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Oxygen improves blood flow, restores more function in spinal cord injuries: U of A study

A new discovery at the University of Alberta will fundamentally alter how we view spinal cord function and rehabilitation after spinal cord injuries.

Neuroscientists found that spinal blood flow in rats was unexpectedly compromised long after a spinal cord injury (chronically ischemia), and that improving blood flow or simply inhaling more oxygen produces lasting improvements in cord oxygenation and motor functions, such as walking.

Previous work had shown that while blood flow was temporarily disrupted at the injury site, it resumed rapidly, and it was more or less assumed that the blood flow was normal below the injury. This turns out to be wrong.

"We've shown for the first time that spinal cord injuries (SCI) lead to a chronic state of poor blood flow and lack of oxygen to neuronal networks in the spinal cord," says co-principal investigator Karim Fouad, professor, Faculty of Rehabilitation Medicine and Canada Research Chair for spinal cord injury. "By elevating oxygen in the spinal cord we can improve function and re-establish activity in different parts of the body."

Published in Nature Medicine on May 1, 2017, the study demonstrates chronic ischemic hypoxia (lack of blood and oxygen) after spinal cord injury and how blood flow plays a key role in the cause and treatment of motor disorders. Simply put, this could mean restored activity and ability in parts of the body that stopped working after spinal cord injury in the near future.

The discovery, like most "eureka moments" in science, happened by accident. The lead author Yaqing (Celia) Li, rehabilitation science post-doctoral fellow, and David Bennett, co-principal investigator and professor, Faculty of Rehabilitation Medicine, were looking at the injured spinal cord of a rat under a microscope and noticed the capillaries contracting in response to application of dietary amino acids like tryptophan.

"I thought, 'why would capillaries contract, when conventionally arteries are the main contractile vessels, and why should dietary amino acids circulating in the blood cause these contractions?'" says Bennett. "That is just plain weird, that what you eat should influence blood flow in the spinal cord." So they set out to answer these questions.

Li, Bennett and Fouad found that the AADC (Aromatic l-amino acid decarboxylase) enzyme that converts dietary amino acids into trace amines was upregulated in specialized cells called pericytes that wrap capillaries. Unexpectedly, these trace amines produced in the pericytes caused them to contract, clamping down on the capillaries and reducing blood flow. This surprising finding led them to make basic measurements of blood flow and oxygenation below the spinal cord, which led to the discovery of the chronic ischemic hypoxia. They reasoned that the capillaries were excessively constricted by these pericytes after SCI, since there is ample supply of tryptophan. So they decided to try blocking AADC to improve blood flow.

"Since blood flow below the injury is compromised, the neuronal networks function poorly with a lack of oxygen. So we blocked the AADC enzyme and found that it improved blood flow and oxygenation to the networks below the injury," Bennett says. "More importantly, this allowed the animals to produce more muscle activity."

As an alternative treatment to blocking the AADC enzyme in the spinal cord of rats, the neuroscientists exposed the animals to higher oxygen levels and even they were surprised to see what happened next. "The rat could walk better!" Fouad says. "The change in oxygen restored function, albeit temporarily."

Though the team knows their discovery can have big implications in the world of neuroscience, rehabilitation and spinal cord injury, they are quick to mention a disclaimer.

"There is still a long way to go when it comes to treatment and helping patients with spinal cord injuries," says Fouad. "But this discovery has helped us understand the etiology of spinal cord injuries in a way we never did before. We can now design treatments that improve blood flow to produce long-term rehabilitation after SCI.

Possibly even simple therapies such as exercise or just breathing will play a role in preventing long-term hypoxia and damage to the spinal cord. It's a small but important step in the right direction, stemming from studying an obscure enzyme in the spinal cord -- and that's the beauty of basic science."

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City of Hope researchers find regular use of aspirin can lower risk of breast cancer for women

A new study, using data from the California Teachers Study, identifies low-dose aspirin as a potential cancer prevention tool

DUARTE, Calif. -- A City of Hope-led study found that the use of low-dose aspirin (81mg) reduces the risk of breast cancer in women who are part of the California's Teacher's Study. This study -- which is the first to suggest that the reduction in risk occurs for low-dose aspirin -- was proposed by City of Hope's Leslie Bernstein, Ph.D., professor and director of the Division of Biomarkers of Early Detection and Prevention, and published online in the journal, Breast Cancer Research.

Bernstein and her colleagues saw an overall 16 percent lower risk of breast cancer in women who reported using low-dose aspirin at least three times per week. Such regular use of low-dose aspirin reduced the risk by 20 percent of estrogen or progesterone receptor positive, HER2 negative breast cancer, which is the most common breast cancer subtype.

"The study found an interesting protective association between low-dose aspirin and breast cancer," said lead author Christina A. Clarke, Ph.D., M.P.H., from the Cancer Prevention Institute of California. "We did not by and large find associations with the other pain medications like ibuprofen and acetaminophen. We also did not find associations with regular aspirin since this type of medication is taken sporadically for headaches or other pain, and not daily for prevention of cardiovascular disease."

This study differed from other studies that have looked at aspirin and cancer risk because it focused on the dose levels of the aspirin women had taken and tracked the frequency of the use of low-dose aspirin as opposed to regular aspirin. It was also able to look in detail at subtypes of breast cancer.

"We already knew that aspirin is a weak aromatase inhibitor and we treat women with breast cancer with stronger aromatase inhibitors since they reduce the amount of estrogen postmenopausal women have circulating in their blood," said Bernstein. "We thought that if aspirin can inhibit aromatase, it ought to reduce the likelihood that breast cancer would develop and it could also be an effective way to improve breast cancer patients' prognosis once they no longer take the more potent aromatase inhibitors." Bernstein added, "Aspirin also reduces inflammation, which may be another mechanism by which aspirin taken regularly can lower risk of breast cancer developing or recurring."

As part of the study, researchers analyzed data recorded in questionnaires submitted by 57,164 women in the California's Teacher's Study. In 2005, participants answered questions regarding family history of cancer and other conditions, use of aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDS), menstrual and reproductive history, use of hormones, weight and height, living environment, diet, alcohol use and physical activity. In the ensuing years before 2013, 1,457 of these participants developed invasive breast cancer.

The team of researchers chose to focus on low-dose "baby" aspirin, because not only is it inexpensive and readily available as potential means of prevention, but because there are already a lot of people

already taking it for prevention of other diseases such as heart disease and even colon cancer.

Now that we have some data separating low-dose from higher-dose aspirin, more detailed research can be undertaken to understand the full value of low-dose aspirin for breast cancer prevention," said Clarke."

Other collaborating authors include Alison J. Canchola, M.S., and Lisa M. Moy, M.P.H., from the Cancer Prevention Institute of California, and Susan L. Neuhausen, Ph.D., The Morris & Horowitz Families Professor in Cancer Etiology & Outcomes Research, Nadia T. Chung, M.P.H., and James V. Lacey Jr., Ph.D., M.P.H., from City of Hope.

Research reported in Breast Cancer Research was supported through grants from the National Cancer Institute and the California Breast Cancer Research Fund under grant numbers: R01 CA77398 and 97-10500. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Earthquakes can make thrust faults open violently and snap shut

Experiments reveal a new mechanism that could explain the source of a destructive feature of the 2011 Tohoku earthquake

It is a common trope in disaster movies: an earthquake strikes, causing the ground to rip open and swallow people and cars whole. The gaping earth might make for cinematic drama, but earthquake scientists have long held that it does not happen.

Except, it can, according to new experimental research from Caltech.

The work, appearing in the journal Nature on May 1, shows how the earth can split open -- and then quickly close back up -- during earthquakes along thrust faults.

Thrust faults have been the site of some of the world's largest quakes, such as the 2011 Tohoku earthquake off the coast of Japan, which damaged the Fukushima nuclear power plant. They occur in weak areas of the earth's crust where one slab of rock compresses against another, sliding up and over it during an earthquake.

A team of engineers and scientists from Caltech and École normale supérieure (ENS) in Paris have discovered that fast ruptures propagating up toward the earth's surface along a thrust fault can cause one side of a fault to twist away from the other, opening up a gap of up to a few meters that then snaps shut.

Thrust fault earthquakes generally occur when two slabs of rock press against one another, and pressure overcomes the friction holding them in place. It has long been assumed that, at shallow depths the plates would just slide against one another for a short distance, without opening.

However, researchers investigating the Tohoku earthquake found that not only did the fault slip at shallow depths, it did so by up to 50 meters in some places. That huge motion, which occurred just offshore, triggered a tsunami that caused damage to facilities along the coast of Japan, including at the Fukushima Daiichi Nuclear Power Plant.

In the Nature paper, the team hypothesizes that the Tohoku earthquake rupture propagated up the fault and--once it neared the surface -- caused one slab of rock to twist away from another, opening a gap and momentarily removing any friction between the two walls. This allowed the fault to slip 50 meters.

That opening of the fault was supposed to be impossible.

"This is actually built into most computer models of earthquakes right now. The models have been programmed in a way that dictates that the walls of the fault cannot separate from one another," says Ares Rosakis, Theodore von Kármán Professor of Aeronautics and Mechanical Engineering at Caltech and one of the senior authors of the Nature paper. "The findings demonstrate the value of experimentation and observation. Computer models can only be as realistic as their built-in assumptions allow them to be."

The international team discovered the twisting phenomenon by simulating an earthquake in a Caltech facility that has been unofficially dubbed the "Seismological Wind Tunnel." The facility started as a collaboration between Rosakis, an engineer studying how materials fail, and Hiroo Kanamori, a seismologist exploring the physics of earthquakes and a coauthor of the Nature study. "The

Caltech research environment helped us a great deal to have close collaboration across different scientific disciplines," Kanamori said. "We seismologists have benefited a great deal from collaboration with Professor Rosakis's group, because it is often very difficult to perform experiments to test our ideas in seismology."

At the facility, researchers use advanced high-speed optical diagnostics to study how earthquake ruptures occur. To simulate a thrust fault earthquake in the lab, the researchers first cut in half a transparent block of plastic that has mechanical properties similar to that of rock. They then put the broken pieces back together under pressure, simulating the tectonic load of a fault line. Next, they place a small nickel-chromium wire fuse at the location where they want the epicenter of the quake to be. When they set off the fuse, the friction at the fuse's location is reduced, allowing a very fast rupture to propagate up the miniature fault. The material is photoelastic, meaning that it visually shows -- through light interference as it travels in the clear material -- the propagation of stress waves. The simulated quake is recorded using high-speed cameras and the resulting motion is captured by laser velocimeters (particle speed sensors).

"This is a great example of collaboration between seismologists, tectonisists and engineers. And not to put too fine a point on it, US/French collaboration," says Harsha Bhat, coauthor of the paper and a research scientist at ENS. Bhat was previously a postdoctoral researcher at Caltech.

The team was surprised to see that, as the rupture hit the surface, the fault twisted open and then snapped shut. Subsequent computer simulations--with models that were modified to remove the artificial rules against the fault opening--confirmed what the team observed experimentally: one slab can twist violently away from the other. This can happen both on land and on underwater thrust faults, meaning that this mechanism has the potential to change our understanding of how tsunamis are generated.

The paper is titled "Experimental evidence that thrust earthquake ruptures might open faults." The lead author is Vahe Gabuchian (MS '08, PhD '15), a former PhD student at Caltech's Graduate Aerospace Laboratories (GALCIT), and coauthors include Raúl Madariaga of ENS. This research was funded by the National Science Foundation. The study can be found online at http://www.nature.com/nature/journal/vaop/ncurrent/full/nature22045.html

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Doctors should question the value of most heavily promoted drugs

Findings suggest pharmaceutical promotion should be met with healthy scepticism

Top promoted drugs are less likely than top selling and top prescribed drugs to be effective, safe, affordable, novel, and represent a genuine advance in treating a disease, argue US researchers in The BMJ today.

Tyler Greenway and Joseph S Ross, based at Yale University, say clinicians "should question the value of drugs being most heavily promoted by pharmaceutical manufacturers before prescribing them."

US physicians receive billions of dollars each year from drug companies as part of drug promotion. Yet studies have shown that greater contact with drug sales representatives is associated with an increased likelihood of prescribing brand name medications when cheaper alternatives exist.

And more recent studies have shown that payments from drug companies are associated with a greater likelihood of prescribing promoted drugs.

However, since August 2013, legislation has required the industry to publicly disclose all payments to physicians of $10 (£8; €9) or more or $100 in aggregate. This led to the Open Payments Database, which archives all industry payments to individual physicians and teaching hospitals.

Greenway and Ross therefore decided to assess the health "value" of drugs being most aggressively promoted to physicians to better understand implications of pharmaceutical promotion for patient care.

They identified the 25 drugs associated with the largest total payments to physicians and teaching hospitals from August 2013 to December 2014, including all direct and indirect payments, such as speaker fees

for education lectures, consulting fees, and honorariums, as well as payments in kind, such as the value of food and gifts.

However, they excluded research payments, royalties, and licensing fees, which are typically not promotional.

Next, they estimated drugs' value to society using five proxy measures: innovation; effectiveness and safety; generic availability (a measure of affordability); clinical value (inclusion on the WHO list of essential medicines); and 'first line' status (recommended as a first line therapy).

They also determined the top 25 drugs by 2014 US sales and the top 25 most prescribed drugs in the US during 2013.

Not all the differences were significant. But one that was showed that top selling and top prescribed drugs, not top promoted drugs, are more likely to represent the ideal drug that is effective, safe, affordable, novel, and represents a genuine advance in treating a disease.

For example, only one of the top promoted drugs was on the WHO essential medicines list, compared with nine top selling drugs and 14 top prescribed drugs.

Fewer top promoted drugs were considered 'first line' treatments than top prescribed drugs, while generic equivalents were available for 15 (63%) top promoted drugs, eight (32%) top selling drugs, and all top prescribed drugs.

These findings raise concerns about the purpose of pharmaceutical promotion and its influence on patient care, say the authors.

They say efforts are needed to better evaluate the value of drugs, ensuring that this information is readily available at the point of care so that it can inform clinical decision making, promoting use of higher value medicines.

And they suggest that clinicians should consider taking steps to limit their exposure to industry promotion and consider engaging with non-commercial educational outreach programmes that provide evidence based recommendations about medication choices.

http://go.nature.com/2pQ9mD9

Party drug's power to fight depression puzzles scientists

Ketamine can ease depression in hours, but researchers might have misjudged how it works.

Sara Reardon

The anaesthetic ketamine — a hallucinogenic club drug also known as Special K — has tantalized researchers who are seeking new ways to treat depression. The drug can lift a person's mood in hours, even when depression is severe. But several 'ketamine-like' medications have failed to alleviate depression in clinical trials over the past decade.

Now, some researchers think they know why. Emerging evidence suggests that scientists have misunderstood how ketamine fights depression. So they might have attempted to mimic the wrong biological mechanism when designing drugs to improve mood while avoiding the disorienting ketamine high.

On 20 May, researchers at a meeting of the Society of Biological Psychiatry in San Diego, California, will present results suggesting that some of ketamine's power comes from its ability to affect brain cells called glia, which support neurons. Their finding adds to recent studies contradicting a long-held idea that the drug works mainly by blocking proteins called NMDA receptors, on the surface of brain cells, which transmit signals between those cells.

At the upcoming meeting, a team led by neuroscientist Mark Rasenick of the University of Illinois at Chicago will report on tests of antidepressant drugs in cultured rat glial cells. All of the drugs that the researchers studied caused a cluster of proteins to shift position in the glial cells' membranes, signalling to the cells to form new connections with their neighbours. But ketamine produced this effect in 15 minutes, as compared to 3 days for conventional antidepressants.

Moreover, drugs that block NMDA receptors but are not antidepressants did not show the effect at all. This suggests that

ketamine's ability to bind to NMDA receptors might not be its primary weapon against depression.

Rasenick's team is not the first to suggest a different target for ketamine. A paper published in *Nature* in May 2016 concluded that one of ketamine's breakdown products — not the drug itself — probably lifted depression in mice[1]. And this compound affected cell proteins called AMPA receptors, instead of NMDA receptors.

The team behind the study plans to test the breakdown product in clinical trials later this year. But study co-author Carlos Zarate, a psychiatrist at the US National Institute of Mental Health in Bethesda, Maryland, says that it is too early to abandon the NMDA-receptor hypothesis, and more data are needed.

Others agree. "We have to be careful not to interpret [the latest] clinical findings as definitively negative," says Gerard Sanacora, a psychiatrist at Yale University in New Haven, Connecticut. Rodent studies have shown, for example, that blocking NMDA receptors can have an antidepressant effect[2].

And there could be more-prosaic explanations for why so many ketamine-like drugs that target NMDA receptors — including candidates from the drug giants Roche, Pfizer and AstraZeneca — have failed in clinical trials. Participants might have received doses that were too small or infrequent to buoy their moods. And in trials with control groups, the placebo effect can make it difficult to determine whether a psychiatric drug is working.

Ketamine copycats

Creating an effective substitute for ketamine remains the goal for many researchers. Although a growing number of physicians prescribe ketamine for their patients, the drug must be administered intravenously. It can also produce disorienting 'out of body' feelings, and it has the potential for abuse.

The companies that are still testing drugs to inhibit NMDA receptors are trying to make sense of the latest findings on ketamine and its would-be imitators. "We do need to tease all this apart," says David Nicholson, chief research-and-development officer at Allergan in Parsippany, New Jersey. In February, Allergan began treating around 500 people with a molecule called rapastinel, which binds to NMDA receptors and showed promising results in earlier trials.

Yet, the most enduring mystery involves ketamine itself, as researchers try to untangle what makes the drug so potent. Alan Schatzberg, a psychiatrist at Stanford University in California suspects that ketamine could act against depression in many ways: jump-starting the process by some as-yet-unknown mechanism, perhaps, and then blocking NMDA receptors to permanently rewire the brain.

Schatzberg also points out that ketamine can act similarly to morphine and rapidly bind to opioid receptors in the brain, which could explain why its effects are apparent within hours. And some studies have found that people with depression are more likely to benefit from ketamine if they do experience that out-of-body feeling, suggesting that it might be related to the drug's main mechanism[3].

In the meantime, the hunt continues for drugs that can replicate ketamine's mood-boosting power. That could be difficult, says Steven Levine, a psychiatrist and president of Ketamine Treatment Centers in New York City. "Ketamine is a dirty, dirty drug," he says. "It goes a lot of places, it does a lot of things."

Nature 545, 17 (04 May 2017) doi:10.1038/545017a

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Pill for Exercise? Chemical Builds Stamina in Mice, Study Finds

Endurance athletes such as marathon runners and long-distance cyclists know that it takes years of training to build stamina. But new research in mice suggests that it may not take much time at all.

By Tracy Staedter, Live Science Contributor

In the study, scientists gave mice that were typically sedentary a chemical called GW1516 for eight weeks, and found that these mice were able to run on a treadmill for 270 minutes before they showed signs of fatigue. Mice in a control group that did not receive the pill could run on the treadmill for only about 160 minutes.

The chemical is thought to work by interacting with a gene involved in the switch from burning the body's stores of sugar to burning fat, according to the findings, published today (May 2) in the journal Cell Metabolism.

"If you reprogram the genetics, you can acquire that level of fitness without having to expend a lot of energy," said Ronald Evans, an author of the study and a molecular and developmental biologist at the Salk Institute in La Jolla, California.

It's not clear whether the chemical would work the same way in humans. But if it did, the results from the study could one day lead to a pill that controls a network of genes, turning them on and off to selectively burn fat and sugar, much like exercise training. Such a therapy could mimic the benefits of exercise for those with limited mobility, such as the elderly, obese or physically impaired.

In the new study, Evans and his team built on earlier work in which they found a kind of biological sensor called PPARD that, during exercise, senses fat in the muscle and then turns genes on and off to burn fat and preserve sugar.

Previous work also showed that GW1516 interacted with that sensor, activating the same set of genes as those that would be triggered by exercise. For example, in one study, Evans and his team gave GW1516 to normal mice for four weeks and showed that it controlled their weight and insulin response. But it didn't seem to influence endurance in sedentary mice.

In the new study with sedentary mice, they increased the dose of GW1516 and gave the compound over a longer period.

When the scientists analyzed muscle tissue from the mice, they found a few interesting things. First, the tissue did not show any of the physiological changes associated with fitness training. There was no increase in the number of blood vessels or mitochondria, the power plants in cells that generate more than 90 percent of the energy.

"What's interesting to me here is that there is no change in fiber type or mitochondrial content, and that the improvement in endurance from GW1516 is primarily, or overwhelmingly, due to differences in glucose management," said Evan Williams, senior research scientist at the Institute of Molecular Systems Biology at ETH Zurich, a university in Switzerland known for its science and technology programs. Williams is not a part of this research study.

Second, Evans and his team saw that the chemical had affected a network of 975 genes. Genes that were involved in burning fat were turned on and up, and genes involved in the breakdown of sugar for energy were silenced.

The scientist think that, at least in muscle, the PPARD sensor facilitates the switch to burning fat for energy, not sugar, Evans said. Even though muscle tissue can burn both, the brain can use only sugar from the blood for energy. And that is where endurance comes from, Evans said. When sugar levels in the blood drop, the brain is affected, and fatigue sets in.

Endurance athletes that push themselves to their limits and deplete their sugar reserves ultimately "hit the wall," or "bonk," as it's colloquially called. But if their muscles could burn less sugar and reserve it for the brain, they could push back the wall.

If the GW1516 chemical sounds like a performance enhancing drug, it is, Evans said. The compound, which is not an approved drug for use in humans in the United States, is being made and used in Russia, Evans said. "That doesn't mean we shouldn't develop the drug for the people who need it," he said.

Marc Hamilton, a professor at the University of Houston and director of Texas Obesity Research Center at the Texas Medical Center, said he is skeptical that any drug would be powerful enough to raise fat and glucose metabolism in people, even to the degree that occurs

during moderate exercise, which has been shown to be safe and without hazardous side effects.

Such a solution should "come through an innovative breakthrough by creating physiologically effective exercise-like metabolism in any body by better forms of natural muscular activity, without the risks of drugs and high effort exercise prescriptions," said Hamilton, who was not a part of this study.

Williams, at ETH Zurich, said he is curious about future studies that will focus on whether GW1516 can be used as a therapy.

"The experiments in this paper are geared towards supporting its ability for athletic performance enhancement," he said. "It'd be useful to see additional research on this compound in models that represents metabolic diseases or some sort of dystrophy."

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At last, a clue to where cancer metastases are born

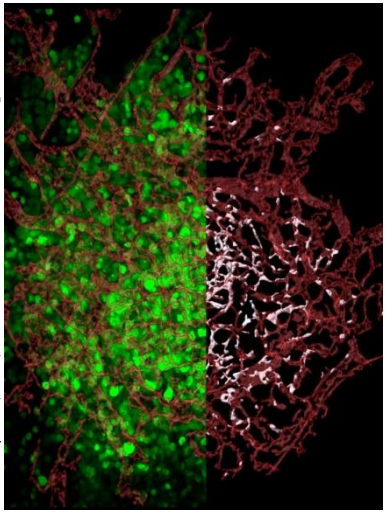
Tumor cells shown to enter bloodstream from deep within early-stage tumors

LA JOLLA, CA - Even in remission, cancer looms. Former cancer patients and their doctors are always on alert for metastatic tumors. Now scientists at The Scripps Research Institute (TSRI) have discovered why some cancers may reoccur after years in remission.

The findings, published recently in the journal Cell Reports, show that invasive tumors can begin sending out tumor cells far earlier than previously thought. These escaping cells--which can enter the bloodstream before the primary tumor is detected--may seed secondary tumors that don't show up for years.

Importantly, the scientists demonstrated that the escaping tumor cells reach the bloodstream by entering blood vessels deep within the dense tumor core, upending the long-held belief that metastatic cells come from a tumor's invasive borders.

"The actual process of cancer cell dissemination via hematogenous routes is a relatively under-studied process, but we finally have an answer as to where it takes place," said TSRI Assistant Professor Elena Deryugina, who led the study in a long-term collaboration with TSRI Staff Scientist William Kiosses.



On the left, stained red blood vessels weave between florescent green tumor cells. On the right, the researchers have mapped exactly where tumor cells (white) have entered blood vessels. The image shows that more cells enter blood vessels in the tumor's core than its invasive border. **Elena Deryugina and William Kiosses**

Metastasis Appears to Start Early

Doctors typically describe tumors in four stages: A solid tumor is more or less confined during stages 0 and 1, but starts invading nearby tissues at stage 2. It is believed that the tumor begins to send the cells to distant organs only after extensive invasion into the adjacent stroma (a nearby tissue or organ) at stage 3. Stage 4 is usually associated with the presence of secondary tumors described as metastases.

In their new study, the researchers wanted to take a closer look at this conventional view of cancer cell spread.

Using cancer cell lines generated from human fibrosarcoma and carcinoma tumors, the researchers found that primary tumors can send out cells early on--independent of cancer invasion into adjacent tissue. This could explain why doctors often see secondary tumors appearing earlier than they would have predicted.

This finding may also shed light on why patients with early stage tumors still have a risk of developing metastatic disease. "These metastases may have been seeded when the primary tumor was even too small to be visualized," Deryugina said.

Peering through dense primary tumors had been a roadblock in cancer studies until now, and this new discovery was possible because the researchers developed of animal models that allowed for microscopic analysis of tumor cell dissemination. Specifically, adapted mouse ear and chick embryo models let the scientists examine developing tumors through relatively thin tissue layers.

Cancer Cells Escape from Tumor Core

The new study is also the first to examine entire tumors to find out exactly where escaping cells come from. The scientists tagged human tumor cells with a florescent protein to distinguish them from the cells of a tumor-bearing animal. Using high-resolution confocal microscopy techniques spearheaded by Kiosses, the researchers mapped in 3-D all blood vessels across entire tumors, from the tumors' dense cores to their invasive tendrils.

The researchers mapped the location of every tumor cell relative to the center of the closest blood vessel--or visualized within blood vessels. This approach gave the researchers a way to finally analyze the escape process, called intravasation, and to demonstrate where intravasating cells enter blood vessels. The researchers were surprised by what they found: The vast majority of tumor cells entered blood vessels within the tumor core, not in the invasive tendrils.

This discovery challenges the long-held assumption that tumor cells enter the bloodstream only after they invade adjacent stroma and reach tumor-converging blood vessels. Instead, the researchers found that fewer than 10 percent of escaped cells intravasated from the stroma-invading sprouts.

This makes sense, Deryugina said, because the newly formed vessels in the tumor core are ideal highways for escaping tumor cells.

A 2015 study by Deryugina and TSRI colleagues showed that these new vessels in the tumor core are structurally sound but permeable enough to give tumor cells a chance to slip into the bloodstream for a ride to other areas of the body. In contrast, blood vessels converging on the tumor border are less welcoming--their walls are more mature and almost impossible for tumor cells to break through.

Deryugina said it has been extremely satisfying to finally discover the primary location where tumor cells intravasate, even if the data contradict conventional cancer models.

This finding could be important for cancer patients. The research suggests a primary tumor does not have to be highly invasive to seed metastases. In fact, doctors may want to reconsider the time frame for the onset of cancer cell dissemination. While invasive tumors are more likely to manifest intravasation, the two processes--intravasation and invasion--appear to be independent of each other.

The researchers also found that levels of a protein called EGFR could be a good indicator of whether tumor cells would intravasate. EGFR appeared to regulate a tumor's ability to induce blood vessels that support cancer cell escape. "Therefore, the data indicate the importance of harnessing the EGFR activity early on in cancer patients," said Deryugina.

Next, the researchers plan to investigate the functional roles of different cell types within a primary tumor, such as inflammatory leukocytes, which also may be critically important for supporting intratumoral cancer cell intravasation.

The study, "Intratumoral Cancer Cell Intravasation Can Occur Independent of Invasion into the Adjacent Stroma," was supported by the National Institutes of Health (grants R01CA105412, R01CA129484 and R01CA157792).

http://wb.md/2qMuTuj

Who Needs a Statin? DNA Beats Current Risk Calculators

A middle-aged man whose brother recently had an MI wanted to know his cardiac risk and what steps he could take to avoid heart disease.

John Mandrola, MD

It's hard to believe that answering this central question of cardiology would be the same now as it was decades ago. We would calculate his cardiac risk using *basic* factors: smoking, age, blood pressure, and cholesterol levels.

Imprecise is a generous word to describe this method of predicting future cardiac events or tailoring preventive therapies. Consider, for instance, the most likely outcome for patients taking a statin drug for primary prevention is the same if they didn't take it—nothing.[1]

A recent paper in the *Journal of the American Medical Association* compared statin eligibility based on either the US Preventive Services

Task Force (USPSTF) and ACC/AHA recommendations.[2] On Twitter, Dr Eric Topol, the editor in chief of Medscape and a leading genomics researcher, wrote: "The debate about which statin guideline for primary prevention is archaic in an era with validated genetic risk scores (GRS)."

This spurred me to look at the evidence for genetic risk scores. I came away impressed and cautiously optimistic.

Background

The challenge of using genetic data to predict coronary artery disease (CAD) is that, unlike monogenetic diseases such as long-QT syndrome, CAD stems from many genes and environmental factors.

We have known for years—from genomewide association studies—that there are numerous genetic loci associated with CAD[3-5]. At these loci are single nucleotide polymorphisms (SNPs, a variation in one base pair) that may individually or together influence the risk of developing CAD.

The problem is that the *individual* predictive power of these SNPs is small. That's where risk scores become useful. These *poly*genetic scores cull many SNPs into a composite score.

This may sound technical, but it's not. Recent advances have reduced the cost of genotyping; identifying disease-associated SNPs is no longer beyond the realm of clinical use.

Dr Pradeep Natarajan, a cardiologist and genetics researcher at Harvard, told me that there is no standard test that you can order now but risk scores can be easily calculated from genomewide arrays that some direct-to-consumer (DTC) genetic testing companies provide. For example 23andMe used to report a gene risk score for CAD, but the FDA asked the company to stop (it can report on some conditions). Dr Topol and other researchers from Scripps are now in beta-testing for a no-cost mobile app (MyGeneRank) that takes a user's 23andMe data and delivers a genetic cardiac risk score.[6]

Compelling Evidence

Dr Gad Abraham (University of Melbourne, Australia) and colleagues asked whether a genomic risk score (GRS) comprising more than 49K SNPs could predict CAD.[7] They divided the score into quintiles from low to high risk, then validated its predictive ability in five prospective cohort studies—three FINRISK cohorts (*n*=12,676) and two Framingham Heart Study cohorts (*n*=3406). They also validated the score in a smaller Dutch cohort (ARGOS) of individuals with familial hypercholesterolemia.

There were four main findings of this paper:

- ***The GRS associated with incident CAD in both the FINRISK and Framingham cohorts* independently *of established risk factors, including family history.***
- ***The GRS also associated with CAD in a high-risk group of patients with familial hypercholesterolemia.***

The curious will note, as the study authors did, that these findings suggest genomic risk exerts its effect through molecular pathways largely independent of cholesterol, blood pressure, and smoking.

- ***The GRS modestly improved on the 10-year prediction of current risk-factor–based scores.***
- ***Fourth, and most important, the GRS captured differing trajectories of cumulative CAD risk, For instance, applying Kaplan-Meier estimates of CAD events to the FINRISK cohorts revealed that men with the highest genetic risk reached a 10% level of cumulative risk 18 years earlier than men with the lowest genetic risk.***

These are impressive findings, but there are limitations.

First, the differing trajectories of CAD incidence based on genetic risk were of lesser magnitude in women, which may be due to lower CAD event rates in women. Second, although the GRS modestly improved risk prediction of the *population*, some *individuals* who had an event were reclassified from higher risk per traditional risk calculation to lower risk based on the genetic score. Finally, the cohorts used in this study (and most studies of genetic risk scores) consisted largely of

individuals of European descent. Utility of risk scores in people of varying ancestry requires validation.

Guiding Statin Therapy

Publishing in the *Lancet*, an international group of researchers used data from two community cohort studies and four randomized trials of statins (in both primary and secondary prevention) to validate a genetic risk score and determine those individuals who may derive greater benefit from statin therapy.[8]

The big finding from this study of more than 48K subjects was that patients with high genetic risk scores derived much greater risk reduction from statin therapy. The associations followed a gradient, with increasing relative risk reductions across low (13%), intermediate (29%), and high (48%) genetic-risk categories. Specifically, when the authors applied the gene risk score to the primary-prevention statin trials, they observed an approximate threefold *decrease* in the number needed to treat (NNT) to prevent one CAD event. For example, the NNT for high-genetic risk individuals in the ASCOT trial[9] was 20 (vs 72 for total coronary events in the original paper) and in JUPITER[10] it was 25.

Dr Natarajan and colleagues confirmed these gradients of risk reduction based on genetic risk scores in a meta-analysis of three primary-prevention statin trials.[11] In addition, they applied the gene score to participants in two observational cohort studies and noted that each standard-deviation increase in risk score associated with a 1.32-fold greater likelihood of having coronary artery calcification (CAC) and a 10% higher burden of carotid plaque.

A crucial factor to consider is that the search for genomic links to CAD continues.[12] Gene risk scores will get better as more SNPs are found.

Conclusions

I'm a clinician, not a geneticist, but the lack of excitement over *the potential* of genetic risk scores is surprising. Consider the statin debates. While nearly everyone agrees that statin benefit outweighs harm for secondary prevention, the argument in primary prevention turns on the smallness in absolute benefit (or high NNT). Gene scores may change that debate. If confirmed, a threefold reduction in the NNT for statin therapy has immense value—on both a patient and population level.

But the use of gene scores go beyond statin decisions. Knowledge is power. Heart disease may be a major killer, but it's highly preventable. The MI-GENES study randomized 200 patients to disclosure of CAD risk via a conventional risk score or traditional scoring plus a genetic risk score. The group with the added genetic info had lower LDL-C levels at 6 months than those given only a conventional risk score.[13]

The value in medical tests lie in their ability to change behavior or therapy. Obviousness dictates that (some) people at high risk might try to lower their risk. And the evidence—from a study of more than 55K individuals—is that among individuals at high genetic risk, adherence to a healthy lifestyle associated with a 50% lower risk of CAD relative to those with unfavorable lifestyles.[14]

Dr Natarajan reminded me that gene scores, unlike CAC scans, are not age-dependent and can identify higher risk people at younger ages. This is key because atherosclerosis is a chronic lifelong disease and the young stand to gain the most from preventive strategies.[1]

Of course, genetic risk scores need more study. I favor slow science. But the evidence looks promising. I'm afraid that in a few years we may look back on this data and think: what took us so long to see the signal in the genes?

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http://bit.ly/2qDuIUT

Scientists suggest the world should brace itself for a new wave of biological invasions

Our rapidly changing world will bring new types of invaders

We are all becoming increasingly familiar with the impacts of invasive species. Knotweed from Japan can destroy building foundations, zebra mussels from eastern Europe can clog-up drinking water pipes, and an Asian fungus is causing ash tree die-back in our forests. Now an international team of scientists has identified how our rapidly changing world will bring new types of invaders, often from very unexpected places.

Invasive non-native species are among the greatest drivers of biodiversity loss on the planet and cost the British economy £1.7bn each year. "Our study found that environmental change, new biotechnology and even political instability are all likely to result in new invasions that we should all be worried about" said Dr. David Aldridge of Cambridge University, who hosted the meeting of 17 scientists from across four continents.

Globalization of the Arctic, emergence of invasive microbial pathogens, advances in genomic modification technology, and changing agricultural practices were judged to be among the 14 most significant issues potentially affecting how invasive species are studied and managed over the next two decades. "We have identified some potential game-changers" said Prof. Anthony Ricciardi from McGill University, who led the study.

Globalization of the Arctic

Until now, the Arctic has been among the least accessible regions on the planet, escaping extensive alien species invasions like those that have affected temperate and tropical areas of the world. However, the rapid loss of sea ice is opening the region to shipping, oil and mineral extraction, fishing, tourism, and shoreline development -- all of which facilitate introductions of alien species.

The loss of sea ice is also creating a major new corridor for international shipping between the Pacific and Atlantic Oceans, which will affect invasion risks throughout the Northern Hemisphere. "The gold rush has begun for major expansion of human activities in the Arctic, with the potential for large-scale alien species transfers" says Dr. Greg Ruiz (Smithsonian Environmental Research Center).

Emergence and spread of invasive microbial pathogens

Disease-causing bacteria, water molds, fungi and viruses are being given increasing opportunities to spread into regions where they never previously existed and where they may attack new hosts. They can also undergo rapid genetic changes that cause previously innocuous forms to become virulent.

Invasive microbes have devastated populations of animal and plants that have had no evolutionary exposure and thus no immunity to them. Recent examples include: the chytrid fungus "Bsal" that is killing salamanders in Europe; the white-nose fungus that is destroying bat colonies in North America; and sea star wasting disease along the Pacific coast of North America, considered to be among the worst wildlife die-offs ever recorded. The proliferation of microbial pathogens is a burgeoning threat to biodiversity, agriculture, forestry and fisheries.

Biotechnological advances and applications

Advances in genomic modification tools hold both promise and challenges for managing invasive species. Very recently, genetically modified versions of an invasive mosquito were released in the Florida Keys in a controversial attempt to interfere with the mosquito's reproductive life cycle, thereby preventing it from vectoring the spread of invasive Zika, Dengue and Chikungunya viruses to humans. "The push to use genetically modified agents to control invasive species will continue to grow", says Prof. Hugh MacIsaac (University of Windsor), "and with it will come public opposition and the view that we are opening Pandora's Box".

Changing agricultural practices

The team also identified changing agricultural practices as a potential source of invasion threats. Virtually unregulated new agricultural crops and practices open the door to potentially disastrous unintended consequences. An Asian cricket species reared for "cricket flour" -- all the rage in the USA - has already established in the wild. Worse, as a disease ravages this species, farmers have imported other kinds of crickets that might well invade in nature.

But possibly the biggest threat of all is the growing use by agribusiness of soil bacteria and fungi to increase crop production. "The cultivation and distribution of 'growth enhancing' microbes could cause some crop plants or plant species residing near agricultural fields to become invasive pests" says Prof. Daniel Simberloff (University of Tennessee).

Invasive species denialism

An additional challenge is public perception of invasion science. Scientific evidence on invasive species impacts is under attack, with much of the opposition value-based rather than science-based. This form of science denialism involves a rejection of peer-reviewed evidence along with an attempt to re-frame, downplay or even deny the role of invasive alien species in global environmental change.

"Denialism in science is not new, but its growth in the context of invasive species is especially worrying for people trying to conserve unique native biodiversity" says Prof. Tim Blackburn (University College London). "Manufacturing doubt about the negative impacts of invasive species can delay mitigating action to the point where it is too late."

The horizon scan was conducted at Cambridge University's David Attenborough Building and is published in the journal Trends in Ecology and Evolution (TREE).

http://bit.ly/2qDAEqA

One step closer to finding out how wine may protect your neurons

Researchers have now found out how wine compounds are protective against neuronal death: they should pass through your stomach first.

Let it be no misunderstanding: heavy alcohol intake has severe harmful effects. But already for several years, researchers have been finding that moderate wine intake can be beneficial in delaying the onset of cognitive impairments in aging and neurodegenerative diseases like Parkinson's and Alzheimer's disease. Dr. Esteban-Fernández from the Institute of Food Science Research in Madrid and her colleagues have been investigating the molecular mechanisms underlying the neuroprotective actions of wine, recently published in Frontiers in Nutrition.

Instead of investigating wine directly, they studied the compounds that are left after the wine has passed through the gut: the so-called wine-derived human gut metabolites. They selected some of these metabolites based on their presence in the urine and feces of people consuming wine on a regular and moderate basis. To explore the neuronal effect of these compounds, they added them to human cells under stress conditions that normally lead to neuronal cell dysfunction and death. These conditions are related to the initial stages of some neurodegenerative disorders.

They found that the metabolites are protecting the cells from dying due to the stress conditions. The most striking result, however, was that the metabolites are active at different points in the cell signaling cascade that is leading to this cell death. The exact composition of the wine metabolites is therefore important in the protective neuronal effect. And this composition depends on your gut microbiota composition, as the intestinal flora breaks down the wine into the different metabolites.

"In other words, differences in our gut microbiota are leading to the different metabolites. Which underpins the idea that humans benefit from food in different ways", Dr. Esteban-Fernández explains. "This individual difference is a factor not to be neglected to understand the health effects of certain foods. We are now in need to advance our understanding of the effect of diet in the promotion of normal brain function."

"It is very important to understand that certain food compounds are responsible for this health benefit in protecting against the onset of neurodegenerative diseases; no medication was involved. I am not advocating to replace medicines by diet, but I want to raise more awareness how your diet is helping to prevent diseases or reduces the risk of getting sick. It is more than feasible to go to the supermarket and buy vegetables and fruit: it depends only on the individuals to maintain a balanced diet."

As she works on the role of diet in health maintenance and disease prevention, Dr. Esteban-Fernández takes her own nutrition very serious. "I am really aware about the importance of a healthy diet enriched in vegetables, fruits, and reduced industrial saturated fats. Although I try to maintain my dietary habits as good as possible, I think it is also important to not get too obsessed. Society is nowadays full of false myths about diet, and it is the role of both science and media to avoid the spread of these rumors, as well as make people aware of the importance of diet for your health."

http://bit.ly/2qDBeen

Gaining Weight In Middle Age? It's This Molecule's Fault, Scientists Say

It's common for people to pack on more pounds as they age, but now a new study may have an explanation for this weight gain — and it has nothing to do with exercise or poor food choices.

By Rachael Rettner, Senior Writer | May 3, 2017 06:42pm ET

Researchers identified an enzyme that appears to increase its activity in animals as they age. The increase in this enzyme's activity may play a role in the weight gain and fitness decline that come with aging, they said.

In experiments in mice on a high-fat diet, the researchers found that mice that had this enzyme blocked gained less weight than normal mice.

"Our society attributes the weight gain and lack of exercise at mid-life … primarily to poor lifestyle choices and lack of will power," study author Dr. Jay Chung, head of the Laboratory of Obesity and Aging Research at the National Heart, Lung, and Blood Institute, said in a statement. "But this study shows that there is a genetic program driven by an overactive enzyme that promotes weight gain and loss of exercise capacity at mid-life," Chung said. [The Best Way to Keep Weight Off]

Because the new study was conducted in mice, researchers don't yet know if blocking this enzyme in humans will have the same effect.

But the researchers said that, with more research, the findings could potentially lead to the development of new weight loss medications that would block this enzyme.

Chung said he has always been puzzled by the tendency of adults to gain weight as they age — the average American gains 30 pounds from ages 20 to 50, even though people don't usually eat more food during this period, he said.

Chung and his colleagues looked for molecular changes that occurred in animals during middle age and found that an enzyme called DNA-dependent protein kinase, or DNA-PK, increases in activity with age.

Their research showed that this enzyme is involved in metabolism (such as the conversion of nutrients to fat) and in the production of mitochondria, or the "powerhouses" in cells that turn nutrients into energy. It's known that as people age, they see a drop in the number of mitochondria.

In the study, the researchers found that giving mice that were on a high-fat diet a drug that inhibits DNA-PK led to a weight gain in those mice that was 40 percent less, compared to mice that were also on this diet but didn't receive the drug.

In addition, mice that received the drug saw an increase in the number of mitochondria in their skeletal muscle cells, and experienced increased aerobic fitness.

"Our studies indicate that DNA-PK is one of the drivers of the metabolic and fitness decline that occurs during aging, which makes staying lean and physically fit difficult" in older age, Chung said. [How to Lose Weight in 2017 (and Keep It Off for Good)]

However, the researchers noted that the findings don't mean people should abandon diet and exercise as they get older, since these are still the primary tools for fighting obesity. Middle-age adults should continue with these practices, even if it takes a while to see results, they said.

The study was published in the May issue of the journal Cell Metabolism.

http://bit.ly/2pjyzSu

Discovery of a Zika antibody offers hope for a vaccine

Researchers have found natural antibodies that prevent Zika infection by latching onto a part of the virus.

A research team based at The Rockefeller University has identified a potent new weapon against the Zika virus in the blood of people who have been infected by it. This discovery could lead to new ways of fighting the disease, including a vaccine.

In blood samples taken from subjects in Mexico and Brazil, the scientists found antibodies--proteins produced by the immune system--that block the virus from initiating an infection. These antibodies appeared to have been initially generated in response to an earlier infection by a related virus that causes dengue. One such antibody, which they call Z004, was particularly effective at neutralizing Zika.

"These antibodies could be very useful in the near future. One could envision, for example, administering Z004 to safely prevent Zika among pregnant women or others at risk of contracting the disease," says Davide F. Robbiani, a research associate professor in Michel Nussenzweig's lab. He and Leonia Bozzacco, a research affiliate in Charles M. Rice's lab, led the study, which appears in Cell on May 4.

The team's detailed examination of the interaction between this antibody and the virus also revealed a new potential strategy for developing a vaccine.

A precise target

A mosquito-borne virus, Zika usually causes mild symptoms in those who contract it. However, dramatic effects can appear in the next generation. Babies born to women infected during pregnancy are at risk of devastating neurodevelopmental abnormalities. The only way to prevent Zika is to avoid mosquito bites; there are currently no vaccines or other medical measures to do so.

An infection begins when the virus, traveling in a spherical particle studded with the viral envelope protein, latches onto a host cell and forces its way in. Faced with a viral threat, the human immune system

generates antibodies that recognize the virus and stop it from invading cells. The team set out to find antibodies tuned to a particular target: a part of Zika's envelope protein, which the virus needs to launch an attack.

Five out of six

Through collaborators working in Pau da Lima, Brazil, and Santa Maria Mixtequilla, Mexico, they obtained blood samples from more than 400 people, collected shortly after Zika was circulating.

Individual responses to the same pathogen can vary greatly. Yet a deeper analysis of samples from six of the volunteers with the most promising antibodies revealed a surprise: Five of them contained the same species of nearly identical antibodies. This similarity suggested these molecules were particularly good at fighting the virus.

When the team examined these closely related antibodies' performance against Zika, one stood out: Z004, an antibody from a Mexican volunteer's blood. When given to mice rendered vulnerable to Zika, the antibody protected them from developing serious infections.

A shared ridge

To get a closer look at the interaction between the antibody and a fragment of the virus' envelope protein, scientists in Pamela J. Bjorkman's lab at Caltech determined the molecular structure formed as the two units interacted. Their detailed maps revealed how the antibody pinches a ridge on the virus when it binds to it.

While some efforts to develop a vaccine use all or most of the virus to stimulate the immune system, the researchers believe it could be safer to employ only a tiny fragment containing this ridge.

Zika isn't the only virus to sport the ridge, as it is also present in envelopes of other viruses in the same family. The dengue 1 virus, a close relative of Zika and one of four types of dengue, has a ridge that is remarkably similar to Zika's. When pitted against dengue 1, Z004 neutralized it as well.

A look back at samples from the Brazilians, collected six months before Zika arrived by a team led by Albert Ko of Yale University, revealed evidence of prior dengue 1 infections in some--and a potential explanation as to why certain people's immune systems fared better against Zika.

"Even before Zika, their blood samples likely had antibodies that could interact with this same spot on the envelope protein," says Margaret R. MacDonald, a research associate professor in Rice's lab. "It appears that, much like a vaccine, dengue 1 can prime the immune system to respond to Zika."

Nussenzweig is the Zanvil A. Cohn and Ralph M. Steinman Professor and Rice is the Maurice R. and Corinne P. Greenberg Professor in Virology.

http://bit.ly/2pUrqT6

508 million-year-old fossil a gripping find

New sea creature sheds light on the origins of the planet's most abundant and diverse group of organisms.

What do ants, centipedes and lobsters have in common? They're all masters of the pincer movement, members of the most abundant and diverse group of organisms on Earth. Known as mandibulates, their common trait is a pair of specialised appendages (mandibles) for grasping, crushing and cutting food.

Tokummia katalepsis specimen showing a pair of large pincers (maxillipeds) at the front. **Jean-Bernard Caron / Royal Ontario Museum**

Which is why the discovery of this exceptionally well-preserved fossil, named Tokummia katalepsis, by Canadian palaeotolongists is so important.

"Before now we've had only sparse hints at what the first arthropods with mandibles could have looked like," explains Cédric Aria, of the University of Toronto, "and no idea of what could have been the other

key characteristics that triggered the unrivaled diversification of that group."

The fossil, from 508 million-year-old sedimentary rocks near Marble Canyon, British Columbia, shows the 10-centimetre-long sea creature with broad serrated mandibles as well as large but specialised anterior claws called maxillipeds. "The pincers of Tokummia are large, yet also delicate and complex," Aria says, "reminding us of the shape of a can opener, with their couple of terminal teeth on one claw, and the other claw being curved towards them."

http://bit.ly/2qPSN7r

Swearing aloud can make you stronger

That is the conclusion of research being presented today by Dr Richard Stephens from Keele University to the Annual Conference of the British Psychological Society in Bright

In the research, Dr Stephens and his team conducted two experiments. In the first, 29 participants completed a test of anaerobic power -- a short, intense period on an exercise bike -- after both swearing and not swearing. In the second, 52 participants completed an isometric handgrip test, again after both swearing and not swearing.

The results showed that the participants produced more power if they had sworn in the first experiment and a stronger handgrip if they had sworn in the second. Dr Stephens said:

"We know from our earlier research that swearing makes people more able to tolerate pain. A possible reason for this is that it stimulates the body's sympathetic nervous system -- that's the system that makes your heart pound when you are in danger.

"If that is the reason, we would expect swearing to make people stronger too -- and that is just what we found in these experiments.

"But when we measured heart rate and some other things you would expect to be affected if the sympathetic nervous system was responsible for this increase in strength, we did not find significant changes.

"So quite why it is that swearing has these effects on strength and pain tolerance remains to be discovered. We have yet to understand the power of swearing fully."

For further information BEFORE THE CONFERENCE contact the British Psychological Society Press Centre: 0116 252 9500 / 07773 173 510 or email presscentre@bps.org.uk
Paper title: 'Effect of swearing on strength and power performance'

http://bit.ly/2pnE1V9

Grandparents who practice outdated health myths may pose safety threat on grandchildren

New research reveals nearly one-quarter of grandparents rearing offspring's children don't know proper sleeping position for babies, a major risk factor for SIDS

NEW HYDE PARK, NY - Many grandparents raising their grandchildren practice outdated health and parenting myths that could potentially pose serious risks to young children, according to illuminating new research by a Northwell Health pediatrician.

The study, one of a trio led by senior investigator Andrew Adesman, MD, is scheduled for presentation at the Pediatric Academic Societies Meeting being held in San Francisco from May 6-9. Dr. Adesman, Chief of Developmental and Behavioral Pediatrics at Cohen Children's Medical Center in New Hyde Park, focused his research on the particular difficulties facing grandparents solely raising their offspring's children.

"When grandparents step up to the plate, it can be wonderful for grandchildren but can also pose challenges in terms of lifestyle, finances and mental and physical health to a somewhat older or elderly cohort," said Dr. Adesman. "In their questionnaires, a fairly large sample size of grandparents felt they were doing a good job but acknowledged they didn't have the support they often needed and that their role could be alienating in terms of their own peer group."

More than 7 million grandchildren in the United States were being raised solely by their 2.7 million grandparents in 2012, according to the US Census Bureau. Factors contributing to this growing

phenomenon include the opioid epidemic, parental incarceration or problems with parents' physical or mental health, Dr. Adesman said.

In the decades since grandparents raised their own children, certain parenting practices and health beliefs have evolved - catching some grandparents unaware and potentially threatening their grandchildren's safety. For example, in one of Dr. Adesman's studies, "Potential Health Risks to Children When Grandparents Raising Their Grandchildren Subscribe to Out-Dated Health Beliefs," 44 percent of the 636 grandparents who completed a detailed questionnaire mistakenly believed that "ice baths are a good way to bring down a very high fever." In fact, ice baths pose a hypothermia risk.

Perhaps more notably, nearly one-quarter of these grandparents did not know that "infants should be put to sleep on their back, not on their stomach or side" - a major risk factor for sudden infant death syndrome (SIDS).

Pediatricians can help grandparents raising their grandchildren by updating them on current health care beliefs and parenting methods, Dr. Adesman said. "It's important that pediatricians not make the mistake of taking for granted that because these grandparents have raised children already, they have the wisdom of the ages," he added.

In his two other related studies, Dr. Adesman and his team surveyed 774 grandparents who identify as the primary caregiver of one or more grandchildren. One questionnaire aimed to characterize these grandparents' sources of support and evaluate their impact, as well as identify unmet needs for support.

The study, "Adequacy of Psychosocial Supports for Grandparents Raising Their Own Grandchildren," showed that one in 10 grandparents reported they didn't have any support systems at the time they answered the survey, while an additional 12 percent said their support system didn't meet their most important needs. In addition, 71 percent reported that their parenting responsibilities had limited their ability to socialize with friends, and nearly one-third indicated that raising their grandchild had affected their spouse or relationship unfavorably.

Many respondents expressed interest in receiving counseling (43 percent) or participating in a support group (61 percent), and those who lacked an adequate support system were less likely to report feeling generally happy (54 percent vs. 86 percent).

"One major takeaway from this study is that for grandparents who are raising grandchildren, their parenting can often take a toll in terms of their own physical and emotional health, and support groups can make a difference," said Dr. Adesman, noting that grandparenting support groups can be found in most major cities.

Dr. Adesman's remaining study, "Parenting Experiences and Self-Perceived Parenting Abilities of Grandparents Raising Their Own Grandchildren" covered parenting experiences, self-perceptions, challenges and other factors affecting these grandparents. Research showed that nearly one-third reported having a medical problem that interfered with their ability to care for their grandchild. Additionally, many said that choosing to parent their grandchild had negatively affected their own emotional (40.3 percent) or physical (32.4 percent) health.

"I think pediatricians need to also evaluate not just the health and well-being of the child, but really ask about the physical and social health of the grandparent that has assumed responsibility for raising that child as well," Dr. Adesman suggested. "Because although the grandparents often elected to take on this role, it's not something they planned for and it can represent a challenge in many domains. Many grandparents are up to the challenge, but it may come with certain costs."

http://bit.ly/2qOU67x

Noisy knees may be an early sign of knee osteoarthritis

People who hear sounds in or around their knee joint may be at increased risk of developing knee osteoarthritis

A new study using data from the Osteoarthritis Initiative, a multi-center observational study of nearly 3500 participants, indicates that people who hear grating, cracking, or popping sounds in or around their knee joint may be at increased risk of developing knee osteoarthritis.

This was a study of people who were at high risk for developing knee osteoarthritis. Among those who developed it within a year, more than 75% had signs of osteoarthritis on radiographic images but no frequent knee pain at the start of the study. The findings may be helpful for identifying individuals at risk for knee osteoarthritis, potentially assisting with earlier diagnosis and intervention.

"Many people who have signs of osteoarthritis on x-rays do not necessarily complain of pain, and there are no known strategies for preventing the development of pain in this group of people," said Dr. Grace Lo, lead author of the Arthritis Care & Research study and an Assistant Professor of Medicine at Baylor College of Medicine in Houston. "This study suggests that if these people have noisy knees, they are at higher risk for developing pain within the next year compared with the people who do not have noisy knees. Future studies that target people who have x-ray signs of osteoarthritis, and who do not complain of pain but do report noisy knees, hold the promise of identifying interventions that can prevent knee pain."

http://bbc.in/2qORaYF

Jurassic animal found on Skye 'fed milk to young'

Palaeontologists believe an animal that lived in what is now Skye 165 million years ago fed milk to its young.

Milk teeth have been discovered in the fossil jaw of a juvenile Wareolestes rex, a species of mammal from the Middle Jurassic.

Scientists suggest adult females secreted milk on to a bare patch of skin for their young to lap up.Nipple s and suckling as seen in modern mammals had still to evolve when Wareolestes rex lived.

The two centimetre-long jaw was found on Skye in 2015 and is one of the most complete fossils of the early mammal to be found outside of China. Single teeth of Wareolestes rex have previously been found in England.

Palaeontologists from National Museums Scotland in Edinburgh and the University of Oxford have been examining the fossil from Skye. Using micro-CT scanning technology, they have identified milk teeth and, inside the jaw, adult teeth that had not erupted through the gums.

An illustration of Wareolestes rex Elsa Panciroli

The scientists said this showed that Wareolestes rex replaced its teeth once, like humans and other modern mammals. It had a set of milk teeth, followed by a set of adult teeth. This pattern of tooth replacement was an important step in the evolution of mammals and is linked to the production of milk to feed young, the scientists said.

Elsa Panciroli, the PhD student who led the research of the fossil, said: "This is such an exciting discovery. "It's one of the most complete Middle Jurassic mammal fossils described from Scotland.

"This was a juvenile animal that was losing its milk teeth and the permanent teeth were just breaking through the gums. "Tooth replacement like this tells us this early mammal fed on milk provided by the parent until it grew to adult size." She added: "Wareolestes would have cared for its young, which is a behaviour we associate with modern mammals."

Living in a period when dinosaurs were the dominant animal, Wareolestes rex were a large mammal for the time, with adults growing to the size of a guinea pig. The method of Wareolestes rex delivery of milk to its young is similar to that of platypus.

During the Middle Jurassic, Skye was covered in lagoons and filled with turtles, crocodiles, pterosaurs and dinosaurs. Mainland Scotland was an island surrounded by a semi-tropical sea filled with marine reptiles and ammonites.

http://bit.ly/2pR2moX

Deadly infection spread by contaminated heart surgery machines

People undergoing heart surgery may be getting infected with a deadly strain of bacteria, spread by machines used to cool blood.

By Clare Wilson

The design of blood-cooling machines is flawed, Daniel Diekema at the University of Iowa told the European Congress of Clinical Microbiology and Infectious Diseases in Vienna, Austria, last week. "This was an infection risk that was hiding in plain sight for decades," Diekema said.

The risk arises during open-heart surgery when inserting a device, such as a valve or blood-vessel graft. This process requires a machine to cool and later warm up the blood. During the operation, machines contaminated by the bacteria can blow them out into the operating room, where they can land on the devices to be implanted.

It was thought that the microbe, called *Mycobacterium chimaera* and common in soil and water, was present in only a certain brand of blood-cooling machine, due to factory contamination. But doctors are now reporting that other machines seem to be affected too, and there is no known way of decontaminating them.

The problem is causing alarm among doctors worldwide, because *M. chimaera* infection is difficult to treat. There are 110 known cases of this happening in heart patients so far, and half of those infected have died.

Indestructible biofilm

The problem is that once *M. chimaera* gets into an implant, it forms an indestructible "biofilm" which antibiotics can't penetrate, said Diekema. "It results in continuous reseeding [of the bacteria] in the bloodstream."

People who show signs of infection are usually treated first with antibiotics, but Diekema said the only solution was additional surgery to replace the implant.

According to the US Centers for Disease Control and Prevention, even if a hospital has had one case of infection in this way, the observed risk to other patients is very low – between 1 in 1000 and 1 in 100.

However, there may have been many more cases than the 110 identified so far. *M. chimaera* is difficult to grow in the lab, so tests of samples from machines or patients may wrongly come back negative. It can also take months or years before an infected person shows symptoms, such as weight loss, tiredness and night sweats.

Patients warned

Hospitals around the world have started notifying patients who are at risk to tell them to watch out for symptoms, mainly if the type of machine first identified as contaminated was used in their surgery. In the UK, Public Health England has sent letters to doctors warning them that any patient who has had valve replacement or valve repair surgery could be at risk – although they have not specified any particular brand of machine.

A spokesperson for Public Health England says the Medicines Healthcare Regulatory Agency is working with manufacturers of blood-cooling machines to engineer "solutions which could be safely and universally implanted".

One solution may be to use long tubing, so the machine can be placed outside the operating room, Diekema said. Alternatively, venting the machine's exhaust outside the room might work.

http://wb.md/2pktFo8

Using Over-the-Counter Analgesics Safely: What Patients Don't but Should Know

Over-the-counter (OTC) analgesics are among the most commonly used nonprescription medicines in the United States,[1] yet not every OTC pain reliever is appropriate for every patient.

Charles P. Vega, MD

Over-the-Counter Analgesics

As healthcare professionals, we play an important role in helping patients make the most appropriate choice.

The topic of OTC analgesics can be easily overlooked among the other priorities we face during a clinical exam. Nevertheless, given the scope and impact of these drugs on patients' everyday lives, best practices dictate that we proactively discuss their use at every visit.

Consider this typical scenario: A woman comes to my office for a clinical visit. She tells me she takes seven prescription medications to manage multiple chronic conditions and that she doesn't take any other medications. After more discussion, I discover that she also takes naproxen, ibuprofen, acetaminophen, ibuprofen/diphenhydramine, and acetaminophen/hydrocodone (which was prescribed for her by another physician).

When I asked her why she didn't mention these other medications, she tells me that she doesn't consider these "medicine" because I didn't prescribe them, and she doesn't take them every day. Unfortunately, what she doesn't realize is that, with her heart failure, chronic renal failure, history of stroke, and use of multiple medications with the same active ingredients, she was inadvertently putting her health at risk. Sound familiar?

A Review of the Risks

To further illustrate why these in-depth conversations with patients about OTC pain-reliever use are important, consider the findings of a recent survey involving 1300 US adults[2] conducted by the US Pain Foundation. The results revealed that 94% of Americans depend on OTC analgesics for pain management and many of them do so without considering factors that could seriously impact their health.

The remainder of the key findings are just as eye-opening. When asked about decisions regarding which OTC pain reliever to use:

- ***Nearly half (45%) do not consider the prescription medicines they are currently taking.***
- ***More than half (58%) do not consider their preexisting health conditions.***
- ***Two-thirds (65%) do not consider other OTC medicines they are taking.***
- ***Three out of four (73%) of those aged 60 and older do not consider their age.***
- ***One in five (20%) do not consider any of these important safety factors.[2]***

Healthcare professionals routinely ask patients about their prescription medications. We need to ensure that we are also asking about the use of OTC medications, including OTC pain relievers, to provide appropriate guidance based on each patient's health history or risk/benefit profile. Not having the complete picture can lead to serious consequences.

For example, when taken regularly, nonsteroidal anti-inflammatory drugs (NSAIDs) can elevate a patient's cardiovascular risk, and this risk can be even greater for patients with known cardiovascular disease.[3] Taking NSAIDs for longer than 3 months has been associated with gastric ulceration rates between 15% and 35%,[4] warranting the use of caution when recommending these medicines.

Similarly, it is important to be aware of hepatic risk factors when recommending acetaminophen to a patient. Acetaminophen hepatotoxicity is still the most common cause of acute liver failure in the United States.[5] Many patients who experienced acetaminophen toxicity were not aware that they were misusing the medication.[6] Educating patients on the many medications that contain acetaminophen, as well as the appropriate maximum daily dose, is a key step in ensuring that patients use this medication appropriately.

Ensuring Patient Safety

Practitioners know that OTC analgesics are ubiquitous. It is critical that we assess their use when performing a medication reconciliation.

I consider the following safety factors when recommending an OTC pain reliever to my patients.

- ***Age: Patients over the age of 60 are at an increased risk for gastrointestinal bleeding with NSAIDS.***
- ***Coexisting medical conditions: Patients with gastritis or stomach ulcers, renal abnormalities, cardiovascular risks, liver disease or cirrhosis, hypertension, or asthma have increased health risks with both NSAIDs and acetaminophen.***

- ***Concomitant medicines: Patients who take anticoagulants/antiplatelet medications,[7,8] corticosteroids, certain antihypertensive agents,[9] or aspirin face increased risks when also taking NSAIDs. This also applies to patients who are taking other medications containing the same analgesic components.***

In addition, I remind my patients to always read and follow the drug facts label each time they reach for any OTC medication.

We all appreciate that OTC analgesics play an important role in improving patients' well-being. They are generally safe and effective when used as directed. With enhanced patient communication and education around OTC pain relievers, healthcare professionals can make well-informed decisions about their patients' treatment plan and help their patients make informed choices.

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http://bit.ly/2qQUeTe

WHO Plans to Bring Cheap Biosimilar Cancer Drugs to Poor

The copies will not be exactly identical to the originals

Reporting by Ben Hirschler; editing by David Clarke

LONDON (Reuters) - The World Health Organization (WHO) is to launch a pilot project this year to assess cheap copies of expensive biotech cancer drugs in a bid to make such medicines more widely available in poorer countries.

The U.N. agency said on Thursday it would invite drugmakers in September to submit applications for prequalification of so-called biosimilar versions of two such drugs on its essential medicines list, Roche's Rituxan and Herceptin. WHO also plans to explore options for prequalifying biosimilar insulin.

The move is a boost for biosimilars which are expected to account for a growing proportion of treatments, particularly for cancer, as patents on the original branded products expire.

The WHO plays a critical role in monitoring drug quality in poorer countries through its prequalification program, which ensures that treatments supplied by U.N. agencies such as UNICEF are of acceptable quality. The program is also used by many governments to guide the bulk purchase of medicines.

"Innovator biotherapeutic products are often too expensive for many countries, so biosimilars are a good opportunity to expand access and support countries to regulate and use these medicines," said WHO Assistant Director General Marie-Paule Kieny.

Roche's Rituxan, known generically as rituximab, is used principally to treat blood cancers, while Herceptin, or trastuzumab, is a treatment for breast cancer.

The complex nature of biological medicines, which are made inside living cells, means copies can never be exactly the same as the original. But a growing number of such drugs have been approved as similar enough to do the job in several markets.

http://bit.ly/2qgMAVQ

Decades of data on world's oceans reveal a troubling oxygen decline

A new analysis of decades of data on oceans across the globe has revealed that the amount of dissolved oxygen contained in the water - an important measure of ocean health - has been declining for more than 20 years.

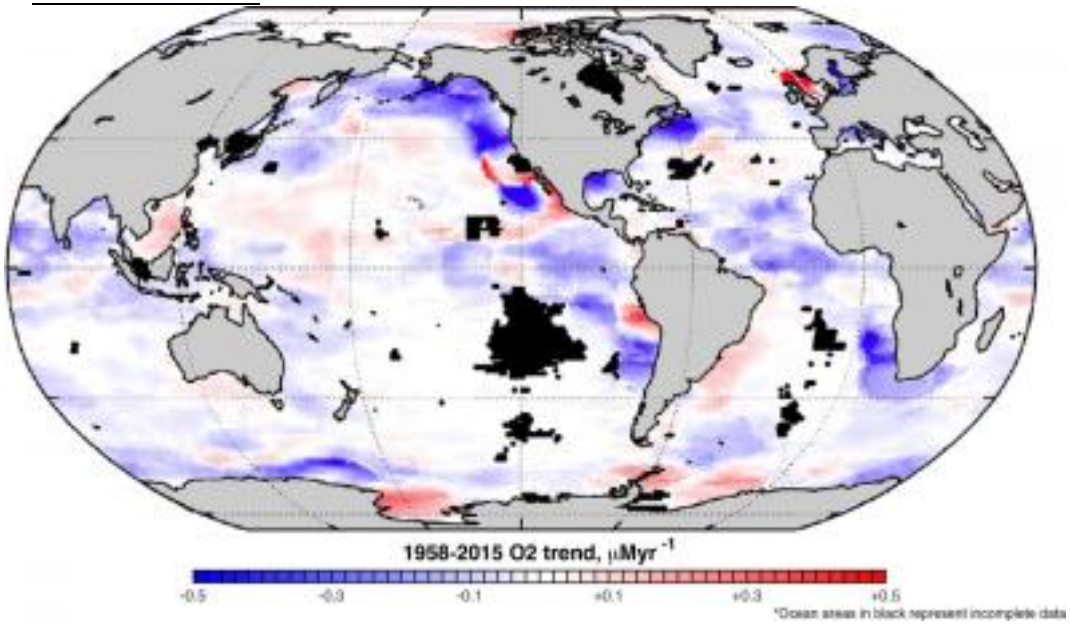
Researchers at Georgia Institute of Technology looked at a historic dataset of ocean information stretching back more than 50 years and searched for long term trends and patterns. They found that oxygen levels started dropping in the 1980s as ocean temperatures began to climb.

"The oxygen in oceans has dynamic properties, and its concentration can change with natural climate variability," said Taka Ito, an associate professor in Georgia Tech's School of Earth and Atmospheric Sciences who led the research. "The important aspect of our result is that the rate of global oxygen loss appears to be exceeding the level of nature's random variability."

The study, which was published April in Geophysical Research Letters, was sponsored by the National Science Foundation and the National Oceanic and Atmospheric Administration. The team included researchers from the National Center for Atmospheric Research, the University of Washington-Seattle, and Hokkaido University in Japan.

Falling oxygen levels in water have the potential to impact the habitat of marine organisms worldwide and in recent years led to more frequent "hypoxic events" that killed or displaced populations of fish, crabs and many other organisms.

Researchers have for years anticipated that rising water temperatures would affect the amount of oxygen in the oceans, since warmer water is capable of holding less dissolved gas than colder water. But the data showed that ocean oxygen was falling more rapidly than the corresponding rise in water temperature.



Global map of the linear trend of dissolved oxygen at the depth of 100 meters. **Georgia Tech**

"The trend of oxygen falling is about two to three times faster than what we predicted from the decrease of solubility associated with the ocean warming," Ito said. "This is most likely due to the changes in ocean circulation and mixing associated with the heating of the near-surface waters and melting of polar ice."

The majority of the oxygen in the ocean is absorbed from the atmosphere at the surface or created by photosynthesizing phytoplankton. Ocean currents then mix that more highly oxygenated water with subsurface water. But rising ocean water temperatures near the surface have made it more buoyant and harder for the warmer surface waters to mix downward with the cooler subsurface waters. Melting polar ice has added more freshwater to the ocean surface - another factor that hampers the natural mixing and leads to increased ocean stratification.

"After the mid-2000s, this trend became apparent, consistent and statistically significant—beyond the envelope of year-to-year

fluctuations," Ito said. "The trends are particularly strong in the tropics, eastern margins of each basin and the subpolar North Pacific."

In an earlier study, Ito and other researchers explored why oxygen depletion was more pronounced in tropical waters in the Pacific Ocean. They found that air pollution drifting from East Asia out over the world's largest ocean contributed to oxygen levels falling in tropical waters thousands of miles away.

Once ocean currents carried the iron and nitrogen pollution to the tropics, photosynthesizing phytoplankton went into overdrive consuming the excess nutrients. But rather than increasing oxygen, the net result of the chain reaction was the depletion oxygen in subsurface water. That, too, is likely a contributing factor in waters across the globe, Ito said.

More information: Takamitsu Ito et al, Upper Ocean Otrends: 1958-2015, Geophysical Research Letters (2017). DOI: 10.1002/2017GL073613

http://bit.ly/2qRYDGd

Ancient Meteor Strike Triggered Eruptions Lasting Up to a Million Years

A huge meteor that hit Earth about 2 billion years ago was responsible for explosive and long-lived volcanic eruptions, scientists have found.

By Charles Q. Choi, Live Science Contributor

A giant meteor impact on Earth nearly 2 billion years ago triggered more explosive and long-lived volcanic eruptions than previously thought, a new study finds.

This finding sheds light on how meteor bombardment may have dramatically shaped the evolution of the early Earth, researchers in the new study said.

Meteor strikes have left giant craters all over Earth. For instance, the cosmic impact that scientists think ended the age of dinosaurs about 66 million years ago left behind a crater more than 110 miles (180 kilometers) wide near the town of Chicxulub (CHEEK-sheh-loob) in Mexico. [In Photos: The Impact Craters of North America]

Gargantuan craters are seen pockmarking the rest of the solar system as well. Recent studies of such impact craters on the moon, Mercury, Venus and Mars suggested that meteor strikes could trigger volcanic activity.

However, over the course of millions of years, geological activity has eradicated the vast majority of ancient impact craters on Earth. This has limited research into whether meteor strikes could also set off volcanism on Earth, said study senior author Balz Kamber, a geochemist in Trinity College Dublin in Ireland, and his colleagues.

To see what effects giant impacts might have had on the surface of the Earth, the researchers analyzed one of the oldest meteor craters on the planet, the 1.85-billion-year-old Sudbury basin in Canada. It's also the second-largest and best-preserved crater on Earth, measuring about 93 to 161 miles (150 to 260 km) in diameter. A 2015 study estimated that the crater may have been created by a comet about 9.3 miles (15 km) wide.

From 2013 to 2014, the scientists in the new study collected samples from the 0.93-mile-thick (1.5 km) layer of rock that filled the Sudbury crater. Although the crater is easy for researchers to get to, "there are lots and lots of blackflies in the spring, and later mosquitoes, and in the summer, there are a lot of blueberries, and so a lot of black bears," Kamber said.

The scientists examined 139 samples from 15 locations in the crater. Their analysis suggested that this material not only consisted of rock that had melted from the heat of the impact, but was also peppered with tiny fragments of volcanic rock.

The researchers noted that these volcanic rocks often had very distinctive angular shapes resembling crab claws. These shapes form when gas bubbles expand in molten rock that then catastrophically explodes, a feature of violent eruptions involving water, such as those seen under glaciers in Iceland, the researchers explained. They said these angular Sudbury volcanic rocks likely arose when seawater flooded the crater floor, either gradually or suddenly.

In addition, the scientists found that the composition of these volcanic-rock fragments varied in nature, with some originating from molten crust and others from "a deeper magma source," Kamber said. These findings suggested that the volcanic activity that created these rocks changed over time and was therefore prolonged, he said.

How long might this meteor-triggered volcanism have lasted? "I think 1 million years would have been an upper limit," Kamber said. "Hundreds of thousands of years is a more reasonable estimate."

These findings shed light on how meteors could have influenced the evolution of early Earth, Kamber said.

"About 3.8 billion to 4 billion years ago, we know the inner solar system experienced heavy bombardment from impactors," Kamber said. The oldest rocks on the planet coincide with the last peak of this bombardment, suggesting that "the older rocks on Earth were somehow destroyed by this bombardment," he said. "The bombardment alone would not have done sufficient damage to have caused the comprehensive loss of primordial rocks on Earth, but if that bombardment also triggered additional eruptions, that could have buried the primordial rocks and plowed them back into the mantle."

The scientists said they are now investigating whether the deep magma they detected in the crater came from the deep crust or from the mantle layer just beneath Earth's crust. They detailed their findings April 22 in the Journal of Geophysical Research: Planets.

http://bit.ly/2pmnBeV

How Electrified Steel Could Suck Toxic Metals From the Ocean

After a century of strip mining and deforestation, New Caldonia researchers are working to de-contaminate marine waters

By Michael Allen, Hakai Magazine smithsonian.com

When heavy rain hits New Caledonia, the rivers run red.

Located about 1,200 kilometers east of Australia, New Caledonia has one of the world's most extensive coral reef ecosystems, and about 10 percent of the world's nickel. More than a century of strip mining and deforestation in the French Pacific territory has created some of the highest levels of soil erosion in the world. Rainforest cover has been reduced from 70 percent to 20 percent, and when it rains, water and earth run unimpeded off the hillsides into rivers and the sea, taking nickel and other toxic metals with them.

Ultimately, these metals—mainly nickel, cobalt, iron, and chromium—end up in the food chain. Oysters that live near rivers that run past mining sites contain 20 times more nickel than those living near other rivers. Eels near the coast have higher concentrations of nickel and other metals than those farther out to sea.

“The consequences of this kind of pollution are disastrous,” says Peggy Gunkel-Grillon, an environmental chemist from the University of New Caledonia. The toxic metals move up the food chain and accumulate in top predators, she says.

But evidence about the toxicological effects of nickel on marine creatures and people is limited. “In New Caledonia, we are beginning to study the impact of metals on the environment—this is a new topic for the government and scientists,” says Yannick Dominique, an ecotoxicologist at New Caledonian consultancy Bioeko. Dominique is part of a new government project examining levels and sources of metal exposure in people in New Caledonia.

In humans, research has linked exposure to nickel—often through smoking cigarettes or industry—to an increased prevalence of type 2 diabetes, and the World Health Organization classifies pure nickel as a carcinogen. Little is known, however, about the effect of consuming water and foods that are high in nickel.

Thinking about the threat of nickel runoff, Gunkel-Grillon and her colleagues wondered if something could be done.

In marine industries, artificial rock-like formations are created around structures such as wind turbines and offshore oil platforms to protect them from erosion. These barriers are created from calcium-based materials in the seawater that are attracted to and build up around electrically charged metal structures. The researchers wondered if this

process could be pushed a step further. That is, if electrically charged metals can attract calcium-based materials, could calcium-based formations attract heavy metal pollutants?

In laboratory experiments, Gunkel-Grillon is working with Marc Jeannin, an engineer from France's Université de La Rochelle, to develop a method to extract nickel from the seawater off New Caledonia.

By placing galvanized steel in seawater, and charging it with a weak electrical current, the researchers have shown that they can pull metal ions out of the solution, trapping them in calcified deposits that grow on the steel electrode.

In a proof-of-concept laboratory test, the scientists dipped small pieces of electrified steel into seawater spiked with nickel. After seven days, they found that up to 24 percent of the nickel added to the water was trapped.

But the real challenge, says Gunkel-Grillon, is to see if their technique will translate to real-world conditions. This next step is already underway in a New Caledonian lagoon. In late March, the scientists placed a larger-scale experiment in Numbo Bay, which is the industrial zone of the capital city, Nouméa.

If these experiments work, the scientists envision an even larger, permanent structure of galvanized electrodes that sit vertically in the water.

"By placing our device at the mouths of rivers, effluents, ports, or any other places where such pollution can occur, we will be able to limit the contamination of dissolved nickel," says Gunkel-Grillon.

The local electrical grid powers the New Caledonian experiment, but it should be possible to run such a setup with wind turbines or solar panels in the future.

Metal contamination in the marine environment is a problem the world over, and this solution holds great promise. The team has also used the technique to trap lead, and Jeannin says he sees no reason why it can't work for other metallic elements as well.

"Older harbors can have a fairly high level of contaminants such as metals and heavy metals in their sediments," says Philippe Andréani, CEO of Géocorail, a company that develops artificial marine structures for erosion protection. "It comes from the antifouling paints used in the past on the hulls, and from other sources. Harbors are not very deep, so turbulence caused by vessel propellers tends to lift the sediments and release their pollutants."

Géocorail has patented a different version of a metal-trapping electrode, which is being tested in a couple of French harbors.

By next spring, the results from the New Caledonian field test will be in, and the scientists should know whether this technique can help with toxic metal pollution.

"When we obtain the deposits from the seawater, we will be able to check what metallic elements have been trapped, including all the metal pollutants that are present in the New Caledonia lagoon," says Jeannin.

http://bit.ly/2pc7jtN

Fukushima accident gave everyone an X-ray's worth of radiation

First global survey of radiation exposure caused by the meltdown of nuclear reactors at the Fukushima-Daiichi nuclear plant

By Andy Coghlan

"We don't need to worry," says Nikolaos Evangeliou at the Norwegian Institute for Air Research, whose team has conducted the first global survey of radiation exposure caused by the meltdown of three nuclear reactors at the Fukushima-Daiichi nuclear plant in Japan after a tsunami struck in 2011.

Evangeliou's team has calculated the approximate exposure of everyone on Earth to two radioactive isotopes of caesium, using all the data available so far. Most of this came from the Comprehensive Test Ban Treaty Organization, which monitors radiation in the environment using a global network of measuring stations.

"More than 80 per cent of the radiation was deposited in the ocean and poles, so I think the global population got the least exposure," Evangeliou told the annual meeting of the European Geosciences Union in Vienna, Austria, last month. He has estimated the dose that most individuals received to be 0.1 millisievert. "What I found was that we got one extra X-ray each," says Evangeliou.

Impact on wildlife

Even in Japan, the average person's radiation dose was low: 0.5 millisieverts, which is close to the annual recommended limit for breathing in naturally occurring radon gas. In comparison, the average annual exposure from background levels of radiation in the UK is around 2.7 millisieverts a year.

Doses were unsurprisingly higher for residents of Fukushima and neighbouring areas during the first three months of the accident, ranging from 1 to 5 millisieverts. But such doses are still relatively low – a typical CT scan delivers 15 millisieverts, for example, while it takes 1000 millisieverts to cause radiation sickness.

But Evangeliou says that the effects on wildlife around the plant might be more severe. Already, he says, increased levels of radiation around Fukushima have been linked to declines in bird populations there between 2011 and 2014. "There have also been reports of declines in other species such as insects and some mammals," he says.

However overall, Evangeliou says the hazards posed by fallout from the Chernobyl nuclear accident in Ukraine in 1986 are still much greater than those from Fukushima, because the fallout was larger, and it fell upon more densely populated areas.

http://bit.ly/2qRKNE1

New theory on how Earth's crust was created

Where did Earth's silica-enriched crust come from?

More than 90% of Earth's continental crust is made up of silica-rich minerals, such as feldspar and quartz. But where did this silica-enriched material come from? And could it provide a clue in the search for life on other planets?

Conventional theory holds that all of the early Earth's crustal ingredients were formed by volcanic activity. Now, however, McGill University earth scientists Don Baker and Kassandra Sofonio have published a theory with a novel twist: some of the chemical components of this material settled onto Earth's early surface from the steamy atmosphere that prevailed at the time.

First, a bit of ancient geochemical history: Scientists believe that a Mars-sized planetoid plowed into the proto-Earth around 4.5 billion years ago, melting the Earth and turning it into an ocean of magma. In the wake of that impact—which also created enough debris to form the moon—the Earth's surface gradually cooled until it was more or less solid. Baker's new theory, like the conventional one, is based on that premise.

The atmosphere following that collision, however, consisted of high-temperature steam that dissolved rocks on the Earth's immediate surface—"much like how sugar is dissolved in coffee," Baker explains. This is where the new wrinkle comes in. "These dissolved minerals rose to the upper atmosphere and cooled off, and then these silicate materials that were dissolved at the surface would start to separate out and fall back to Earth in what we call a silicate rain."

To test this theory, Baker and co-author Kassandra Sofonio, a McGill undergraduate research assistant, spent months developing a series of laboratory experiments designed to mimic the steamy conditions on early Earth. A mixture of bulk silicate earth materials and water was melted in air at 1,550 degrees Celsius, then ground to a powder. Small amounts of the powder, along with water, were then enclosed in gold palladium capsules, placed in a pressure vessel and heated to about 727 degrees Celsius and 100 times Earth's surface pressure to simulate conditions in the Earth's atmosphere about 1 million years after the moon-forming impact. After each experiment, samples were rapidly quenched and the material that had been dissolved in the high temperature steam analyzed.

The experiments were guided by other scientists' previous experiments on rock-water interactions at high pressures, and by the McGill team's own preliminary calculations, Baker notes. Even so, "we were surprised by the similarity of the dissolved silicate material produced by the experiments" to that found in the Earth's crust.

Their resulting paper, published in the journal Earth and Planetary Science Letters, posits a new theory of "aerial metasomatism"—a term coined by Sofonio to describe the process by which silica minerals condensed and fell back to earth over about a million years, producing some of the earliest rock specimens known today.

"Our experiment shows the chemistry of this process," and could provide scientists with important clues as to which exoplanets might have the capacity to harbor life Baker says.

"This time in early Earth's history is still really exciting," he adds. "A lot of people think that life started very soon after these events that we're talking about. This is setting up the stages for the Earth being ready to support life."

More information: Don R. Baker et al, A metasomatic mechanism for the formation of Earth's earliest evolved crust, Earth and Planetary Science Letters (2017). DOI: 10.1016/j.epsl.2017.01.022

http://bit.ly/2pVQ0MM

Giving a single, high dose of radiation directly to the site of a prostate tumor is safe

And results in high patient satisfaction

Vienna, Austria: Doctors have found that treating prostate cancer with a single, high dose of radiation delivered precisely to the site of the tumour results in good quality of life and fewer trips to the hospital, with adverse side effects that are no worse than if the radiation treatment had been given in several lower doses.

Dr Alfonso Gomez-Iturriaga, from the Hospital de Cruces, Baracaldo, Spain, told the ESTRO 36 conference that results were encouraging from the phase II trial of high-dose rate (HDR) brachytherapy, delivered in a single fraction of 19Gy [1], to 45 patients with prostate cancer that was at low or intermediate risk of spreading elsewhere in the body.

"Our study demonstrates that patients do not suffer higher toxicity or a worse quality of life than might be expected with other methods of delivering radiation treatment. In fact, patients are very satisfied with this single outpatient treatment, which they find convenient and which allows them to return rapidly to normal activities.

"It is too early to say that this strategy can be used outside the trial setting, but it seems quite clear that the toxicity and impact on quality of live are very low. Longer follow-up for at least five years is needed to demonstrate definite cancer control."

HDR brachytherapy involves the very precise positioning of catheters, with the aid of ultrasound, at the site of the tumour while the patient is under spinal or general anaesthetic. A radioactive source (iridium-192) is delivered via the catheters to the target, avoiding other structures such as the bladder and the bowel, so that they deliver the maximum dose precisely to the target. The treatment usually takes about 30 minutes.

"The combination of a short lapse of time, real-time 3D visualisation of the target and needles positioning using ultrasound, and the ability to optimise the dose (high doses to target and low doses to surrounding organs at risk), allows for an extraordinary control over the dose administration. To the patient the main advantage is to get the radiotherapy in just one day. Although the brachytherapy is done in an operating room, it is an outpatient procedure and the patient avoids daily radiation treatment," said Dr Gomez-Iturriaga.

Although it has been thought that HDR brachytherapy could be used for treating prostate cancer, until now there has been limited evidence of its safety and efficacy. In this study, 45 consecutive patients received HDR brachytherapy at the Hospital de Cruces between January 2014 and July 2016. The patients had low- or intermediate-risk prostate cancer, mild to moderate symptoms, a tumour volume

that was 60cc or less, and had not yet had surgery or androgen deprivation therapy.

After a follow-up time that ranged from three to 31 months (median average was 16 months), there were no serious (grade 3) adverse side effects from the treatment; six patients had moderate (grade 2) bowel or bladder problems (diarrhoea or needing to pass urine frequently or urgently).

In terms of quality of life, the need to pass urine urgently declined significantly between the first and sixth month after treatment and had returned to normal after a year. There were no significant changes in bowel movements, sexual or hormonal functioning. Sixty percent of patients who had normal sexual functioning before the treatment continued to function normally afterwards. Six months after the radiation therapy, 77% of patients said they were "extremely satisfied" with their treatment and quality of life and 23% were "very satisfied".

Dr Gomez-Iturriaga said these were excellent results in terms of patient satisfaction, quality of life, toxicity and tolerability, as well as safety.

"The precise control over dose delivery inherent in HDR brachytherapy is not readily achievable with low-dose rate (LDR) brachytherapy because of several factors: movement of the radioactive seeds away from the target site, swelling of the prostate after the implant and uncertain dose delivery outside the prostate, which can all contribute to less than optimal dose distributions," he said. "With LDR brachytherapy the actual dose distribution achieved is not known until the post plan quality assurance is completed, several weeks after the treatment. In contrast, with HDR brachytherapy, what you plan to treat is exactly what is actually administered."

President of ESTRO, Professor Yolande Lievens, head of the department of radiation oncology at Ghent University Hospital, Belgium, said: "As radiation oncologists we are working constantly to try to reduce the impact of radiation therapy on patients' lives while maintaining and improving the efficacy of the treatment. Although these results are preliminary in that it is too early to affirm the actual control of the tumour, they suggest that it may be possible to reduce the number of trips to hospital for patients and, at, the same time, to target the treatment more precisely, thereby avoiding adverse side effects. However, we need to follow these patients for longer to ensure the cancer continues to be controlled successfully."

Abstract no: OC-0270, "Prostate 2" proffered papers session, 10.30-11.30 hrs (CEST) on Sunday, 9 May, Room Stolz 1-2.

[1] Radiation dose is measured in units called grays, with one gray (Gy) equivalent to absorbing one joule of radiation energy per kilogram of body tissue.