http://www.medscape.com/viewarticle/811846?src=rss

PSA Screening Does More Harm Than Good, Says New Analysis

To the ongoing debate over whether routine screening for prostate cancer reduces prostate cancer mortality comes a new analysis that suggests that it does more harm than good.

Roxanne Nelson

AMSTERDAM —The total harms that men experience in terms of impotence, incontinence, and other side effects from prostate cancer treatment can severely affect their quality of life, lead author Mathieu Boniol, MD, said here at the European Cancer Conference 2013 (ECCO-ESMO-ESTRO).

Dr. Boniol and colleagues conducted a systematic review of the literature for data on results of prostate-specific antigen (PSA) testing, biopsy rates, and mortality/associated side effects from radical prostatectomy, as well as hospitalization rates associated with biopsy. They also used data from the European Randomized Study of Screening for Prostate Cancer, which is the study showing the most favorable outcomes for PSA screening.

Overall, they found that the harms outweigh the benefits on a population level. This should further discourage the use of routine PSA testing for prostate cancer in the general population, Dr. Boniol said.

He did acknowledge, however, that there are high-risk groups, such as men with a family history of aggressive disease, who can benefit from PSA testing.

"Presently, we do not know if PSA screening decreases mortality," said Dr. Boniol, who is research director at the International Prevention Research Institute (IPRI) and a professor at Strathclyde Institute for Global Public Health at IPRI, Lyon, France. "We have conflicting data. It may save lives, but is testing helpful in the general population?"

The United States Preventive Service Task Force (USPSTF) recently recommended against routine screening with PSA for men who are symptomatic. However, this recommendation has invoked a great deal of controversy and disagreement among physicians and professional organizations.

In Europe, screening varies considerably from country to country, because there is no standard policy across the continent. But Dr. Boniol stated that PSA testing was widely implemented in France, where 55% of men between the ages of 55 and 69 years received PSA testing. He pointed out that family doctors routinely add PSA when ordering routine blood work.

"In France, a large proportion of men are receiving this test," he said during a press briefing. "More than 80% of men aged 65 years have received a PSA test during the past 3 years."

Dr. Boniol emphasized that according to statistics, PSA testing has not lowered prostate cancer mortality. In the 1980s, before the advent of testing, the incidence of prostate cancer in France was 5%, and disease-specific mortality was 2%. But in the era of testing, he explained, incidence is now 14%. "But the risk of dying did not go up, it is still 2%." "We are now finding cancers that never would have appeared in these men," he said, pointing out that upon autopsy, about 70% of men have changes in the prostate that are indicative of cancer, but it is disease that never would have been fatal.

Harms Outweigh Benefit

Dr. Boniol and colleagues estimated the total harm that men would endure if exposed to PSA testing by applying different side-effect estimates to a virtual population of 1000 individuals aged 55 to 69 years. They also included a group of 1000 unscreened men as a control group.

Under the best scenario from prostate cancer screening efficiency, the prevention of 1 death from prostate cancer is associated with a significant additional adverse event burden from undergoing biopsy and from the treatment of the diagnosed disease. These can severely affect the patient's quality of life and argue against using PSA for mass screening, they say.

In a group of 1000 men, the authors estimated that there will be 116 biopsies and 60 cases of prostate cancer. Overall, there will be 119 deaths in this population, of which 5.17 would be as a result of prostate cancer. In the population exposed to screening, there would be 270 biopsies performed and 96 prostate cancers diagnosed. The mortality would be similar, with 191 deaths overall and 4.1 from prostate cancer. For 1 cancer death to be prevented among 1000 men, there would have to be an additional 154 biopsies, of which 9 would require hospitalization for severe adverse events; another 0.2 deaths would result from biopsy complications.

There would be 35 additional prostate cancers diagnosed primarily from low-risk men (32 cases). These cases would be associated with 12 additional cases of impotence, 2 cases of incontinence, and 1 case of fecal incontinence.

The authors note that a high percentage of prostate cancer–related surgery (18%) was performed on men who were older than 70 years. In addition, 183 deaths (0.15%) occurred 60 days after prostate cancer surgery. The overall risk of dying was 0.11% for men aged 40 to 69 years, and this number jumped to 0.36% for those 70 years or older 60 days after surgical intervention.

Awaiting a Tiebreaker

Breast, colorectal, and cervical cancers have well-established screening programs, and prostate cancer could benefit from a similar program because it is a very common cancer, commented Jack Cuzick, PhD, professor of epidemiology at the Wolfson Institute of Preventive Medicine at Queen Mary University of London, United Kingdom.

Dr. Cuzick gave a related talk on prostate cancer screening during European Cancer Conference 2013.

He reminded the audience of the 2 major trials that gave conflicting results as to the benefit of screening. The ERSPC (European Randomized Screening for Prostate Cancer) showed that routine screening lowered prostate cancer mortality, whereas the PLCO (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial) did not show an effect.

Although a number of reasons have been suggested to explain the differences between the 2 trials, Dr. Cuzick noted that a large, currently ongoing trial "may be the tiebreaker."

The UKCAP/PROTECT trial includes 450,000 men and is expected to report its findings in 2016.

"One of the real challenges, and in my mind, the major challenge that has to be resolved before we can really embrace screening is to separate the indolent from aggressive cancers," said Dr. Cuzick. "There is a crucial need to identify which cancers are likely to be fatal, and new molecular markers are needed."

"In countries like the US, where screening is done routinely, the incidence is almost 8-fold higher than mortality, so if you have prostate cancer, there is little chance of dying from it," he continued. "Yet most of these men are having radical treatment. If we can identify which men are likely to benefit from radical treatment accurately, we might be able to get those gains from screening, without overtreatment."

Offering his own opinion, Dr. Cuzick concluded that he does not think we will be ready for prostate cancer screening in the general population until better markers are established.

The study was funded by the International Prevention Research Institute, Lyon, France.

http://arstechnica.com/science/2013/09/strange-unpredictable-chemistry-at-high-pressure/

Strange, unpredictable chemistry at high pressure

Extreme pressure has "a completely different atomic table," vital to understanding space.

by John Timmer - Sept 30 2013, 7:15am TST

The Institute for Advanced Study, which has played host to such luminaries as Albert Einstein and Kurt Gödel, is holding a series of talks to celebrate the birthday of another one of its famous faculty: Freeman Dyson. Dyson made important contributions to a huge variety of fields and gave us the concept of the Dyson Sphere. The talks in his honor covered many of the fields that he influenced, and here, we'll describe the talk by chemist Russel Hemley.

Pretty much everyone agrees that the Universe is run by physics. But for a lot of science, there are so many complicating factors and abstractions that stand between the physics and phenomena we see. Most people would put the boundaries somewhere in fields like biology and geology. Hemley would place a clear boundary at chemistry.

Hemley focuses on extreme conditions, saying that "we have a completely different atomic table at extreme pressures." The elements we're familiar with under normal conditions tend to see their behaviors shift down and to the right as pressures increase. This leads to unexpected results. At 20 GigaPascals (each GigaPascal is about 10,000 atmospheres of pressure), O_2 breaks down and forms an eight-atom box—which happens to be a brilliant scarlet in color. Add another 10GPa, and it turns into a superconductor, as do sulfur, boron, and lithium.

Lithium and other metals also undergo multiple phase transitions, gradually opening up into a complex lattice with open spaces internally. Rather than circulating freely, the electrons often get stuck in these spaces. Hemley referred to this as "electret bonding" and described it as being entirely new.

And it isn't just the elemental properties that change; their reactivity changes. "There is no such thing as a noble element from the perspective of hydrogen," Hemley said, going on to describe a Xenon-hydrogen compound that exists at high temperatures. Every Xenon atom gets surrounded by eight molecules of hydrogen, each of which takes electrons from it.

Hemley said the reason for all these changes comes back to the orbitals occupied by electrons. We tend to think of atoms as solid spheres defined by their outermost electrons (he illustrated this with a photo of a stack of cannon balls). But the reality is that these orbitals can change based on the environment the atom finds itself in. Under pressure, these orbits gradually distort and undergo further changes, some of which may lead to the electrons being booted from orbitals entirely.

The nature of those changes can be difficult to predict from physical principles, and our models of the changes often fail to anticipate the things we see in experiments. (Which is why Hemley suggested that there's a big gap

between physics and chemistry.) So, although we have many models of some of the bizarre things that happen at high pressures, we're not sure how likely they are to reflect reality (this is especially true for hydrogen).
Why does any of this matter? A lot of the material in the natural world is held at extreme pressures: the core of the Earth, the atmosphere of Jupiter, the environments of what now appear to be countless exoplanets like the Super Earths we're discovering. If we're going to understand the environments on these planets, then we may have to understand how minerals we think are familiar behave in a very different pressure regime.
More real-world data may be on the way shortly. Hemley said that the Sloan Foundation is now funding a Deep Carbon Observatory to understand what's happening to carbon compounds that end up at depth below the Earth's crust. And he's excited to see the Juno probe arrive at Jupiter. Some models of hydrogen at pressure suggest that its conducting phase would occur relatively high in Jupiter's atmosphere, which may mean that the giant planet's magnetic field will be generated outside its core.
Juno might be able to determine whether Jupiter has a core as well.

http://www.eurekalert.org/pub_releases/2013-09/uow-zpa093013.php

Zinc, proteins, and an essential cellular balancing act

Shortage of zinc may contribute to diseases like Alzheimer's and Parkinson's

MADISON — Scientists at the University of Wisconsin-Madison have made a discovery that, if replicated in humans, suggests a shortage of zinc may contribute to diseases like Alzheimer's and Parkinson's, which have been linked to defective proteins clumping together in the brain.
With proteins, shape is everything. The correct shape allows some proteins to ferry atoms or molecules about a cell, others to provide essential cellular scaffolding or identify invading bacteria for attack. When proteins lose their shape due to high temperature or chemical damage, they stop working and can clump together — a hallmark of Parkinson's and Alzheimer's. The UW researchers have discovered another stress that decreases protein stability and causes clumping: a shortage of zinc, an essential metal nutrient.
Zinc ions play a key role in creating and holding proteins in the correct shape. In a study just published in the online Journal of Biological Chemistry, Colin MacDiarmid and David Eide show that the gene Tsa1 creates "protein chaperones" that prevent clumping of proteins in cells with a zinc shortage. By holding proteins in solution, Tsa1 prevents damage that can otherwise lead to cell death.
For simplicity, the researchers studied the system in yeast — a single-celled fungus. Yeast can adapt to both shortages and excesses of zinc, says MacDiarmid, an associate scientist. "Zinc is an essential nutrient but if there's too much, it's toxic. The issue for the cell is to find enough zinc to grow and support all its functions, while at the same time not accumulating so much that it kills the cell."
Cells that are low in zinc also produce proteins that counter the resulting stress, including one called Tsa1. The researchers already knew that Tsa1 could reduce the level of harmful oxidants in cells that are short of zinc. Tsa1, MacDiarmid says, "is really a two-part protein. It can get rid of dangerous reactive oxygen species that damage proteins, but it also has this totally distinct chaperone function that protects proteins from aggregating. We found that the chaperone function was the more important of the two."
"In yeast, if a cell is deficient in zinc, the proteins can mis-fold, and Tsa1 is needed to keep the proteins intact so they can function," says Eide, a professor of nutritional science. "If you don't have zinc, and you don't have Tsa1, the proteins will glom together into big aggregations that are either toxic by themselves, or toxic because the proteins are not doing what they are supposed to do. Either way, you end up killing the cell."
While the medical implications remain to be explored, there are clear similarities between yeast and human cells. "Zinc is needed by all cells, all organisms, it's not just for steel roofs, nails and trashcans," Eide says. "The global extent of zinc deficiency is debated, but diets that are high in whole grains and low in meat could lead to deficiency."
If low zinc supply has the same effect on human cells as on yeast, zinc deficiency might contribute to human diseases that are associated with a build-up of "junked" proteins, such as Parkinson's and Alzheimer's. Eide says a similar protective system to Tsa1 also exists in animals, and the research group plans to move ahead by studying that system in human cell culture.

http://www.eurekalert.org/pub_releases/2013-09/afps-tpr093013.php

Testosterone promotes reciprocity in the absence of competition

Boosting testosterone can promote generosity, but only when there is no threat of competition

Boosting testosterone can promote generosity, but only when there is no threat of competition, according to new research published in Psychological Science, a journal of the Association for Psychological Science. The findings show that testosterone is implicated in behaviors that help to foster and maintain social relationships, indicating that its effects are more nuanced than previously thought.

"Testosterone may mediate competitive and potentially antisocial behavior when social challenges or threats need to be confronted and handled," explains lead researcher Maarten Boksem of Rotterdam School of Management, Erasmus University (RSM) in the Netherlands. "But it can also induce prosocial behavior in the absence of these threats, when high status and good reputation are best served by positive behavior."
Animals studies have shown that testosterone plays an important role in dominance behavior, so Boksem and colleagues reasoned that testosterone in humans would also increase a drive for social status.
"But we doubted that this drive would automatically result in aggressive and antisocial behaviors," says Boksem. "We hypothesized that testosterone could perhaps also lead to prosocial behavior if such behavior would be beneficial for maintaining or obtaining social status."
To test this hypothesis, the researchers had 54 female volunteers ingest a liquid solution several hours before participating in an investing game — some volunteers received a placebo solution, while others received a solution with added testosterone.
In the investing game, participants were given €20 (about $27 USD) and were instructed that they could keep the amount they wanted and invest whatever remained with a trustee (another participant). The invested portion would be tripled and split by the trustee, who would keep whatever portion she wanted and return the rest to the investor.
If participants were completely trusting, they could invest all €20 and hope that the trustee would split the final €60 equally. If they wanted to play it safe, they could keep the €20 for themselves.
Each participant took turns playing both investor and trustee. When they were the trustee, they were always given €60, indicating that the investor had entrusted them with the task of splitting up the whole sum.
As investors, participants who received testosterone were, on average, stingier — they placed less trust in the trustee and kept more of their initial money. Participants who received the placebo, on the other hand, were more trusting investors, choosing to invest about €3.20 more than those who received testosterone.
Just as the researchers predicted, testosterone seemed to promote antisocial behavior in response to a potential threat — in this case, a threat to financial resources.
But the opposite effect emerged when participants played the role of trustee. In this case, participants given testosterone chose to give more money back to the investor than participants who had been given a placebo. The results suggest that the trustees felt a responsibility to repay the trust that the investor ostensibly placed in them.
"While we expected the decrease in trust found in the first scenario, the increase in reciprocity was surprisingly strong and robust," Boksem notes. "Testosterone had a more pronounced effect on prosocial behavior than on antisocial behavior."
The fact that testosterone can promote prosocial behavior, at least in certain contexts, provides a more nuanced account than the traditional view of testosterone as being involved in purely aggressive and antisocial behavior, says Boksem. The researchers hope to run a similar study in men and they are currently investigating additional types of social behavior under various conditions of social threat.
For more information about this study, please contact: Maarten A. S. Boksem at maarten@boksem.nl.
Along with Boksem, co-authors on this research include Pranjal Mehta, Bram Van den Bergh, and Ale Smidts of Rotterdam School of Management, Erasmus University (RSM); Veerle van Son, Karin Roelofs, and Alan Sanfey of Radboud University, Nijmegen; and Stefan Trautmann of Tilburg University. All co-authors are in the Netherlands.
This research was supported by the Erasmus Research Institute of Management (ERIM).
http://pss.sagepub.com/content/early/2013/09/26/0956797613495063.abstract

http://www.eurekalert.org/pub_releases/2013-09/eeco-rsh093013.php

Research shows how aspirin may act on blood platelets to improve survival in colon cancer patients

Researchers believe they have discovered how aspirin improves survival in patients diagnosed with colon cancer, the 2013 European Cancer Congress (ECC2013) [1] heard today (Monday).

Although previous research has shown that taking low dose aspirin after being diagnosed with colon cancer improves patient outcome, the reasons why this happens remain unknown. The new research has shown that aspirin improves outcome in patients whose tumour cells express a specific protein on their surface; the protein is known as Human Leukocyte Antigen class I (HLA class I), a cell-surface protein produced by a collection of genes involved in the functioning of the immune system.
The results mean that HLA class I could be used in the future to predict whether or not a patient would benefit from aspirin. The findings also suggest that aspirin's role in improved patient survival could be explained by the interaction of the body's immune system with the effect of aspirin on platelets (cell fragments in the blood that are involved in clotting).

Dr Marlies Reimers, MD, a PhD student, in the Department of Surgery, Leiden University Medical Center, The Netherlands, said: "We think that platelets are involved in cancer spreading to other parts of the body by shielding tumour cells in the bloodstream so that they cannot be recognised by the immune system and can finally colonise distant organs. Aspirin could help to 'unmask' those tumour cells by attacking platelet formation, so that the immune cells can detect and eliminate them."

Dr Reimers and her colleagues used tissue microarray technology [2] to investigate the pattern of protein expression in colon cancer patients whose aspirin use after cancer diagnosis was known and who were registered with the Eindhoven Cancer Registry between 1998 and 2007.

They studied 999 colon cancers to look at HLA class I expression, and expression of the COX-2 enzyme. They also extracted DNA from 663 tumours to look for mutations in the PIK3CA gene. Both COX-2 expression and PIK3CA mutations are known to be involved in the onset of cancer.

They found that low dose (80mg a day) aspirin use after diagnosis improved survival only in patients with tumours expressing HLA class I; if these patients used aspirin they were half as likely to die during the average four years of follow-up as patients with tumours expressing HLA class I that did not use aspirin. This effect of aspirin was not seen in patients without HLA class I expression.

"Therefore, HLA class I might serve as a predictive biomarker to help identify patients who would benefit from aspirin therapy after diagnosis," said Dr Reimers.

"Our results showed that there was no difference in the effect of aspirin in relation to COX-2 expression and PIK3CA mutation."

Until now it was assumed that COX-2 expression or PIK3CA gene mutation played a role in the effectiveness of aspirin use.

Dr Reimers explained: "When we stratified our analyses for COX-2 expression and PIK3CA mutation status, we did not see differences in survival benefit. For example, patients with aspirin use after diagnosis with strong COX-2 expressing tumours had the same survival benefit as tumours with weak COX-2 expression."

Dr Reimers and her colleagues believe their results suggest that aspirin may be acting on two different pathways in colon cancer: one in the preventive setting and the other through the control of metastasis – the spread of cancer to other parts of the body from its primary site.

She said: "The first pathway is through PIK3CA mutations and COX-2 expression in the tumours, which seem to show more effect in the preventive setting. Studies of hereditary colorectal cancers have shown that aspirin can help to prevent the onset of cancer by limiting the formation of polyps in the bowel, which are often the forerunners of cancer, and that this is linked to PIK3CA mutations and COX-2 expression.

"The second pathway, revealed by our results today, is more involved in metastasis, by influencing the platelets in the bloodstream. Although speculative, it may be that the interaction of platelets with HLA positive tumour cells circulating in the blood promotes the metastatic potential of these cells. Aspirin interferes with this interaction, thereby decreasing the risk of metastatic disease and colon cancer-related death."

The researchers say that more evidence from larger studies and clinical trials is required to support their findings.

Some randomised clinical trials have started in the UK and one in Asia – a multi-centre prospective randomised controlled phase III trial of aspirin use in colorectal cancer patients, called the ASCOLT study.

Professor Peter Naredi, who is a member of the Board of Directors of the European CanCer Organisation (ECCO), commented: "The results presented by Dr Reimers and colleagues are very interesting.

The idea that aspirin can enhance the effect of our immune system and that we might be able to identify those cancer patients who best benefit from it, is worth further studies.

Ongoing placebo-controlled randomised trials evaluating the effect of aspirin in colorectal cancer can hopefully strengthen the evidence that aspirin is useful in patients with HLA class 1 expression." [3]

[1] The 2013 European Cancer Congress is the 17th congress of the European CanCerOrganisation (ECCO), the 38th congress of the European Society for Medical Oncology (ESMO) and the 32nd congress of European Society for Therapeutic Radiology and Oncology (ESTRO).

[2] Tissue microarray technology involves using a punching instrument to precisely place up to 1000 tissue samples in a paraffin block for analysis of multiple components.

[3] Professor Naredi is professor of surgery and chair of the department of surgery, Sahlgrenska University Hospital, Gothenburg, Sweden.

[4] This study received no external funding.

http://bit.ly/1bl0mGC

First physical evidence of why you're an owl or a lark

They say the early bird catches the worm, but night owls may be missing far more than just a tasty snack.

11:26 30 September 2013 by Linda Geddes

Researchers have discovered the first physical evidence of structural brain differences that distinguish early risers from people who like to stay up late. The differences might help to explain why night owls seem to be at greater risk of depression.

Around 10 per cent of people qualify as morning people or larks, and a further 20 per cent are night owls – with the rest of us falling somewhere in between. Your lark or night owl status is called your chronotype.

Previous studies have suggested that night owls experience worse sleep, more tiredness during the day and consume greater amounts of tobacco and alcohol. This has prompted some to suggest that they are suffering from a form of chronic jet lag.

To investigate further, Jessica Rosenberg at RWTH Aachen University in Germany and colleagues used diffusion tensor imaging to scan the brains of 16 larks, 23 night owls and 20 intermediate chronotypes. They found a reduction in the integrity of night owls' white matter – brain tissue largely comprised of fatty insulating material that speeds up the transmission of nerve signals – in areas associated with depression.

"We think this could be caused by the fact that late chronotypes suffer from this permanent jet lag," says Rosenberg, although she cautions that further studies are needed to confirm cause and effect.

Skewed body clocks

Although the team controlled for tobacco and alcohol use, it's possible that gene variants that skew people's body clocks towards nocturnal living could affect the structure of the brain. It's also not clear whether the structural changes have any implications for people's health.

"It's interesting that there are individual differences, but we need to understand what is causing them and find ways of creating environments in which those differences can be attenuated," says Derk-Jan Dijk, director of the Surrey Sleep Research Centre in Guildford, UK, who was not involved in the study.

Rosenberg suggests that people's work schedules should change to fit in with their natural sleep patterns, but Djik says there may be an easier way. For example, research published last month suggests that night owls who cut their exposure to artificial light and boosted their exposure to sunlight found their body clocks shifted towards earlier waking and sleeping (Current Biology, DOI: 10.1016/j.cub.2013.06.039).

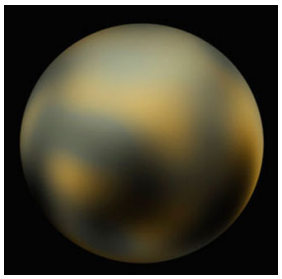
Journal reference: Neuroimage, DOI: 10.1016/j.neuroimage.2013.07.086

http://www.scientificamerican.com/article.cfm?id=air-apparent-plutos-eternal-atmosphere

Air Apparent: Pluto's Eternal Atmosphere

New observations suggest the small world's air never vanishes

By Ken Croswell



A World With Atmosphere: Pluto is never airless. **Image: NASA, ESA, and M. Buie (Southern Research Institute)**

Although billions of kilometers from the sun, frigid Pluto has an Earthly air: an atmosphere made mostly of nitrogen, the same gas that constitutes 78 percent of the air we breathe. But Pluto pursues such an elliptical orbit around the sun that all of that gas might freeze onto its surface when farthest and coldest. On May 4, however, Pluto passed in front of a star in the constellation Sagittarius, allowing observers to watch the atmosphere block some of the star's light and deduce that the air is so substantial it never disappears.

That passage was key to understanding the atmosphere's future, says Catherine Olkin, a planetary scientist at the Southwest Research Institute in Boulder, Colo., whose team tracked the so-called occultation. In work submitted to Icarus she and her colleagues report that Pluto's atmosphere is now thicker than ever before seen. Astronomers discovered the atmosphere in 1988, when Pluto occulted another star. An airless Pluto would have cut off the star's light abruptly, but instead the starlight faded gradually, revealing air with roughly one one-hundred-thousandth the surface pressure of our own—equivalent to the terrestrial atmosphere 80 kilometers high.

Pluto is so distant that completing a single orbit takes it 248 years. Pluto came closest to the sun in 1989 and has been receding from the star ever since. When Pluto ventures out to its most distant point, in 2113, it will be 3 billion kilometers farther, and sunlight on its surface will be 36 percent weaker, than in 1989. "Many scientists have predicted that Pluto's atmosphere would collapse as it traveled away from the sun," Olkin says. "Receiving less sunlight, the gas would condense onto the surface." Mars, whose orbit is also rather elliptical, temporarily loses a quarter of its air every time its southern hemisphere experiences winter, when Martian gas freezes onto the south polar cap.

Pluto is mostly rock, but its crust consists of water ice. At Pluto's temperature of approximately 40 kelvins (–233 Celsius), water is as hard as rock, constituting a stage on which nitrogen and also methane dance back and forth between ice and gas.
The new observations indicate that Pluto's air is now three times denser than in 1988, contradicting models that predicted the atmosphere would someday vanish. Instead, Olkin says, the higher pressure accords with a model indicating that the region around a hundred meters below the surface retains heat during Pluto's close encounters with the sun and releases that heat only slowly, thereby keeping the surface warm enough so that some of the nitrogen always stays gaseous. "As Pluto goes around the sun, its atmosphere does not completely condense," Olkin says. Her work implies that Pluto's water-ice layer is compact, because a porous subsurface would quickly lose its warmth.
"It's a nice piece of work," says John Stansberry, a planetary scientist at the Space Telescope Science Institute. "These kinds of observations are critical for studying seasonal evolution on Pluto." Stansberry worries, however, that Pluto is more complex than the model assumes, which means the atmosphere's behavior is less clear than Olkin asserts. "Based on these results, it's certainly fair to say that Pluto's atmosphere is not going to collapse any time soon, but to say it's going to be there in 2140 is maybe stretching it a bit," Stansberry says.
Both Olkin and Stansberry do agree on a far more famous controversy: Pluto is a planet. In 2005 astronomers discovered Eris, a distant world proclaimed to be larger than Pluto, adding to arguments that Pluto should lose its planetary status and prompting predictions that a plethora of worlds surpassing Pluto in size awaited discovery.
But things didn't work out that way. In 2010 Eris passed in front of a star and failed to live up to the hype. The short duration of the occultation revealed Eris to be just 2,326 kilometers across—versus about 2,350 kilometers for Pluto. And no one has ever found anything else orbiting the sun beyond Neptune's path exceeding Pluto’s size.
Pluto's diameter, however, is uncertain: It could be as small as 2,300 kilometers or as large as 2,400 kilometers. Ironically, the villain is the atmosphere, which bends starlight during occultations and complicates measurements of its diameter.
Fortunately, help is on the way. In July 2015 NASA's New Horizons spacecraft will sail past Pluto and its five known moons. "I'm not sure what we'll see, but I can't wait to get there," Olkin says. "It's going to revolutionize our view."

http://www.eurekalert.org/pub_releases/2013-10/p-sws092413.php

Scientists who share data publicly receive more citations

Long-lived citation benefit, and an increase in data reuse over time is seen for gene expression studies

A new study finds that papers with data shared in public gene expression archives received increased numbers of citations for at least five years. The large size of the study allowed the researchers to exclude confounding factors that have plagued prior studies of the effect and to spot a trend of increasing dataset reuse over time. The findings will be important in persuading scientists that they can benefit directly from publicly sharing their data.
The study, which adds to growing evidence for an open data citation benefit across different scientific fields, is entitled "Data reuse and the open citation advantage". It was conducted by Dr. Heather Piwowar of Duke University and Dr. Todd Vision of the University of North Carolina at Chapel Hill, and published today in PeerJ, a peer reviewed open access journal in which all articles are freely available to everyone.
The study examined citations to over ten thousand articles that generated new gene expression data, a quarter of which had data publicly archived in the GEO and ArrayExpress repositories. Papers with publicly available data received about 9% more citations overall, with the difference increasing over time. The researchers concluded that much of this citation difference was due to actual data reuse.
"Professional advancement in science is still highly dependent on how well your paper gets cited, even in a field like genomics where the data underlying that paper may have far more scientific impact over the long term." said Dr. Vision, a biologist affiliated with the National Evolutionary Synthesis Center and the Dryad Digital Repository. "Until the happy day when hiring and promotion committees catch up with how to value data sharing for its own sake, it is comforting to know that scientists can still receive credit for data sharing in a currency that counts."
The researchers also mined the full text of articles for references to dataset identifiers in order to study trends in data reuse directly. They took the unusual step of discussing the obstacles they encountered in the paper. Dr. Piwowar, at the time of the study a postdoc with the DataONE project, said "We need more open and cohesive infrastructure to support collecting evidence about the process and products of science. This evidence is needed

to inform important policy decisions. For example, data archiving requirements, infrastructure, and education should be informed by evidence about how data is and is not reused."
The mined references revealed that scientists generally stopped publishing papers using their own datasets within two years, while other scientists continued to reuse their data for at least six years. It also showed that data reuse is on the rise. "Not only were the number of reuse papers higher", says Dr. Piwowar, "but analyses from 2002 to 2004 were reusing only one or two datasets, while a quarter of the studies by 2010 were using three or more."
https://peerj.com/articles/175 - your readers will be able to freely access this article at this URL.
Citation to the article: Piwowar HA, Vision TJ. (2013) Data reuse and the open data citation advantage. PeerJ 1:e175 http://dx.doi.org/10.7717/peerj.175
Other Information: The raw data behind this study are publicly available in the Dryad Digital Repository at http://doi.org/10.5061/dryad.781pv. This link will only work after Oct 1st
Funding: This study was funded by U.S. National Science Foundation grants to the DataONE (OCI-0830944) and Dryad (DBI-0743720) projects, and a Discovery grant to Michael Whitlock from the Natural Sciences and Engineering Research Council of Canada.

http://www.eurekalert.org/pub_releases/2013-10/bmj-ea092713.php

Exercise 'potentially as effective' as many drugs for common diseases

More trials urgently needed to inform treatment decisions

The researchers argue that more trials comparing the effectiveness of exercise and drugs are urgently needed to help doctors and patients make the best treatment decisions. In the meantime, they say exercise "should be considered as a viable alternative to, or alongside, drug therapy."
Physical activity has well documented health benefits, yet in the UK, only 14% of adults exercise regularly, with roughly one third of adults in England meeting recommended levels of physical activity. In contrast, prescription drug rates continue to skyrocket, sharply rising to an average of 17.7 prescriptions for every person in England in 2010, compared with 11.2 in 2000. But there is very little evidence on how exercise compares with drugs in reducing the risk of death for common diseases.
So researchers based at the London School of Economics, Harvard Pilgrim Health Care Institute at Harvard Medical School and Stanford University School of Medicine set out to compare the effectiveness of exercise versus drugs on mortality across four conditions (secondary prevention of coronary heart disease, rehabilitation of stroke, treatment of heart failure and prevention of diabetes).
Secondary prevention refers to treating patients with existing disease before it causes significant illness.
They analysed the results of 305 randomised controlled trials involving 339,274 individuals and found no statistically detectable differences between exercise and drug interventions for secondary prevention of heart disease and prevention of diabetes. Among stroke patients, exercise was more effective than drug treatment, while for heart failure, diuretic drugs were more effective than exercise and all other types of drug treatment.
The authors point out that the amount of trial evidence on the mortality benefits of exercise is considerably smaller than that on drugs, and this may have had an impact on their results.
They argue that this "blind spot" in available scientific evidence "prevents prescribers and their patients from understanding the clinical circumstances where drugs might provide only modest improvement but exercise could yield more profound or sustainable gains in health."
Despite this uncertainty, they say that, based on the available data, physical activity is potentially as effective as many drug interventions – and call for more trials to address the disparity between exercise and drug-based treatment evidence. "In cases where drug options provide only modest benefit, patients deserve to understand the relative impact that physical activity might have on their condition," they conclude.

http://www.eurekalert.org/pub_releases/2013-10/usmc-lcb093013.php

Less can be more when removing lymph nodes during breast cancer surgery

A conservative approach to removing lymph nodes is associated with less harm for breast cancer patients and often yields the same results as more radical procedures, researchers at UT Southwestern Medical Center have found.

DALLAS - In the Oct. 2 edition of the Journal of the American Medical Association, lead author Dr. Roshni Rao, associate professor of surgery at UT Southwestern, and other investigators from the Harold C. Simmons Cancer Center reviewed studies on patient outcomes of women who had received various forms of surgical treatment, ranging from removal of one lymph node to prevent the spread of breast cancer to removing the entire network of lymph nodes spanning the armpits.
Until recently, clinical practice guidelines advised complete axillary node dissection – removal of all 20-30 axillary nodes – if a woman's sentinel node biopsy was positive. The sentinel node is generally the first node to

which cancer cells will spread from a primary tumor. A positive sentinel lymph node biopsy indicates the tumor has metastasized and can be used to determine the stage of the cancer. Axillary lymph nodes are distributed at the edge of the chest muscles and into the armpits and lower neck.
For women with no suspicious axillary nodes who undergo breast-conserving therapy, there is little evidence of benefit in doing a complete axillary node dissection compared with sentinel node biopsy alone, the reviewers reported. Breast conserving therapy is defined as partial mastectomy followed by whole breast radiation.
"In the past, axillary nodal status was a critical factor considered in therapy decisions," said Dr. Rao, a breast cancer surgeon. "With the validation of sentinel lymph node biopsy, the same staging information can be obtained with less morbidity and risk to the patient. And now that decisions regarding chemotherapy are often guided by molecular tumor profiling in an era of personalized medicine, there are other avenues to explore beyond aggressive surgeries."
To assess the effect of the guidelines, Dr. Rao and her colleagues reviewed the risks and benefits of sentinel node biopsy as compared with complete axillary node dissection in previous published research. They also compared these procedures with nonsurgical interventions (i.e., additional radiation) in women with breast cancer who do not have palpable lymph nodes or ultrasound evidence that their cancer has spread to the axillary nodes.
They also reviewed the rate of recurrence of axillary node metastases, mortality, morbidity, and complications associated with each intervention, using online medical databases. In all, more than 1,000 results were examined from 17 studies to write the JAMA review.
Avoiding axillary surgery if possible is important, Dr. Rao said, because it can cause shoulder and arm symptoms including lymphedema, severe pain or numbness, and reduced range of motion, and it generally involves longer stays in the hospital, as opposed to sentinel node surgery.
Other authors include Dr. David Euhus, professor of surgery, a Simmons Cancer Center member and part of the Division of Surgical Oncology; Dr. Charles Balch, professor of surgery, oncology and dermatology and Deputy Director of the Johns Hopkins Institute for Clinical and Translational Research; and Helen Mayo, Faculty Associate in the UT Southwestern Library.

http://www.eurekalert.org/pub_releases/2013-10/tmsh-idc100113.php

Inexpensive drug costing less than 3 dollars may minimize damage from heart attack

Collaborative study by Spain and Icahn School of Medicine at Mount Sinai shows potential benefits of administering beta-blocker medication to heart attack patients in ambulance

Early treatment of heart attack patients with an inexpensive beta-blocker drug called metoprolol, while in transit to the hospital, can significantly reduce damage to the heart during a myocardial infarction, according to clinical trial study results published Oct. 1 in the journal Circulation. The study was a collaboration between Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC) in Spain and Icahn School of Medicine at Mount Sinai in New York.
The study, involving emergency ambulances and seven hospitals across Spain, shows this simple, low-cost intervention strategy with metoprolol could be easily extended throughout the world, to provide significant clinical benefit and could change current treatment practice for heart attack patients. Currently, patients receive no medication before undergoing routine angioplasty, the standard treatment for removing a heart blockage that causes a heart attack and damages heart tissue.
Borja Ibáñez, MD, PhD, head of the Experimental Cardiology Group at CNIC and clinical cardiologist at the Hospital Clínico San Carlos in Spain, is the joint lead investigator of this novel study with Valentín Fuster, MD, PhD, General Director of CNIC, who also serves as Director of Mount Sinai Heart and Physician-in-Chief at The Mount Sinai Medical Center. Also, Dr. Fuster will begin his term in 2014 as the next Editor-in-Chief of the Journal of the American College of Cardiology (JACC).
Metoprolol, a drug of the beta-blocker family, has been available for more than 30 years to treat arterial hypertension and other cardiovascular conditions. In this new study, the team of researchers were able to examine the potential usefulness of metoprolol after a heart attack. The clinical trial named METOCARD-CNIC is the first to test metoprolol therapy, at a cost less than three dollars (or less than two euros), in heart attack patients undergoing standard angioplasty treatment procedures.
According to researchers, the potential savings from this medical therapy intervention may go far beyond the low cost of metoprolol itself, since patients experiencing less-extensively damaged heart muscle are less likely to need more costly treatments such as an implantable defibrillator or to require costly hospitalization for treatment of heart failure. Dr. Ibáñez explains, "the savings in healthcare costs will run into millions; a per-patient outlay of less than two euros (or less than three dollars) will over the years save thousands." Currently, researchers are now carrying out a cost-effectiveness analysis to give a firm estimate of the expected savings.

An acute myocardial infarction, or heart attack, is caused by a sudden obstruction of one of the coronary arteries. A blockage requires immediate medical attention and the response time is critical. With every minute that the artery is blocked, the cells of the heart die becoming necrotic, in exponentially growing numbers. According to researchers, the best strategy for limiting the size of an infarct is to carry out the angioplasty procedure as soon as possible. A delay in reopening the coronary artery could mean a larger region of damaged or necrotic tissue. When necrosis is extensive, the heart loses a large part of its pumping strength, which does not recover.

In addition to the high risk of death during the infarction, survivors are likely to suffer from heart failure and severe arrhythmias, and often may die in the months or years following the attack. "The larger the infarct (death of cardiac muscle), the greater the probability that survivors will suffer these complications in the future," says co-lead investigator Dr. Fuster, who also serves as Director of the Zena and Michael A. Wiener Cardiovascular Institute and the Marie-Josée and Henry R. Kravis Center for Cardiovascular Health at The Mount Sinai Medical Center.

Therefore, Dr. Fuster stresses reducing the amount of tissue that is damaged or dies during an infarction is of the utmost importance. Over the last several decades investigators have searched unsuccessfully for a complementary therapy that would further reduce the extent of heart damage.

A total of 270 patients with infarction were recruited since 2010 in four of Spain's regions including: Madrid, Galicia, León, and Cantabria. In the randomized study, patients were assigned to receive either intravenous metoprolol or a placebo treatment at the moment of diagnosis of a myocardial infarction during ambulance transit to the catheterization laboratory. Hospitals in Spain participating in the METOCARD-CNIC trial included: Hospital Clínico San Carlos, Hospital de La Princesa, Hospital 12 de Octubre, Hospital Puerta de Hierro, and Hospital Quirón (Madrid), Hospital Meixoeiro (Galicia), Hospital de León (León), and Hospital Marqués de Valdecilla (Cantabria).

The efficacy of the medical intervention was evaluated by magnetic resonance imaging (MRI) a week after the infarction. MRI measured the mass of damaged heart tissue in all patients. The results showed patients who received metoprolol had much smaller infarcts than those who received the control treatment, and that this smaller infarct size was linked to greater heart contractility.

"MRI is a unique tool for studying heart tissue that enables us to explore in exquisite detail heart function, necrosis, the state of the microcirculation, and many other parameters that are critical in determining the post-infarction status of the myocardium," says Dr. Fuster.

The MRI scans were analyzed at the central CNIC laboratory by cardiologists blinded to the treatment. The CNIC team of cardiologists are experts in this analysis, and most of them received their training from Dr. Fuster at The Mount Sinai Medical Center in New York through a bilateral training agreement with the CNIC.

Initial research investigations about the potential benefits of metoprolol were first launched at The Mount Sinai Medical Center in 2006 while Dr. Ibáñez was working there with Dr. Fuster and Mount Sinai's Juan Badimon, PhD, Director of the Atherothrombosis Research Unit at its Cardiovascular Institute. Their preclinical research findings about metoprolol in animal models, analyzed using MRI and published in the journal Circulation in 2007, showed early administration of metoprolol during heart attack increased myocardial salvage and led to the translational medicine potential for human clinical trial.

The research team is currently investigating the molecular mechanism underlying the therapeutic action of metoprolol. Antonio Fernández-Ortiz, MD, PhD, co-investigator on the METOCARD-CNIC study and leader of this sub-study, explains that "this project analyzes the effect of metoprolol on the interaction of blood platelets with inflammatory cells, which might explain the benefit of early treatment with this drug as soon as possible after diagnosis of a heart attack."

Researchers are planning to extend the clinical trial to a much larger number of patients in a multinational study, to demonstrate not only a reduced infarct size, but also a reduced mortality in patients who receive early metoprolol during transit to hospital. The CNIC research team, colleagues in the emergency services, and hospitals are already working on the logistics of a new international clinical trial.

In an editorial accompanying the published article in Circulation, experts from the Technische Universität and the Munich Heart Alliance, Gjin Ndrepepa and Adnan Kastrati, affirmed that, if confirmed by a subsequent analysis of large numbers of patients, the results of METOCARD-CNIC trial are likely to lead to a change in clinical practice: "In this regard, a pharmaco-protective strategy able to reduce infarct size by 20 percent when used in conjunction with primary PCI nurtures great hope in clinical benefit." In addition, Dr. Ibáñez adds: "the professionals of the emergency ambulance services were the driving force of this study. Their hard work is a professional and human example to us all; we are deeply humbled by the readiness of so many professionals to commit themselves 24 hours a day, 365 days a year to an altruistic project."

Funding for this METOCARD-CNIC clinical trial study was received from the Spanish Ministry of Economy and Competitiveness, a competitive research grant from the CNIC, and the assignation of CNIC as a Severo Ochoa center in 2011. Additionally, support was received from the Spanish Ministry of Health, Social Services and Equality, Philips, the Fundación Mutua Madrileña, and from members of the Pro-CNIC Foundation, which manages private contributions to the CNIC.

http://www.eurekalert.org/pub_releases/2013-10/uocb-blk100113.php

Bad luck? Knocking on wood can undo jinx: study

Knocking on wood is the most common superstition in Western culture used to reverse bad fortune or undo a "jinx."

Other cultures maintain similar practices, like spitting or throwing salt, after someone has tempted fate. Even people who aren't particularly superstitious often participate in these practices. A new study from the University of Chicago Booth School of Business finds that these superstitions actually do "reverse" perceived bad fortune.

People believe that negative outcomes are especially likely after a jinx. If someone says, "No one I know will ever get into a car accident," for example, it often feels that a car accident is likely to occur. But people's elevated concerns after tempting fate can be eliminated if they engage in a ritual to undo that bad luck.

Noting that many of the most common rituals for undoing bad luck – knocking on wood, spitting, and throwing salt – all seem to involve movements that exert force away from a person, researchers set out to test whether the avoidant nature of the action is key for reducing the negative expectations and heightened concern generated by tempting fate.

"Our findings suggest that not all actions to undo a jinx are equally effective. Instead, we find that avoidant actions that exert force away from one's representation of self are especially effective for reducing the anticipated negative consequences following a jinx" says Jane Risen, associate professor of behavioral science at Chicago Booth. Risen conducts research in the areas of judgment and decision-making, intuitive belief formation, magical thinking, stereotyping and managing emotion.

"Engaging in an avoidant action seems to create the sense that the bad luck is being pushed away," Risen says.

Titled "Reversing One's Fortune by Pushing Away Bad Luck," the study was published in the Journal of Experimental Psychology: General. Co-authors are Yan Zhang of National University of Singapore and former Chicago Booth student, and Christine Hosey, a current Chicago Booth student.

In five separate experiments, researchers had participants either tempt fate or not and then engage in an action that was either avoidant or not. The avoidant actions included those that were superstitious – like knocking on wood – or non-superstitious – like throwing a ball.

They found that those who knocked down (away from themselves) or threw a ball believed that a jinxed negative outcome was less likely than participants who knocked up (toward themselves) or held a ball. In addition, the researchers found that engaging in an avoidant action had its effect by leading people to have a less vivid mental image of the negative event.

http://bit.ly/GFl8GA

Once infertile woman gives birth after novel Japanese surgical experiment

A 30-year-old infertile woman gave birth after surgeons removed her ovaries and re-implanted tissue they treated in a lab, researchers have reported.

New York – The experimental technique was only tried on a small group of Japanese women with a specific kind of infertility problem, but scientists hope it can also help those in their early 40s who have trouble getting pregnant because of their age.

The new mother gave birth to a son in Tokyo last December, and she and the child continue to be healthy, said Dr. Kazuhiro Kawamura of the St. Marianna University School of Medicine in Kawasaki. He and others describe the technique in a report published online Monday by the Proceedings of the National Academy of Sciences.

The mother, who was not identified, had been diagnosed with primary ovarian insufficiency, an uncommon form of infertility sometimes called premature menopause. It appears in about 1 percent of women of childbearing age. The cause of most cases is unknown, but the outcome is that the ovary has trouble producing eggs. That leaves women with only a 5 to 10 percent chance of having a baby unless they get treated. The standard treatment is using donor eggs.

After the experimental procedure, Kawamura and colleagues were able to recover eggs from five of their 27 patients. One woman went on to have a miscarriage, one did not get pregnant, and two more have not yet attempted pregnancy, Kawamura said.

The approach differs from what has been done to preserve fertility in some cancer patients who had normal ovarian tissue removed and stored while they underwent cancer treatments, and then put back. The new work involved ovaries that were failing to function normally.

In the ovary, eggs mature in structures called follicles. For women with the condition the new study targeted, the follicles are either missing or failing to produce eggs. The experimental treatment was designed to stimulate dormant follicles.
First, the women's ovaries were removed and cut into strips, which were then frozen. Later, the strips were thawed and cut into tiny cubes, a step intended to stimulate maturation of the follicles. Then the cubes were treated with drugs to stimulate further development of the follicles. Finally, the cubes were transplanted just under the surface of the women's fallopian tubes.
Within six months, eight women showed signs of follicle maturation, and five of them produced eggs for fertilization in the lab with their husbands' sperm. The fertilized eggs were grown into early embryos that were frozen for preservation. In the three attempts at pregnancy, one or two embryos were implanted in the women.
The researchers found that half the 27 patients had no follicles at all, which meant the treatment could not help them, said Aaron Hsueh of Stanford University, senior author of the study. He also said researchers hope to find a way to stimulate follicles without removing the ovaries.
Dr. Sherman Silber of the Infertility Center of St. Louis criticized the approach, saying he has had success by using drugs rather than surgery to treat the condition. He also disagreed with the researchers' explanation for why their treatment worked.
Some other experts said treatment with drugs often does not work. Still, the new results, experts cautioned, must be viewed as preliminary.
"It shows a lot of promise (but) I don't think it's even close to being ready" for routine use, said Dr. Mark Sauer of the Columbia University Medical Center in New York. Dr. Amber Cooper of Washington University in St. Louis called the technique "very much an experimental method."
The reported efficiency is very low, and the possible health risk to babies born from the method is unknown, said David Albertini of the University of Kansas Medical Center. "One success does not mean we have a treatment. . . . Stay tuned," he said.
He and others were also skeptical of the researcher's suggestion that the procedure would help women between the ages of 40 and 45. Eggs from women of that age often show genetic abnormalities, many of which would prevent a live birth, said Dr. Marcelle Cedars of the University of California, San Francisco Medical Center. Stimulating egg production wouldn't overcome that problem, she said.
Kawamura released a photo of himself holding the newborn shortly after delivering him. He said the mother hopes to have another child with one of the frozen embryos in storage from her treatment.

http://www.sciencedaily.com/releases/2013/09/130930211701.htm

Concerns Over Mercury Levels in Fish May Be Unfounded

New research from the Children of the 90s study at the University of Bristol suggests that fish accounts for only seven per cent of mercury levels in the human body.

In an analysis of 103 food and drink items consumed by 4,484 women during pregnancy, researchers found that the 103 items together accounted for less than 17 per cent of total mercury levels in the body.
Concerns about the negative effects of mercury on fetal development have led to official advice warning against eating too much fish during pregnancy. This new finding, published today in Environmental Health Perspectives, suggests that those guidelines may need to be reviewed.
Previous research by Children of the 90s has shown that eating fish during pregnancy has a positive effect on the IQ and eyesight of the developing child, when tested later in life. Exactly what causes this is not proven, but fish contains many beneficial components including iodine and omega-3 fatty acids.
After fish (white fish and oily fish) the foodstuffs associated with the highest mercury blood levels were herbal teas and alcohol, with wine having higher levels than beer. The herbal teas were an unexpected finding and possibly due to the fact that herbal teas can be contaminated with toxins.
Another surprise finding was that the women with the highest mercury levels tended to be older, have attended university, to be in professional or managerial jobs, to own their own home, and to be expecting their first child.
Overall, however, fewer than one per cent of women had mercury levels higher than the maximum level recommended by the US National Research Council. There is no official safe level in the UK.
The authors conclude that advice to pregnant women to limit seafood intake is unlikely to reduce mercury levels substantially.
Speaking about the findings, the report's main author, Professor Jean Golding OBE, said:
'We were pleasantly surprised to find that fish contributes such a small amount (only seven per cent) to blood mercury levels. We have previously found that eating fish during pregnancy has many health benefits for both mother and child. We hope many more women will now consider eating more fish during pregnancy. It is

important to stress, however, that pregnant women need a mixed balanced diet. They should include fish with other dietary components that are beneficial including fruit and vegetables.'

Jean Golding, Colin D. Steer, Joseph R. Hibbeln, Pauline M. Emmett, Tony Lowery, Robert Jones. Dietary Predictors of Maternal Prenatal Blood Mercury Levels in the ALSPAC Birth Cohort Study. Environmental Health Perspectives, 2013; DOI: 10.1289/ehp.1206115

http://phys.org/news/2013-10-universally.html

Making clean drinking water universally available is 'achievable'

Making clean drinking water globally accessible is one of the biggest challenges of this century. Yet a new study by Oxford University contends that this goal is achievable if the key elements of good governance and management are adopted.

Phys.org - It proposes a framework built on examples of good practice in South Asia and sub-Saharan Africa – areas which the authors argue present the most severe challenges of all the developing countries. The study warns, however, that the scale of investment necessary to update the often neglected, ageing infrastructure of pipelines or water pumps goes beyond the narrow project timeframes favoured by politicians.

The findings are published in a landmark collection of papers on water security, risk and society by the journal Philosophical Transactions of the Royal Society A.

The study says the problem of providing clean water is most acute in developing countries, particularly in Africa, where creaking infrastructures struggle to keep pace with fast-growing urban populations; in rural areas, millions of water pumps stand unused waiting to be repaired. Despite hitting the Millennium Development Goal for drinking water access in 2012, over 780 million people still do not have safe and reliable drinking water, says the report, resulting in largely preventable health problems that most affect women and children.

Based on nine case studies in Cambodia, India, Kenya, Uganda and Senegal, the authors analysed new data in rural and urban areas to compare what the authors call the under-researched aspects of water security: the institutional side of how water supplies are delivered, their operation and management systems. They examined water payment systems and the quality of service, such as how quickly leaks or pumps were fixed, and whether populations had water on demand or a regularly disrupted service.

The study suggests that a critical factor in all cases is to have a good system for maintaining existing water supplies. Additionally, new information systems were found to be important for improving the way the quality of service was monitored. In West Africa, for instance, a structured crowd sourcing platform is used by water scheme managers to input weekly data via a mobile phone application; in East Africa, a mobile-enabled monitoring system is leading to faster repair times for water pumps.

Late bills are still a huge problem in developing countries, so consequently there is often a failure to recoup the service costs needed to invest in the infrastructure. The study highlights a successful mobile water payment system adopted in one Kenyan city, which was the preferred way of paying bills for 85% of customers who would otherwise often have to queue in water company offices. More efficient and transparent payment systems were not only found to reduce debts, but also helped root out corrupt practices which diverted water payments into illegitimate channels.

The study warns that barriers to progress include the vested interests of individuals benefiting from the status quo, and misguided public investments which are short-term and without any real measures of performance. However, the authors argue that these findings provide concrete evidence to demonstrate how drinking water risks can be managed and reduced 'even in the most difficult and challenging contexts'.

Lead author Dr Rob Hope, from the Smith School of Enterprise and the Environment at the University of Oxford, said: 'We hope this study provides a framework to design policy and guide investments to systematically reduce drinking water risks in urban and rural contexts. These case studies demonstrate a variety of approaches taken by countries in some of the most challenging circumstances.

'They set benchmarks by which others can measure their own progress. Our examples include water managers who have introduced both bonus systems to reward good performance and competitions between different areas to drive up standards of service. Some water service providers have found ways of giving subsidies to expand access to water customers on the lowest incomes. There are other examples of initiatives to promote greater efficiency which can mean leaks or water pumps get fixed more quickly or water rationing can be replaced with a continuous service.

'Despite the often gloomy outlook voiced by some on the prospects for making drinking water more accessible, these case studies in sub-Saharan Africa and South Asia show there are realistic pathways to transform water services, thereby potentially improving the health of the millions of people who depend upon them.'

Meanwhile, in the same collection of papers in the journal, Professor David Bradley of Oxford University writes that the monitoring programme developed to measure the success of the Millennium Development Goals

(MDGs) for improving domestic water supply and basic sanitation worldwide has been effective. His paper discusses whether the successor to the MDGs for 2015 on water security will also include water for agriculture, flood control and the environment after 2015.

More information: Rob Hope study: rsta.royalsocietypublishing.org/content/371/2002/20120417.full
David Bradley study: rsta.royalsocietypublishing.org/content/371/2002/20120420.full

http://bit.ly/GFBWwh

Pharmaceutical Industry Scrambles to Fast-Track Drugs

"Breakthrough therapy" status is much sought after, but there is confusion about its definition and impact

By Heidi Ledford and Nature magazine | Tuesday, October 1, 2013 | 2

The experimental cancer drug ibrutinib has wowed in clinical trials, beating deadly blood cancers without the painful side effects of currently approved therapies. And it has raced through development and regulatory hurdles, in part thanks to a US program to accelerate the development of particularly promising drugs, says its developer Pharmacyclics, based in Sunnyvale, California.

The US Food and Drug Administration (FDA) launched the 'breakthrough therapy' designation in 2012, and the label has been eagerly embraced by the pharmaceutical industry. Recent months have seen a steady stream of drugs being submitted for review. For some firms — particularly young ones — the designation can bring an extra boost of cash by raising investor confidence.

But for all the fanfare, the industry is also watching closely to see exactly what benefits can be gained by having a drug reviewed through this route. "It's like winning a beauty pageant," says Timothy Coté, a former director of the FDA's Office of Orphan Products Development who now runs a consultancy called Coté Orphan Consulting in Silver Spring, Maryland. "It doesn't have specific tangible outcomes, but it does appear to have enlivened the community."

The breakthrough therapy designation was created by the FDA Safety and Innovation Act, a law that requires the agency to fast-track promising drugs for serious or life-threatening conditions. The FDA aims to do this by meeting early and often with developers, as well as working with them to design clinical trials that deliver the needed data quickly and efficiently.

The industry leapt on the opportunity, so far submitting 99 applications for the designation. But the flurry of applications may partly be a product of confusion, says Coté: the FDA has avoided laying out detailed descriptions of what constitutes a breakthrough, and some companies are unsure of the criteria. "Most biotech chief executives with something in the clinic think that they're already there," Coté says — but 47 of the applications submitted in the past year have been denied. In most cases the denials are due to insufficient clinical data, the FDA says.

Although the lack of clear guidelines could be deemed confusing, the FDA's avoidance of hard-and-fast criteria can actually be an advantage for some drugs, says Keith Flaherty, an oncologist at Massachusetts General Hospital in Boston. He was pleased, for example, to see the FDA bestow breakthrough status on a melanoma therapy called lambrolizumab. The drug, which is made by Merck (based in Whitehouse Station, New Jersey), is one of several in development that stimulate the immune system to fight cancer by blocking a protein called PD1. Lambrolizumab works in only about 38% of patients, which is well below the response rate for some other cancer drugs in development. However, doctors champion it because it has tolerable side effects and can yield unusually long-lasting responses. "Having it get that designation really put a spring in the step of many people in our community," says Flaherty. "It showed us that the FDA really gets the importance of these drugs."

There are lingering concerns that other aspects of the drug-development process might delay the ultimate impact of the breakthrough-designated compounds. Jeff Allen, executive director of the patient-advocacy group Friends of Cancer Research in Washington DC, notes that drugs are increasingly developed alongside medical tests that will select the patients who are most likely to benefit from them. The new law does not address the development of such tests, but unless their evaluation and approval is accelerated, a breakthrough drug — even if approved — may not achieve its full potential in the clinic, he says.

Coté, despite being a fan of the program, says that it might not have much of an impact on review times because the FDA has always prioritized promising applications. The biggest benefit, says Steven Grossman, founder of the consultancy HPS Group in Silver Spring, might be for small companies that can use the designation to get the FDA's attention earlier in development than they normally might.

Financial analysts expect ibrutinib to be approved by the end of the year, and Coté thinks that most of the breakthrough designees will ultimately prevail. "If the FDA likes what you're doing, that can't be a bad thing," he says.

http://www.eurekalert.org/pub_releases/2013-10/afps-ecm100113.php

Eye contact may make people more resistant to persuasion

Making eye contact has long been considered an effective way of drawing a listener in and bringing him or her around to your point of view.

But new research shows that eye contact may actually make people more resistant to persuasion, especially when they already disagree. The new findings are published in Psychological Science, a journal of the Association for Psychological Science.

"There is a lot of cultural lore about the power of eye contact as an influence tool," says lead researcher Frances Chen, who conducted the studies at the University of Freiburg, Germany, and is now an assistant professor at the University of British Columbia. "But our findings show that direct eye contact makes skeptical listeners less likely to change their minds, not more, as previously believed," says Chen.

To investigate the effects of eye contact in situations involving persuasion, Chen and colleagues took advantage of recently developed eye-tracking technology.

They found that the more time participants spent looking at a speaker's eyes while watching a video, the less persuaded they were by the speaker's argument – that is, participants' attitudes on various controversial issues shifted less as they spent more time focusing on the speaker's eyes.

Spending more time looking at the speaker's eyes was only associated with greater receptiveness to the speaker's opinion among participants who already agreed with the speaker's opinion on that issue.

A second experimental study confirmed these findings.

Participants who were told to look at the speaker's eyes displayed less of a shift in attitudes than did those participants who were told to look at the speaker's mouth. The results showed that participants who looked at the speaker's eyes were less receptive to the arguments and less open to interaction with the advocates of the opposing views, and were thus more difficult to persuade.

According to Julia Minson of the Harvard Kennedy School of Government, co-lead researcher of the studies, the findings highlight the fact that eye contact can signal very different kinds of messages depending on the situation. While eye contact may be a sign of connection or trust in friendly situations, it's more likely to be associated with dominance or intimidation in adversarial situations. So, while we might be tempted make the demand, "Look at me when I'm talking to you!" of a listener, this demand may have unintended consequences: "Whether you're a politician or a parent, it might be helpful to keep in mind that trying to maintain eye contact may backfire if you're trying to convince someone who has a different set of beliefs than you," says Minson.

The researchers are planning to look at whether eye contact may be associated with certain patterns of brain activity, the release of stress hormones, and increases in heart rate during persuasion attempts.

"Eye contact is so primal that we think it probably goes along with a whole suite of subconscious physiological changes," says Chen.

Co-authors on the study include Julia Minson of the Harvard Kennedy School, and Maren Schöne and Markus Heinrichs of the University of Freiburg.

The article abstract is available online: http://pss.sagepub.com/content/early/2013/09/25/0956797613491968.abstract

F. S. Chen is supported by a research fellowship from the Alexander von Humboldt Foundation. M. Heinrichs gratefully acknowledges grant support from the Swiss National Science Foundation (SNSF; PP001-114788) and the German Research Foundation (DFG; He 5310/1-1).

http://www.sciencedaily.com/releases/2013/10/131001124020.htm

Compound May Keep Survivors of Brain Aneurysms from Succumbing to Stroke

Johns Hopkins researchers, working with mice, say they have identified a chemical compound that reduces the risk of dangerous, potentially stroke-causing blood vessel spasms that often occur after the rupture of a bulging vessel in the brain.

They say their findings offer clues about the biological mechanisms that cause vasospasm, or constriction of blood vessels that reduces oxygen flow to the brain, as well as potential means of treating the serious condition in humans.

When an aneurysm -- essentially a blister-like bulge in the wall of a blood vessel -- bursts, blood spills into the fluid-filled space that cushions the brain inside the skull. If a patient survives a ruptured aneurysm, between 20 and 40 percent of the time, this brain bleed, called a subarachnoid hemorrhage, will lead to an ischemic stroke within four to 21 days, even when the aneurysm is surgically clipped.

"We're a long way from applying this to humans, but it's a good start," says Johns Hopkins neurosurgery resident Tomas Garzon-Muvdi, M.D., M.Sc., one of the authors of the study led by Rafael J. Tamargo, M.D., and described in the October issue of the journal Neurosurgery.

To conduct their experiments, Garzon-Muvdi and his colleagues took blood from mouse leg arteries and injected it behind their necks to mimic what happens in a subarachnoid hemorrhage. Then they gave the mice a compound called (S)-4-carboxyphenylglycine (S-4-CPG), a placebo or nothing at all. The mice given S-4-CPG developed less vasospasm, looked better and were more active than those in the other two groups.
The scientists also found concentrations of the drug in the brains of the mice, showing that it was able to cross the often impermeable blood-brain barrier. The researchers chose the compound because it is similar to drugs that have been used in stroke research in rodents. It is not approved for any use in humans.
Garzon-Muvdi explains that when blood vessels break anywhere but the brain, the body's immune cells easily clear the blood cells and their remnants from the area. This is what happens with a bruise, when immune cells rush to the area, and a chemical cascade scavenges and disperses the remnants of excess blood components. When a blood vessel bursts in the space around the brain, however, the blood is trapped. A subsequent inflammatory response brings key immune system cells into the space, where they secrete the neurotransmitter glutamate outside of the blood vessels where it shouldn't be, promoting dangerous vasospasm in those blood vessels. This can lead to ischemic stroke, the most common type of stroke, caused by a blockage of a blood vessel in the brain. Death or serious disability may result.
The Johns Hopkins researchers say S-4-CPG keeps glutamate "in check," prevents or reduces vasospasm and allows oxygen-filled blood to continue flowing into the brain.
According to the National Institutes of Health, subarachnoid hemorrhage caused by a cerebral aneurysm that breaks open occurs in about 40 to 50 out of 100,000 people over age 30. Patients may die immediately, but those who survive are still at elevated risk for developing an ischemic stroke in the days afterward. These patients are often watched very carefully in the intensive care unit for one to two weeks to search for early signs of vasospasm so that doctors can take steps to prevent or limit damage from a stroke.
In the ICU, doctors can order regular angiograms or ultrasounds to measure blood flow in vessels. If need be, they can increase blood pressure to send blood through vessels faster in the hopes of counteracting the constriction.
A drug to prevent stroke after a serious subarachnoid hemorrhage that follows the rupture of an aneurysm would improve quality of life for patients, Garzon-Muvdi says, and could potentially save millions of dollars in health care costs if patients don't have to endure extensive hospital stays to monitor for a delayed stroke.

http://www.eurekalert.org/pub_releases/2013-10/lu-kmb100213.php

Key mechanism behind herpes revealed

Researchers at Lund University in Sweden have for the first time managed to measure the internal pressure that enables the herpes virus to infect cells in the human body.

The discovery paves the way for the development of new medicines to combat viral infections. The results indicate good chances to stop herpes infections in the future.
A virus comprises a thin shell of protein, within which are its genes. A long-standing theory has been that a virus has high internal pressure because it is so tightly packed with genetic material. The pressure means that they can infect a cell by ejecting the genes at high force and speed. The cell is then duped into becoming a small 'virus factory' that produces new viruses, multiplying the number. However, no one has previously succeeded in measuring the internal pressure of a virus that can infect humans.
Biochemist Alex Evilevitch from Lund University and Carnegie Mellon University in Pittsburgh, USA, has measured the pressure inside the herpes virus HSV-1 (herpes simplex virus 1) together with a research team in the US. The study has been published in the Journal of the American Chemical Society, JACS.
"The pressure explains the way all eight known herpes viruses that infect humans inject their genes into our cells", said Alex Evilevitch.
This includes both of the two most common forms of herpes, which cause cold sores and genital herpes, as well as Varicella zostervirus, which causes chickenpox and shingles, Epstein-Barr virus, which leads to glandular fever, and viruses linked to various forms of cancer.
In previous studies, Alex Evilevitch has also demonstrated that bacteriophages, viruses that infect bacteria, have a high internal pressure. Bacteriophages and herpes viruses separated in evolution billions of years ago, but have retained the same pressure-driven method of ejecting their genes. Evilevitch therefore believes this must be a key mechanism for viral infection.
The discovery could lead to new drugs. The medication that exists to combat viral infections is very specialised and if a virus mutates, which often happens, the medicine can become less effective. However, if a treatment could be developed that reduces the pressure within the virus shell, it would probably be possible to fight many

different types of viral infection with the same drug. In addition, the medication would work even if the virus mutated, because mutations do not affect the internal pressure of a virus.
"The results of the present study are the first step towards the goal of developing a drug of this type, and we already have positive preliminary data that shows that the herpes infection can be stopped. It feels great to know that this research will help to fight infections that are as yet incurable", said Alex Evilevitch.
The study was funded by the Swedish Research Council, the National Science Foundation and the National Institutes of Health (NIH).

http://www.sciencedaily.com/releases/2013/10/131001151132.htm

Researchers Propose New Theory to Explain Seeds of Life in Asteroids

A new look at the early solar system introduces an alternative to a long-taught, but largely discredited, theory that seeks to explain how biomolecules were once able to form inside of asteroids.

A new look at the early solar system introduces an alternative to a long-taught, but largely discredited, theory that seeks to explain how biomolecules were once able to form inside of asteroids. In place of the outdated theory, researchers at Rensselaer Polytechnic Institute propose a new theory -- based on a richer, more accurate image of magnetic fields and solar winds in the early solar system, and a mechanism known as multi-fluid magneto-hydrodynamics -- to explain the ancient heating of the asteroid belt.
Although today the asteroid belt between Mars and Jupiter is cold and dry, scientists have long known that warm, wet conditions, suitable to formation of some biomolecules, the building blocks of life, once prevailed. Traces of bio-molecules found inside meteorites -- which originated in the asteroid belt -could only have formed in the presence of warmth and moisture. One theory of the origin of life proposes that some of the biomolecules that formed on asteroids may have reached the surfaces of planets, and contributed to the origin of life as we know it.
"The early sun was actually dimmer than the sun today, so in terms of sunlight, the asteroid belt would have been even colder than it is now. And yet we know that some asteroids were heated to the temperature of liquid water, the 'goldilocks zone,' which enabled some of these interesting biomolecules to form," said Wayne Roberge, a professor of physics within the School of Science at Rensselaer, and member of the New York Center for Astrobiology, who co-authored a paper on the subject with Ray Menzel, a graduate student in physics. "Here's the question: How could that have happened? How could that environment have existed inside an asteroid?"
In the paper, titled "Reexamination of Induction Heating of Primitive Bodies in Protoplanetary Disks" and published today in The Astrophysical Journal, Menzel and Roberge revisit and refute one of two theories proposed decades ago to explain how asteroids could have been heated in the early solar system. Both of the established theories -- one involving the same radioactive process that heats the interior of Earth, and the other involving the interaction of plasma (super-heated gases that behave somewhat like fluids) and a magnetic field -- are still taught to students of astrobiology. Although radioactive heating of asteroids was undoubtedly important, current models of radioactive heating make some predictions about temperatures in the asteroid belt that are inconsistent with observations.
Motivated by this, Roberge and Menzel reviewed the second of the two theories, which is based on an early assessment of the young sun and the premise that an object moving through a magnetic field will experience an electric field. According to this theory, as an asteroid moves through the magnetic field of the solar system, it will experience an electric field, which will in turn push electrical currents through the asteroid, heating the asteroid in the same way that electrical currents heat the wires in a toaster.
"It's a very clever idea, and the mechanism is viable, but the problem is that they made a subtle error in how it should be applied, and that's what we correct in this paper," said Roberge. "In our work, we correct the physics, and also apply it to a more modern understanding of the young solar system."
Menzel said the researchers have now definitively refuted the established theory.
"The mechanism requires some extreme assumptions about the young solar system," Menzel said. "They assumed some things about what the young sun was doing which are just not believed to be true today. For example, the young sun would have had to produce a powerful solar wind which blew past the asteroids, and that's just no longer believed to be true."
The solar wind, and the plasma stream it produced, was not as powerful as early theorists assumed, and the researchers have corrected those calculations based on the current understanding of the young sun. Roberge said the early theorists also incorrectly calculated the position of the electric field asteroids would have experienced. Roberge said that, in reality, an electric field would have permeated the asteroid and the space around it, a mistake very few researchers would have realized.

"We've calculated the electric field everywhere, including the interior of the asteroid," Roberge said. "How that electric field comes about is a very specialized thing; about 10 people in the world study that kind of physics. Fortunately, two of them are here at RPI working together."
What emerges, Menzel and Roberge said, is a new possibility, based on the corrected understanding of the electric fields the asteroids would have experienced, the solar wind and plasma conditions that would have prevailed, and a mechanism known as multi-fluid magneto-hydrodynamics.
Magneto-hydrodynamics is the study of how charged fluids -- including plasmas -- interact with magnetic fields. The magnetic fields can influence the motion of the charged fluid, or plasma, and vice versa. Magneto-hydrodynamics had a moment of fame as the propulsion system for an experimental nuclear submarine in the 1990 movie The Hunt for Red October.
Multi-fluid magneto-hydrodynamics are an even more specialized variation of the mechanism that apply in situations where the plasma is very weakly ionized, and the neutral particles behave distinctly from the charged particles.
"The neutral particles interact with the charged particles by friction," Menzel said. "So this creates a complex problem of treating the dynamics of the neutral gas and allowing for the presence of the small number of charged particles interacting with the magnetic field."
Menzel and Roberge said their new theory is promising, but it raises many questions that merit further exploration. "We're just at the beginning of this. It would be wrong to assert that we've solved this problem," Roberge said. "What we've done is to introduce a new idea. But through observations and theoretical work, we know have a pretty good paradigm."
And much as Menzel and Roberge benefited from recent progress in understanding the physical conditions in an emerging planetary system, they hope their own work will advance the field of astrophysics.
"There are a lot of byproducts of this work because, in the course of doing this, we had to really zero in on how an asteroid interacts with the plasma of the young solar system," said Roberge. "There are a lot of physical processes that we had to consider that have not been considered in this context before."
Raymond L. Menzel, Wayne G. Roberge. Reexamination of Induction Heating of Primitive Bodies in Protoplanetary Disks. The Astrophysical Journal, 2013

http://www.sciencedaily.com/releases/2013/10/131002134405.htm

You Say He's Just a Friend, but Your Voice Says Differently

Think your partner is cheating? His or her voice may be a dead giveaway.

New research by Albright College associate professor of psychology Susan Hughes, Ph.D., has found that men and women alter their voices when speaking to lovers versus friends and that such variations can potentially be used to detect infidelity.
"It's not just that we change the sound of our voice, but that others can easily perceive those changes," said Hughes, an expert in evolutionary psychology and voice perception. The findings are included in a new article, "People Will Know We Are in Love: Evidence of Differences Between Vocal Samples Directed Toward Lovers and Friends," published this month in the Journal of Nonverbal Behavior. The study is co-authored by Jack LaFayette, director of institutional research at Albright, and Sally D. Farley, former assistant professor of psychology at Albright, who now teaches at the University of Baltimore.
The study looked at how individuals alter their voices, or engage in voice modulation, when speaking to romantic partners versus same-sex friends during brief telephone conversations. Researchers recruited 24 callers who were newly in love and still in the so-called honeymoon period. Callers were asked to phone their romantic partners, as well as a close same-sex friend, and in both cases engage in a conversation asking specifically "how are you?" and "what are you doing?"
Researchers then played the recordings to 80 independent raters who judged the samples for sexiness, pleasantness and degree of romantic interest. Raters were exposed to only one end of the conversation and, in some cases, for only 2 seconds. Still, raters were able to correctly identify, with greater than chance accuracy, whether the caller was speaking to a friend or lover, leading researchers to believe that people will alter their voice to communicate their relationship status.
"Vocal samples directed toward romantic partners were rated as sounding more pleasant, sexier and reflecting greater romantic interest than those directed toward same-sex friends," according to the article.
Researchers also performed a spectrogram analysis on the samples to examine pitch and found that both men and women tend to mimic or match the pitch of their romantic partners. Women will use a lower pitch, while men will employ a higher one when speaking to their romantic partner. According to the article, this effect "represents desire for affiliation and intimacy" and is a "way to communicate affection and relational connection -- 'I am one with you.'"

Researchers were, however, surprised by the results of the paralanguage analysis. Paralanguage samples are stripped of their content, while maintaining elements such as inflection and intonation. In these samples, raters could sense stress, nervousness and lack of confidence in the voices of callers speaking to their lovers, which could be attributed to the early stages of romantic love. "There was vulnerability associated with the voices of those newly in love. Perhaps people don't want to be rejected," said Hughes.

Sally D. Farley, Susan M. Hughes, Jack N. LaFayette. People Will Know We Are in Love: Evidence of Differences Between Vocal Samples Directed Toward Lovers and Friends. Journal of Nonverbal Behavior, 2013; 37 (3): 123 DOI: 10.1007/s10919-013-0151-3

http://www.sciencedaily.com/releases/2013/10/131002185238.htm

Long-Term Cognitive Impairment Too Common After Critical Illness

Patients treated in intensive care units are entering with no evidence of cognitive impairment but oftentimes leaving with deficits similar to those seen in patients with traumatic brain injury

Patients treated in intensive care units across the globe are entering their medical care with no evidence of cognitive impairment but oftentimes leaving with deficits similar to those seen in patients with traumatic brain injury (TBI) or mild Alzheimer's disease (AD) that persists for at least a year, according to a Vanderbilt study published in the New England Journal of Medicine.

The study, led by members of Vanderbilt's ICU Delirium and Cognitive Impairment Group, found that 74 percent of the 821 patients studied, all adults with respiratory failure, cardiogenic shock or septic shock, developed delirium while in the hospital, which the authors found is a predictor of a dementia-like brain disease even a year after discharge from the ICU.

Delirium, a form of acute brain dysfunction common during critical illness, has consistently been shown to be associated with higher mortality, but this large study of medical and surgical ICU patients demonstrates that it is associated with long-term cognitive impairment in ICU survivors as well.

At three months, 40 percent of patients in the study had global cognition scores similar to patients with moderate TBI, and 26 percent scored similar to patients with AD. Deficits occurred in both older and younger patients, irrespective of whether they had coexisting illness, and persisted to 12 months, with 34 percent and 24 percent still having scores similar to TBI and AD patients, respectively.

"As medical care is improving, patients are surviving their critical illness more often, but if they are surviving their critical illness with disabling forms of cognitive impairment then that is something that we will have to be aware of because just surviving is no longer good enough," said lead author Pratik Pandharipande, M.D., MSCI, professor of Anesthesiology and Critical Care.

"Regardless of why you come in to an ICU, you have to know that, on the back end of your critical care, you are very likely to be suffering cognitively in ways similar to a TBI patient or an AD patient, except that most of the medical profession doesn't even know that this is happening and few around you suspect anything, leaving most to suffer in silence," said senior author Wes Ely, M.D., professor of Medicine.

"Delirium in critically ill, hospitalized adults is a serious yet understudied issue," said Molly Wagster, Ph.D., chief of the Behavioral & Systems Neuroscience Branch in the National Institute on Aging, part of the NIH. "These new findings provide important evidence of the extent of the problem, the imperative for greater recognition and the pressing need for solutions."

Ely said at least some component of this brain injury may be preventable through efforts to shorten the duration of delirium in the ICU by using careful delirium monitoring and management techniques, including earlier attempts at weaning from sedatives and mobility protocols that can save lives and reduce disability.

"Even after the patient leaves the hospital, we think that cognitive rehabilitation might be helpful to somebody like this, and we have some early preliminary data supporting this," he said.

P.P. Pandharipande, T.D. Girard, J.C. Jackson, A. Morandi, J.L. Thompson, B.T. Pun, N.E. Brummel, C.G. Hughes, E.E. Vasilevskis, A.K. Shintani, K.G. Moons, S.K. Geevarghese, A. Canonico, R.O. Hopkins, G.R. Bernard, R.S. Dittus, E.W. Ely. Long-Term Cognitive Impairment after Critical Illness. New England Journal of Medicine, 2013; 369 (14): 1306 DOI: 10.1056/NEJMoa1301372

http://www.eurekalert.org/pub_releases/2013-10/osu-ha100113.php

How a 'mistake' in a single-cell organism is actually a rewrite essential to life

Finding reveals new way that RNA genetic information is 'edited'

COLUMBUS, Ohio – A tiny but unexpected change to a segment of RNA in a single-cell organism looks a lot like a mistake, but is instead a change to the genetic information that is essential to the organism's survival.

Scientists have discovered this RNA "edit" in Trypanosoma brucei, a parasite that causes sleeping sickness in Africa and Chagas disease in Latin America. Though the organism is a model system for this work, the finding could lead to a new drug target to fight the parasite if higher species don't share this genetic behavior.

Some of the organism's genetic activity was already known. In the case of gene products called tRNAs, which help assemble the amino acids that make proteins, T. brucei was known to have only one tRNA with a specific segment of RNA that ensures the tRNA's proper function. Additionally, examples of RNA editing have been discovered before. But in this case, the way genetic information necessary for the protein production process was changed – through a swap of three nucleotides for three others that are completely out of place – has never been seen before.

"These are changes for which no chemistry is known and has never been described. We don't know what enzyme is involved and that is the million-dollar question: What mechanism is doing this? We haven't a clue," said Juan Alfonzo, professor of microbiology at The Ohio State University and senior author of the study.

"If the activity is unique to a trypanosome, then you have a good drug target. If it is widespread, then you have to reconsider one more time what coding sequences really mean in the sense that you can indeed change them in a very programmed fashion by activities that don't exist – that have not been described," said Alfonzo, also an investigator in Ohio State's Center for RNA Biology.

The work is the result of Alfonzo's longtime collaboration with co-lead author Christopher Trotta, senior director of biology at PTC Therapeutics in South Plainfield, N.J.

The study appears online in the journal Molecular Cell and is scheduled for print publication on Oct. 24.

The finding was not only unexpected, but serendipitous. Alfonzo's lab was analyzing an enzyme affecting T. brucei's tRNA behavior in response to a request from Trotta, a drug developer who is considered a pioneer of research on tRNAs. To begin the analysis, Alfonzo sought to identify the intron, a specific segment of RNA, that needs to be removed before the tRNA can participate in the selection of the right amino acids during protein production.

This critical function of removing the intron is called splicing – in essence, a pre-requisite chemical reaction affirming that tRNA can deliver the correct instructions for protein production. If a tRNA is not spliced, it will not work in protein production and the cell will die.

The trouble was, Alfonzo couldn't locate the intron that he knew was there. After multiple attempts, he found that the intron's sequence in this organism changed after transcription, the point at which a copy of RNA is made from a DNA sequence as the first step of gene expression.

This edit – hard to find because of its odd nature – consisted of a change to three nucleotides, the molecules that form DNA and RNA. Because of its rarity and unusual nature, it is called a noncanonical edit.

"It's noncanonical because it is not typical. It is completely not typical," Alfonzo said. "And for the first time, we show the biological significance. We show that if you don't edit, you don't splice. This editing is required for splicing, and splicing is required for functionality. Otherwise, cells die."

Previously known methods of RNA editing include deamination, the removal of sections of molecules from the RNA that change the message from the DNA, and nucleotide insertion, deletion or exchange. The editing described here is a swap of three nucleotides for three others that, according to the rules of biology, do not belong where they end up. This is why it looks like a mistake.

Colleagues have suggested that this edit should have been identified by researchers who do deep sequencing, which involves repeated readings of all nucleotides within an RNA molecule, Alfonzo noted. But he is not surprised that technology didn't yield these results. "In massive sequencing, you match RNAs to the sequence in the genome. Any mismatch is called a sequence mistake and is thrown in the trash. So this noncanonical editing may well be in the trash bin of many of these deep sequencing researchers," he said.

This work is partially supported by a grant from the National Institutes of Health.

Additional co-authors include Mary Anne Rubio, Zdeněk Paris, Kirk Gaston, Ian Fleming and Paul Sample, all of Ohio State's Department of Microbiology and Center for RNA Biology. Alfonzo is also a member of the Ohio State Biochemistry Program.

http://www.eurekalert.org/pub_releases/2013-10/luhs-ors100313.php

Old remedy shows promise as new chemo drug for bladder cancer

Active ingredient of ipecac syrup inhibits growth of cancer cells

MAYWOOD, Il. – An old home remedy called ipecac syrup, once stocked in medicine cabinets in case of accidental poisoning, is showing promise as a new chemotherapy drug for bladder cancer.

Years ago, ipecac syrup was used to induce vomiting in poisoning cases.

Now a Loyola University Medical Center study has found that the active ingredient of ipecac syrup effectively inhibits the growth of bladder cancer cells, especially when combined with a standard chemotherapy drug.

The study by corresponding authors Kimberly Foreman, PhD, Gopal Gupta, MD, and colleagues is published online ahead of print in The Journal of Urology.

The active ingredient of ipecac syrup comes from the flowering plant Psychotria ipecacuanha. The drug no longer is recommended to induce vomiting. Studies have shown that vomiting after swallowing poison does not help, and sometimes can harm. Moreover, ipecac syrup can be abused by people with eating disorders.
Two small studies published in 1969 and 1970 found that the active ingredient of ipecac syrup, emetine dihydrochloride, helped in treating bladder cancer. Recent studies have found emetine also can kill leukemia cells.
In the new study, Loyola researchers exposed cell lines of normal and cancerous bladder cells to emetine alone and to emetine plus cisplatin. (Cisplatin is the standard chemotherapy drug for advanced bladder cancer.)
The study found, for the first time, that:

Emetine alone inhibits the proliferation of bladder cancer cell lines.
Emetine acts synergistically with cisplatin to inhibit bladder cancer proliferation better than either drug does alone.
Emetine has little effect on normal cells.

Bladder cancer is the fourth most common cancer in men and the 9th most common cancer in women. But even with aggressive surgery and chemotherapy, the five-year survival rate for patients with advanced Stage 4 bladder cancer is only 4 to 20 percent.
"There is an urgent need to develop new drug combinations," Dr. Gupta said. "Our study demonstrates that combining emetine with cisplatin is potentially beneficial, and merits further study in clinical trials."
Dr. Gupta is an assistant professor in the departments of Urology and Surgery and in the Oncology Research Institute of Loyola University Chicago Stritch School of Medicine. Dr. Foreman is an associate professor in the Department of Pathology and the Oncology Research Institute. Other authors are John Jesse III, a Stritch student, and Paul Kuo, MD, FACS, chair of Loyola's Department of Surgery and director of the Oncology Research Institute.

http://www.medscape.com/viewarticle/811891?src=rss

Fill 'er Up! Health Effects of Coffee

Best Evidence Review of Health Effects of Coffee

Charles P. Vega, MD

Coffee is one of the most frequently consumed beverages on earth, yet there remain many questions regarding its effects on health. A recent observational study made headlines for finding a positive association between heavy coffee consumption and an increased risk for death among men, but the research had some substantial limitations. Other research certainly suggests that coffee can reduce the risk for diabetes and cardiovascular events. Overall, however, patients will probably have far more to gain by addressing other lifestyle and diet issues besides coffee drinking in their quest for a longer, happier life.

The Study

Liu J, Sui X, Lavie CJ, et al. Association of coffee consumption with all-cause and cardiovascular disease mortality. *Mayo Clin Proc.* 2013 Aug 15. [Epub ahead of print]

The Background

"Doctor, I made some of those changes we talked about last time!" my patient relates with enthusiasm. I am genuinely excited. Ten tortillas per day, lots of *Hogan's Heroes* reruns, and problem alcohol drinking is no way to go through life, son.
"I stopped drinking coffee!" And my hopes vanish faster than the Baconator® my patient inhaled immediately before his appointment with me. Coffee?! That was never part of the conversation. I can't help but look at my e-chart; yep, 1 cup of coffee each morning. In my analysis, he's safe as kittens regarding any health risk from coffee consumption.
This scene has played out time and again in my practice, and it has reinforced to me that many adults consider coffee drinking a guilty pleasure. If so, there are many guilty individuals out there. According to trade association reports, 83% of US adults now drink coffee, a 5% increase since 2012 and part of an upward trend over the past 2 decades.[1] The majority of Americans drink coffee on a daily basis, and the average number of cups per day among daily drinkers is 3.1.[2]
But what are the health risks associated with that cup of joe? A new study will give anyone in line at their favorite coffee shop something serious to consider.

Study Synopsis

This prospective study recruited adults between the ages of 20 and 87 years for over 30 years, ending in 2002. Patients with a history of cardiovascular disease, cancer, or abnormal exercise stress testing were excluded from the current analysis.
Participants completed health questionnaires that included questions regarding coffee consumption. They also underwent a baseline examination that included laboratory analyses and an exercise stress test. Mortality data were culled from national and state databases.

The main study outcome was the relationship between coffee consumption and mortality risk. These results were adjusted to account for demographics, chronic disease, and other health habit information. They were not stratified according to lab results.

Data for study analysis came from 43,727 adults; 77% of the cohort was male, and the average age at the time of enrollment was 43 years. Participants were predominantly white, at the higher end of the socioeconomic spectrum, and well educated. Approximately one quarter of the study cohort had hypertension or hyperlipidemia.

A minority of participants (19% of men and 21% of women) never drank coffee, while approximately a third (35.2% of men and 33.5% of women) drank 22 or more cups of coffee per week. Coffee consumption was associated with higher rates of smoking and lower levels of cardiorespiratory fitness.

The most surprising finding from the multivariate adjustment analysis was that men who drank at least 28 cups of coffee per week experienced a hazard ratio of 1.21 for all-cause mortality (95% confidence interval, 1.04-1.40) when compared with men who did not drink coffee. There were also nonsignificant increases in the risk for mortality associated with drinking any amount of coffee, from 1 to 28 cups per week among men. However, there was no significant effect of coffee consumption on the risk for mortality among women.

An association between heavy coffee consumption and a higher risk for cardiovascular mortality specifically was found on initial analysis among men, but this association was rendered nonsignificant after adjustment for cardiorespiratory fitness. Subgroup analysis found that any mortality risk associated with coffee was most pertinent for men and women younger than 55 years of age. Adjustment for body mass index did not significantly alter the study's main findings, and coffee did not promote a higher risk for mortality among smokers.

The strengths of this study are its size and length of follow-up. It would be difficult to create meaningful results for mortality outcomes from a smaller study. The natural limitation to an observational study is confounding data, and the researchers made adjustments to account for important confounders, including an objective test to measure exercise tolerance. They did not adjust their results based on laboratory data such as lipid levels.

This research has other major limitations. Participants' coffee consumption was measured only at baseline and changes were not assessed. While the researchers noted that adults' coffee-drinking habits change little over time, certainly the culture of coffee and coffee consumption has undergone a revolution during the study period between 1971 and 2002. It is hard to believe that there have not been changes in the ways that people prepare and consume coffee over 3 decades.

This leads to another major study limitation: a failure to define their main variable. Not only was the type of coffee -- caffeinated vs decaffeinated, for example -- not evaluated as part of the study methods, but the authors failed to define the measurement of a cup of coffee in the first place. In America's "Supersize It!" culture, there are some massive cups of coffee out there (the average coffee mug holds 9 ounces), so any reasonable analysis should account for the exact volume of coffee consumed.[2]

Discussion

This is not the first study performed on the health effects of coffee, and the subject remains controversial. It is interesting that the results of this study buck the trend of recent, high-quality research that suggests that coffee improves health outcomes.

Coffee can raise blood pressure acutely, but the consensus appears to be that it has a negligible role in promoting hypertension. In one systematic review of observational studies, only mild coffee consumption of 1-3 cups per day was associated with a higher risk for hypertension compared with no coffee consumption.[3] A more recent review found that the cumulative effect of coffee consumption on blood pressure was less than 1 mm Hg, and coffee did not promote hypertension.[4]

Coffee has more mixed effects on other important cardiovascular risk factors. A meta-analysis of 12 studies found that coffee increased serum levels of total cholesterol, low-density lipoprotein cholesterol, and triglycerides, with a dose-response effect.[5] In contrast, a meta-analysis of 18 studies with over 400,000 participants in total found that each additional cup of coffee consumed daily was associated with a 7% reduction in the risk for incident type 2 diabetes.[6]

Given these variable effects on cardiovascular disease risk factors, how does coffee consumption affect the rates of actual cardiovascular events? Previous research found a positive association between coffee intake and the risk for either myocardial infarction or cardiovascular death.[7] However, a recent review found that moderate coffee consumption reduced the risk for heart failure, with a peak protective effect at 4 servings per day.[8] This same review also found that high levels of coffee consumption might increase heart failure risk. A review of 9 cohort studies found that at least 4 cups of coffee per day reduced the risk for stroke by 17% compared with abstinence from coffee.[9]

What about mortality outcomes among coffee drinkers vs nondrinkers? Research is mixed in this area as well. In an observational study of 37,742 Japanese women, coffee consumption had no significant effect on the overall risk for mortality, but there was a clear reduction in the risk for death due to coronary heart disease among coffee drinkers.[10] Another study examined mortality outcomes associated with coffee among 3837 patients with diabetes.[11] Like the current study by Liu and colleagues, it featured a broad age range among its subjects. However, in contrast to the current research, coffee consumption was associated with a lower risk for mortality, even at levels of greater than 6 cups per day. Finally, data from the Health Professionals Follow-Up Study and Nurses' Health Study, which featured similar largely white and well-educated populations in comparison with the current study, demonstrated no effect of coffee consumption on the risk for mortality among men and a lower risk for mortality among women who drank coffee.[12] Again, the benefit among women was principally for cardiovascular mortality.

Conclusion

The results of the current study made national headlines but really provide more questions than answers when it comes to the major health effects of coffee consumption. It should be emphasized that the higher risk for death in this study was limited to men at the highest levels of coffee consumption. Other good evidence suggests that coffee is not deleterious to health and does not promote early mortality.

Moderation is key to most things in life, and individuals who are heavy coffee drinkers should consider reining in their rampant coffee habit. However, patients may also overestimate the risks of drinking coffee. If they choose to cut back on moderate consumption of coffee, physicians should inform them that they may not be reducing their risk for diabetes or improving their for mortality. At the same time, such changes in and of themselves can be empowering and can serve as teachable moments to encourage other salutary behaviors that have a better chance of improving morbidity and mortality.

Clinical Pearls

• The current study finds that coffee is associated with a higher risk for mortality but only among men who drank an average of at least 4 cups of coffee per day. There were significant limitations in this observational study.

• Previous research has found that coffee consumption can increase serum lipid levels. Coffee appears to have a negligible effect on the risk for hypertension.

• In contrast, coffee consumption appears to reduce the risk for incident diabetes.

• The overall record of coffee on cardiovascular and mortality outcomes is mixed. The evidence appears strongest for a reduction in the risk for cardiovascular death among women who drink coffee.

• There is insubstantial evidence to recommend against moderate consumption of coffee among adults.

References

1. Food Manufacturing. Consumer trends: 83 percent of Americans drink coffee. April 8, 2013. http://www.foodmanufacturing.com/news/2013/04/consumer-trends-83-percent-americans-drink-coffee Accessed September 9, 2013.

2. Statistic Brain. Coffee drinking statistics. http://statisticbrain.com/coffee-drinking-statistics/ Accessed September 9, 2013.

3. Zhang Z, Hu G, Caballero B, Appel L, Chen L. Habitual coffee consumption and risk of hypertension: a systematic review and meta-analysis of prospective observational studies. Am J Clin Nutr. 2011;93:1212-1219. Abstract

4. Steffen M, Kuhle C, Hensrud D, Erwin PJ, Murad MH. The effect of coffee consumption on blood pressure and the development of hypertension: a systematic review and meta-analysis. J Hypertens. 2012;30:2245-2254. Abstract

5. Cai L, Ma D, Zhang Y, Liu Z, Wang P. The effect of coffee consumption on serum lipids: a meta-analysis of randomized controlled trials. Eur J Clin Nutr. 2012;66:872-877.

6. Huxley R, Lee CM, Barzi F, et al. Coffee, decaffeinated coffee, and tea consumption in relation to incident type 2 diabetes mellitus: a systematic review with meta-analysis. Arch Intern Med. 2009;169:2053-2063. Abstract

7. Greenland S. A meta-analysis of coffee, myocardial infarction, and coronary death. Epidemiology. 1993;4:366-374. Abstract

8. Mostofsky E, Rice MS, Levitan EB, Mittleman MA. Habitual coffee consumption and risk of heart failure: a dose-response meta-analysis. Circ Heart Fail. 2012;5:401-405. Abstract

9. Kim B, Nam Y, Kim J, Choi H, Won C. Coffee consumption and stroke risk: a meta-analysis of epidemiologic studies. Korean J Fam Med. 2012;33:356-365. Abstract

10. Sugiyama K, Kuriyama S, Akhter M, et al. Coffee consumption and mortality due to all causes, cardiovascular disease, and cancer in Japanese women. J Nutr. 2010;140:1007-1013. Abstract

11. Bidel S, Hu G, Qiao Q, Jousilahti P, Antikainen R, Tuomilehto J. Coffee consumption and risk of total and cardiovascular mortality among patients with type 2 diabetes. Diabetologia. 2006;49:2618-2626. Abstract

12. Lopez-Garcia E, van Dam RM, Li TY, Rodriguez-Artalejo F, Hu FB. The relationship of coffee consumption with mortality. Ann Intern Med. 2008;148:904-914. Abstract

http://www.bbc.co.uk/news/health-24387491

Body clock 'reset button' found

Drugs that rapidly tweak the body clock in order to avoid jet lag and the pains of shift work have moved a step closer after research in Japan.

The team at Kyoto University has found the clock's 'reset button' inside the brain. Their study, published in the journal Science, showed the button could be used to switch the clock to a new time zone in a single day.

Experts said the team was "close to the money" in the hunt for a jet lag cure. There are clocks throughout the body and a "master clock" in the brain, keeping the body in sync with the world around it to make people sleepy at night.

Anyone who has ever done shift work or a long-haul flight has experienced the disrupted sleep and hunger patterns of a body clock which is out of tune with the rising and setting of the sun. The clock uses light to help keep track of time, but it is naturally stubborn and adjusts slowly. The rough rule is that for every time zone crossed it takes a full day for the body to catch up. Fly from London to Beijing and it would take a week for the body clock to fully adapt.

Loosen up

The team in Japan have come up with a way to get the master clock to be a bit more flexible. It is a group of 10,000 brain cells - about the same size as a grain of rice - which constantly talk to each other to keep a strict control over the time. The scientists found that interfering with the vasopressin receptors, essentially a brain cell's ears that allow it to keep in touch with its neighbours, let the clock shift rapidly.

Genetically modified mice which had no vasopressin receptors were able to adjust to the clocks being put back eight hours within a single day, while normal mice took six days.

When the clocks were put forward eight hours then it took normal mice eight days to adapt, but those without vasopressin receptors adjusted in two. Similar results were then achieved in normal mice using a drug.

'Remarkable'

The study's authors concluded: "Studies have shown that chronic jet lag and rotating shift work can increase an individual's risk of developing hypertension, obesity, and other metabolic disorders. "Our results identify vasopressin signalling as a possible therapeutic target for the management of circadian rhythm [body clock] misalignment."

Dr Michael Hastings, a Medical Research Council body clock researcher, told the BBC's Science in Action programme: "It's a remarkable study, it really is very exciting for our field. "There's been many false dawns when it comes to a cure for jet lag, but I think this time they're close to the money."

However, he cautioned that vasopressin receptors were also heavily involved in kidney function so any drug developed would need to be designed carefully to target the body clock without disrupting the kidneys.

Dr Hastings added that with an increasingly 24-7 society a drug which can adjust the body clock could, in theory, improve the health of shift workers.

"The issue here in terms of public health is rotational shift work, the epidemiological evidence that we have now shows that if a worker has spent a working life doing rotational shift work they're at higher risk of contracting certain forms of cancer, cardiovascular disease or metabolic syndrome like diabetes."

http://www.eurekalert.org/pub_releases/2013-10/miot-sss100413.php

Surprisingly simple scheme for self-assembling robots

In 2011, when an MIT senior named John Romanishin proposed a new design for modular robots to his robotics professor, Daniela Rus, she said, "That can't be done."

Written by Larry Hardesty, MIT News Office

CAMBRIDGE, MA -- Two years later, Rus showed her colleague Hod Lipson, a robotics researcher at Cornell University, a video of prototype robots, based on Romanishin's design, in action. "That can't be done," Lipson said.

In November, Romanishin — now a research scientist in MIT's Computer Science and Artificial Intelligence Laboratory (CSAIL) — Rus, and postdoc Kyle Gilpin will establish once and for all that it can be done, when they present a paper describing their new robots at the IEEE/RSJ International Conference on Intelligent Robots and Systems. Known as M-Blocks, the robots are cubes with no external moving parts. Nonetheless, they're able to climb over and around one another, leap through the air, roll across the ground, and even move while suspended upside down from metallic surfaces.

Inside each M-Block is a flywheel that can reach speeds of 20,000 revolutions per minute; when the flywheel is braked, it imparts its angular momentum to the cube. On each edge of an M-Block, and on every face, are cleverly arranged permanent magnets that allow any two cubes to attach to each other.

"It's one of these things that the [modular-robotics] community has been trying to do for a long time," says Rus, a professor of electrical engineering and computer science and director of CSAIL. "We just needed a creative insight and somebody who was passionate enough to keep coming at it — despite being discouraged."

Embodied abstraction

As Rus explains, researchers studying reconfigurable robots have long used an abstraction called the sliding-cube model. In this model, if two cubes are face to face, one of them can slide up the side of the other and, without changing orientation, slide across its top.

The sliding-cube model simplifies the development of self-assembly algorithms, but the robots that implement them tend to be much more complex devices. Rus' group, for instance, previously developed a modular robot called the Molecule, which consisted of two cubes connected by an angled bar and had 18 separate motors. "We were quite proud of it at the time," Rus says.

According to Gilpin, existing modular-robot systems are also "statically stable," meaning that "you can pause the motion at any point, and they'll stay where they are." What enabled the MIT researchers to drastically simplify their robots' design was giving up on the principle of static stability. "There's a point in time when the cube is essentially flying through the air," Gilpin says. "And you are depending on the magnets to bring it into alignment when it lands. That's something that's totally unique to this system."

That's also what made Rus skeptical about Romanishin's initial proposal. "I asked him build a prototype," Rus says. "Then I said, 'OK, maybe I was wrong.'"

Sticking the landing

To compensate for its static instability, the researchers' robot relies on some clever engineering. On each edge of a cube are two cylindrical magnets, mounted like rolling pins. When two cubes approach each other, the magnets naturally rotate, so that north poles align with south, and vice versa. Any face of any cube can thus attach to any face of any other.

The cubes' edges also have a slight bevel, so when two cubes are face to face, there's a slight gap between their magnets. When one cube begins to flip on top of another, the bevels, and thus the magnets, touch. The connection between the cubes becomes much stronger, anchoring the pivot. On each face of a cube are four more pairs of smaller magnets, arranged symmetrically, which help snap a moving cube into place when it lands on top of another.

As with any modular-robot system, the hope is that the modules can be miniaturized: the ultimate aim of most such research is hordes of swarming microbots that can self-assemble, like the "liquid steel" androids in the movie "Terminator II." And the simplicity of the cubes' design makes miniaturization promising.

But the researchers believe that a more refined version of their system could prove useful even at something like its current scale. Swarms of mobile cubes could temporarily repair bridges or buildings during emergencies, or raise and reconfigure scaffolding for building projects. They could assemble into different types of furniture or heavy equipment as needed. And they could swarm into environments hostile or inaccessible to humans, diagnose problems, and reorganize themselves to provide solutions.

Strength in diversity

The researchers also imagine that among the mobile cubes could be special-purpose cubes, containing cameras, or lights, or battery packs, or other equipment, which the mobile cubes could transport. "In the vast majority of other modular systems, an individual module cannot move on its own," Gilpin says. "If you drop one of these along the way, or something goes wrong, it can rejoin the group, no problem."

In ongoing work, the MIT researchers are building an army of 100 cubes, each of which can move in any direction, and designing algorithms to guide them. "We want hundreds of cubes, scattered randomly across the floor, to be able to identify each other, coalesce, and autonomously transform into a chair, or a ladder, or a desk, on demand," Romanishin says.

http://www.bbc.co.uk/news/technology-24381149

23andMe's 'build-a-baby' patent criticised

A US patent for a database that uses DNA testing to tell prospective parents which traits their future offspring may inherit has been criticised by experts.

23andMe says its Family Traits Inheritor Calculator can predict the risk of inheriting specific diseases as well as details such as height, weight, eye colour and even personality. Couples send the firm a saliva sample to see what their babies might be like. But critics have called the project "ethically and socially treacherous".

Designer babies

The patent suggests the database could also be used by fertility clinics to find appropriate donors. But the Mountain View, California-based firm was quick to say this was no longer part of its plan. "At the time

23andMe filed the patent, there was consideration that the technology could have potential applications for fertility clinics so language specific to the fertility treatment process was included in the patent," it said in a blog post.
"The company never pursued the concepts discussed in the patent beyond our Family Traits Inheritance Calculator, nor do we have any plans to do so." Instead it described the tool for prospective parents as "an enjoyable way to dip their toes into genetics".
But critics remain concerned that such technology could be misused.
"It would be highly irresponsible for 23andMe or anyone else to offer a product or service based on this patent," said Marcy Darnovsky, executive director of the Center for Genetics and Society. "It amounts to shopping for designer donors in an effort to produce designer babies. "We believe the patent office made a serious mistake in allowing a patent that includes drop-down menus for which to choose a future child's traits.
"A project like this would also be ethically and socially treacherous."

http://www.bbc.co.uk/news/technology-24381149

Genepeeks firm to offer 'digital baby' screen for sperm donors

A service that digitally weaves together the DNA of prospective parents to check for potential disease in thousands of "virtual babies" is set to launch in the US by December.

By Paul Rincon Science editor, BBC News website

New York start-up Genepeeks will initially focus on donor sperm, simulating before pregnancy how the genetic sequence of a female client might combine with those of different males. Donors that more often produce "digital children" with a higher risk of inherited disorders will be filtered out, leaving those who are better genetic matches. Everything happens in a computer, but experts have raised ethical questions.
"We are just in the business right now of giving prospective mothers, who are using donor sperm to conceive, a filtered catalogue of donors based on their own underlying genetic profile," Genepeeks co-founder Anne Morriss told BBC News. "We are filtering out the donor matches with an elevated risk of rare recessive paediatric conditions." Ms Morriss, an entrepreneur, gave a presentation on the company at the Consumer Genetics Conference in Boston last week.

Advancing technology

She was motivated in part by her own experience of starting a family. Her son was conceived with a sperm donor who happened to share with Morriss the gene for an inherited disorder called MCADD.
MCADD (medium-chain acyl-CoA dehydrogenase deficiency) prevents those affected from converting fats to sugar. It can be fatal if it is not diagnosed early. Luckily, in Ms Morriss's case, the condition was picked up in newborn screening tests. "My son has a pretty normal life," Ms Morriss said, "but about 30% of children with rare genetic diseases don't make it past the age of five."
Genepeeks has formalised a partnership with a sperm bank - the Manhattan Cryobank - and has a patent pending on the DNA screening technology. The start-up benefits from the rapid pace of change in genetic technology.
Indeed, six months ago, Genepeeks' founders decided it was able to use a superior system for DNA analysis (called "targeted exon sequencing") than the one originally envisaged - a result, says Anne Morriss, of falling costs and increased flexibility. For couples planning babies, other companies already screen one or both partners for genes that could cause disease if combined with a similar variant - so-called "carrier screening".

Digital filter

One academic who studies the use of genetic technology commented: "This is like that, but ramped up 100,000 times."
Ms Morriss's business partner, Prof Lee Silver, a geneticist and expert on bioethics at Princeton University, New Jersey, told BBC News: "We get the DNA sequence from two prospective parents. We simulate the process of reproduction, forming virtual sperm and virtual eggs. We put them together to form a hypothetical child genome.
"Then we can look at that hypothetical genome and - with all the tools of modern genetics - determine the risk that the genome will result in a child with disease. We're looking directly for disease and not carrier status. For each pair of people that we're going to analyse, we make 10,000 hypothetical children."
The process will be run for the client and each potential donor one by one, scanning for some 600 known single-gene recessive conditions. In this way, the highest-risk pairings can be filtered out.
Anne Morriss added: "At this stage our clients won't be receiving any genetic information back. We're very much focused on the practical utility of helping prospective parents who want to protect their future kids, giving them the option of additional analysis to what is currently being offered in the industry."

But the company's founders have plans to expand the screening beyond single-gene recessive disorders to more complex conditions in which multiple genes play a part.
Indeed, going to the trouble of simulating thousands of digital children deliberately lays the ground for this: "[It's] impossible to get towards an accurate risk calculation in any other way," said Anne Morriss.
And in a video produced by the company, Prof Silver says: "My hope for the future is that any people who want to have a baby can use this technology to greatly reduce the risk of disease being expressed in their child."

Donor ethics

To some, such a prospect might appear like a step towards designer babies - until now the preserve of science fiction literature and films such as Gattaca, which envisaged a future of genetic "haves" and "have-nots".
Bio-ethicists approached by the BBC said Genepeeks was a logical outcome of the increasing demand for more information when making reproductive decisions.
However, some raised potential concerns about risk communication and the expansion of screening beyond rare single-gene disorders. But they suggested there were few, if any, regulatory barriers.
One ethicist told BBC News: "The biggest question for me, just from the outset, is the understanding of uncertainty. Even people who have been doing genomics for years still have a hard time figuring out exactly what a risk for a particular genetic predisposition really means for a family.
"Gene-environment interactions can lead to people either having disease or not having disease."
Dr Ewan Birney, associate director of the European Bioinformatics Institute in Hinxton, UK, echoed the point: "It's good that they're focusing on the carrier status of these rare Mendelian disorders where it's potentially more clear-cut. That said, these things are more complex than they first seem," he said.
"I'm sure the scientists appreciate that complexity. But when transmitting that complexity to everyday people, these things can sound more absolute than they really are."
He added: "The thing I would want to stress here is just how complex this is. It's great that people are thinking of using this technology in lots of different ways, but our knowledge gap is very large."
Risk communication to clients was, said Anne Morriss, "absolutely critical to anyone in this industry".
"We have to be crystal clear about what we're testing for, what risks we're helping to reduce; that there's no guarantee you won't give birth to a sick child," she said.
Prof Mildred Cho, associate director of the Stanford Center for Biomedical Ethics in California, raised questions over whether the sperm donor should also receive information about their genome gleaned from the screening process. "Unlike hair colour, occupation or family history - those are things, presumably, the donor already knows - the thing that's different about this that I see is it could create information that the donor doesn't already have. It also has implications for the donor's other biological family members," Prof Cho told BBC News.
This week it also emerged that California-based consumer genetics company 23andMe had submitted the patent on a DNA analysis tool for planning a child.

http://www.eurekalert.org/pub_releases/2013-10/idso-nvr100313.php

Norovirus vaccine reduces symptoms of illness by more than half, early research shows

An investigational vaccine appears generally well tolerated and effective against the most common strain of norovirus, reducing the main symptoms of the gastrointestinal (GI) infection, vomiting and/or diarrhea, by 52 percent, suggests research being presented at IDWeek 2013™.

SAN FRANCISCO –Currently, there is no treatment or cure for norovirus, the most common cause of severe GI infection in the United States. Norovirus is highly contagious. Significant outbreaks occur in health care facilities, childcare centers and other places where people are in close quarters, including in the military and on cruise ships. Each year, 19 to 21 million Americans – one in 15 – are infected and as many as 800 die, according to the Centers for Disease Control and Prevention (CDC). In addition, one recent evaluation reports that the overall cost of the disease in the United States is $5.5 billion annually.
"Norovirus truly is a global issue and most if not everyone has experienced it to some degree," said David I. Bernstein, MD, MA, professor of pediatrics at Cincinnati Children's Hospital Medical Center and the University of Cincinnati and lead author of the study. "The results of our study are promising and our next step is to test this vaccine in a real-world setting."
The randomized, multi-center study included 98 people who agreed to drink water containing a significant dose of the virus, 50 who received the injected vaccine and 48 who received a placebo injection that did not contain the vaccine. Neither the participants nor the researchers knew in advance who received the vaccine and who did not. In the vaccine group, 26 (52 percent) were infected, as were 29 (60 percent) of those in the non-vaccine

group. In people who received the vaccine, 10 (20 percent) suffered from mild, moderate or severe vomiting and/or diarrhea versus 20 (42 percent) in the non-vaccine group, a 52 percent reduction in symptoms.
The vaccine targets two genotypes of norovirus: GI.1 and GII.4, the latter of which is now the leading cause of outbreaks in the United States.
Norovirus can spread from person to person through infected food or water or contaminated surfaces. The best prevention is proper hand washing, but the virus is so contagious that people can become ill even from contact with viral particles in the air. Not everyone who is exposed to norovirus becomes infected and of those who are infected, not everyone gets sick, said Dr. Bernstein. But it nonetheless is very common, and can be serious, particularly for children and older adults.
"If the vaccine continues to prove as effective as our initial results indicate, it could be used for specific populations or situations – in those at a higher risk of severe disease such as the elderly or at high risk for infection or transmission such as in day care, people going on a cruise, those in nursing homes or in the military," said Dr. Bernstein. "Or it could be offered to everyone, since all of us are exposed at one time or another."
Co-authors of the study, sponsored by Takeda Pharmaceutical Company Limited, are Robert L. Atmar, MD and David Y. Graham, MD, Baylor College of Medicine; G. Marshal Lyon, MD, MMSc, Emory University School of Medicine; John J. Treanor, MD, University of Rochester Medical Center; Wilbur H. Chen, MD, MS, University of Maryland School of Medicine; Robert W Frenck, MD and Xi Jiang PhD, Cincinnati Children's Hospital Medical Center; Jan Vinjé, PhD, Centers for Disease Control and Prevention; Mohamed S. AL-Ibrahim, MD, Shin Nippon Biomedical Laboratories; Jill Barrett, MPH, The EMMES Corp.; Charles Richardson, PhD, Robert Goodwin, PhD, Astrid Borkowski, MD, PhD, Ralf Clemens, MD, PhD, and Paul M. Mendelman, MD, Takeda Vaccines.

AT A GLANCE

An investigational vaccine reduces symptoms of norovirus gastrointestinal (GI) infection by 52 percent, an early study shows.
Norovirus is the most common cause of GI illness, sickening one in 15 Americans every year, and killing as many as 800.
In the randomized multicenter study, people drank water infected with the virus. Those who had been vaccinated experienced a 52 percent reduction in vomiting and/or diarrhea versus those who did not receive the vaccine.
If further testing proves the vaccine effective, it might be offered to the general population, or people most likely to be exposed to norovirus, such as those in the military, who are going on cruises, or who live in nursing homes.

http://bit.ly/195Qxdv

'Higgsogenesis' Proposed to Explain Dark Matter

Interactions of Higgs bosons and anti-Higgs in early universe may also have caused the observed asymmetry between matter and antimatter

By Eugenie Samuel Reich and Nature magazine | Saturday, October 5, 2013 | 7

A key riddle in cosmology may be answered by the 2012 discovery of the Higgs boson—now a leading contender for the 2013 Nobel Prize in Physics on October 8.
Two physicists suggest that the Higgs had a key role in the early universe, producing the observed difference between the number of matter and antimatter particles and determining the density of the mysterious dark matter that makes up five-sixths of the matter in the universe.
In a paper accepted for publication in Physical Review Letters, Sean Tulin of the University of Michigan in Ann Arbor and Géraldine Servant of the Catalan Institute for Research and Advanced Study in Barcelona, Spain, say that there may have been an asymmetry in the early universe between the Higgs boson and its antimatter counterpart, the anti-Higgs.
It is thought that the Higgs does not currently have an antiparticle, but the standard cosmological model allows for there to have been both Higgs bosons and anti-Higgs bosons in the very early universe. Tulin and Servant's idea is that there was an imbalance between the numbers of these particles. The Higgs interacts with ordinary matter, and that imbalance in the number of Higgs and anti-Higgs particles could have translated into an asymmetry in the amount of matter and antimatter."We really make the Higgs a key player, whereas in many other cosmological theories it's just a by-product," says Tulin.
The team has dubbed the idea Higgsogenesis, after baryogenesis, the name of an early-universe process that has been proposed to create more baryons (particles including protons and neutrons) than antibaryons.
"Higgsogenesis is an alternative," says Tulin.

Missing particles

Tulin and Servant show that if the Higgs also interacted with dark matter—for example by generating dark-matter particles when it decays—it could produce a ratio of dark to visible matter that is just what we see in the universe today. Servant says that one consequence of the Higgs interacting in this way would be a new potential

test for dark matter, which has so far proven difficult to see directly. When the Higgs decays to other particles in the Large Hadron Collider at CERN, Europe's particle-physics laboratory near Geneva, Switzerland, it would occasionally form dark-matter particles that could not be detected. Higgs decays at the LHC have not yet been studied closely enough to tell whether this is happening, but could be in future, Servant says.

Other groups are also pursuing Higgsogenesis. In July, theorist Sacha Davidson of the University of Lyons in France and her colleagues uploaded a paper to the preprint server arXiv investigating what would be required to produce the asymmetry between the Higgs and anti-Higgs that would kick off Higgsogenesis in the early universe. They found that a relatively simple theory—in which the standard model of particle physics includes all the normal particles, as well as two Higgs and one extra, unobservable Higgs-like particle—can produce an asymmetry of the type that Servant and Tulin propose.

Manoj Kaplinghat, a theoretical physicist at the University of California, Irvine, likes Tulin and Servant's proposal because of its simplicity. "We know that the Higgs exists, we know there's dark matter and matter–antimatter asymmetry, and they're trying to put three empirical facts together," he says. "It's a minimal approach and that makes it interesting."

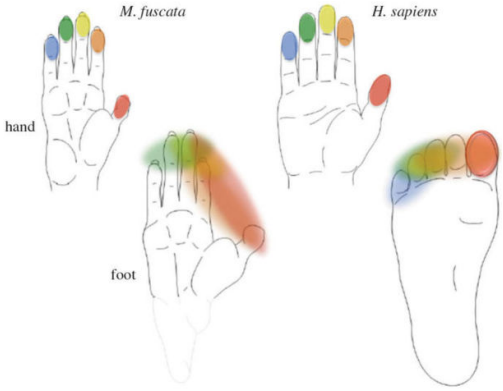
http://www.sciencedaily.com/releases/2013/10/131006204157.htm

What Evolved First, a Dexterous Hand or an Agile Foot?

Resolving a long-standing mystery in human evolution, new research from the RIKEN Brain Science Institute indicates that early hominids developed finger dexterity and tool use ability before the development of bipedal locomotion.

Combining monkey and human behavior, brain imaging, and fossil evidence, a research team led by neurobiologist Dr. Atsushi Iriki and including Dr. Gen Suwa, an anthropologist from the University of Tokyo Museum, have overturned the common assumption that manual dexterity evolved after the development of bipedal locomotion freed hominid hands to use fingers for tool manipulation.

In a study published today in Philosophical Transactions of the Royal Society, the researchers employed functional magnetic resonance imaging in humans and electrical recording from monkeys to locate the brain areas responsible for touch awareness in individual fingers and toes, called somatotopic maps. With these maps, the researchers confirmed previous studies showing that single digits in the hand and foot have discrete neural locations in both humans and monkeys.



Shape of the hand and foot in two primate species. The fingers are represented independently (colour coded) in the primate somatosensory cortex (SI). By contrast, the representations of the toes are fused, with the exception of the big toe in humans. **(Credit: Image courtesy of RIKEN)**

However, the researchers found new evidence that monkey toes are combined into a single map, while human toes are also fused into a single map, but with the prominent exception of the big toe, which has its own map not seen in monkeys. These findings suggest that early hominids evolved dexterous fingers when they were still quadrupeds. Manual dexterity was not further expanded in monkeys, but humans gained fine finger control and a big toe to aid bipedal locomotion.

"In early quadruped hominids, finger control and tool use were feasible, while an independent adaptation involving the use of the big toe for functions like balance and walking occurred with bipedality," the authors explained.

The brain study was supported by analysis of the well-preserved hand and feet bones of a 4.4 million year-old skeleton of the quadruped hominid Ardipithecus ramidus, a species with hand dexterity that preceded the human-monkey lineage split.

The findings suggest that the parallel evolution of two-legged locomotion and manual dexterity in hands and fingers in the human lineage were a consequence of adaptive pressures on ancestral quadrupeds for balance control by foot digits while retaining the critical capability for fine finger specialization.

"Evolution is not usually thought of as being accessible to study in the laboratory," stated Dr. Iriki, "but our new method of using comparative brain physiology to decipher ancestral traces of adaptation may allow us to re-examine Darwin's theories."

T. Hashimoto et al. Hand Before Foot? cortical somatotopy suggests manual dexterity is primitive and evolved independently of bipedalism. Philosophical Transactions of the Royal Society B, 2013 DOI: 10.1098/rstb.2012.0417

http://phys.org/news/2013-10-minamata-mercury-treaty-conference-japan.html

'Minamata' mercury treaty conference kicks off in Japan

A UN conference to sign a historic treaty aimed at reining in the use and emission of mercury began Monday in Kumamoto, near Minamata, the site of Japan's worst-ever industrial poisoning.

Delegates from some 140 countries and regions are scheduled to attend the five-day conference in the country's southwest, organisers said.

The conference comes after a January agreement on details of the world's first legally binding treaty on mercury, a highly toxic metal.

Preparatory meetings kicked off Monday at the venue, the organisers said, while local media said the treaty is likely to be adopted unanimously on Thursday.

The treaty has been named the Minamata Convention on Mercury, in honour of the Japanese city around 2,000 people died and many more were made sick by mercury dumped by a local factory.

Delegates are to visit Minamata on Wednesday to mourn the victims.

The treaty will take effect once ratified by 50 countries—something organisers expect will take three to four years.

Mercury, also known as quicksilver, is found in products ranging from electrical switches, thermometers and light-bulbs, to amalgam dental fillings and even facial creams.

Serious mercury poisoning affects the body's immune system and development of the brain and nervous system, posing the greatest risk to foetuses and infants.

The treaty sets a phase-out date of 2020 for a long line of products including mercury thermometers, while the text gives governments 15 years to end all mercury mining.

But environmental groups say the treaty falls short in addressing artisanal small-scale gold mining, a major source of large amounts of the heavy metal, which also directly threatens the health of miners.

http://www.bbc.co.uk/news/health-24427951

Cellular 'shipping' wins Nobel Prize

Three scientists have won the Nobel Prize for medicine or physiology after discovering how cells precisely transport material.

James Rothman and Randy Schekman, both from the US, and Thomas Sudhof, from Germany, shared the prize.

They found the way "vesicles" act like a fleet of ships transporting their goods to the exact location.

It is crucial for the way the brain communicates, the release of hormones and parts of the immune system.

The prize committee said the findings: "Had a major impact on our understanding of how cargo is delivered with timing and precision within and outside the cell.

"Without this wonderfully precise organisation, the cell would lapse into chaos."

A defective vesicle transport system is implicated in diabetes and brain disorders.