivated whole virus Ebola vaccine through irradiation and the preservative formalin failed to protect monkeys exposed to the Ebola virus and were abandoned. Although the new vaccine has surpassed that hurdle, human trials are expensive and complex, costing millions of dollars.

The Ebola vaccine study conducted by Kawaoka was supported by the National Institutes of Health and by the Japanese Health and Labour Sciences Research Grants.

In addition to Kawaoka, co-authors of the new Science report include Halfmann, Lindsay Hill-Batorski and Gabriele Neumann of UW-Madison and Andrea Marzi, W. Lesley Shupert and Feldmann of the National Institute of Allergy and Infectious Diseases.

http://www.eurekalert.org/pub_releases/2015-03/fi-fr031815.php

Forsyth research explains why popular antacids may increase chance of bone fractures

New study provides best explanation for side effect of prescription and over-the-counter heartburn medications used by 100 million Americans

CAMBRIDGE, Mass - Newly published research from the Forsyth Institute details a discovery explaining why the 100 million Americans estimated to be taking prescription and over-the-counter antacid and heartburn medications may be at an increased risk of bone fractures.

The new report from Forsyth, published in the March issue of the prestigious medical research journal PLOS Genetics, explains that stomach acid in the gastrointestinal tract plays an important role in helping the intestines absorb and transfer calcium to the skeletal system. While the introduction of proton pump inhibitor-based antacids reduces the level of acidity in the stomach to bring relief to patients, the reduction also interrupts and even stops the gut from absorbing much needed calcium.

The connection between proton pump inhibitors and bone fractures has been well established, with the Food and Drug Administration in 2010 requiring a warning label placed on all product packaging. Other research has indicated these medications may block the absorption of important nutrients, but until this study it was not known how or why this was happening in the body.

"The regulation of bone mass by the gastrointestinal tract represents a remarkable example of an unexpected and important relationship between these two systems that is only now becoming fully appreciated," said Dr. Ricardo Battaglino of the Forsyth Institute. "It could help us better understand and find new ways to treat common clinical conditions that currently require medications which have been linked to weakened bones, such as popular antacids."

Over-the-counter and prescription antacids are used by 100 million Americans to treat heartburn and related conditions. It is the third highest selling drug category with $14 billion in annual sales according to the American Academy of Family Physicians. Fractures at the hip, wrist, arm, ribs and even vertebrae - especially in individuals aged 50 and older - can permanently impair quality of life and result in an expensive drain on the American healthcare system.

This research study, titled "Osteopetrorickets due to Snx10 Deficiency Results from Both Failed Osteoclast Activity and Loss of Gastric Acid-dependent calcium Absorbtion," was conducted in mice by The Forsyth Institute and the published report is authored by Battaglino, Liang Ye, Lelsie R. Morse, Li Zhang, Hajime Sasaki, Jason C. Mills, Paul R. Odgren, Greg Sibbel, and Ariane Zamarioli. To learn more, visit http://www.forsyth.org.

http://www.eurekalert.org/pub_releases/2015-03/ason-wtd031915.php

What to do with kidneys from older deceased donors?

Study reveals which patients on the transplant waiting list are most likely to benefit from such organs

-***For older patients in need of a kidney transplant, rapid transplantation from an older deceased donor is superior to delayed transplantation from a younger donor.***

-***Kidneys from older donors do not have sufficient longevity to provide younger patients with a lifetime of kidney function, but they do have sufficient longevity to provide older patients who have a shorter life expectancy with a lifetime of kidney function.***

-***More than 100,000 people in the United States are waiting for a kidney transplant.***

Washington, DC - A new study highlights the best way to use kidneys from older deceased donors, providing the most benefits to patients and addressing the worsening organ shortage. The study's findings, which appear in an upcoming issue of the Journal of the American Society of Nephrology (JASN), could lead to changes in current transplant allocation policies.

The number of patients waiting for a kidney transplant in the United States recently eclipsed 100,000, yet most kidneys recovered from deceased donors aged 65 years or older are discarded.

To investigate how to optimally increase the use of such "expanded criteria donor kidneys," a team led by John Gill MD, MS, Caren Rose, PhD, (University of British Columbia, in Canada), and Elke Schaeffner, MD (Charité University Medicine, in Berlin) conducted a series of analyses of data from the Eurotransplant Senior Program and the United States Renal Data System. They found that in patients in need of a transplant who are at least 60 years old, rapid transplantation from an older deceased donor is superior to delayed transplantation from a younger donor. The researchers also discovered that kidneys from older donors do not have sufficient longevity to provide younger patients with a lifetime of kidney function, but they do have sufficient longevity to provide older patients who have a shorter life expectancy with a lifetime of kidney function.

"Older patients derive a survival benefit from rapid transplantation with an older donor kidney, while younger patients do not derive a benefit from transplantation from an older kidney," said Dr. Gill. "Ensuring older patients can access older donor kidneys should be a priority in the United States. This may involve increased utilization of older donor kidneys or possibly excluding younger patients from receiving these kidneys."

Study co-authors include Ulrich Frei, MD and Jagbir Gill MD, MS.

Disclosures: The authors reported no financial disclosures.

The article, entitled "A Lifetime of Allograft Function with Kidneys from Older Donors," will appear online at http://jasn.asnjournals.org/ on March 26, 2015.

http://www.medscape.com/viewarticle/842103

Budesonide Has Potential for Lung Cancer Chemoprevention

Inhaled glucocorticosteroids might have potential as a chemopreventive agent for lung cancer, new research shows.

Roxanne Nelson, RN

At 5-year follow-up, nonsolid nodules detected with low-dose CT were significantly smaller in people who used inhaled budesonide for 1 year than in those who did not, according to updated results from a phase 2b randomized study. A subset of these nodules could be precursors of adenocarcinoma.

The results were published online February 11 in the *Annals of Oncology*.

The use of inhaled budesonide had no effect on the number of new lesions or the number of cases of lung cancer, although the study was underpowered to assess cancer incidence as an end point, note Giulia Veronesi, MD, from the division of thoracic surgery at the European Institute of Oncology in Milan, and colleagues.

"To demonstrate a reduction in the cancer rate, we need a longer follow-up and a much larger population," Dr Veronesi told *Medscape Medical News*. Budesonide was only used for 1 year, and 5 years of follow-up might not be sufficient for assessing the progression of premalignant lesions to cancer, she explained.

But the persistent effect on nonsolid nodules "suggests biologic activity and the possibility that such nodules could be intermediate end points in future chemoprevention trials," the researchers report.

The inhaled corticosteroid can prevent the progression of the lung lesions to infiltrating tumors.

"These results, if validated in additional studies, may be of conical importance for subjects with initial precancerous lesions that are typically multifocal slow-growing ground-glass opacities that can evolve into adenocarcinomas with time," said Dr Veronesi. "For these subjects, the inhaled corticosteroid can prevent the progression of the lung lesions to infiltrating tumors." Thus, the effects of budesonide on the development of lung cancer "deserves continuing investigation," she noted.

Merit Further Exploration

These results are interesting because there are not very many positive studies in terms of the chemoprevention of lung cancer, said Samjot Singh Dhillon, MD, associate professor of oncology, chief of pulmonary medicine, and cochief of endoscopy at the Roswell Park Cancer Institute in Buffalo, New York.

"However, this hypothesis will need further exploration, and current evidence is not enough to start using inhaled budesonide for the prevention of lung cancer," Dr Dhillon told *Medscape Medical News*. "The nodules were very small, and minor variations in size can occur just due to technique and interpreter variability." He pointed out that "techniques like volumetric assessment were not available." In addition, "most of the small lesions are generally benign."

Although ground-glass changes can occur because of premalignant changes, these can also be caused by inflammation, fluid, blood, pus, or mucus in the airway.

"Budesonide has a known anti-inflammatory effect, and without biopsy, it is hard to tell what exactly was treated," Dr Dhillon explained. "The reason for the persistence of the effect for 5 years is also unclear."

"The side effects of inhaled steroids, including bone loss and increased risk of pneumonia, need to be weighed when considering this treatment for the prevention of lung cancer in patients who do not otherwise need it for their asthma or chronic obstructive lung disease," he said. But Dr Dhillon agrees that the positive results are interesting and merit further exploration.

"There are companies working on and testing new formulations of budesonide to reduce the size of the molecules, with the objective of having a deeper diffusion of the inhaled compound in the periphery of the lung," said Dr Veronesi.

In the meantime, the researchers are evaluating oral low-dose aspirin as a chemopreventive agent in a similar population.

Nodule Size Significantly Smaller

In a study that was nested in the ongoing prospective COSMOS lung screening trial, Dr Veronesi and her colleagues evaluated the effect of budesonide on lung nodules detected with low-dose CT in 202 current and former smokers.

All of the participants had 'target' nodules, which had persisted for at least 1 year but did not require any additional diagnostic assessment. They received inhaled budesonide 800 µg twice daily or placebo for 1 year.

The primary study end point was the effect of budesonide on target nodule size, determined with a per person analysis.

At 1 year, there was no significant difference in nodule size between the budesonide and placebo groups (2% vs 1%) (*Cancer Prev Res (Phila).* 2011;4:34-42). However, when a per lesion analysis was conducted, the association between budesonide and the regression of nonsolid target nodules was significant (P = .02). Although both target and nontarget nonsolid nodules seemed to regress in the budesonide group, the difference between the two groups did not reach significance.

Five years after the baseline assessment, the researchers analyzed the evolution in the size of the nodules in both groups.

At 5-year follow-up, the mean size of both target and nontarget nonsolid nodules had decreased a significant 2.42 mm from baseline in the budesonide group (from 5.03 to 2.61 mm; P = 0.029). In contrast, the mean size had increased by 0.42 mm in the placebo group (from 5.26 to 5.68 mm).

The decrease was less pronounced in partially solid nodules, but the mean change in maximum diameter was still greater in the budesonide group than in the placebo group (–0.79 vs +0.10 mm; P = .252).

During the follow-up period, five participants were diagnosed with lung cancer (all adenocarcinomas); three were from the budesonide group and two were from the placebo group.

This trial was supported by the National Cancer Institute Division of Cancer Prevention. The authors have disclosed no relevant financial relationships.

Ann Oncol. Published online February 11, 2015. Abstract

http://bit.ly/1IHkbIf

Why Would Cooling Rice Make it Less Caloric?

Scientists suggest a new way to prepare rice that they say could help slow the worldwide obesity epidemic

By Laura Clark

Fans of leftovers, listen up: refrigerating rice cooked with just a teaspoon of coconut oil could cut the amount of calories we absorb from it by up to 60 percent, according to a team of scientists from Sri Lanka.

The researchers, who recently made a presentation on the subject to the American Chemical Society, developed the new cooking method while seeking out “food-based solutions” to combat growing global obesity rates. And they deemed rice,

which remains a mealtime staple in many countries where sedentary lifestyles are becoming more common, a good place to start.

As a type of carb, the starch in rice is broken down by our bodies into simple sugars, explains Michelle Roberts, health editor at BBC News. Those sugars get stored and then converted into glucose, which helps give us energy. But when the body has more glucose than it can use, that can add up to fat. Rice, however, has two types of starches - digestible and indigestible - and only the carbs our digestive system can absorb get broken down into sugars.

So the research team set out to find a way to make more of the starches in rice indigestible, which would then make it less caloric. And how can you do that? It all comes down to the preparation, they say.

If you simmer rice for forty minutes in a little bit of coconut oil, as the researchers recommend, the oil "enters the starch granules in the rice, changing their structure to be resistant to the enzymes that would normally break down the starch during digestion," explains Alexandra Ossola over at Popular Science.

Then comes the key component: refrigeration. "The cooling is essential because amylose, the soluble part of the starch, leaves the granules during gelatinization," said research team leader Sudhair A. James. "Cooling for 12 hours will lead to formation of hydrogen bonds between the amylose molecules outside the rice grains which also turns it into a resistant starch."

The more resistant starch, the fewer calories we can absorb. The team notes that you can still re-heat the specially prepared rice without accruing any additional calories. (Whether it still tastes any good is a whole separate question.)

http://bit.ly/19ewoaR

The Navajo Nation Will Have the First Junk Food Tax in the U.S.

The Navajo National Council approved a 2 percent increase in sales tax on foods like pastries, fried foods, desserts, chips and soda

By Marissa Fessenden

How should governments govern soda? An outright ban on large sugary drinks? A tiny tax? Or not at all? This debate has been playing in New York, Berkeley, and places in between - and one community recently made drastic moves to target people's eating habits. The Navajo National Council just announced that they have approved a 2 percent increase in sales tax on foods like pastries, fried foods, desserts, chips and sodas, reports Leilani Clark for Mother Jones. She writes:

Authored by the Diné Community Advocacy Alliance (DCAA), a grassroots organization of community volunteers, the legislation was modeled on existing taxes on tobacco and alcohol, as well as other fat and sugar tax initiatives outside the United States. The act follows on the heels of a spring 2014 amendment that removed a 5 percent tribal sales tax on fresh fruits and vegetables.

Called the Healthy Diné Nation Act, this law hasn't attracted the same amount of media attention as New York's infamous soda ban. But it will bring the total tax on low-nutrition foods to 7 percent. All the revenue from the increase will go toward a fund to build "wellness centers, parks, basketball courts, trails, swimming pools, picnic grounds and health education classes," reports Alysa Landry for Indian Country. She adds:

An estimated 10 percent of the Navajo population has diabetes, said David Foley, an epidemiologist for the Navajo Nation Division of Health. In numbers, that's about 24,600 people. Another 75,000 people are pre-diabetic.

The junk food tax is unprecedented, not just in Indian Country but in the nation as a whole, said Crystal Echo Hawk, executive director of the Notah Begay III Foundation, a non-profit organization that combats obesity and diabetes among Natives.

"This is the only one in the country, so the national significance of this cannot be underplayed," she said. "Bigger cities have been trying to get something like this passed for years, and the Navajo Nation is the first to get it done."

Whether the tax will help health outcomes for the Navajo population remains to be seen. Landry points out that the border towns around the reservation will still sell junk food without the extra tax. However, previous soda taxes, such as the one in Mexico that began at the start of 2014, do seem to show some effect on soda sales - though to what extent is debated, reports Tamar Haspel for the Washington Post. Haspel suggests that taxing added sugar in the supply chain itself might be a more effective approach. She writes:

If we tax sugar, high-fructose corn syrup, fruit juice concentrate and other added sugars at the point where they're manufactured or imported (we already do tax imported sugar), we essentially tax everything with added sugar, commensurate with its sugar content (with the exception of foods already manufactured before we import them). An "input tax," it's called.

The Navajo Nation's tax is somewhere between a soda tax and an input tax. Whether the tax and the fund to create active spaces for the tribe helps remains to be seen. And there is probably a timeline: The tax hike will expire at the end of 2018 unless the Council votes to extend it.

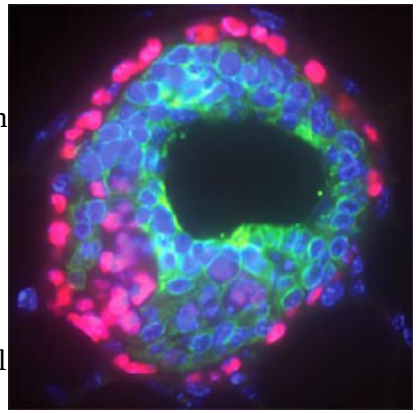
http://www.eurekalert.org/pub_releases/2015-03/qiom-tst032615.php

The switch that might tame the most aggressive of breast cancers

Australian researchers have found that so-called 'triple-negative breast cancers'[1] are two distinct diseases that likely originate from different cell types.

This helps explain why survival prospects for women with the diagnosis tend to be either very good or very bad. The Sydney-based research team has found a gene that drives the aggressive disease, and hopes to find a way to 'switch it off'. The aggressive form of triple-negative breast cancer appears to arise from stem cells, while the more benign form appears to arise from specialised cells.

Stem cells have many of the same features as cancers. They are plastic and flexible, and have the ability to proliferate and spread into other tissues - deadly traits in cancers. Previous studies have shown that breast stem cells are needed for breast growth and development during puberty and pregnancy, although how they evolve from stem cells into specialist cells has been unclear.



The new study has shown that a gene known as 'inhibitor of differentiation 4' (ID4) determines whether a stem cell remains a stem cell, or whether it differentiates into a specialist cell. Notably, when the high levels of ID4 in a stem cell are 'switched off', other genes that drive cell specialisation are 'switched on'.

Id4+ stem cells are in red, luminal cells in green, and all cells are marked with blue nuclear dye. **Garvan Institute of Medical Research**

Drs Alex Swarbrick and Simon Junankar from Sydney's Garvan Institute of Medical Research spearheaded this large interdisciplinary study,2 which links the development of the mammary gland in mice with human breast cancer. Its main finding, that ID4 not only 'marks', but appears to control, the highly aggressive form of triple negative breast cancer is published online today in Nature Communications.

"We found that ID4 is produced at high levels in roughly half of all triple negative breast cancers, and that these cancers have a particularly poor prognosis," said project leader Dr Alex Swarbrick. "We also showed that if you block the ID4 gene in experimental models of triple negative breast cancer, the tumour cells stop dividing." It is interesting to note that blocking ID4 switches on the oestrogen receptor3 and several other genes expressed by the best-prognosis breast cancer. "Oestrogen receptor-positive breast cancers have a relatively good prognosis because the drug Tamoxifen is very effective at blocking the oestrogen receptor and hence their growth" noted Swarbrick. "We speculate, therefore, that by blocking ID4 it might be possible to turn stem-cell-like breast cancers into less aggressive breast cancers that may even respond to tamoxifen. If we are correct, that would be remarkable."

The next step for Dr Swarbrick and his team will be to study the biochemistry of ID4 in a cell - to determine how best to block it in people. There are also plans to undertake therapeutic experiments in mice to test whether or not switching off ID4 sensitises a tumour to tamoxifen.

"We don't know yet whether we are seeing a real oestrogen-dependent cancer after ID4 is blocked - one with an effective oestrogen receptor - or just a caricature of one. "We're very fortunate that our collaborator in Cambridge UK is a world expert on oestrogen receptor function. "We also have technologies that allow us to study processes on a genome-wide scale - so we can map the interactions of ID4 comprehensively."

[1.] *Triple-negative breast cancers, which make up around 15% of all breast cancers, lack any of the three receptors (oestrogen, progesterone or HER2) that would make them responsive to targeted drugs. Overall, patients have a higher risk of disease recurrence and shorter survival than those with other breast cancers.*

http://www.eurekalert.org/pub_releases/2015-03/chla-ffm032615.php

First fully-implantable micropacemaker designed for fetal use

Novel device has received Humanitarian Use Device designation from FDA

Children's Hospital Los Angeles

A team of investigators at Children's Hospital Los Angeles and the University of Southern California have developed the first fully implantable micropacemaker designed for use in a fetus with complete heart block. The team has done preclinical testing and optimization as reported in a recent issue of the journal Heart Rhythm. The micropacemaker has been designated a Humanitarian Use Device by the US Food & Drug Administration (FDA). The investigators anticipate the first human use of the device in the near future.

"Up until now, the pacemaker devices that have been used in an attempt to treat this condition in a fetus were designed for adults," said Yaniv Bar-Cohen, MD, pediatric cardiologist at CHLA and lead author on the paper. "We have lacked an effective treatment option for fetuses."

With each beat of a healthy heart, an electrical signal moves from the upper to the lower chambers of the heart. As this signal moves, it results in the heart contracting and pumping blood. Congenital heart block is a defect of the heart's electrical system that originates in the developing fetus, greatly slowing the rate of the heart and impacting its ability to pump blood. Although the condition can be diagnosed in utero, all attempts to treat the condition with a standard pacemaker have failed.

"We now have a pacemaker that can be implanted in utero, potentially without harm to the fetus or the mom," said Ramen H. Chmait, MD, Director of the CHLA-USC Institute for Maternal-Fetal Health. "This novel device provides a real opportunity to prevent miscarriage and premature birth in babies affected with these abnormalities."

The size of the adult device requires a small part to be implanted in the fetus and the rest to remain externalized. This design has uniformly failed, likely due to fetal movement causing the electrodes to become dislodged from the heart.

"Building on our experience of using microfabrication techniques to create biomedical devices, we have developed a micropacemaker small enough to reside entirely within the fetus," said Gerald E. Loeb, MD, professor of Biomedical Engineering at the Viterbi School of Engineering at USC. "This will allow the fetus to move freely without risk of dislodging the electrodes."

Each year, approximately 500 pregnancies in the U. S. are affected by fetal heart block and could be candidates for receiving this device.

Additional members of the investigational team include: Michael J. Silka, MD and Jay D. Pruetz, MD, Children's Hospital Los Angeles; Adriana N. Vest and Li Zhou, Department of Biomedical Engineering, USC; and Catalina Guerra, DVM, Los Angeles Biomedical Research Institute, Harbor-UCLA. Funding has been provided by NIH grant R01HD075135, the Southern California Clinical and Translational Science Institute, the Robert E. and May R. Wright Foundation, and the Coulter Foundation.

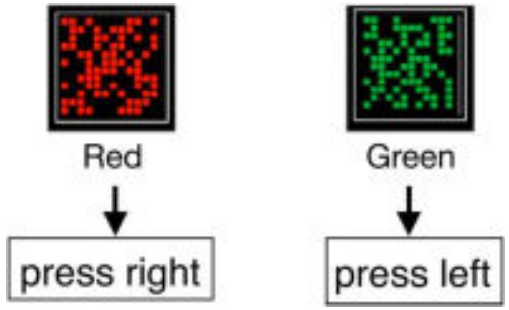
http://www.eurekalert.org/pub_releases/2015-03/pu-wai032715.php

When attention is a deficit

How the brain switches strategies to find better solutions

Sometimes being too focused on a task is not a good thing. During tasks that require our attention, we might become so engrossed in what we are doing that we fail to notice there is a better way to get the job done.

For example, let's say you are coming out of a New York City subway one late afternoon and you want to find out which way is west. You might begin to scan street signs and then suddenly realize that you could just look for the setting sun.



Volunteers played a game where they had to press one button or another depending on the location of squares on a screen. Participants that switched to a strategy based on the color of the squares were able to improve their performance on the game. **Schuck, et al.**

A new study explored the question of how the brain switches from an ongoing strategy to a new and perhaps more efficient one. The study, conducted by researchers at Princeton University, Humboldt University of Berlin, the Bernstein Center for Computational Neuroscience in Berlin, and the University of Milan-Bicocca, found that activity in a region of the brain known as the medial prefrontal cortex was involved in monitoring what is happening outside one's current focus of attention and shifting focus from a successful strategy to one that is even better. The researchers published the finding in the journal Neuron.

"The human brain at any moment in time has to process quite a wealth of information," said Nicolas Schuck, a postdoctoral research associate at Princeton and first author on the study. "The brain has evolved mechanisms that filter that information in a way that is useful for the task that you are doing. But the filter has a disadvantage: you might miss out on important information that is outside your current focus."

Schuck and his colleagues wanted to study what happens at the moment when people realize there is a different and potentially better way of doing things. They asked volunteers to play a game while their brains were scanned with magnetic resonance imaging (MRI). The volunteers were instructed to press one of two buttons depending on the location of colored squares on a screen. However, the game contained a hidden pattern that the researchers did not tell the participants about, namely, that if the squares were green, they always appeared in one part of the screen and if the squares were red, they always appeared in another part. The researchers refrained from telling players that they could improve their performance by paying attention to the color instead of the location of the squares.

Not all of the players figured out that there was a more efficient way to play the game. However, among those that did, their brain images revealed specific signals in the medial prefrontal cortex that corresponded to the color of the squares. These signals arose minutes before the participants switched their strategies. This signal was so reliable that the researchers could use it to predict spontaneous strategy shifts ahead of time.

"These findings are important to better understand the role of the medial prefrontal cortex in the cascade of processes leading to the final behavioral change, and more generally, to understand the role of the medial prefrontal cortex in human cognition," said Carlo Reverberi, a researcher at the University of Milan-Bicocca and senior author on the study. "Our findings suggest that the medial prefrontal cortex is 'simulating' in the background an alternative strategy, while the overt behavior is still shaped by the old strategy."

The study design - specifically, not telling the participants that there was a more effective strategy - enabled the researchers to show that the brain can monitor background information while focused on a task, and choose to act on that information. "What was quite special about the study was that the behavior was completely without instruction," Schuck said. "When the behavior changed, this reflected a spontaneous internal process."

Before this study, he said, most researchers had focused on the question of switching strategies because you made a mistake or you realized that your current

approach isn't working. "But what we were able to explore," he said, "is what happens when people switch to a new way of doing things based on information from their surroundings." In this way, the study sheds light on how learning and attention can interact, he said.

Schuck designed and conducted the experiments while a graduate student at Humboldt University and the International Max Planck Research School on the Life Course (LIFE) together with the other authors, and conducted the analysis at Princeton University in the laboratory of Yael Niv, assistant professor of psychology and the Princeton Neuroscience Institute in collaboration with Reverberi. The study has relevance for the question of how the brain balances the need to maintain attention with the need to incorporate new information about the environment, and may eventually help our understanding of disorders that involve attention deficits.

http://www.eurekalert.org/pub_releases/2015-03/uow--ssi032015.php

Sexual selection isn't the last word on bird plumage, UWM study shows

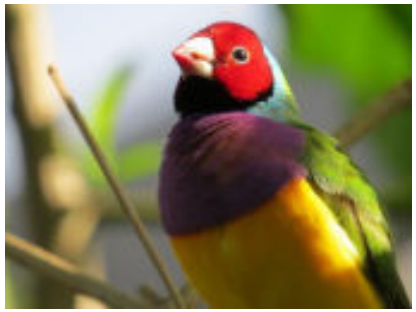
Survival shapes feather color as much as the need to attract mates

In the world of bird fashion, the guys seem to have all the fun: brighter feathers, sharper accessories, more pizzazz.

Researchers going back to Charles Darwin have focused on the contrast between the sexes, attributing the males' brighter colors to their need to attract mates.

A group of researchers at University of Wisconsin-Milwaukee took a different approach, testing a hypothesis that evolution has actually resulted in similarities among the sexes as much as differences.

Looking at nearly 1,000 species of birds, they found that while males often have brighter feathers than females, the two sexes have come closer together in color over time to blend into their surroundings and hide from predators. Natural selection - during migration, breeding in subtropical locales and care of young - is as powerful as sexual selection. "Although most studies of bird plumage focus on dichromatism, evolutionary change has most often led to similar, rather than different, plumage in males and females," the authors write.



The Gouldian finch was one of 977 species examined by UWM biologist Peter Dunn and his research partners in a worldwide study of the evolution of bird colors. This photograph shows a male. **Peter Dunn**

Peter Dunn and Linda Whittingham, professors of biological sciences at UW-Milwaukee, wrote the paper with Jessica Armenta, a former UW-Milwaukee graduate student who now teaches at Austin Community College in Texas.

"Our study shows that ecology and behavior are driving the color of both sexes, and it is not due to sexual selection," they write.

The paper, "Natural and sexual selection act on different axes of variation in avian plumage color," is being published in "Science Advances."

Armenta spent four years collecting data from 977 species of birds from six museums in the U.S. and Australia. She looked at six birds of each species, three males and three females. Dunn and Whittingham analyzed the data, assigning each bird a color score based on scales of brightness and hue. They examined plumage color in relation to 10 measures of natural and sexual selection.

"Researchers have called for separate analyses of each sex for over a decade, but this is the first large-scale study to examine the color of each sex in relation to indices of both natural and sexual selection," they write.

When the sexes became more similar in color, they did so for reasons of natural selection. When the color gap increased, it had more to do with sexual selection, they found. Dunn hopes the findings will send future research in new directions.

"A lot of research has focused on how plumage color is related to mating success, especially in males," he says, "so this should hopefully get researchers to think more about how color affects survival, especially predation and foraging success, in both sexes." Within the larger findings is another surprise: male birds with multiple mates actually tend to be duller in color than their female counterparts. Male red-winged blackbirds, for example, can have up to a dozen mates but are less colorful than their consorts. "The reason for this is that males in these species often have a lot of black plumage," Dunn says.

http://bit.ly/1BT3OCr

Major Science Publisher Admits "Fabricated" Peer Reviews

But are BioMed Central's retractions just the tip of the iceberg?

By Erin Blakemore

Peer review is at the heart of scientific publishing. But its rigor has come into question lately - and news that a major publisher has retracted scientific papers could point to a wider peer review problem in progress.

BioMed Central, a U.K.-based science publisher with 277 peer-reviewed journals in its catalog, has retracted 43 scientific papers, Fred Barbash reports for the *Washington Post*. He notes that though most of the papers come from Chinese universities, a representative told him that rather than being an issue of China, the retractions come from "a broader problem of how scientists are judged."

Retraction Watch's Cat Ferguson spoke with Elizabeth Moylan, BioMed Central's senior editor of scientific integrity, who noted that some of the peer review concerns stem from suspicions about third-party involvement:

Some of the manipulations appear to have been conducted by third-party agencies offering language-editing and submission assistance to authors. It is unclear whether the authors of the manuscripts involved were aware that the agencies were proposing fabricated reviewers on their behalf or whether authors proposed fabricated names directly themselves.

When Barbash spoke to BioMed Central's associate editorial director for research integrity, she confirmed that the publisher had received a number of "very convincing" peer review reports. However, odd email addresses and multiple reviews in different specialized fields raised red flags, which were confirmed when they learned that the scientists who had supposedly penned the reviews "hadn't written them at all."

But the problem doesn't seem to be unique to BioMed Central. Barbash notes that the Committee on Publication Ethics issued a statement warning of "systematic, inappropriate attempts to manipulate the peer review process of several journals across publishers." It's an issue that has galvanized people like the anonymous founders of PubPeer, an anonymous feedback tool that lets scientists provide post-publication peer review without revealing their identities.

"While standard 'pre-publication' peer review often does improve the quality of published work, it is also clear that it lets through a huge number of mistakes, and a surprising amount of misconduct," they told *Vox*'s Julia Belluz earlier this month. "And the system as it stands has great difficulty in correcting work once published." For now, BioMed Central is retracting, rather than correcting, the falsely peer-reviewed articles.

http://nyti.ms/1a67qeU

Weed Killer, Long Cleared, Is Doubted

World Health Organization has declared that glyphosate, the active ingredient in Roundup, "probably" causes cancer in people

By ANDREW POLLACK

Thirty years ago, an Environmental Protection Agency committee determined that the popular weed killer Roundup might cause cancer. Six years later, in 1991, the agency reversed itself after re-evaluating the mouse study that had been the basis for the original conclusion. Now the issue is back again, in an even bigger way.

An agency of the World Health Organization has declared that glyphosate, the active ingredient in Roundup, "probably" causes cancer in people. One piece of evidence the agency cites is that same mouse study. The declaration drew an angry response from Monsanto, the maker of Roundup, which has accused the agency of having an "agenda" and "cherry picking" the data to support its case.

The conclusion is "starkly at odds with every credible scientific body that has examined glyphosate safety," Philip Miller, Monsanto's vice president for global regulatory affairs, told reporters on Tuesday. That includes a recent review by German government regulators on behalf of the European Union.

The new controversy and the reversal by the E.P.A. decades ago demonstrate how the same data can be interpreted differently and how complicated and politically perilous such a decision can be. But the discrepancy between Monsanto and the health organization can be partly explained by the specific way its agency analyzes the data.

Officials at the agency, the International Agency for Research on Cancer, said they had no agenda other than to inform the World Health Organization. They said the conclusion was based on studies of people, laboratory animals and cells.

"All three lines of evidence sort of said the same thing, which is we ought to be concerned about this," said Aaron Blair, a retired epidemiologist from the National Cancer Institute who was chairman of the group of 17 reviewers from around the world; agreement on the classification was unanimous.

Glyphosate, introduced in the 1970s, is the most widely used herbicide in the world, sprayed on farms, in forests, on road sides and in gardens, and has a reputation for being benign, as pesticides go. It is now generic and used in many products, not only Roundup.

Use of glyphosate has soared in the last two decades because of Monsanto's Roundup Ready crops, which account for most corn and soybeans grown in the United States. These crops are genetically engineered to withstand glyphosate, allowing farmers to spray their fields without harming the crops.

Monsanto executives said this week that they did not expect the agency's action to affect sales. But that could depend on whether regulators around the world impose restrictions on glyphosate use after the W.H.O. pronouncement. A spokesman for the California Office of Environmental Health Hazard Assessment said it was evaluating whether products containing glyphosate might have to be labeled as posing a cancer hazard under the state's Proposition 65.

Some consumer and environmental groups said on Friday that the findings strengthen the case for the labeling of genetically modified foods. They also called upon the E.P.A. to re-evaluate glyphosate and a newer weed killer from Dow Chemical that combines glyphosate and another herbicide, 2,4-D.

The E.P.A. said it would consider the W.H.O. agency's finding in its own review of glyphosate. The E.P.A. has maintained its classification of glyphosate as

having “evidence of noncarcinogenicity for humans” since 1991, including through a review last year.

The International Agency for Research on Cancer looks at a very narrow question: whether a substance or behavior might cause cancer under some circumstances, even if those circumstances are unlikely to occur. It does not weigh the benefit versus the risks of a chemical, leaving that up to national regulators.

The agency classifies alcoholic beverages as human carcinogens, along with tobacco, arsenic and asbestos. Working the night shift or being a hairdresser are classified as probably cancer-causing, the same as glyphosate, because one job disrupts the body’s circadian rhythms and the other involves exposure to dyes. Coffee is a “possible” carcinogen, a lower level.

Over all, the agency has reviewed 983 things like chemicals and occupations. About half could not be classified based on the evidence. Only one compound, caprolactam, which is used to make a type of nylon, had enough evidence in its favor to be judged “probably not” carcinogenic.

There are also differences in interpretation. Monsanto and some regulators say the preponderance of studies shows no cancer risk from glyphosate. But for the W.H.O. agency, a few positive findings can be enough to declare a hazard, even if there are negative studies as well.

Kathryn Z. Guyton, a senior toxicologist at the agency, said the reviews also considered only studies published in journals or government documents that were publicly available. That typically excludes many studies done by chemical companies to get regulatory approval.

She also said the reviewers did not include the German regulatory report because it has not been ratified by the European Food Safety Authority.

It is a bit difficult to judge how the W.H.O. agency reviewers arrived at their conclusion. Eventually, it will publish a detailed monograph. For now, there is only a brief paper published March 20 in The Lancet Oncology, a medical journal. In that paper, the reviewers cited studies from the United States, Canada and Sweden suggesting that people exposed to glyphosate had a higher incidence of non-Hodgkin’s lymphoma, even after correcting for exposure to other chemicals. But a large and long study of pesticide applicators on American farms did not find any problems. Dr. Miller of Monsanto accused the agency of “disregarding” this study, though it is clearly mentioned in the Lancet article. Dr. Guyton said because of that study the reviewers concluded that there was only “limited” evidence from human studies that glyphosate could cause cancer.

The Lancet article cited several animal studies. As few as two are needed to establish carcinogenicity, Dr. Guyton said.

There are several ways to measure a possible effect. Are there more cancers in animals exposed to the chemical than in a control group? Do higher doses mean more cancers? Are the rates higher than expected based on historical data? In many studies, not all three measures are positive.

Take the mouse study at issue in the E.P.A. review 30 years ago and also cited by the W.H.O. agency. There were three cases of a rare type of kidney cancer in 50 male mice fed the highest dose. That type of tumor is rare, so it strengthens the case, Dr. Blair said. “They literally don’t occur, but they occurred when rodents were dosed with this stuff,” he said. While the W.H.O. agency’s reviewers focused on the rise in cancer with dose, the E.P.A. reviewers in 1991 said the findings were not meaningful, in part because there was no statistically significant difference over all between the exposed mice and the control group.

Another finding cited by the W.H.O. agency was of an increased rate of hemangiosarcoma, a cancer of the blood vessels, in male mice, as discussed in a document issued by the W.H.O. and the Food and Agriculture Organization in 2004. The authors of that document dismissed the significance of the finding, and said that over all, the study had “produced no signs of carcinogenic potential at any dose.”

The 2004 document then discussed four rat studies that it said also showed no evidence of carcinogenicity. One of those studies was also cited by the W.H.O. agency reviewers as evidence of carcinogenicity. Dr. Guyton said the agency reviewers “don’t report the authors’ conclusion. They report their own conclusions on that data.”

Another sign of whether something can cause cancer is whether it causes mutations or chromosomal damage. Bacterial tests do not show that glyphosate causes mutations. But the reviewers said there was evidence of chromosomal damage in studies involving animal and human cells.

The agency assessment began about a year ago with a literature search and culminated this month, when the working group met in Lyon, France. Reviewers had no ties with the pesticide industry, Dr. Guyton said.

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Why Don't Animals Get Schizophrenia (and How Come We Do)?

Research suggests an evolutionary link between the disorder and what makes us human

March 24, 2015 |By Bret Stetka

Many of us have known a dog on Prozac. We've also witnessed the eye rolls that come with canine psychiatry. Doting pet owners - myself included - ascribe all sorts of questionable psychological ills to our pawed companions. But the science does suggest that numerous non-human species suffer from psychiatric symptoms.

Birds obsess; horses on occasion get pathologically compulsive; dolphins and whales - especially those in captivity - self-mutilate. And that thing when your dog woefully watches you pull out of the driveway from the window - that might be DSM-certified separation anxiety. "Every animal with a mind has the capacity to lose hold of it from time to time" wrote science historian and author Dr. Laurel Braitman in "Animal Madness."

But there's at least one mental malady that, while common in humans, seems to have spared all other animals: schizophrenia. Though psychotic animals may exist, psychosis has never been observed outside of our own species; whereas depression, OCD, and anxiety traits have been reported in many non-human species. This begs the question of why such a potentially devastating, often lethal disease - which we now know is heavily genetic, thanks to some genomically homogenous Icelanders and plenty of other recent research - is still hanging around when it would seem that genes predisposing to psychosis would have been strongly selected against. A new study provides clues into how the potential for schizophrenia may have arisen in the human brain and, in doing so, suggests possible treatment targets. It turns out psychosis may be an unfortunate cost of our big brains - of higher, complex cognition.

The study, led by Mount Sinai researcher Dr. Joel Dudley, proposed that since schizophrenia is relatively prevalent in humans despite being so detrimental - the condition affects over 1% of adults - that it perhaps has a complex evolutionary backstory that would explain its persistence and exclusivity to humans.

Specifically they were curious about segments of our genome called human accelerated regions, or HARs. HARs are short stretches of DNA that while conserved in other species, underwent rapid evolution in humans following our split with chimpanzees, presumably since they provided some benefit specific to our species. Rather than encoding for proteins themselves, HARs often help regulate neighboring genes. Since both schizophrenia and HARs appear to be for the most part human-specific, the researchers wondered if there might be a connection between the two.

To find out, Dudley and colleagues used data culled from the Psychiatric Genomics Consortium, a massive study identifying genetic variants associated with schizophrenia. They first assessed whether schizophrenia-related genes sit close to HARs along the human genome - closer than would be expected by chance. It turns out they do, suggesting that HARs play a role in regulating genes contributing to schizophrenia. Furthermore, HAR-associated schizophrenia genes were found to be under stronger evolutionary selective pressure compared with other schizophrenia genes, implying that the human variants of these genes are beneficial to us in some way despite harboring schizophrenia risk.

To help understand what these benefits might be, Dudley's group then turned to gene expression profiles. Whereas gene sequencing provides an organism's genome sequence, gene expression profiling reveals where and when in the body certain genes are actually active. Dudley's group found that HAR-associated schizophrenia genes are found in regions of the genome that influence other genes expressed in the prefrontal cortex, a brain region just behind the forehead involved in higher order thinking - impaired PFC function is thought to contribute to psychosis.

They also found that these culprit genes are involved in various essential human neurological functions within the PFC, including the synaptic transmission of the neurotransmitter GABA. GABA serves as an inhibitor or regulator of neuronal activity, in part by suppressing dopamine in certain parts of the brain, and it's impaired transmission is thought to be involved in schizophrenia. If GABA malfunctions, dopamine runs wild, contributing to the hallucinations, delusions and disorganized thinking common to psychosis. In other words, the schizophrenic brain lacks restraint.

"The ultimate goal of the study was to see if evolution may help provide additional insights into the genetic architecture of schizophrenia so we can better understand and diagnose the disease," says Dudley. Identifying which genes are most implicated in schizophrenia and how they're expressed could lead to more effective therapies like, say, those influencing the function of GABA.

But the findings also offer a possible explanation for why schizophrenia arose in humans in the first place, and why it doesn't seem to occur in other animals. "It's been suggested," Dudley explains, "that the emergence of human speech and language bears a relationship with schizophrenia genetics, and incidentally also autism. Indeed, language dysfunction is a feature of schizophrenia, and GABA is critical to speech, language and many other aspects of higher-order cognition. The fact that our evolutionary analysis converged on GABA function in the prefrontal cortex seems to tell an evolutionary story connecting schizophrenia risk with intelligence."

Put another way, with complicated, highly social human thought - and the complicated genetics at the root of higher cognition - perhaps there's just more that can go wrong: complex function begets complex malfunction.

Dudley is careful not to exaggerate the evolutionary implications of his work. "It is important to note that our study was not specifically designed to evaluate an "evolutionary trade-off," he says, "but our findings support the hypothesis that evolution of our advanced cognitive abilities may have come at a cost - a predisposition to schizophrenia." He also acknowledges that the new work didn't identify any "smoking gun genes" and that schizophrenia genetics is profoundly

complex. Still, he feels that evolutionary genetic analysis can help identify the most relevant genes and pathologic mechanisms at play in schizophrenia, and possibly other mental illnesses that preferentially affect humans as well - specifically neurodevelopmental disorders related to higher-cognition and GABA activity, including autism and ADHD.

In fact, a new study published in *Molecular Psychiatry* reports a link between gene variants associated with autism spectrum disorder and better cognitive function in people without the disorder. The findings may help explain why those with autism sometimes exhibit extraordinary skill at certain cognitive abilities. They also support Dudley's speculation that higher cognition might have come at a price. As we broke away from our primate cousins our genomes - HARs especially - hastily evolved, granting us an increasing cache of abilities that other species lack. In doing so, they may have left our brains prone to occasional complex dysfunction - but also capable of biomedical research aimed at one day, hopefully, curing the ailing brain. As Dudley and others untangle the genetic underpinnings of schizophrenia and other mental illnesses in search of improved diagnosis and treatment, at least our pugs, poodles and pot-bellied pigs seem to be psychosis free.