http://www.eurekalert.org/pub_releases/2012-03/miot-mrs031912.php

MIT research: Study finds room to store CO2 underground

New MIT analysis shows there's enough room to safely store at least a century's worth of US fossil fuel emissions

A new study by researchers at MIT shows that there is enough capacity in deep saline aquifers in the United States to store at least a century's worth of carbon dioxide emissions from the nation's coal-fired powerplants. Though questions remain about the economics of systems to capture and store such gases, this study addresses a major issue that has overshadowed such proposals.

The MIT team's analysis - led by Ruben Juanes, the ARCO Associate Professor in Energy Studies in the Department of Civil and Environmental Engineering, and part of the doctoral thesis work of graduate students Christopher MacMinn PhD '12 and Michael Szulczewski - is published this week in the Proceedings of the National Academy of Sciences.

Coal-burning powerplants account for about 40 percent of worldwide carbon emissions, so climate change "will not be addressed unless we address carbon dioxide emissions from coal plants," Juanes says. "We should do many different things" such as developing new, cleaner alternatives, he says, "but one thing that's not going away is coal," because it's such a cheap and widely available source of power.

Efforts to curb greenhouse gases have largely focused on the search for practical, economical sources of clean energy, such as wind or solar power. But human emissions are now so vast that many analysts think it's unlikely that these technologies alone can solve the problem. Some have proposed systems for capturing emissions - mostly carbon dioxide from the burning of fossil fuels - then compressing and storing the waste in deep geological formations. This approach is known as carbon capture and storage, or CCS.

One of the most promising places to store the gas is in deep saline aquifers: those more than half a mile below the surface, far below the freshwater sources used for human consumption and agriculture. But estimates of the capacity of such formations in the United States have ranged from enough to store just a few years' worth of coal-plant emissions up to many thousands of years' worth.

The reason for the huge disparity in estimates is twofold. First, because deep saline aquifers have no commercial value, there has been little exploration to determine their extent. Second, the fluid dynamics of how concentrated, liquefied carbon dioxide would spread through such formations is very complex and hard to model. Most analyses have simply estimated the overall volume of the formations, without considering the dynamics of how the CO2 would infiltrate them.

The MIT team modeled how the carbon dioxide would percolate through the rock, accounting not only for the ultimate capacity of the formations but the rate of injection that could be sustained over time. "The key is capturing the essential physics of the problem," Szulczewski says, "but simplifying it enough so it could be applied to the entire country." That meant looking at the details of trapping mechanisms in the porous rock at a scale of microns, then applying that understanding to formations that span hundreds of miles.

"We started with the full complicated set of equations for the fluid flow, and then simplified it," MacMinn says. Other estimates have tended to oversimplify the problem, "missing some of the nuances of the physics," he says. While this analysis focused on the United States, MacMinn says similar storage capacities likely exist around the world.

Howard Herzog, a senior research engineer with the MIT Energy Initiative and a co-author of the PNAS paper, says this study "demonstrates that the rate of injection of CO2 into a reservoir is a critical parameter in making storage estimates."

When liquefied carbon dioxide is dissolved in salty water, the resulting fluid is denser than either of the constituents, so it naturally sinks. It's a slow process, but "once the carbon dioxide is dissolved, you've won the game," Juanes says, because the dense, heavy mixture would almost certainly never escape back to the atmosphere.

While this study did not address the cost of CCS systems, many analysts have concluded that they could add 15 to 30 percent to the cost of coal-generated electricity, and would not be viable unless a carbon tax or a limit on carbon emissions was put in place.

While uncertainties remain, "I really think CCS has a role to play," Juanes says. "It's not an ultimate salvation, it's a bridge, but it may be essential because it can really address the emissions from coal and natural gas."

The research was supported by grants from the U.S. Department of Energy, the MIT Energy Initiative, the Reed Research Fund, the Martin Family Society of Fellows for Sustainability and the ARCO Chair in Energy Studies.

http://www.eurekalert.org/pub_releases/2012-03/aha-sbp031412.php

Sudden blood pressure drop with position change linked to higher risk of heart failure

People whose blood pressure drops rapidly when they move from lying down to standing may have a higher risk of developing heart failure

People whose blood pressure drops rapidly when they move from lying down to standing, known as orthostatic hypotension, may have a higher risk of developing heart failure, according to research published in Hypertension, an American Heart Association journal.

The link between orthostatic hypotension and heart failure was stronger in people 45-55 years old compared to those 56-64, researchers said. High blood pressure, which was present in over half of people who developed heart failure, may be partially responsible for the association.

Over an average 17.5 years of follow-up, researchers looked at the association between orthostatic hypotension and developing heart failure. They measured patients' blood pressure while lying down and shortly after standing up.

They defined orthostatic hypotension as a decrease of 20 points or more in the systolic (top number) or a decrease of 10 or more points in the diastolic (bottom number) blood pressure measurements.

The researchers, who based the definition of heart failure on either hospital admission or death certificate diagnoses, found:*

* About 11 percent of patients who developed heart failure had orthostatic hypotension at the start of the study, compared with only 4 percent of those who did not develop heart failure.
* People with orthostatic hypotension had 1.54 times the risk of developing heart failure than those without orthostatic hypotension; however, after excluding those with high blood pressure, the risk fell to 1.34 times.

"Orthostatic hypotension appears to be related to the development of heart failure along with other conditions known to cause heart failure," said Christine DeLong Jones, M.D., study lead author and preventive medicine resident at the University of North Carolina at Chapel Hill.

"Hypertension, diabetes and coronary heart disease are already known to contribute to a person's risk of developing heart failure. Orthostatic blood pressure measurement may supplement what is already known about the risk for heart failure and requires no additional equipment, just a standard blood pressure cuff."

Researchers found that even when adjusting for existing diseases, such as high blood pressure, diabetes, and coronary heart disease, participants with orthostatic hypotension at the start of the study were still more likely to develop heart failure than those without it.

The study is the first of its kind to include both Caucasian and African-Americans. Prior studies in Europe included mostly Caucasians. "The association of orthostatic hypotension with heart failure did not vary greatly when we compared white and African-American participants," Jones said.

Study participants were part of the Atherosclerosis Risk In Communities (ARIC) Study, an ongoing longitudinal study of men and women in communities throughout the United States.

Heart failure, which affects about 5.7 million people in the United States and caused over 281,000 deaths in 2008, cost the healthcare system about $34.4 billion in 2010, according to the American Heart Association.

The disease occurs when the heart pumps inefficiently, which results in inadequate delivery of blood to the body's cells and organs. Discovering factors that may predict heart failure is important to preventing the disease, Jones said.

The National Heart, Blood, and Lung Institute funded the study. Co-authors are: Christine DeLong Jones, M.D., M.S.; Laura Loehr, M.D., Ph.D.; Nora Franceschini, M.D., M.P.H.; Wayne D. Rosamond, Ph.D.; Patricia P. Chang, M.D., M.H.S; Eyal Shahar, M.D.; David J. Couper, Ph.D.; and Kathryn M. Rose, Ph.D. Author disclosures and sources of funding are on the manuscript.

http://www.nature.com/news/satellites-expose-8-000-years-of-civilization-1.10257

Satellites expose 8,000 years of civilization

Archaeologists develop large-scale method to identify ancient human settlements.

Virginia Gewin

Hidden in the landscape of the fertile crescent of the Middle East, scientists say, lurk overlooked networks of small settlements that hold vital clues to ancient civilizations.

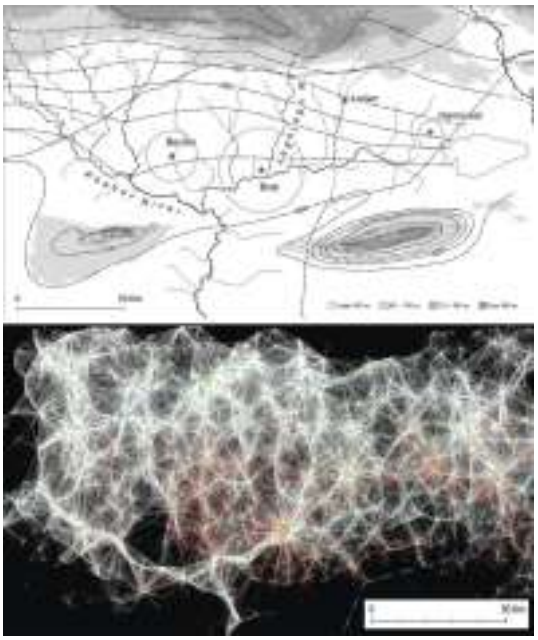
Beyond the impressive mounds of earth, known as tells in Arabic, that mark lost cities, researchers have found a way to give archaeologists a broader perspective of the ancient landscape.

By combining spy-satellite photos obtained in the 1960s with modern multispectral images and digital maps of Earth's surface, the researchers have created a new method for mapping large-scale patterns of human settlement.

The approach, used to map some 14,000 settlement sites spanning eight millennia in 23,000 square kilometres of northeastern Syria, is published today in the Proceedings of the National Academy of Sciences1.

"Traditional archaeology goes straight to the biggest features - the palaces or cities - but we tend to ignore the settlements at the other end of the social spectrum," says Jason Ur, an archaeologist at Harvard University in Cambridge, Massachusetts, who is co-author of the study. "The people who migrated to cities came from somewhere; we have to put these people back on the map."

Such comprehensive maps promise to uncover long-term trends in urban activity. "This kind of innovative large-scale application is what remote sensing has been promising archaeology for some years now; it will certainly help us to focus our attention on the big picture," says Graham Philip, an archaeologist at Durham University, UK.



Analysis of the locations of ancient settlements can reveal the many connections between them.

Soil signatures

The satellite-based method relies on the fact that human activity leaves a distinctive signature on the soil, called anthrosols. Formed from organic waste and decayed mud-brick architecture, anthrosols are imbued with higher levels of organic matter and have a finer texture and lighter appearance than undisturbed soil - resulting in reflective properties that can be seen by satellites.

To sift through satellite images for those signatures, co-author Bjoern Menze, a research affiliate in computer science at the Massachusetts Institute of Technology in Cambridge, built on his skills from his day job identifying tumours in clinical images.

Menze trained software to detect the characteristic wavelengths of known anthrosols in images spanning 50 years of seasonal differences. This automation was key. "You could do this with the naked eye using Google Earth to look for sites, but this method takes the subjectivity out of it by defining spectral characteristics that bounce off of archaeological sites," says Ur.

Menze and Ur also used digital elevation data collected in 2000 by the space shuttle as part of NASA's Shuttle Radar Topography Mission (SRTM). This information enabled the authors to estimate the volume of the larger sites for the first time - and to use this volume as a proxy for a site's longevity. The bigger the mound, the longer the settlement survived.

Tony Wilkinson, an archaeologist at Durham University and Ur's former mentor, says that being able to measure the volume of many sites over large areas remotely is a breakthrough.

However, Philip cautions that the resolution of the SRTM data may be too coarse to provide an accurate measurement for the volume of the smaller settlements. Nonetheless, he expects that the method will spark new archaeological insights for several different regions.

New life for old hypotheses

The method has already renewed speculation about the importance of water to city development. Surprisingly, this study found that a handful of sites are unexpectedly large given that they are not located near rivers or in areas of high precipitation.

"The settlement known as Tell Brak, for example, is far too large for what one would expect at such a marginal position," says Ur. "This is where things get interesting."

Jennifer Pournelle, a landscape archaeologist at the University of South Carolina in Columbia, agrees. "These findings validate hypotheses I've introduced in southern Iraq - namely that irrigation is an after-effect of urbanization," she says. "It's not what enables a city to develop; it's what keeps them going after soil moisture dries up."

Pournelle says that she plans to adopt this method as soon as possible, and notes that it offers a valuable way to learn more about large regions, particularly when they are remote and difficult to access because of local conflicts. *Nature doi:10.1038/nature.2012.10257*

References *Menze, B. H. & Ur, J. A. Proc. Natl Acad. Sci. USA http://dx.doi.org/10.1073/pnas.1115472109 (2012).*

http://www.bbc.co.uk/news/health-17439490

Mars for the 'average person'

Rocket entrepreneur Elon Musk believes he can get the cost of a round trip to Mars down to about half a million dollars.

The SpaceX CEO says he has finally worked out how to do it, and told the BBC he would reveal further details later this year or early in 2013. Musk is one of Nasa's new commercial partners, building systems to take cargo and crew to the space station. He has developed his own rocket and a capsule for the purpose.

The Falcon 9 launcher and the Dragon vessel are expected to give the first full demonstration of their capabilities next month on an unmanned sortie to the orbiting outpost.

Elon Musk describes his Mars vision in Scott's Legacy, a BBC Radio 4 programme presented by Kevin Fong. The programme examines the future of exploration. It can be heard on iPlayer but you can also listen to Kevin's extended interview with the SpaceX chief on this page. In the discussion, the California entrepreneur says key technology breakthroughs are dramatically lowering the cost of space access to the point where a mission to the Red Planet will very soon become a realistic financial prospect.

"My vision is for a fully reusable rocket transport system between Earth and Mars that is able to re-fuel on Mars - this is very important - so you don't have to carry the return fuel when you go there," he said.

"The whole system [must be] reusable - nothing is thrown away. That's very important because then you're just down to the cost of the propellant. "We will probably unveil the overall strategy later this year in a little more detail, but I'm quite confident that it could work and that ultimately we could offer a round trip to Mars that the average person could afford - let's say the average person after they've made some savings."

The entrepreneur described this as about half a million dollars. He conceded the figure was unlikely to be the opening price - rather, the cost of a ticket on a mature system that had been operating for about a decade. Nonetheless, Musk thought such an offering could be introduced in 10 years at best, and 15 at worst.

"Land on Mars, a round-trip ticket - half a million dollars. It can be done," he asserts.

Leaving aside how one might define the wealth of an "average person", this is quite a claim. To put it in some context - Nasa itself is commissioning its own rocket and capsule system from more established aerospace companies that the agency expects eventually to use on Mars missions. Few elements of this multi-billion-dollar system will be re-useable and its maiden manned flight - probably a loop around the Moon - may not occur until the early 2020s. A Nasa-led manned mission to the Red Planet is unlikely to happen until the 2030s, and that could be optimistic.

There will be some who will see Elon Musk's latest remarks as little more than bluster. After all, SpaceX still has much to prove in the here and now. It has still only ever launched a rocket seven times, and the first three failed. That space station re-supply mission has also repeatedly slipped on its schedule, say the doubters. Space is difficult and SpaceX has yet to show it has suddenly become easy, they add.

Even so, Nasa itself is expecting big things from Musk's team, and is pushing Congress to release more money in 2013 to seed the development of commercial spaceflight systems like those from SpaceX.

In his BBC interview, Musk talks about the importance of his Falcon 9-Heavy vehicle. This rocket will be substantially bigger than the simple variant due to fly next month, and should be capable of putting more than 53 tonnes (117,000lb) of payload in a low-Earth orbit - more than twice that of the space shuttle.

Musk believes the Falcon Heavy will be transformative because it will substantially reduce the cost of carrying a given mass into space - breaking the barrier of $1,000 per pound lifted.

He cites the advanced design of its structure, its avionics, its engines and its launch operation as important contributions to the template of low cost. But it will be by making this vehicle totally reusable, by recovering all its parts to put back on the launch pad, that will ultimately slash the cost of space access, he contends.

"If you had to buy a new plane every time you flew somewhere, it would be incredibly expensive," Musk says. "A 747 costs something like $300m and you'd need two of them to do a round trip. And yet people aren't paying half a billion dollars to fly from LA to London, and that's because that 747 can be used tens of thousands of times.

"We must get to the same position in rocketry. That's really what's critical; in order to get a two orders of magnitude improvement beyond Falcon Heavy (in other words to get down to the $10 or $20 per pound to orbit range), you have to have high levels of reusability. "You need to be in the position where it is the cost of the fuel that actually matters and not the cost of building the rocket in the first place."

This episode of Scott's Legacy was first broadcast on BBC Radio 4 on Tuesday 20 March, and is repeated on Thursday 22 March at 21:02 GMT. It is also available on the iPlayer.

http://www.physorg.com/news/2012-03-reveals-ancestors-bipedal-power.html

Study reveals why our ancestors switched to bipedal power

Our earliest ancestors may have started walking on two limbs instead of four in a bid to monopolise resources and to carry as much food as possible in one go, researchers have found.

PhysOrg.com - A study published in the journal Current Biology this week, investigated the behaviour of modern-day chimpanzees as they competed for food resources, in an effort to understand why our "hominin", or "human-like" ancestors became bipedal.

Its findings suggest that chimpanzees switch to moving on two limbs instead of four in situations where they need to monopolize a resource, usually because it may not occur in plentiful supply in their habitat, making it hard for them to predict when they will see it again. Standing on two legs allows them to carry much more in one go because it frees up their hands.

The joint University of Cambridge and Kyoto University team of biological anthropologists, led by PhD student Susana Carvalho and Professor Tetsuro Matsuzawa, conclude that our earliest hominin ancestors may have lived in shifting environmental conditions in which certain resources were not always easy to come by. Over time, intense bursts of bipedal activity may have led to anatomical changes that in turn became the subject of natural selection where competition for food or other resources was strong.

Professor William McGrew, from the Department of Archaeology and Anthropology, University of Cambridge, said: "Bipedality as the key human adaptation may be an evolutionary product of this strategy persisting over time. Ultimately, it set our ancestors on a separate evolutionary path."

Lack of evidence in the fossil record means that researchers remain divided over when these ancestors became bipedal. It is widely believed that they did so because of climatic changes, which reduced forested areas and forced them to move longer distances across open terrain more often. The new research digs deeper, however, by attempting to explain what particular pressures within that context forced those hominins to modify their posture and resort to moving on their legs. The team theorized that the reason for this change may have something to do with the need to transport resources with maximum efficiency. Because bipedal movement is sometimes observed in modern great apes, they decided to monitor the behaviour of chimpanzees and, if possible, determine when and why they resorted to moving on two legs.

Two surveys were carried out. The first was in Kyoto University's "outdoor laboratory" of a natural clearing in Bossou Forest, Guinea. Here, the researchers allowed the chimpanzees access to different combinations of two different types of nut – the oil palm nut, which is naturally widely available, and the coula nut, which is not, so the latter is an "unpredictable" resource.

Their behavior was monitored in three different situations: (a) when only oil palm nuts were available, (b) when a small number of coula nuts was available, and (c) when coula nuts were the majority available resource.

When the rare coula nuts were available only in small numbers, the chimpanzees transported far more in one go. Similarly, when coula nuts were the majority resource, the chimpanzees ignored the oil palm nuts altogether. Clearly, the chimpanzees regarded the coula nuts as a more highly-prized resource and competed for them more intensely.

In such high-competition settings, the frequency of cases in which the chimpanzees started moving on two legs increased by a factor of four. Not only was it obvious that bipedal movement allowed them to carry more of this precious resource, but also that they were actively trying to move as much as they could in one go by using everything available – even their mouths.

The second survey was a 14-month study of Bossou chimpanzees crop-raiding, a situation in which they have to compete for rare and unpredictable resources. Here, 35% of their activity involved some sort of bipedal movement, and once again, this behaviour appeared to be linked to a clear attempt to carry as much as possible in one go. The study concludes that unpredictable resources, like the coula nut in the field survey, are seen by chimpanzees as more valuable. When these resources are scarce and access to them is on a "first-come, first-served" basis, they are more prone to switch to bipedal movement, because it allows them to carry more of the resource at once.

For our early ancestors, unpredictable access to vital resources may have been a frequent occurrence because of climatic shifts and rapid environmental change. Those who resorted to bipedal movement may have had an advantage, and gradually, anatomical change may have taken place as they used this strategy again and again. Once that happened, ability to move more easily on two legs may have become a selection pressure, so that over many generations, it became the norm.

More information: *The full report, Chimpanzee carrying behavior and the origins of human bipedality, is available in the March 20 issue of Current Biology: http://www.cell.com/current-biology/Provided by University of Cambridge*

http://www.physorg.com/news/2012-03-group-madagascar-unique-animals-rafts.html

Research group suggests Madagascar's unique animals arrived on rafts

Since Madagascar was first visited by people there has been speculation about the unique plants and animals on the world's fourth largest island; where ninety percent of the wildlife is found nowhere else

PhysOrg.com - Ever since the island of Madagascar was first visited by people, some two thousand years ago, there has been speculation about the unique plants and animals that live on the world's fourth largest island; one where roughly ninety percent of the wildlife is found nowhere else.

For many years, it was believed they came to be there during the time when the island was still physically connected to Africa, but that reasoning has fallen by the wayside as it has been shown that the island separated some 88 million years ago, while most of the animals that live there didn't arrive till just 60 million years ago, forcing evolutionary scientists to search for other explanations.

Now new evidence by an international group of researchers is proposing that the animals got there by floating on rafts during a time when prevailing currents would have made the journey more plausible. They have published a paper on their ideas in the Proceedings of the National Academy of Sciences.

Today, the distance between Madagascar and Africa is about 250 miles (400 kilometers), far enough to make the journey by raft virtually impossible due to a lack of fresh water to drink, not to mention overheating and sunburn.

But, say the researchers, some 60 million years ago, things were different. During that time, the island was in a slightly different position. In particular, its northernmost edge hadn't started creeping into the southern equatorial current, which means ocean currents would have been able to flow from west to east, which would have helped tremendously.

If the animals were to ride over, they would have done so accidentally due to finding themselves marooned on a raft made of natural vegetation torn from the ground during a cyclone, examples of which have been seen often enough in modern times to prove that it can happen. If such a situation did occur, it's possible the small raft could have been blown far out to sea by a storm that also deposited enough water on the raft to allow any animals aboard to survive the trip from Africa, or even Asia.

The researchers came to these conclusions after building a database of all the animals on the island and then working backwards using genetic evidence to pinpoint almost precisely the time frame that they diverged from their African cousins. Once they had that, they studied research findings regarding conditions on the Earth in that area and found that it was likely that the ocean currents could have been flowing east to west due to tectonic shifting.

The research team suggests that the animals would also have had time on their side. Over a span of millions of years, a rare event such as animals floating over could have occurred often enough to account for the animals that did make it over and who eventually began reproducing.

The team also points out that once the island shifted enough to change ocean currents, the numbers of animals reaching Madagascar diminished greatly, which explains why those that did make the trip lived in almost complete isolation, giving rise to the evolution of such exotic species.

More information: Spatial and temporal arrival patterns of Madagascar's vertebrate fauna explained by distance, ocean currents, and ancestor type, PNAS, Published online before print March 19, 2012, doi: 10.1073/pnas.1113993109

Abstract

How, when, and from where Madagascar's vertebrates arrived on the island is poorly known, and a comprehensive explanation for the distribution of its organisms has yet to emerge. We begin to break that impasse by analyzing vertebrate arrival patterns implied by currently existing taxa. For each of 81 clades, we compiled arrival date, source, and ancestor type (obligate freshwater, terrestrial, facultative swimmer, or volant). We analyzed changes in arrival rates, with and without adjusting for clade extinction. Probability of successful transoceanic dispersal is negatively correlated with distance traveled and influenced by ocean currents and ancestor type. Obligate rafters show a decrease in probability of successful transoceanic dispersal from the Paleocene onward, reaching the lowest levels after the mid-Miocene. This finding is consistent with a paleoceanographic model [Ali JR, Huber M (2010) Nature 463:653–656] that predicts Early Cenozoic surface currents periodically conducive to rafting or swimming from Africa, followed by a reconfiguration to present-day flow 15–20 million years ago that significantly diminished the ability for transoceanic dispersal to Madagascar from the adjacent mainland.

http://www.eurekalert.org/pub_releases/2012-03/msu-csp032012.php

Curcumin shows promise in attacking Parkinson's disease

A compound found in the spice turmeric is proving effective at preventing clumping of a protein involved in Parkinson's disease

EAST LANSING, Mich. - Curcumin, a compound found in the spice turmeric, is proving effective at preventing clumping of a protein involved in Parkinson's disease, says a Michigan State University researcher.

A team of researchers led by Basir Ahmad, an MSU postdoctoral researcher, demonstrated earlier this year that slow-wriggling alpha-synuclein proteins are the cause of clumping, or aggregation, which is the first step of diseases such as Parkinson's. A new study led by Ahmad, which appears in the current issue of the Journal of Biological Chemistry, shows that curcumin can help prevent clumping. "Our research shows that curcumin can rescue proteins from aggregation, the first steps of many debilitating diseases," said Lisa Lapidus, MSU associate professor of physics and astronomy who co-authored the paper with Ahmad. "More specifically, curcumin binds strongly to alpha-synuclein and prevents aggregation at body temperatures."

Lapidus' lab uses lasers to study protein folding. Proteins are chains of amino acids that do most of the work in cells. Scientists understand protein structure, but they don't know how they are built – a process known as folding. Lapidus' team is shedding light on the process by correlating the speed at which protein folds with its tendency to clump or bind with other proteins. When curcumin attaches to alpha-synuclein it not only stops clumping, but it also raises the protein's folding or reconfiguration rate. By bumping up the speed, curcumin moves the protein out of a dangerous speed zone allowing it to avoid clumping with other proteins.

Finding a compound that can fix a protein when it first begins to misfold can lead scientists to identify drugs that can treat certain diseases. Doctors won't be prescribing curcumin pills any time soon, though, Lapidus said.

"Curcumin's usefulness as an actual drug may be pretty limited since it doesn't go into the brain easily where this misfolding is taking place," she said. "But this kind of study showcases the technique of measuring reconfiguration and opens the door for developing drug treatments."

http://www.eurekalert.org/pub_releases/2012-03/joci-nel031912.php

New evidence links Alzheimer's disease and diabetes

An emerging body of research suggests that Alzheimer's disease may be linked to insulin resistance, constituting a third type of diabetes.

This model is based on several observations including an increased risk of developing Alzheimer's disease for diabetic patients, and reduced insulin levels in the brain tissue of Alzheimer's disease patients. Though intriguing, the existing evidence does not reveal if defective insulin signaling is causative of Alzheimer's or how insulin resistance impacts cognitive function. Two back-to-back research articles in the Journal of Clinical Investigation – led by Konrad Talbot, Steve Arnold and colleagues at the University of Pennsylvania and by Fernanda De Felice, Sergio Ferreria and colleagues at the University of Rio de Janeiro - address the connection between insulin resistance and Alzheimer's disease.

The University of Pennsylvania team examined insulin signaling in human brain tissue postmortem, and concluded that the activation state of many insulin signaling molecules were highly related to memory and cognitive function. They further suggest that insulin resistance is a common and early feature of Alzheimer's disease. The De Felice group further observed impaired insulin signaling in Alzheimer's brain tissue in rodent and non-human primate model systems as well as from tissue from human patients.

They went on to show in a mouse model system of Alzheimer's disease that treatment with a new anti-diabetic drug normalized insulin signaling and remarkably improved cognitive function. Cumulatively, these two new studies strongly support a connection between insulin resistance and Alzheimer's disease and provide hope for new therapeutics in Alzheimer's disease treatment.

An anti-diabetes agent protects the mouse brain from defective insulin signaling caused by Alzheimer's disease–associated Aß oligomers View this article at: http://www.jci.org/articles/view/57256?key=de0efc001f2106f5edc4

http://news.discovery.com/history/madagascar-women-120320.html

Madagascar Founded By Women

The discovery negates a prior theory about how the island was first found.

By Jennifer Viegas

Madagascar was first settled and founded by approximately 30 women, mostly of Indonesian descent, who may have sailed off course in a wayward vessel 1200 years ago. The discovery negates a prior theory that a large, planned settlement process took place on the island of Madagascar, located off the east coast of Africa. Traditionally it was thought to have been settled by Indonesian traders moving along the coasts of the Indian Ocean.

Most native Madagascar people today, called Malagasy, can trace their ancestry back to the founding 30 mothers, according to an extensive new DNA study published in the latest Proceedings of the Royal Society B,. Researchers focused on mitochondrial DNA, passed down from mothers to their offspring. Scientists assume some men were with the women.

"I'm afraid this wasn't a settlement by Amazon seafarers!" lead author Murray Cox told Discovery News. "We propose settlement by a very small group of Indonesian women, around 30, but we also presume from the genetics that there were at least some Indonesian men with them. At this stage, we don't know how many."

Cox, a senior lecturer at Massey University's Institute of Molecular BioSciences, and his colleagues analyzed genetic samples from 2745 individuals hailing from 12 Indonesian archipelago island groups. They then compared the results with genetic information from 266 individuals from three Malagasy ethnic groups: Mikea hunter-gatherers, semi-nomadic Vezo fishermen and the dominant Andriana Merina ethnic group.

Many Malagasy carry a gene tied to Indonesia. The DNA detective work indicates just 30 Indonesian women founded the Malagasy population, with a much smaller biological contribution from Africa. The women may have mated with their male Indonesian travel companions, or with men from Africa.

"The small number of Indonesian women is consistent with a single boatload of voyagers," Cox said, adding that "typical Indonesian trading ships in the mid first millennium A.D. could hold around 500 people. "

The distance between Indonesia and Madagascar is close to 5000 miles, so the women and their travel mates must have had quite a journey, especially if it was unintended. The small founder population of Indonesian women makes this scenario fairly unlikely," Cox said. "Instead, our new evidence favors a small movement of people, and perhaps even an unplanned crossing of the Indian Ocean."

Scant archaeological evidence, consisting of a few bones marked by stone tools and an increased rate of forest fires, suggests people may have first visited, but not settled, Madagascar around 2000 years ago. Even that is very recent in terms of overall human history.

Madagascar was one of the last places on earth to have been settled, with remote islands like New Zealand, Hawaii and Easter Island being in the short group of places that were settled later - about 900 years ago.

"Our best argument is that these islands were just extremely difficult to get to," Cox said.

Matthew Hurles, a senior group leader at the Wellcome Trust Sanger Institute, has also studied the genetic heritage of Madagascar's native people. He and his team also noted the Indonesian connection.

"Malagasy peoples are a roughly 50:50 mix of two ancestral groups: Indonesians and East Africans," Hurles said. "It is important to realize that these lineages have intermingled over intervening centuries since settlement, so modern Malagasy have ancestry in both Indonesia and Africa."

Cox concluded, "It is worth emphasizing that Madagascar wasn't a 'sealed box' after its initial settlement. There are notable later contributions by Africans, Arabs and Europeans. All of these contributions show up in the DNA of Malagasy today."

http://www.bbc.co.uk/news/health-17443454

Daily aspirin 'prevents and possibly treats cancer'

Taking a low dose of aspirin every day can prevent and possibly even treat cancer, fresh evidence suggests.

By Michelle Roberts Health reporter, BBC News

The three new studies published by The Lancet add to mounting evidence of the drug's anti-cancer effects.

Many people already take daily aspirin as a heart drug. But experts warn that there is still not enough proof to recommend it to prevent cancer cases and deaths and warn that the drug can cause dangerous side effects like stomach bleeds.

Prof Peter Rothwell, from Oxford University, and colleagues, who carried out the latest work, had already linked aspirin with a lower risk of certain cancers, particularly bowel cancer. But their previous work suggested people needed to take the drug for about 10 years to get any protection.

Now the same experts believe the protective effect occurs much sooner - within three to five years - based on a new analysis of data from 51 trials involving more than 77,000 patients. And aspirin appears not only to reduce the risk of developing many different cancers in the first place, but may also stop cancers spreading around the body. The trials were designed to compare aspirin with no treatment for the prevention of heart disease. But when Prof Rothwell's team examined how many of the participants developed and died from cancer, they found this was also related to aspirin use.

Halting cancer spread

Taking a low (75-300mg) daily dose of the drug appeared to cut the total number of cancer cases by about a quarter after only three years - there were nine cancer cases per 1,000 each year in the aspirin-taking group,

compared with 12 per 1,000 for those taking dummy pills. It also reduced the risk of a cancer death by 15% within five years (and sooner if the dose was higher than 300mg) And if patients stayed on aspirin for longer, their cancer death risk went down even further - by 37% after five years.

Low-dose aspirin also appeared to reduce the likelihood that cancers, particularly bowel, would spread (metastasise) to other parts of the body, and by as much as half in some instances.

In absolute numbers, this could mean for every five patients treated with aspirin one metastatic cancer would be prevented, the researchers estimate. At the same time, aspirin cut the risk of heart attacks and strokes, but it also increased the risk of a major bleed. However this elevated bleeding risk was only seen in the first few years of aspirin therapy and decreased after that.

Critics point out that some of the doses given in the study were much higher than the 75mg dose typically given in the UK. Also, some very large US studies looking at aspirin use were not included in the analysis. The researchers acknowledge both of these points in their published papers.

Prof Rothwell says for most fit and healthy people, the most important things they can do to reduce their lifetime cancer risk is to give up smoking, take exercise and have a healthy diet.

After that aspirin does seem to reduce the risk further - only by a small amount if there is no risk factor, but if there is a family history for something like colorectal cancer, it tips the balance in favour of aspirin, he said.

Prof Peter Johnson, of Cancer Research UK, said it was still a good idea for people thinking of taking aspirin to discuss it with their GP because of the possible side effects. But he said the work was exciting and suggested aspirin might be beneficial for treating and preventing cancer, which is something the charity is exploring in its own research. "We now need some definitive advice from the government as to whether aspirin should be recommended more widely," he said.

The National Institute for Health and Clinical Excellence (Nice), which issues treatment guidelines for the NHS, has not yet been asked by the government to look at the topic but a spokesman for the Department of Health said they were considering how best to advise the public about the benefits and risks of aspirin.

Meanwhile, the leader of an ongoing UK trial looking at cancers of the gastrointestinal tract said their results - as yet unpublished - suggested no preventative effect of aspirin after following patients for several years.

Professor Janusz Jankowski of Barts and The London School of Medicine and Dentistry said: "So far aspirin cancer prevention effects have not been seen in this major UK study after > 4.5 years of therapy. "

http://www.bbc.co.uk/news/health-17442996

Arm blood pressure differences 'predict death risk'

A large difference between the blood pressure in each arm suggests a bigger risk of dying early, researchers claim.

By Helen Briggs Health editor, BBC News website

A study of 230 high blood pressure patients found those with big differences in systolic pressure were more likely to die from heart attack, stroke or other causes. More heart health checks may be needed in those with different readings, says the British Heart Foundation.

Not all medics follow national guidance to measure blood pressure in both arms. Dr Christopher Clark from the Peninsula College of Medicine and Dentistry at the University of Exeter, who led the study, published in the British Medical Journal, said the message to doctors was simple. "Sorry guys, but you really need to follow the guidelines by measuring both arms when you're assessing blood pressure," he told the BBC.

He said patients with high blood pressure who routinely checked their blood pressure at home should also follow the advice. "If they are being treated on the basis of their blood pressure, it's important to know if there's a difference between arms so they know their treatment is based on the correct measurements in the future."

A previous analysis of 28 study papers in The Lancet also found that a large difference in readings could mean an increased risk of vascular disease and death.

Maureen Talbot, senior cardiac nurse at the British Heart Foundation, said: "This study supports national guidelines, which recommend that blood pressure readings are taken in both arms. It is normal to have a small difference in your blood pressure readings between arms. "However, a big difference between your readings may carry risks, so more tests could be needed to check your heart health. If you want to find out your blood pressure, visit your GP or practice nurse to have it measured."

People with different readings in each arm may have peripheral vascular disease, which often shows no symptoms.

Stopping smoking, or medication to lower blood pressure or cholesterol, may help reduce the risk of heart problems or stroke in these patients.

http://www.physorg.com/news/2012-03-electricity-trees.html

Electricity from trees

Scientists have long-suspected an association between trees and electricity. A team of researchers may have finally discovered the link.

Plants have long been known as the lungs of the earth, but a new finding has found they may also play a role in electrifying the atmosphere.

Scientists have long-suspected an association between trees and electricity but researchers from Queensland University of Technology (QUT), in Brisbane, Australia, think they may have finally discovered the link.

Dr Rohan Jayaratne and Dr Xuan Ling from QUT's International Laboratory for Air Quality and Health (ILAQH), led by Professor Lidia Morawska, ran experiments in six locations around Brisbane, including the Brisbane Forest Park, Daisy Hill and Mt Coot-tha. They found the positive and negative ion concentrations in the air were twice as high in heavily wooded areas than in open grassy areas, such as parks.

Dr Jayaratne, who is also a member of QUT's Institute of Health and Biomedical Innovation (IHBI), said that natural ions in the air were mainly created by ionisation due to two processes - radiation from the trace gas radon in air and cosmic radiation from space. Radon is a by-product of the radioactive decay of radium which is present in minute quantities in rocks and is continually exhaled by the ground.

"Because radium is found in rocks and radon is soluble in water, ground water is particularly rich in radon," he said. "Trees act as radon pumps, bringing the gas to the surface and releasing it to the atmosphere through transpiration - a process where water absorbed by the root system is evaporated into the atmosphere from leaves. This is especially prevalent for trees with deep root systems, such as eucalypts."

The QUT scientists estimated that, in a eucalyptus forest, trees may account for up to 37 per cent of the radon in the air when transpiration rates were highest.

Dr Jayaratne said though there was still a lot more research which needed to be done in relation to the role of ions, the findings, which were published in the journal Environmental Science and Technology, have potentially important implications for the atmosphere, climate and human health.

"Although there is an established link between airborne particles and human health, the role of ions is largely unknown," he said. "However, we do know that approximately one-half of the particles that we inhale during normal breathing are retained in our respiratory system and it has been shown that charged particles were more likely to be deposited in the lungs than uncharged particles. "We do not believe that ions are dangerous - the danger comes from the pollutants. If there are no dangerous particles in the air to attach to the ions there is no risk of ill health." *Provided by Queensland University of Technology*

http://www.bbc.co.uk/news/science-environment-17248776

Mercury has been 'dynamic world'

The planet Mercury was once an active and dynamic planet, according to new evidence from a Nasa spacecraft.

By Paul Rincon Science editor, BBC News website, The Woodlands, Texas

Data from the American Messenger probe shows that impact craters on the planet's surface were distorted by some geological process after they formed. The findings, reported in Science magazine, challenge long-held views about the closest world to the Sun. Another study looking at Mercury's gravity field shows that the planet has an unusual internal structure. As well as being published in the journal Science, the research has also been presented here at the Lunar and Planetary Science Conference in The Woodlands, Texas.

"Many scientists believed that Mercury was much like the Moon - that it cooled off very early in Solar System history, and has been a dead planet throughout most of its evolution," said Maria Zuber, from the Massachusetts Institute of Technology (MIT). "Now, we're finding compelling evidence for unusual dynamics within the planet, indicating that Mercury was apparently active for a long time."

Dr Zuber and her colleagues used laser measurements from Messenger to map out a large number of impact craters, and found that many had tilted over time. This suggests that geological processes within the planet have re-shaped Mercury's terrain after the craters were created.

Observations of Caloris Basin, the planet's largest impact feature, show that portions of the crater floor stand higher than its rim, suggesting that forces within Mercury's interior pushed the surface up after the initial collision event.

The researchers also identified an area of lowlands near Mercury's north pole that could have migrated there over the course of the planet's evolution. A process called polar wander can cause geological features to shift around on a planet's surface. In theory, the process of convection going on within the mantle could drive such changes. But Dr Zuber said this would be unusual in Mercury's case, because the mantle is so thin.

Another potential explanation could be that features on the surface were distorted as the planet's interior cooled and contracted. This fits in with observations that some surface features on Mercury have been exposed to high levels of stress.

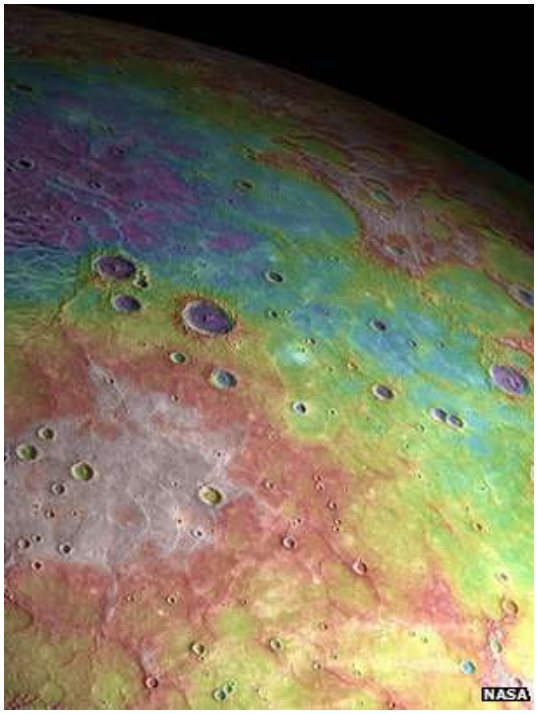
Scientists had long known that the planet possessed a large, iron-rich core and relatively thin outer shell.

Several theories had been put forward to explain this, including the idea that Mercury was struck early in its history by a large space rock, stripping away much of the original crust and mantle.

Messenger's measurements of the planet's gravity field have now confirmed an exceptionally large iron core which is partially liquid. This core makes up about 85% of the planet's radius, with the outer shell occupying about 15% - about as thin as the peel on an orange. But this thin outer shell is also surprisingly dense.

In order to explain this, Dave Smith, from Nasa's Goddard Space Flight Center, and colleagues propose that the core is surrounded by a solid layer of iron sulphide - a type of structure not known to exist on any other planet. The iron sulphide layer is in turn encased by a thin mantle and crust made from silicate rock.

"We had an idea of the internal structure of Mercury, [but] the initial observations did not fit the theory so we doubted [them]," said Dr Smith. "We did more work and concluded the observations were correct, and then reworked the theory... it's a nice result."



A broader view: Some areas (white) have clearly been deformed and risen over time

Mercury Messenger is the first ever mission to orbit the first planet from the Sun. Messenger took up that position in March 2011, and has since circled the planet twice a day, collecting nearly 100,000 images and more than four million measurements of the surface.

Throughout its mission, the spacecraft has had to contend with tidal forces from the Sun, which have tugged the probe out of its preferred orbit, as well as "sunlight pressure" in which photons, or packets of light, from our star "press" on the spacecraft. The team has periodically had to adjust the probe's orbit and apply corrections to its measurements to account for the Sun's effects.

http://bit.ly/Gzw8qr

NCBI ROFL: Which brand of ball point pen is best for an emergency airway puncture?

Airflow efficacy of ballpoint pen tubes: a consideration for use in bystander cricothyrotomy.

OBJECTIVE:To examine the suitability of commonly available ballpoint pens as a substitute emergency tracheostomy tube.

METHODS: Commonly available ballpoint pens were examined and compared against two standard cricothyroidotomy sets. The pens were evaluated for dimensions, speed of construction of a temporary tracheostomy tube and airway resistance with differing flow rates.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Emerg Med J. 2010 Apr;27(4):317-20.

Airflow efficacy of ballpoint pen tubes: a consideration for use in bystander cricothyrotomy.

Owens D, Greenwood B, Galley A, Tomkinson A, Woolley S

Princess of Wales Hospital, Bridgend, Wales CF31 1RQ, UK.

Abstract

OBJECTIVE: To examine the suitability of commonly available ballpoint pens as a substitute emergency tracheostomy tube.

METHODS: Commonly available ballpoint pens were examined and compared against two standard cricothyroidotomy sets. The pens were evaluated for dimensions, speed of construction of a temporary tracheostomy tube and airway resistance with differing flow rates.

RESULTS: Internal diameters of the pens varied considerably. Time taken to construct a temporary tube ranged from 3 to 170 s, and in the majority of pens the airway resistance increased dramatically as the airflow rate increased.

CONCLUSION: Contrary to popular belief, the majority of ballpoint pens appear unsuitable for use as a substitute tracheostomy tube. In this study only two pens fulfilled the criteria for use: the Baron retractable ballpoint and the BIC soft feel Jumbo.

PMID: 20388693 [PubMed - in process]

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http://blogs.scientificamerican.com/disease-prone/2012/03/21/you-should-rub-honey-on-your-everywhere/

You should rub honey on your everywhere

Honey is awesome. I've found its best consumed when combined with nougat and wrapped in dark chocolate but I digress.

By James Byrne | March 21, 2012

Indulge me while I digress my way to diabetes Honey also has some pretty amazing properties, its broadly antimicrobial and seemingly able to promote healing. My Nan would always give me a spoonful of honey alongside other meds when I had colds and flus but as you can see below it can have pretty amazing results on far more serious injuries. Honey's 'healing powers' can be summarised into 5 main ingredients or activities of the components of honey;

Hydrogen peroxide – Honey contains an enzyme called glucose oxidase which breaks down glucose sugars and generates hydrogen peroxide, a kind of bleach, when there is free water available. In case you missed the antimicrobial component it was friggin BLEACH IN YOUR HONEY. I can feel you wondering why bees would bleach their own food supply and it turns out that is very simple. Any available water can cause the honey to spoil so the presence of glucose oxidase in the honey is an inbuilt anti-spoiling mechanism, pretty smart huh?

Sugar – The hydrogen peroxide control mechanism is a back up as very little free water exists in honey. The lack of free water is due to the vast amount of sugar dissolved into honey which gives it a low water activity. This essentially means that honey is more likely to take up water from its surroundings than have water removed from it and if you are a micro-organism it makes it very difficult to survive.

Methylglyoxal or MGO – This compound is an incredibly interesting and powerful antibacterial compound but, it is only found in certain natural honeys (Manuka honey from New Zealand) although it can be made in artificial greenhouses as well. This is the stuff that is making honey a potentially very useful topical salve (with the possibility of other forms of treatment being considered) in medical honey treatments such as MediHoney.

Bee Defensin 1 – Bee Defensin is an antimicrobial peptide (AMP) that for a long time was thought to be exclusively found in the Royal Jelly (The food worker bees make for potential Queen larve). But fairly recent discoveries have found it in the honey, but more on AMPs in a second.

Acidity – Finally, honey is fairly acidic and remains so even when diluted holding a pH of approximately 3.5. Nothing that likes eating you particularly likes living in acid so this property is very important.

No single property is more important than the others and the multifactorial nature of honey's activities is probably the key to its amazing antimicrobial nature. Having said this, Bee Defensin 1 and other identified AMPs in honey such as Apidaecin may have much more involved roles that are only recently being uncovered.

Typically defensins interact with the bacterial membrane and assemble into shapes that facilitate a 'hole-punching' mechanism. The hole-punchers then do just that to the bacterial cell's membrane causing its insides to leak to it's outsides. This is rarely good which may account for the observation that defensins can be found all over the place on the tree of life. They form part of our own innate immune system but you can find them in invertebrates and even in some plants.

Apidaecins, however, work differently. Instead they have been observed moving into the microbial cytoplasm where they bind the protein DnaK. DnaK is involved in helping bacterial cells handle stress (not the 'hard day at the office' kind, the 'my environment is trying to tear me apart' kind). By binding to and inactivating DnaK the bacterial cell cannot respond to a hostile and stressful environment and as a result they die. This ability to induce death via an intracellular mechanism is very attractive to the fields of drug development and structural biology and better yet, a more complete understanding of this mechanism may lead to the development of new antibiotics.

Interestingly, apidaecins seem to also have the ability to alter the host immune system by modifying chemotaxis (movement of cells in the immune system), apoptosis (induced cell death), cytokine/chemokine production (the production of signalling chemicals which direct the immune response), antigen presentation and the Th1/Th2 balance (whether you fight the nasty with B cells or T cells).

In most cases the ability of apidaecins (and their homologues) to modulate the immune system has been done in the the organism the AMP was originally recovered from but some recent work sugests the potential for insect apidaecin to have a crossover effect on a mammalian system. While apidaecin is insect derived it appears to be sufficiently similar in shape to human AMPs that it can interact with and modify the activity of our immune system. When macrophages in particular were incubated with apidaecin they started pumping out chemokines and cytokines that promote increased antimicrobial activity in these cells. Additionally when these cells were stimulated with apidaecins and lipopolysaccharide (a potent immune system activator found on the

surface of many bacterial cells) apidaecin seemed to counter some of the pro-inflammatory effects normally observed with lipopolysaccharide stimulation suggesting it can both promote and regulate the response to microbes.

While only preliminary, it seems honey and it's various components might have more secrets to unveil which will further develop our understanding of the anti-microbial nature of this environmental product and at the same time its pro-immune responses elicited when we use it.

Tavano, R., Segat, D., Gobbo, M., & Papini, E. (2011). The Honeybee Antimicrobial Peptide Apidaecin Differentially Immunomodulates Human Macrophages, Monocytes and Dendritic Cells Journal of Innate Immunity, 3 (6), 614-622 DOI: 10.1159/000327839

Kwakman, P., te Velde, A., de Boer, L., Speijer, D., Vandenbroucke-Grauls, C., & Zaat, S. (2010). How honey kills bacteria The FASEB Journal, 24 (7), 2576-2582 DOI: 10.1096/fj.09-150789

http://www.sciencedaily.com/releases/2012/03/120320161459.htm

Why Getting Healthy Can Seem Worse Than Getting Sick

A new article in The Quarterly Review of Biology helps explain why the immune system often makes us worse while trying to make us well.

ScienceDaily - The research offers a new perspective on a component of the immune system known as the acute-phase response, a series of systemic changes in blood protein levels, metabolic function, and physiology that sometimes occurs when bacteria, viruses, or other pathogens invade the body. This response puts healthy cells and tissue under serious stress, and is actually the cause of many of the symptoms we associate with being sick.

"The question is why would these harmful components evolve," asks Edmund LeGrand (University of Tennessee, Knoxville), who wrote the paper titled with Joe Alcock (University of New Mexico). The researchers contend that answer becomes clear when we view the acute-phase response in terms of what they call "immune brinksmanship."

The immune brinksmanship model "is the gamble that systemic stressors will harm the pathogens relatively more than the host," LeGrand said. The concept, he explains, is akin to what happens in international trade disputes. When one country places trade sanctions on another, both countries' economies take a hit, but the sanctioning country is betting that its opponent will be hurt more.

"One of our contributions here is to pull together the reasons why pathogens suffer more from systemic stress," LeGrand said.

The acute-phase response creates stress in several ways. It raises body temperature and causes loss of appetite and mild anemia. At the same time, certain vital nutrients like iron, zinc, and manganese are partially sequestered away from the bloodstream.

Some of these components are quite puzzling. Why reduce food intake just when one would expect more energy would be needed to mount a strong immune response? Zinc is essential for healthy immune function. Why pull it out of the bloodstream when the immune system is active? The benefits of a stressor like fever are fairly well known; heat has been shown to inhibit bacterial growth and cause infected cells to self-destruct. But what hasn't been clear is why pathogens should be more susceptible to this stress than the host.

LeGrand and Alcock offer some answers. For an infection to spread, pathogens need to multiply, whereas host cells can defer replication. Replication makes DNA and newly forming proteins much more susceptible to damage. It also requires energy and nutrients - which helps explain the benefits of restricting food and sequestering nutrients.

The act of invading a body also requires bacteria to alter their metabolism, which can make them more vulnerable to all kinds of stress, including heat.

Another reason pathogens are more vulnerable to stress is that the immune system is already pummeling them with white blood cells and related stressors at the site of the infection. That means that pathogens are already under local stress when systemic stressors are piled on. "In many ways, the acute-phase response reinforces the stress inflicted on pathogens locally at the infection site," LeGrand said.

As the term "brinksmanship" implies, there's an inherent risk in a strategy that involves harming oneself to hurt the enemy within. This self-harm leaves the body more vulnerable to other dangers, including other infections. Additionally, it is possible for the immune stressors to do more damage than required to control the pathogens.

"But in general, systemic stressors when properly regulated do preferential harm to invaders," LeGrand said. Viewed this way, it's not surprising that natural selection has utilized the stressful parts of the acute-phase response in mammals, reptiles, fish, and even invertebrates.

Journal Reference: *Edmund Kenwood LeGrand, Joe Alcock. Turning Up The Heat: Immune Brinksmanship In The Acute-phase Response. The Quarterly Review of Biology, 2012; 87 (1): 3 DOI: 10.1086/663946*

http://www.sciencedaily.com/releases/2012/03/120321131852.htm

Drug Target for Stimulating Recovery from Stroke Discovered

Removing a matched set of molecules that typically help to regulate the brain's capacity for forming and eliminating connections between nerve cells could aid recovery from stroke even days after the event.

By Bruce Goldman.

ScienceDaily - Investigators at the Stanford University School of Medicine have shown that removing a matched set of molecules that typically help to regulate the brain's capacity for forming and eliminating connections between nerve cells could substantially aid recovery from stroke even days after the event. In experiments with mice, the scientists demonstrated that when these molecules are not present, the mice's ability to recover from induced strokes improved significantly.

Importantly, these beneficial effects grew over the course of a full week post-stroke, suggesting that, in the future, treatments such as drugs designed to reproduce the effects in humans might work even if given as much as several days after a stroke occurs. The only currently available stroke treatment - tissue plasminogen activator, or tPA - must be given within a few hours of a stroke to be effective, and patients' brains must first be scanned to determine whether this treatment is appropriate. Moreover, while tPA limits the initial damage caused by a stroke, it doesn't help the brain restore or replace lost connections between nerve cells, which is essential to recovery.

The mice in the study had been genetically bioengineered to lack certain molecules that one of the Stanford researchers had previously shown to play a major role in modulating the ease with which key nerve-cell connections are made, strengthened, weakened or destroyed in the brain. The molecules in question include "K" and "D," two of the 50 or so members of the so-called MHC class-1 complex, which plays a key role in the function of the immune system. Alternatively, when a receptor called PirB, which binds to these MHC molecules, is not present, the same improved outcome from stroke happens - significant, because receptors make good drug targets.

It was only a few years ago that Carla Shatz, PhD, professor of neurobiology and of biology, and her colleagues surprised the neuroscience and immunology communities by showing that these molecules "moonlight" in the brain, where their job appears to involve inhibiting the readiness of connections among nerve cells (known as synapses) to grow stronger or weaker in response to experience.

Learning and memory require the constant, coordinated strengthening of some synaptic connections and weakening of others. But this very flexibility, if it becomes excessive, is thought to put the brain at risk for conditions such as epilepsy or schizophrenia. The molecules Shatz has been exploring can be seen as providing a measure of stabilizing ballast.

However, in order to re-establish brain functions that have been lost in the massive nerve-cell die-off that follows an extraordinary event such a stroke, it's necessary to restore lost synapses and form new ones at a rapid pace. It's also important to retrain surviving circuits to take over functions formerly served by lost circuits - this is the basis of rehabilitation therapy. Under such circumstances, one might ask, might it be a good idea to ease up on the brake pedal?

"Nobody had ever thought any of these molecules had anything to do with stroke," said Shatz, who is the Sapp Family Provostial Professor and also is the director of Bio-X, Stanford's interdisciplinary biosciences research consortium. "But our lab had shown in 2009 that mice bioengineered to lack them performed like Olympians on motor-learning tasks."

A couple of years ago, Shatz and her colleague, Rona Giffard, MD, PhD, professor of anesthesia and a veteran stroke researcher, grew bored during a scientific meeting and began whispering about their work "to cheer ourselves up," Shatz said. It occurred to them that teaming Shatz's molecules with Giffard's animal-research expertise could provide answers to this question.

The results, published Mar. 22 in Neuron, were unequivocal and potentially quite clinically significant: Mice genetically engineered to lack either K and D or PirB, a major cell-surface receptor for these molecules, experienced markedly better recovery in their motor performance after a stroke than did normal mice. Giffard and Shatz are the senior authors of the Neuron study.

"This is the very first time anyone has looked for a role of these molecules in stroke, or in recovery from stroke," said Giffard. "Targeting recovery, as opposed to just halting the damage, would have the widest possible chance to help patients after stroke, and could help patients who cannot receive tPA."

The collaboration was accelerated by the fact that Jamie Adelson, a PhD candidate in Shatz's laboratory who shared first authorship of the study with postdoctoral researcher George Barreto, PhD, of Giffard's lab, had

worked in the Giffard lab before joining Shatz's group. Tests indicated that concentrations of K and D - which in a healthy brain are already abundant at synapses - rose dramatically in the brain after an induced stroke.

First the researchers trained their mice in certain athletic activities, such as balancing on a spinning horizontal rod at gradually increasing rotation speeds, or traversing the rungs of a small "ladder" suspended horizontally just a half-inch or so above a board. Then the researchers induced strokes in the trained animals by cutting off blood supply to a region of the brain that is involved in motor performance. One week later, the animals lacking K and D had recovered their athletic skills substantially better than the normal animals had.

Moreover, lab tests showed that the stroke-affected area of the K/D-deficient mice was considerably smaller than was the case for the controls. Observations showed that sprouting of new nerve fibers in stroke-affected areas was more abundant in the K/D-deficient mice, too.

Next, the team turned to K and D's counterpart receptor PirB, which binds to K and D as well as to many similar MHC molecules. Shatz has previously shown that this molecule, well-known to immunologists, abounds in the brain. Receptors make excellent targets for therapeutic intervention, as small molecules that bind and block them can often be designed by pharmaceutical and biotech companies and academic pharmacologists. In addition, PirB is the key receptor not only for K and D, but also for all of the roughly 50 different but related MHC molecules that have been identified so far. So blocking PirB could, in theory, be more efficient than attempting to block each of the 50-plus MHC molecules independently or impairing only one or a few of them.

So the Stanford researchers performed similar tests on mice genetically engineered to lack PirB. Just like the mice lacking K and D, PirB-deficient mice recovered their athletic ability better than normal mice did. Not only did PirB-lacking mice's brains show smaller areas affected by the induced stroke than the normal mice's brains did, but these areas also were noticeably smaller one week after the stroke than they were a day afterward, suggesting that restoration of damaged tissue may have occurred. In a dish, glucose- and oxygen-deprived hippocampal slices from the PirB-lacking mice suffered less nerve-cell death than slices from normal mice.

One drug-development expert, Corey Goodman, PhD, called the findings "exciting." Goodman is chair of the board of four biotechnology companies, a board member of two others and co-founder and managing director of venBio LLC, a venture-capital firm. Goodman, who is familiar with the study but was not involved in it, spent 25 years as an academic neuroscientist at Stanford and the University of California-Berkeley before moving into commercial drug development. He noted that, as is typical in early research, what works in a mouse doesn't necessarily translate into human benefits. He said he'd also like to see the results of experiments with normal mice in which MHC/PirB binding could be blocked conditionally (for example, with a small molecule that could enter the brain and bind to, say, PirB), starting at different time points after an induced stroke. "To take this into human trials, you'd need a molecule that could get into the brain and that's very specific to PirB" or MHC molecules, he said. Nevertheless, Goodman pronounced the results "encouraging."

"There is, today, very little we can do for stroke patients, and it has to be done almost immediately," he said. "What makes me optimistic is that this mechanism has to do with growth and repair that takes place days later. This approach has the look of one that might be able to work as long as days and weeks after a stroke."

The study was funded by the National Institutes of Health, the Mathers Charitable Foundation, the Ellison Foundation and a National Defense Science & Engineering Graduate Fellowship.

Additional co-authors were Lijun Xu, MD, Yibing Ouyang, PhD, and Xiaoxing Xiong, MD, of Giffard's lab; and Taeho Kim, PhD, Barbara Brott, PhD, Thorsten Naserke, PhD, and Maja Djurisic, PhD, of Shatz's lab.

Journal Reference: *Jaimie D. Adelson, George E. Barreto, Lijun Xu, Taeho Kim, Barbara K. Brott, Yi-Bing Ouyang, Thorsten Naserke, Maja Djurisic, Xiaoxing Xiong, Carla J. Shatz et al. Neuroprotection from Stroke in the Absence of MHCI or PirB. Neuron, 22 March 2012; 73(6) pp. 1100 - 1107 DOI: 10.1016/j.neuron.2012.01.020*

http://bit.ly/GEYcX1

Reign Check: Abundant Rainfall May Have Spurred Expansion of Genghis Khan's Empire

It is generally thought that changing precipitation patterns impacted the rise of the Mongols and their domination of the Eurasian continent in the 13th century - but was it rain or drought?

By Charles Q. Choi | Wednesday, March 21, 2012 | 10

The Mongol hordes led by Genghis Khan carved out the largest contiguous land empire history has ever witnessed, reaching at its apex from Asia's Pacific coast to eastern Europe and down into Persia and southeastern Asia. Although conventional wisdom suggests drought may have pushed them across the steppe to conquer more bountiful lands, ancient, long-dead trees discovered in a forbidding lava field in Mongolia give evidence that unprecedented rains might actually have helped fuel their expansion.

The Mongols took the Old World by storm in the 13th century. Their invasions and expansion are often attributed to the unstable climate they experienced on the steppes, "with them preying on others because they did not have a constant set of resources," says geographer Amy Hessl at West Virginia University. "Now, we

agree they experienced a variable climate. However, this idea of drought driving the Mongols to expand their territory isn't really based on any climate data from that time, but on inferences based on modern conditions there."

In 2010 Hessl was on a National Geographic–sponsored mission there with forest ecologist Neil Pederson at Columbia University's Lamont–Doherty Earth Observatory to look at the climate history of Mongolia and how climate change might affect the area's wildfire risks. Driving by the Orkhon Valley, the original seat of the Mongol empire, they saw a huge lava field that had been produced by a volcanic eruption 7,000 years ago and checked it for ancient wood. Tree rings can shed light on a region's history - fat rings suggest abundant water that promoted growth, thin ones mean years with less water and growth; the number of rings is linked with how many years a tree has lived - and the live Siberian pines they saw in the area can live about 700 years.

The researchers also took samples from dead wood in the lava field because it can be much older than any living tree there, given how the cold, dry conditions can slow decay. Pinpointing a dead tree's age can be difficult, but a unique growth pattern of fat and thin rings in a living tree might act as a "bar code" to identify wood alive during a specific period such as the 15th century. Seeing the same pattern in living and dead wood of a certain species from the same area reveals that both were alive during the same historical period. Determining the dead wood's age then involves counting back all the rings before that span of time.

All in all, the research team of U.S. and Mongolian scientists sampled 17 trees. "We felt if we got records going back 500 years, that would be fantastic," Pederson recalls. Unexpectedly, they instead discovered two samples with tree rings dating back to A.D. 658, now the longest climate record for this part of the world - and with further research, "we might be able to find tree rings going back maybe 2,000 years," Pederson adds. "We collected these samples as an afterthought when we were exhausted and sick. To find they might go back that far is unbelievable."

A Siberian pine in Mongolia. A Siberian pine in Mongolia. **Image: Amy Hessl**

Surprisingly, their preliminary findings based on the tree ring data suggest the Mongol empire actually rose during a time of abundant rain. These would have turned grasslands there extraordinarily lush, enabled the Mongols to raise vast numbers of horses and other livestock. "There are actually massive wetlands in the area, and during a warm, wet period, they might have been incredibly productive," Hessl says. "There's actually quite a lot of evidence that the Mongols were practicing agriculture around there in the early 1200s, contrary to this image of Mongols as only herders and these horseback hordes."

Although this research is preliminary and needs more data before it can be properly assessed, "I'm not the slightest bit surprised that there are findings that contradict earlier studies," says archaeologist Brian Fagan, professor emeritus at the University of California, Santa Barbara, who did not take part in this study. "It is an area with wildly fluctuating climatic conditions."

This summer, the scientists plan on returning to the lava field to find more and older specimens. The lava field is large, about 50 square kilometers, "and it's very inhospitable - we saw horse skulls everywhere - meaning that people probably didn't venture in too much to gather firewood, and that there may be a lot of ancient wood there," Hessl says. "We'd love to have at least 15 to 20 samples from the 1200s," Pederson notes. "Ideally we'd sample several species of trees from four to five lava fields to get a robust record of drought in central Mongolia for the past 1,000 years."

The researchers also hope to collaborate with ecosystem modeler Hanqin Tian at Auburn University in Alabama, who can use the tree ring climate data to estimate how many animals and other resources the Mongols could have secured from the landscape. In addition, historian Nicola Di Cosmo at the Institute for Advanced Study and his colleagues will comb old manuscripts from China to Europe for references to the climate at the time. Moreover, lake sediment expert Avery Cook Shinneman at the University of Washington also hopes to collect tubes of sediment from lake bottoms in the area for signs of how many livestock might have existed in the past, another sign of the region's past productivity. "Livestock would have disturbed the lake, affecting the sediment in ways we can see, and we can also look for Sporormiella, a tiny spore that thrives in livestock dung," Hessl says.

It may be that climatic changes may not only help explain the expansion of the empire, but its contraction as well. "It may be that a decline in moisture in the Orkhon Valley helped spur the Mongols to relocate their capital to Beijing," Hessl says.

The researchers caution that they are not arguing that climate was the sole or main driver of the rise and fall of the Mongol empire. "Genghis Khan was really key to uniting many tribes together and spurred them to expand in a way that's never been repeated - we just argue that it takes energy to create an empire, just as it does today, and rains may have helped provide the grass that 'powered' their horses," Hessl says. Likewise, "after Genghis Khan died, the empire became somewhat factionalized, with most historians arguing that it became too large to effectively administrate. We're saying maybe climate change may have made managing the empire difficult also."

The fate of the Mongol empire might have lessons for modern life , the researchers say. "The Mongols adapted to changing energy sources and to changing water quality, both of which climate change affected," Hessl says. "Exploring how they adapted might shed light on current challenges we face."

http://www.eurekalert.org/pub_releases/2012-03/hcfa-rpz032212.php

Runaway planets zoom at a fraction of light speed

Not only do runaway planets exist, but some of them zoom through space at a few percent of the speed of light

Seven years ago, astronomers boggled when they found the first runaway star flying out of our Galaxy at a speed of 1.5 million miles per hour. The discovery intrigued theorists, who wondered: If a star can get tossed outward at such an extreme velocity, could the same thing happen to planets?

New research shows that the answer is yes. Not only do runaway planets exist, but some of them zoom through space at a few percent of the speed of light - up to 30 million miles per hour.

"These warp-speed planets would be some of the fastest objects in our Galaxy. If you lived on one of them, you'd be in for a wild ride from the center of the galaxy to the Universe at large," said astrophysicist Avi Loeb of the Harvard-Smithsonian Center for Astrophysics. "Other than subatomic particles, I don't know of anything leaving our galaxy as fast as these runaway planets," added lead author Idan Ginsburg of Dartmouth College.

Such speedy worlds, called hypervelocity planets, are produced in the same way as hypervelocity stars. A double-star system wanders too close to the supermassive black hole at the galactic center. Strong gravitational forces rip the stars from each other, sending one away at high speed while the other is captured into orbit around the black hole.

For this study, the researchers simulated what would happen if each star had a planet or two orbiting nearby. They found that the star ejected outward could carry its planets along for the ride. The second star, as it's captured by the black hole, could have its planets torn away and flung into the icy blackness of interstellar space at tremendous speeds. A typical hypervelocity planet would slingshot outward at 7 to 10 million miles per hour. However, a small fraction of them could gain much higher speeds under ideal conditions.

Current instruments can't detect a lone hypervelocity planet since they are dim, distant, and very rare. However, astronomers could spot a planet orbiting a hypervelocity star by watching for the star to dim slightly when the planet crosses its face in a transit.

For a hypervelocity star to carry a planet with it, that planet would have to be in a tight orbit. Therefore, the chances of seeing a transit would be relatively high, around 50 percent. "With one-in-two odds of seeing a transit, if a hypervelocity star had a planet, it makes a lot of sense to watch for them," said Ginsburg.

Eventually, such worlds will escape the Milky Way and travel through the intergalactic void. "Travel agencies advertising journeys on hypervelocity planets might appeal to particularly adventurous individuals," added Loeb.

http://www.eurekalert.org/pub_releases/2012-03/uosf-sri032112.php

Skull reconstruction immediately following traumatic brain injury worsens brain damage

Delaying surgical repair reduced secondary brain swelling, damage in TBI animal model study

Tampa, FL - Immediate skull reconstruction following trauma that penetrates or creates an indentation in the skull can aggravate brain damage inflicted by the initial injury, a study by a University of South Florida research team reports. Using a rat model for moderate and severe traumatic brain injury, the researchers also showed that a delay of just two days in the surgical repair of skull defects resulted in significantly less brain swelling and damage. The study was published March 16, 2012 in the online journal PloS ONE. While further investigation is needed, the findings have implications for the acute treatment of traumatic brain injury (TBI), considered the signature wound of soldiers who have served in Iraq and Afghanistan, said the study's principal investigator Cesar Borlongan, PhD, professor and vice chair of research at the USF Health Department of Neurosurgery and Brain Repair "A double-edged sword," is how Borlongan describes the inflammation and subsequent swelling of brain tissue that occurs immediately following TBI.

When the brain is initially penetrated - by a bullet, shrapnel, other debris, or even the force of blast waves, for instance - inflammation helps recruit the body's own good (glial) cells to the damaged site to limit localized injury. For a short time, the inflammation-induced edema, or swelling of the brain, is beneficial to help relieve pressure within the skull. However, chronic inflammation precipitates increases in intracranial pressure that perpetuate a vicious cycle leading to secondary cell injury and death.

Cranioplasty is an operation to repair malformations of the skull caused by TBI; the procedure may involve replacing a missing piece of the skull protecting the underlying brain and/or improving the appearance of the skull's surface. Current clinical practice emphasizes performing cranioplasty quickly upon initial hospital admission to help reduce the likelihood of infection or other complications that may arise when the brain is exposed. "Our preclinical study indicates that reconstructing the skull too early in the brain's natural healing process may interfere with critical therapeutic benefits of brain swelling post-TBI," Dr. Borlongan said. "It's better to wait at least two days."

The USF researchers studied rats with moderate and severe TBI. Post-TBI, the animals were randomly assigned to skull bone flap replacement with or without bone wax (a sterile mixture to help control bleeding from bone surfaces); no skull reconstruction; or delayed skull reconstruction with bone wax alone, which was performed two days following TBI. The brains of all the animals were analyzed in the laboratory five days after surgery. While immediate reconstruction provided aesthetic repair of the skull fracture, this early surgical procedure, with bone wax alone or with bone wax and skull bone flap, significantly increased cortical brain tissue damage in both moderate and severe animal models.

Overall, whether the rat model was moderate or severe TBI, delayed reconstruction limited the worsening of brain tissue damage compared to immediate reconstruction. In fact, for moderate TBI, the extent of damage observed in the brains of rats that received delayed reconstruction was on a par with that in the animals getting no reconstruction. In those with severe traumatic brain injury, the tissue damage was significantly larger. The authors suggest this may mean a two-day delay, while more beneficial than immediate reconstruction, was not sufficient to counteract the intracranial pressure generated by severe TBI. The researchers concluded that the timing of cranioplasty warrants further evaluation in both laboratory and clinical settings.

"Our results suggest that delaying cranioplasty until the TBI-induced cerebral swelling has subsided may reduce unwanted exacerbation of cortical damage associated with skull reconstruction," Borlongan said. "We need to carefully weigh the risk of infection that comes from leaving the brain somewhat exposed with the benefit of enhancing the brain's own repair of its cells." "Finding a safe and effective cranioplasty regimen will require determining the optimal period of time when we let the brain repair itself and balancing that with when to best introduce a regimen of surgical skull repair and other potential therapies," said co-author Harry van Loveren, MD, the David W. Cahill endowed professor and chair of the USF Health Department of Neurosurgery and Brain Repair.

The study was supported by the National Institutes of Health National Institute of Neurological Disorders and Stroke, the James and Esther King Foundation for Biomedical Research Program, SanBio Inc., Celgene Cellular Therapeutics, KM Pharmaceutical Consulting and NeuralStem Inc.

Citation: "Immediate, but Not Delayed, Microsurgical Skull Reconstruction Exacerbates Damage in Experimental Traumatic Brain Injury Model;" Loren E. Glover, Naoki Tajiri, Tsz Lau, Yuji Kaneko, Harry van Loveren, Cesario V. Borlongan; PloS ONE 7(3), e33646, March 16, 2012.

http://www.bbc.co.uk/news/health-17457098

Clue to male baldness discovered

A biological clue to male baldness has been discovered, raising the prospect of a treatment to stop or even reverse thinning hair.

By Helen Briggs Health editor, BBC News website

In studies of bald men and laboratory mice, US scientists pinpointed a protein that triggers hair loss. Drugs that target the pathway are already in development, they report in the journal Science Translational Medicine. The research could lead to a cream to treat baldness. Most men start to go bald in middle age, with about 80% of men having some hair loss by the age of 70. The male sex hormone testosterone plays a key role, as do genetic factors. They cause the hair follicles to shrink, eventually becoming so small that they are invisible, leading to the appearance of baldness.

Reverse balding?

Now, researchers at the University of Pennsylvania have analysed which genes are switched on when men start to go bald. They found levels of a key protein called prostaglandin D synthase are elevated in the cells of hair follicles located in bald patches on the scalp, but not in hairy areas.

Mice bred to have high levels of the protein went completely bald, while transplanted human hairs stopped growing when given the protein.

Prof George Cotsarelis, of the department of dermatology, who led the research, said: "Essentially we showed that prostaglandin protein was elevated in the bald scalp of men and that it inhibited hair growth. So we identified a target for treating male-pattern baldness. "The next step would be to screen for compounds that affect this receptor and to also find out whether blocking that receptor would reverse balding or just prevent balding - a question that would take a while to figure out." The inhibition of hair growth is triggered when the protein binds to a receptor on the cells of hair follicles, said Prof Cotsarelis.

Several known drugs that target this pathway have already been identified, he added, including some that are in clinical trials. The researchers say there is potential for developing a treatment that can be applied to the scalp to prevent baldness and possibly help hair regrow.

http://news.sciencemag.org/sciencenow/2012/03/enzyme-melts-cancer-drug-barrier.html

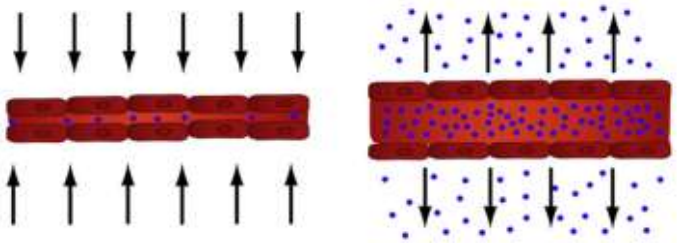
Enzyme 'Melts' Cancer Drug Barrier

Researchers may have found a new way to treat pancreatic tumors, one of the deadliest and most drug-resistant forms of cancer.

by Jocelyn Kaiser on 19 March 2012, 2:09 PM | 0 Comments

Injecting mice with a molecule that melts the tough structure around the tumor allowed a standard chemotherapy drug to better penetrate and destroy cancer cells. The strategy is already being tested in people.

People diagnosed with the most common form of pancreatic cancer, pancreatic ductal adenocarcinoma (PDA), usually don't respond to chemotherapy and only live a few months. Some researchers suspect that one reason is that the pancreatic tumor cells are enmeshed in a tough, fibrous matrix of cells and molecules known as the stroma. This may create fluid pressure within the tumor that is much higher than in the tumor's blood vessels, making it hard for any cancer drugs to diffuse from the blood into the tumor. Adding to the challenge, PDA tumors already have few obvious blood vessels penetrating them.



Going with the flow. Before enzyme treatment, fluid pressure confined a cancer drug (blue) to blood vessels; afterward, it could diffuse into tumor tissue. **Adapted from P. P. Provenzano et al., Cancer Cell 21, © 2012 Elsevier Inc.**

Oncologist and cancer biologist Sunil Hingorani's group at the Fred Hutchinson Cancer Research Center in Seattle, Washington, and collaborators confirmed the extreme fluid pressures in PDA tumors by inserting a special probe into tumors in mice with the disease. The pressures were "astonishing," Hingorani says - 80 to 120 millimeters (mm) of mercury, which is comparable to the pressure of blood being pumped within the heart.

Looking for a way to lower that pressure so that drugs can breach the barrier, Hingorani's group focused on a sugar molecule called hyaluronic acid (HA), which is abundant in the stroma of PDA tumors. The team treated the mice with an enzyme called PEGPH20, which degrades HA. The pressure in the tissue around the tumor began to drop and by 24 hours had reached about 20 mm of mercury, the level seen in normal pancreas tissue. When the researchers cut out the animals' tumors, they were soft and pink, unlike the hard, white tumors from animals that had not received the enzyme, Hingorani says. His team also found that blood vessels in the tumors that had been compressed and hard to see had sprung open.

The next step was to see if chemotherapy drugs would get into a tumor more easily after it was treated with the enzyme. And indeed, when mice with PDA tumors were injected with PEGPH20 and gemcitabine, the standard drug for pancreatic cancer, they lived 70% longer (a median of 92 days) than mice receiving gemcitabine alone and developed fewer metastases, the team reports today in Cancer Cell. That's the longest survival his group has seen in this animal model of pancreatic cancer, Hingorani says.

A formulation of the PEGPH20 enzyme has already been approved by U.S. regulators for a different drug-delivery application. (It's injected under the skin to form a pocket that helps fluids and standard drugs reach blood vessels.) And a trial to test the PEGPH20-gemcitabine combination in pancreatic cancer patients is already under way. Although other tissues in the body contain HA, the enzyme doesn't seem to result in serious side effects in animal studies, says Hingorani, who is working on the trial being run by Halozyme Therapeutics. He says if the treatment is successful, other potential drugs for PDA that had been shelved should be reexamined: "Maybe not enough of the drug got into the tumor," he says.

The results seen in the mice are "exceedingly encouraging," particularly because the animals treated with the enzyme combo developed fewer metastatic tumors, says cancer biologist Dafna Bar-Sagi of New York

University Langone Medical Center. However, she and others caution that the results seen in mice may not translate into people. A few years ago, Hingorani was part of a team that used a different drug to shrink the stroma of PDA tumors. That strategy seemed promising in mice but apparently hasn't worked in the clinic.

Cancer biologist Craig Logsdon of MD Anderson Cancer Center in Houston, Texas, cautions that drug-blocking role of the stroma itself is debatable - he was part of some recent imaging studies that found molecules that penetrated pancreatic tumors. Still, "the disease is so terrible and people are looking for new options," he says. "Let us hope that my analysis is incorrect that this really does improve therapy."

http://www.scientificamerican.com/article.cfm?id=hunters-killed-off-big-animals-australia

Big Kill, Not Big Chill, Finished Off Giant Kangaroos

Scientists have debated whether climate change or human activity wiped out the world's megafauna. In Australia new evidence points to hunting, and only hunting

By David Biello | Thursday, March 22, 2012 | 38

Around 40,000 years ago, the giant kangaroo disappeared from Australia. So did Diprotodon (rhinoceros-size wombats) and Palorchestes (tapirlike marsupials) as well as supersize birds, reptiles and some 50 other so-called megafauna - big animals. And now a record of fungal spores pulled from the swamp at Lynch's Crater in the northeastern corner of the continent reveals humans as the culprit.

"The megafauna declined soon after the time that we know people arrived in the region," explains zoologist Christopher Johnson of the University of Tasmania, lead author of the report published March 23 in Science. "We conclude that humans, not climate, caused the extinction."

BIG KILL: Hunters killed off more than 50 species of large animals in Australia, including Diprotodon optatum pictured here. **Image: © Science/AAAS/Drawing by Peter Murray**

The basis for the charge rests on two mud cores - one stretching from around 130,000 years ago to 24,000 years ago and the other ranging from roughly 50,000 years ago 3,000 years ago. The long core reveals how the local environment reacted to two previous periods of cooling and drying. Judging by the Sporormiella fungus - which only releases its spores when in the dung of plant-eating animals - big animals fared well during these climatic changes, munching happily on the changing vegetation of the area.

That changed roughly 41,000 years ago, when the number of spores in the core "dropped almost to zero," the researchers wrote. The record in mud also notes an increase in charcoal from large-scale fires and new types of vegetation - eucalyptus trees and the like with grasses beneath, much as seen today. A shift in climate could alter plant populations, but this vegetation change actually precedes by roughly 10,000 years the most recent climate shift within the core's age, to cooler and drier conditions. "Climate change played no role in megafaunal extinction in Australia," Johnson concludes.

Using the second core, the researchers then focused on the period between 43,000 years and 38,000 years ago to try to understand how humans eliminated the megafauna. Humans could have hunted them to extinction or set fires that changed the landscape so much that large herbivores could not survive. But examining the core in 100-year increments showed that the shifts in vegetation happened after the near disappearance of Sporormiella spores - not before as would have been expected if fire-triggered vegetation changes had caused the extinctions. "It could not have been vegetation change due to firing of the landscape, as other people have proposed, because those things followed megafaunal decline," Johnson argues.

In fact, the disappearance of the big plant-eaters seems to have set the stage for fires, allowing the buildup of the dry grasses and other fine fuels that spur burning like the catastrophic wildfires still seen in Australia today. At Lynch's Crater, the disappearance of the large plant-eaters saw an increase in grasses within 300 years, then acacias, eucalyptuses and other hard-leaved plants within 400 years, and, ultimately, a rise in the pollen from forest trees some 1,600 years later. Even today, many of the plants still extant in Australia boast features such as protective spines that would discourage grazing by megafauna or big fruit and seeds that could only be dispersed by large animals that no longer exist - a landscape shaped by ghosts. "These plants are now anachronistic," Johnson observes.

The findings seem to close the case against modern human hunters, although they remain to be confirmed at other sites throughout the continent. And, on every continent except Africa, human arrival and large animal

extinctions seem to coincide, so the case may also extend globally. (The reason large animals did not vanish in Africa is perhaps because they co-evolved with us and learned to be wary of this stalking, hairless, upright ape.)

An analysis of ancient DNA from extinct species such as woolly mammoths and rhinoceroses suggests that "climate has been a major driver of population change over the past 50,000 years," according to a 2011 Nature paper that also suggests climate and humans may have colluded to push such species to extinction. (Scientific American is part of Nature Publishing Group.) Johnson, for one, isn't sure climate should be blamed. "Extinctions in other parts of the world were remarkably similar in pattern and severity to those that occurred in Australia," he notes. After all, human hunting wiped out similar species from in neighboring New Zealand less than a millennia ago. "This seems to strengthen the view that human impact - mainly hunting - was the predominant cause in other places as well as in Australia."

As for the specific weapons and techniques, they remain unknown. "It is almost certain that hunting of large animals was one of the things [early Australians] did, but we'll probably never know exactly how they did it," Johnson says. In this case, it wasn't the weapons that fingered the perpetrators but an absence of fungal spores that reveals an ancient human deed.

http://www.sciencedaily.com/releases/2012/03/120322174621.htm

High-Throughput Screening Finds Surprising Properties for Antioxidants

Some Compounds Can Damage DNA, but May Treat Cancer

ScienceDaily - Antioxidants have long been thought to have anti-aging properties, primarily by protecting a person's genetic material from damaging chemicals. The story, however, now appears to be much more complicated.

National Institutes of Health researchers from two institutes and one center have demonstrated that some antioxidants damage DNA and kill cells instead of protecting them. The findings, published in the Proceedings of the National Academy of Sciences on March 19, 2012, also suggest that this surprising capability may be good for treating cancer, but may prove cautionary when using antioxidant-based medicines to treat other disorders, such as diabetes.

"It's an unexpected discovery," says Kyungjae Myung, Ph.D., a senior investigator in the Genetics and Molecular Biology Branch of the National Human Genome Research Institute (NHGRI), and the senior author on the report. "It may have important clinical applications in treating people with cancer, especially if they have failed previous treatments."

Many people attempt to boost their levels of antioxidants by eating fruits and vegetables, nuts and grains, or by taking vitamins such as A, C, E and beta-carotene, among others. Some research suggests that antioxidants soak up compounds called free radicals produced by burning oxygen during normal respiration. Free radicals cause random chemical reactions that can damage cellular components, including DNA, leading to disease. By adding antioxidants to the diet, many people hope to slow down the process that some believe contributes to the normal process of aging.

Dr. Myung did not set out to challenge this anti-aging strategy, and the new findings may not fundamentally alter the approach; much more study will be needed. Instead, his lab studies DNA repair, the enzyme systems within a cell that fix mistakes and other damage that routinely accumulate in DNA as cells simply live and divide to make daughter cells. Researchers know that naturally occurring defects in DNA repair can lead to a number of disorders, including cancer.

To study DNA repair, Dr. Myung's group sought a new way to easily identify chemicals that damage DNA and then use those chemicals to study cellular repair mechanisms, a basic research question. Using a laboratory grown cell line from human kidneys, the NHGRI team, which included Jennifer Fox, Ph.D., lead author and post-doctoral fellow, developed a novel laboratory test, or assay, that readily shows when a chemical exposure damages DNA.

With the test developed, Dr. Myung's team formed collaborations with two other NIH research groups: The first was with what is now the NIH National Center for Advancing Translational Sciences (NCATS). Over the last several years, a team led by Christopher Austin, M.D., head of the NCATS laboratories, has developed high-throughput chemical screening systems using robotics. Dr. Austin agreed to use Dr. Myung's assay to rapidly test thousands of chemicals for their ability to damage DNA. But what chemicals should they test?

In 2008, the NIH Chemical Genomics Center, then part of NHGRI and now at NCATS, the National Institute of Environmental Health Sciences (NIEHS) and the U.S. Environmental Protection Agency (EPA) formed an initiative called Tox21 to develop high-throughput screening tests that measure cellular harm caused by environmental chemicals. The Tox21 team created a library of some 2,000 compounds and agreed to test

them against Dr. Myung's assay. The NHGRI researchers also added a commercially available chemical collection to the screening runs for a total of some 4,000 chemicals.

The screening runs produced surprises, identifying 22 antioxidants that damaged DNA. Three of the antioxidants - resveratrol, genistein and baicalein - are currently used - or being studied - to treat several disorders, including heart disease, type 2 diabetes, osteopenia and osteoporosis and chronic hepatitis, as well as serving as an anti-aging treatment. Not only did the antioxidants damage the DNA, the researchers found, but also, in dividing cells (such as in tumors), the antioxidants can be lethal, killing the disease-causing cells.

"This is what's cool about biology," Dr. Austin said. "Just when we think we understand something, it turns out to be more complex than we thought. Not only did the NHGRI team produce a novel way to measure DNA damage, but their test has given us insights into the effects of chemical compounds that were not seen in more conventional strategies."

The discovery opens up several new lines of research. As a first step, the collaborators are dramatically expanding the number of compounds - more than 300,000 - that will be tested with the new assay. The Tox21 team also has decided to include the NHGRI test in its standard screen for biological harm produced by environmental chemicals.

The clinical implications for these findings are more complicated. This initial discovery is only in lab-grown cell lines, not even in intact organisms. The relevance for humans has yet to be demonstrated. Still, there is plenty of work already underway. Other researcher teams had launched various studies of these DNA-damaging antioxidants in various diseases. For example, 44 studies are currently listed in www.clinicaltrials.gov for resveratrol, which is found in many foods, including red grapes and wine, peanuts and chocolate. The studies focus on treating Alzheimer's disease, type 2 diabetes, obesity, inflammation, colon cancer, multiple myeloma, and testing other anti-aging strategies, among others. The newly reported study does not suggest that resveratrol in red wine is harmful; the dose is probably too low to be significant, Dr. Myung said.

Researchers also have launched 43 studies on genistein, including trials to treat cancers of the prostate, pancreas, bladder, breast, kidney and skin (metastatic melanoma) and as adjunct treatments for rare diseases such as cystic fibrosis.

Even though the antioxidants damaged the DNA, the researchers reported that the chemicals did not cause genetic mutations, another surprise. "Because they don't cause genetic mutations, antioxidants may be useful for treating cancer," Dr. Myung said. "Standard chemotherapy mutates the tumor's DNA, speeding its evolution and sometimes allowing it to escape the toxic treatment intended to kill it. This leads to multi-drug resistance in some cancer patient's disease."

To test whether the antioxidants might help, the NHGRI team borrowed some multi-drug resistant cancer cells from Dr. Michael Gottesman, a National Cancer Institute researcher and NIH Deputy Director for Intramural Research. Although these cells are very resistant to anti-cancer drugs, treatment with resveratrol appeared to sensitize the cancer cells, leading to their death. "Resveratrol," Dr. Myung said, "could prove useful in treating multi-drug resistant cancers." The findings do raise concerns about using antioxidants to treat disorders, as treatment with high doses may cause unexpected DNA damage that leads to other problems. "Clearly," Dr. Myung said, "much more study will be needed."

Journal Reference: *J. T. Fox, S. Sakamuru, R. Huang, N. Teneva, S. O. Simmons, M. Xia, R. R. Tice, C. P. Austin, K. Myung. High-throughput genotoxicity assay identifies antioxidants as inducers of DNA damage response and cell death. Proceedings of the National Academy of Sciences, 2012; DOI: 10.1073/pnas.1114278109*

http://www.sciencenews.org/view/generic/id/339380/title/Vesta_seems_more_planet_than_asteroid_

Vesta seems more planet than asteroid

Spacecraft explorations reveal a layered, beat-up body

By Nadia Drake

THE WOODLANDS, Texas - The enormous asteroid Vesta is more like a small, rocky planet than other space rocks wandering around the asteroid belt between Mars and Jupiter. Among other planetlike characteristics, Vesta's interior is probably divided into layers like Earth's - and scientists have detected traces of an ancient magnetic field.

"We have a hard time working on this body and not thinking about it as a planet," said UCLA's Christopher Russell, principal investigator of the Dawn spacecraft that has been buzzing around Vesta since July.

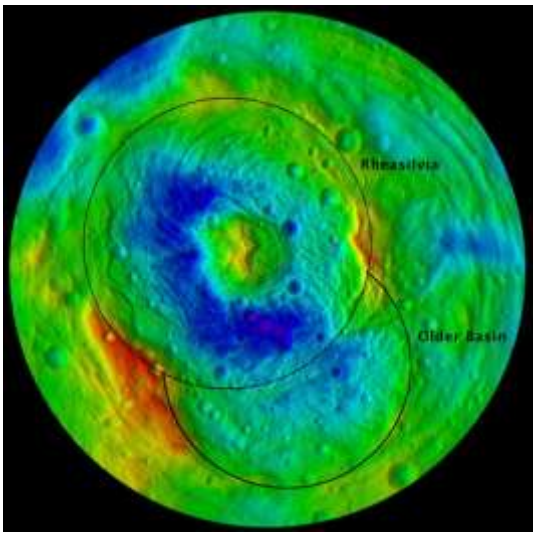
Like Earth, Vesta probably has an iron core, a mantle and crust. Scientists don't know how thick the crust is, but Dawn measurements suggest that the core's radius is between 107 and 113 kilometers, Carol Raymond of the Jet Propulsion Laboratory said on March 22 at the Lunar and Planetary Science Conference. Vesta is only about 530 kilometers across, meaning that the core occupies almost half its diameter. And new gravity maps

from Dawn reveal anomalies in the crust, or areas where there's "likely mantle material close to the surface," Raymond reported.

Other presenters at the meeting relied on data gathered from bits of Vesta that had crashed to Earth.

Two chips off the old Vestal block contain traces of a strong magnetic field, said Roger Fu, a graduate student at MIT, who studied meteorites known as Millbillillie (which landed in Australia in 1960) and ALHA 81001 (found in Antarctica in 1981). The field's strength suggests that an active, liquid metallic core generated the magnetic signature, which became locked into Vesta's crust as the asteroid cooled. "There was a magnetic field on the surface of Vesta after 3.6 billion years ago, and there probably still is," Fu said.

Vesta also bears multiple scars from two giant impacts, including mammoth basins in its south pole and equatorial troughs that formed as the rock's crust reverberated from the impact. The larger impact basin, called Rheasilvia, is well-known: at 505 kilometers across, it consumes essentially the entire south pole and hosts one of the tallest mountains in the solar system, which towers 20 kilometers from the basin's floor.



***A newly identified impact basin (bottom circle) lies buried beneath the asteroid Vesta's famous Rheasilvia basin (top circle), planetary scientists have found.*NASA, JPL-Caltech, UCLA, MPS, DLR, IDA**

But the second impact basin, which sits under and slightly to the side of Rheasilvia, is a newly named structure. Called Veneneia, the basin - described by Paul Schenk from the Lunar and Planetary Institute in Houston - is older than Rheasilvia and about 395 kilometers across.

The double bull's-eye at the south pole suggests that Vesta must be incredibly resilient, Schenk said.

Even so, the impacts probably penetrated Vesta's crust and scattered minerals that normally live deep underground over the surrounding surface. Scientists will continue studying and characterizing these details because even though Vesta might resemble Earth, it embodies one crucial difference: Instead of erasing pages from its history, the asteroid's biography still contains records of its evolution dating back to the dawn of the solar system.

"By studying the surface," Russell said, "we will go back in time right to the beginning of the solar system."

Dawn will hover near Vesta until August, continuing to transcribe the tales it tells. It will then head toward Ceres, the most massive body in the asteroid belt, with a planned arrival in 2015.

http://bit.ly/GK8yST

Reptile grew feather-like structures before dinosaurs

FOSSIL feathers provided the definitive proof that birds descended from dinosaurs.

23 March 2012 by Jeff Hecht

There is one extinct beast that doesn't fit the picture, though. It is called Longisquama insignis, and it lived 230 to 240 million years ago - just before the dinosaurs evolved, and 70 to 80 million years before the first fossils of feathered dinobirds. Why, then, did Longisquama sport what look suspiciously like feathers?

Some palaeontologists think that it didn't: they say that the only known specimen of Longisquama - found in Kyrgyzstan in the 1960s and shown here at life size - was just a run-of-the-mill reptile that died beneath some exotic plant fronds, so the "feathers" were not actually part of the animal. A small group of researchers say Longisquama's feathers are real, and suggest that birds evolved from reptiles like this rather than from feathered dinosaurs. A new analysis suggests neither theory is correct.

"The strange skin appendages of Longisquama are neither scales nor feathers," says Michael Buchwitz of the Freiberg University of Mining and Technology, Germany.

Longisquama insignis

They are perhaps linked to the early evolution of dino and pterosaur fuzz, though."

Buchwitz has reanalysed the original fossil and says that the base of the structures lies so close to the bones of the spine that they were probably anchored deep within the skin. They were definitely attached to the body.

He has also studied recently discovered isolated "feathers" from the same locality, which are better preserved. He says Longisquama's appendages neither branch like real feathers nor vary in structure along their length as feathers do. Most tellingly, each carries a very unfeather-like thick border along one edge.

For all that, Buchwitz says the appendages are clearly similar to the real deal. Like feathers, they have a central filament running along their lengths, for example. He thinks this means that they were constructed using the same developmental genes that later produced feathers.

Longisquama's skeleton is too incomplete to work out its exact evolutionary position, but Buchwitz says the little reptile was probably part of the lineage that gave rise to pterosaurs, crocodiles, dinosaurs and birds.

Many of these groups later evolved their own skin appendages, including filaments on pterosaur wings, quills on the tails of some plant-eating ornithischian dinosaurs, and the proto-feathers of theropod dinosaurs. Longisquama shows that evolution was experimenting with the genes that gave rise to feathers long before any of these animals appeared on the scene.

"It's a very impressive analysis," says Alan Brush, a feather specialist at the University of Connecticut in Storrs.

Larry Martin at the University of Kansas in Lawrence is one of the few researchers who think Longisquama-like reptiles gave rise to birds. He likes the idea that its appendages developed along similar lines to feathers. For most palaeontologists, though, Longisquama is an intriguing evolutionary experiment that apparently left no descendants.

http://seattletimes.nwsource.com/html/health/2017810279_psychoticdrug22.html

Doctors not fully told of downside of antipsychotic drugs, study finds

A new report finds that psychiatrists have not been given a full picture of the effectiveness, or lack thereof, of so-called atypical antipsychotic drugs.

By Brian Vastag

So-called atypical antipsychotic drugs have been blockbusters for the drug industry, pulling in $16 billion in 2010. But a new report finds that psychiatrists have not been given a full picture of their effectiveness.

When seeking approval for eight atypical antipsychotic drugs, drug companies performed 24 studies, according to a Food and Drug Administration (FDA) database. But four of the studies were never published in professional journals, and all four were unflattering for the drug in question.

The class includes big sellers such as Abilify (aripiprazole), Zyprexa (olanzapine), Risperdal (risperidone), and Seroquel (quetiapine). These drugs were developed to treat schizophrenia and related disorders, but physicians also prescribe the drugs "off label" for bipolar disorder, insomnia and other problems.

Three of the unpublished studies showed that the new drug did not perform better than a sugar pill. The fourth study showed that while the antipsychotic drug helped patients more than a placebo, older, less expensive drugs helped patients more.

"That's bad if you're marketing the drug," said Erick Turner, the psychiatrist at Oregon Health & Science University who conducted the new analysis, published Tuesday in the journal PLoS Medicine.

Two of the unpublished studies, which included more than 300 patients, tested Abilify. Both found the drug to be no more effective than a sugar pill in treating schizophrenia.

The two other studies involved Geodon (ziprasidone). One study found Geodon to be no more effective than a placebo. The second found that while Geodon was more effective than a placebo, it was less effective than an older - and much less expensive - drug, Haldol (haloperidol).

Further, four studies of the atypical antipsychotic drug Fanapt (iloperidone) that were published left out unflattering data that showed other drugs worked better.

With this information absent from professional journals, psychiatrists are left with an incomplete picture of how well atypical antipsychotic drugs work. "I think (psychiatrists) should be aware that what they're reading in journal articles could be sanitized," Turner said.

When Turner added the data from the negative, unpublished studies to the positive, published studies, he found the overall effectiveness of this class of drugs in treating schizophrenia fell by a small amount, about 8 percent.

"Overall, the drugs seem to work almost as well as we thought they did," Turner said.

But if the negative data had been published, psychiatrists would have had more complete information to decide which of these drugs - if any - to prescribe.

Turner worked at the FDA earlier in his career, where he discovered he "was living in this highly censored environment" where negative studies never get published.

There's a term in academic medicine for this phenomenon: publication bias. Studies that show a new drug in a positive light get published; those that throw a drug into question get buried.

http://bit.ly/GK7sTH

Are medical students really that clueless about health care costs?

A few months ago, I went to a talk by a health economist.

By Ilana Yurkiewicz | March 23, 2012 | Comments2

"How many of you think cost will factor into your decision-making with patients?" he asked the audience of medical students. About 80 percent raised their hands. Surprised, he commented that when he asked that question ten years ago, maybe 20 percent of his audience raised their hands. "Then again," he joked, "maybe you are only saying 'yes' because you know I'm an economist." Should a $2000 MRI be ordered for a patient complaining of headaches? These are the kinds of questions medical students discuss.

It is difficult to consider a career in medicine today without an awareness of spending. Go to any talk on health care policy, and you will hear a similar message. Health care spending is increasing at an unsustainable rate. The United States spends more per person on health care than any other nation, and yet we are not any healthier for it. If we continue to spend at current rates, we will jeopardize the long-term fiscal stability of our nation. Something is broken. Something needs to be done. Physicians are partially responsible for doing something.

Despite these facts, a common mantra is that medical students are wholly unprepared in this regard. Last week, Dr. Pauline Chen published a piece in the New York Times on a new teaching module that will train doctors to think more about costs. "Today… doctors continue to struggle to reconcile cost consciousness with quality care," she writes. "And doctors-to-be are not getting much help in learning how to do so."

If that was true in the past, steps are being taken to improve the situation. In 2006, Harvard implemented a month-long health care policy course into the first year curriculum. We also take a semester-long ethics class, where the subject of cost and how it plays into patient care comes up often.

A few weeks ago, we turned to rationing. We met a fictional 28-year-old office worker who came to the doctor's office complaining of headaches. Her symptoms fit the classical pattern for tension-type headaches. Yet, worried about a brain tumor, she asked for an MRI. The MRI would cost $1,500 to $2,000, and it would come out of the budget for the rest of health maintenance organization (HMO) patient population. What should we, as doctors-to-be, tell her?

Many of us thought that the rationing line has to be drawn somewhere, and this seemed like a pretty good place. With the chances of a brain tumor in this case "vanishingly low," the MRI struck us as having a pretty poor benefit-cost ratio.

Still, change a few circumstances – such as making the likelihood of the tumor slightly higher than the stated "vanishingly low" – and my feelings about the situation became more complicated. It was easy for some of my classmates to continue to write the patient off as neurotic – but what's so wrong about being health conscious?

All this just goes to show that there is no clear right or wrong in terms of being cost-conscious. There is no model to learn and follow. We read. We debate. We disagree. We try to identify what can be resolved by data, and what is a value judgment. We challenge one another's assumptions, along with our own.

I do realize discussing these patients in the abstract won't necessarily ensure good decision-making when we get into clinic. It is easy to sit around a classroom and debate whether we should give a fictional patient an expensive test under X, Y, and Z circumstances, but quite another to routinely integrate cost, among all other clinical factors, into daily practice. I imagine it will be far more difficult to look a concerned patient in the eye and say no, I cannot provide this service you are requesting. It will be difficult because to cite any reason for denying the service other than cost would be dishonest. And acknowledging that money is a limiting factor in health care is a tough thing to accept.

But, it's a good thing we are having these discussions now. I am grateful that medical education is becoming more well-rounded, and that I will not be thrust into caring for patients with a strong knowledge of the nuts and bolts of clinical medicine but without benchmarks of what's reasonable in terms of cost. Because as much as we might shun cost as a dirty word, antithetical to the noble aims of the physician, it will be relevant to all of our practices.

http://www.bbc.co.uk/news/health-17487999

Hope of a 'pain-free needle' to end injection trauma

Who would argue with a pain-free injection?

By Philippa Roxby Health reporter, BBC News

Nobody loves the thought of a needle piercing their skin, least of all doctors and dentists who have to deal with stressed and anxious patients. Scientists have been working on this problem for a while, but a young British inventor based in Somerset may have come up with the solution.

Oliver Blackwell's device looks like the typical syringes used in hospitals and doctors' surgeries around the country, with one crucial difference. On the front is a much smaller needle which injects a tiny amount of local anaesthetic to ease the pain of the larger needle which follows. It is essentially two injections in one - the first one, virtually pain-free, paving the way for the second one, which is rendered painless. The first injection is "like a fly landing on your palm", the inventor says.

Blackwell, who is 29 and graduated in industrial design from the University of Plymouth, UK, in 2005, says his pain-free needle could be used in millions of procedures every year and reduce the risk of contamination or confusion because staff will only have to deal with one device. "At the moment, if they want to use a local anaesthetic they have to use two needles, find keys and go to the medicine cupboard separately and it all takes time and effort," he says.

He involved experts in his design, enrolling the help of two family doctors and a former president of The Royal College of Anaesthetists. They insisted that it should be easy to use, feel and look familiar and meet the needs of patients and doctors.

Self-vaccination?

Dr Alan McGlennan, lead obstetric anaesthetist at the Royal Free Hospital in London, said the idea of a pain-free needle had value. "Nobody likes having injections, but in my line of work it tends to end up with a needle somewhere." He meets at least one adult every week who is so anxious about needles that their blood pressure rises. Children aged between three and 12 are also particularly prone to needle phobia, he says. "But so much of it is perception rather than reality. For many people it's psychological."

Dr McGlennan has sometimes used a local anaesthetic paste on patients' arms which numbs the skin prior to an injection. This eases the pain, but the needle still has to penetrate the skin. Perhaps, in the future, there will be a way of avoiding needles altogether.

American scientists have tested a vaccine patch on mice, which cuts out the need for painful needles. Instead, the patch has hundreds of microscopic needles which dissolve into the skin. The researchers say that one day it could be used to enable people to vaccinate themselves against flu, for example.

High-speed jet

Several years ago, Japanese scientists claimed they had developed a tiny hypodermic syringe that could be used to give virtually pain-free injections. This could be very good news for people with conditions like diabetes, who require daily injections of insulin to manage their condition. The insujet insulin administration system is intended for people who are uncomfortable injecting themselves with a needle.

When administered, the insulin passes through a small channel, creating a high speed jet that can penetrate the skin and underlying tissue. "Combined with a unique automatic injection system, this results in virtually painless insulin administration," the charity's spokesman Richard Evans explains.

Blackwell's device has been through extensive testing but there are still more trials to come before it can be mass-produced. He has won design awards before and is currently working on a range of different inventions - from agricultural machinery to electrical products and medical devices. "It is all about gaining an insight. You take simple information on board from the experts and adapt your thinking based on their skills." Millions of people will be hoping he gets it right.

http://nyti.ms/GS4pIj

Steps Set for Livestock Antibiotic Ban

The Obama administration must warn drug makers that the government may soon ban agricultural uses of some popular antibiotics

By GARDINER HARRIS

The Obama administration must warn drug makers that the government may soon ban agricultural uses of some popular antibiotics that many scientists say encourage the proliferation of dangerous infections and imperil public health, a federal magistrate judge ruled on Thursday.

The order, issued by Judge Theodore H. Katz of the Southern District of New York, effectively restarts a process that the Food and Drug Administration began 35 years ago, but never completed, intended to prevent penicillin and tetracycline, widely used antibiotics, from losing their effectiveness in humans because of their bulk use in animal feed to promote growth in chickens, pigs and cattle.

The order comes two months after the Obama administration announced restrictions on agricultural uses of cephalosporins, a critical class of antibiotics that includes drugs like Cefzil and Keflex, which are commonly used to treat pneumonia, strep throat and skin and urinary tract infections.

Siobhan DeLancey, an F.D.A. spokeswoman, would not say whether the government planned to appeal. “We are studying the opinion and considering appropriate next steps,” she said.

In a separate move, the F.D.A. is expected to issue draft rules within days that ask drug makers to voluntarily end the use of antibiotics in animals without the oversight of a veterinarian.

But neither the judge's order nor the F.D.A.'s expected rule changes are likely to fundamentally alter the large-scale agricultural uses of antibiotics because farmers and ranchers now say the drugs are being used to prevent animal diseases, not to promote growth. The F.D.A. has so far refused to propose restrictions on antibiotic uses to prevent disease even when the drugs are delivered in feed or water, and Judge Katz's order does not extend to disease prevention uses.

Gwen Venable, a spokeswoman for the U.S. Poultry and Egg Association, said that poultry producers "judiciously use antibiotics to maintain the health of their flocks." "Our association has not had an opportunity to review the judge's order, so we cannot comment on the impact of the specific decision at this time," she said.

Environmentalists and health advocates cheered Judge Katz's ruling, as they have largely cheered the F.D.A.'s incremental efforts to begin restricting some of the less discriminating antibiotic agricultural uses because they welcome any improvement in the decades-old issue. "The rise of superbugs that we see now was predicted by F.D.A. in the '70s," said Jen Sorenson, a lawyer for the Natural Resources Defense Council.

But agricultural trade groups were more critical. Ron Phillips, vice president of public affairs for the Animal Health Institute, an association representing companies that make animal medicine, said that the judge's order could slow efforts to reduce agricultural uses of antibiotics by diverting resources from the agency's collaborative efforts with industry.

Antibiotics were the wonder drugs of the 20th century, and their initial uses in humans and animals were indiscriminate, experts say. Farmers were impressed by the effects of penicillin and tetracycline on the robustness of cattle, chickens and pigs, and added the drugs to feed and water, with no prescriptions or sign of sickness in the animals.

By the 1970s, public health officials had become worried that overuse was leading to the development of killer infections resistant to treatment. In 1977, the F.D.A. announced that it would begin banning some agricultural uses. But the House and Senate appropriations committees passed resolutions against the ban, and the agency retreated.

"In the intervening years, the scientific evidence of the risks to human health from the widespread use of antibiotics in livestock has grown, and there is no evidence the F.D.A. has changed its position that such uses are not shown to be safe," Judge Katz wrote in his order.

Eighty percent of antibiotics bought in the United States are used in animals, not humans. Meanwhile, outbreaks of illnesses from antibiotic-resistant bacteria have grown in number and severity, killing thousands.

Environmental and health groups petitioned the F.D.A. in 1999 and 2005 to restart the process to ban the drugs for promoting animal growth. The Natural Resources Defense Council, the Center for Science in the Public Interest, the Food Animal Concerns Trust, Public Citizen and the Union of Concerned Scientists filed suit against the F.D.A.

On Thursday, Judge Katz ruled that these groups had won their case without need for a trial.

Judge Katz ordered the F.D.A. to alert drug manufacturers that it intended to prohibit the use of penicillin and tetracycline to promote growth in animals. The manufacturers can request a hearing to present evidence that these uses are safe. If the companies have such evidence, the drugs can continue to be used for growth promotion, the judge wrote.

http://bit.ly/GOSzmL

Green tea could mask testosterone doping

ATHLETES who cheat by doping themselves with testosterone may be able to mask their actions by drinking green tea.

24 March 2012 by Peter Aldous

Large quantities might even provide a legal performance boost by raising levels of testosterone in the blood.

Abuse of testosterone is hard to spot because the steroid hormone is found naturally in men and women. Tests rely on detecting an unusual ratio of testosterone to a hormone called epitestosterone in urine.

In lab tests, Declan Naughton and colleagues at Kingston University London discovered that compounds called catechins, found in tea, inhibit an enzyme called UGT2B17. This enzyme attaches glucuronic acid to testosterone, making it more likely to be excreted in urine (Steroids, DOI: 10.1016/j.steroids.2012.02.023).

Catechins are present in green and white tea but not in black. "Levels from a strong cup of green tea match those we used in our experiments," Naughton says. Athletes dosing themselves with testosterone may be able to reduce the amount of hormone entering their urine by drinking green or white tea. Tea alone may also boost circulating levels of testosterone by blocking its excretion.

The researchers have informed the World Anti-Doping Agency in Montreal, Canada, of their findings. If the same effect occurs in human bodies, one answer would be to test athletes' blood, rather than urine.

WADA is aiming to add regular checks of blood steroids to its "biological passports", which monitor athletes for suspicious changes in their physiology. That should foil any attempt to fool the urine test, says Olivier Rabin, WADA's science director.

Rabin also doubts that tea alone will have much effect on performance, compared with the big boosts in testosterone seen in doping cases. "It would be fairly modest," he says.

http://www.eurekalert.org/pub_releases/2012-03/jaaj-iod032212.php

Infusion of drug into the coronary artery may help reduce size of heart damage after heart attack

A bolus dose of drug abciximab into the coronary artery and receiving an anticoagulant resulted in reduction in damage to the heart muscle

Administration of a bolus dose of the anticoagulant drug abciximab into the coronary artery involved in causing a certain type of heart attack among patients who were undergoing a percutaneous coronary intervention and also receiving another anticoagulant resulted in reduction in the size of damage to the heart muscle at 30 days, while a procedure that involved use of a catheter to remove the blood clot blocking that coronary artery did not produce these results, according to a study appearing in JAMA. The study is being published early online to coincide with its presentation at the American College of Cardiology's annual scientific sessions.

"Primary percutaneous coronary intervention [PCI; procedures such as balloon angioplasty or stent placement used to open narrowed coronary arteries] is widely accepted as the most effective reperfusion [restoration of blood flow] modality for ST-segment elevation myocardial infarction [STEMI; a certain pattern on an electrocardiogram following a heart attack]. However, myocardial recovery after primary PCI is often suboptimal despite restoration of coronary blood flow, in part due to thrombus embolization [small blood clots blocking the arteries] resulting in impaired microvascular perfusion [blood flow]," according to background information in the article.

Two strategies proposed to reduce this complication after PCI include bolus (large dose) infusion of intracoronary abciximab and manual thrombus aspiration (use of a catheter for removal of a clot). "However, conflicting results have been reported as to whether intracoronary abciximab and manual aspiration thrombectomy reduce infarct [heart muscle damage] size or improve clinical outcomes, in part because of differences in patient selection, devices, and study methodology."

Gregg W. Stone, M.D., of Columbia University Medical Center and New York–Presbyterian Hospital, New York, and colleague investigated whether bolus intracoronary abciximab, manual aspiration thrombectomy, or both would reduce infarct size in high-risk patients with STEMI.

The study, conducted between November 2009 and December 2011, included 452 patients presenting at 37 sites in 6 countries within 4 hours of STEMI due to blockage in a certain area of the heart (proximal or mid left anterior descending artery occlusion) undergoing primary PCI with the anticoagulant bivalirudin. The patients were randomized to bolus intracoronary abciximab delivered locally (via a drug delivery catheter) at the infarct lesion site vs. no abciximab and to manual aspiration thrombectomy vs. no thrombectomy. Infarct size was assessed at 30 days by cardiac magnetic resonance imaging (cMRI).

Evaluable cMRI results at 30 days were present in 181 and 172 patients randomized to intracoronary abciximab vs. no abciximab, respectively, and in 174 and 179 patients randomized to manual aspiration vs. no aspiration, respectively.

The researchers found that patients randomized to intracoronary abciximab compared with no abciximab had a significant decrease in infarct size measured as a percentage of total myocardial mass (median [midpoint], 15.1 percent vs. 17.9 percent) and absolute infarct mass (median, 18.7 g vs. 24.0 g), but not in abnormal wall motion (the movement of the wall of the heart during contraction) score. Patients randomized to aspiration thrombectomy vs. no aspiration had no significant difference in infarct size (median, 17.0 percent vs. median, 17.3 percent), absolute infarct mass (median, 20.3 g vs. 21.0 g), or abnormal wall motion score.

"The principal findings from this multicenter, prospective, randomized trial in patients presenting early in the course of a large evolving anterior STEMI undergoing primary PCI with bivalirudin anticoagulation are as follows: (1) bolus intracoronary abciximab delivered to the infarct lesion site significantly but modestly reduced the primary end point of infarct size at 30 days; (2) in contrast, manual aspiration thrombectomy did not significantly reduce infarct size; and (3) indices of myocardial reperfusion, ST-segment resolution, and 30-day clinical event rates were not significantly different between the randomized groups," the authors conclude.

(JAMA. 2012;307(17):doi:10.1001/jama.2012.421. Available pre-embargo to the media at www.jamamedia.org)
Editor's Note: This study was sponsored and funded by Atrium Medical. Atrium supplied the local drug delivery catheter. Aspiration catheters were provided at a discount by Medtronic. Bivalirudin was provided at no charge by The Medicines Company. All other study devices and drugs were commercially purchased. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, etc.

http://www.eurekalert.org/pub_releases/2012-03/sfgm-vcc032312.php

Vaccinating chickens could prevent food-borne illness

A vaccine could be developed to prevent Campylobacter being carried in chickens.

This approach could drastically cut the number of cases of food poisoning, saving the UK economy millions each year, says an American scientist presenting his work at the Society for General Microbiology's Spring Conference in Dublin.

Food-borne illness costs the UK an estimated £2 billion each year. Campylobacter is the leading cause of food-borne illness and is responsible for about 30% of cases in the UK. Campylobacter jejuni was responsible for more than 371,000 estimated cases in England and Wales in 2009, resulting in more than 17,500 hospitalizations and 88 deaths.

Campylobacter jejuni is found in the gut of many animals, including chickens. If Campylobacter-contaminated poultry is not prepared and cooked properly, the micro-organism can be transmitted to humans where it may cause severe gastrointestinal disease.

Scientists at Washington State University are studying the maternal antibodies that are passed from hens to their chicks. "These antibodies protect chicks from becoming colonized by Campylobacter in the first week of life," explained Professor Michael Konkel who is leading the research. "Our group has now identified the bacterial molecules that these antibodies attack, which has given us a starting point for a vaccine against Campylobacter," he said. "We have already found that chickens injected with these specific molecules – found on the surface of Campylobacter jejuni – produce antibodies against the bacterium. This response partially protects them from colonization."

A vaccine could be a powerful weapon to help control food-borne illness. "Preventing contamination of poultry at slaughter has not been effective at reducing illness in humans. It has been shown that about 65% of chickens on retail sale in the UK are contaminated with Campylobacter," explained Professor Konkel. "Ideally, the best way to prevent contamination is to stop chickens on the farm from becoming colonized with this microorganism in the first place, which could be achieved by vaccination. Our goal within the next 6 months is to test a vaccine for chickens that will reduce Campylobacter colonization levels. There's still a long way to go, but I'm confident our lab and others are moving in the right direction."

Controlling food-borne illness through vaccination would have a significant impact both in the UK and globally. "A safe food supply is central to human health. If we can decrease the load of human pathogens in food animals, then we can reduce human illness. A 1% reduction in the number of cases of food-borne illness would save the UK around £20 million per year. In developing countries, where people and food animals often share the same environment, diseased animals also pose a direct public health risk; vaccination would help mitigate this risk," said Professor Konkel.

http://www.eurekalert.org/pub_releases/2012-03/acs-pts030512.php

Popcorn: the snack with even higher antioxidant levels than fruits and vegetables

Popcorn's reputation as a snack food that's actually good for health popped up a few notches today

SAN DIEGO - Popcorn's reputation as a snack food that's actually good for health popped up a few notches today as scientists reported that it contains more of the healthful antioxidant substances called "polyphenols" than fruits and vegetables. They spoke at the 243rd National Meeting & Exposition of the American Chemical Society (ACS), the world's largest scientific society, being held here this week.

Joe Vinson, Ph.D., a pioneer in analyzing healthful components in chocolate, nuts and other common foods, explained that the polyphenols are more concentrated in popcorn, which averages only about 4 percent water, while polyphenols are diluted in the 90 percent water that makes up many fruits and vegetables.

In another surprising finding, the researchers discovered that the hulls of the popcorn — the part that everyone hates for its tendency to get caught in the teeth — actually has the highest concentration of polyphenols and fiber. "Those hulls deserve more respect," said Vinson, who is with the University of Scranton in Pennsylvania. "They are nutritional gold nuggets."

The overall findings led Vinson to declare, "Popcorn may be the perfect snack food. It's the only snack that is 100 percent unprocessed whole grain. All other grains are processed and diluted with other ingredients, and

although cereals are called "whole grain," this simply means that over 51 percent of the weight of the product is whole grain. One serving of popcorn will provide more than 70 percent of the daily intake of whole grain. The average person only gets about half a serving of whole grains a day, and popcorn could fill that gap in a very pleasant way."

Vinson cautioned, however, that the way people prepare and serve popcorn can quickly put a dent in its healthful image. Cook it in a potful of oil, slather on butter or the fake butter used in many movie theaters, pour on the salt; eat it as "kettle corn" cooked in oil and sugar — and popcorn can become a nutritional nightmare loaded with fat and calories. "Air-popped popcorn has the lowest number of calories, of course," Vinson said. "Microwave popcorn has twice as many calories as air-popped, and if you pop your own with oil, this has twice as many calories as air-popped popcorn. About 43 percent of microwave popcorn is fat, compared to 28 percent if you pop the corn in oil yourself." Likewise, Vinson pointed out that popcorn cannot replace fresh fruits and vegetables in a healthy diet. Fruits and vegetables contain vitamins and other nutrients that are critical for good health, but are missing from popcorn.

Vinson explained that the same concentration principle applies to dried fruit versus regular fruit, giving dried fruit a polyphenol edge. Previous studies found low concentrations of free polyphenols in popcorn, but Vinson's team did the first study to calculate total polyphenols in popcorn. The amounts of these antioxidants were much higher than previously believed, he said. The levels of polyphenols rivaled those in nuts and were up to 15 times greater than whole-grain tortilla chips.

The new study found that the amount of polyphenols found in popcorn was up to 300 mg a serving compared to 114 mg for a serving of sweet corn and 160 mg for all fruits per serving. In addition, one serving of popcorn would provide 13 percent of an average intake of polyphenols a day per person in the U.S. Fruits provide 255 mg per day of polyphenols and vegetables provide 218 mg per day to the average U.S. diet.

Michael G. Coco, an undergraduate chemistry student at the University of Scranton who participated in the study, said he benefited in several ways. "From working on this project with Dr. Vinson, I've gained experience and many insights in doing scientific research," said Coco. "Besides the obvious things like learning how to use instrumentation and perform analyses, I've also learned that research is extremely satisfying, especially when you discover or think of something no one else has thought of."

The scientists acknowledged funding from the University of Scranton.

Abstract

Popcorn, one of the most popular snacks foods in the world, is known for being a high fiber, healthy food. Research has found that popcorn contains significant amounts of the class of antioxidants known as polyphenols. Being a popular snack food, polyphenols from popcorn are possibly part of a large portion of the polyphenol dietary intake. Popcorn without any oils is also a 100% whole grain food, whose consumption is recommended in the Dietary Guidelines for Americans. Free and total polyphenols for 40 different kernels and ingredients have been quantified using the Folin-Ciocalteu and FRAP assays. The identity of the polyphenols have been identified using UV/Vis HPLC and LC-MS. Ferulic Acid has been identified as one of the major components. By quantifying and identifying the polyphenols in popcorn; some predictions about their bioactivity can be made.

http://www.eurekalert.org/pub_releases/2012-03/w-fyw032112.php

Few young women with cancer take steps to preserve fertility during treatments

A new study has found that very few young women with cancer take steps to preserve their fertility while undergoing cancer therapy.

Also, certain groups of young women are more likely to do so than others. Published early online in Cancer, a peer-reviewed journal of the American Cancer Society, the study indicates that efforts are needed to provide counseling on fertility preservation in reproductive-aged women diagnosed with cancer.

More than 120,000 women under 50 years of age are diagnosed with cancer each year in the United States. As cancer survival rates are improving, quality of life issues are becoming increasingly more relevant. For example, chemotherapy and other cancer therapies often increase a woman's risk of becoming infertile and experiencing early menopause, and a woman may regret losing the ability to bear children because of her cancer treatment. With widely available assisted reproductive techniques such as egg or embryo freezing, women who have been diagnosed with cancer have options to improve their chances of conceiving.

To find out which women are taking advantage of these fertility-preserving techniques, Mitchell Rosen, MD, of the University of California, San Francisco (UCSF), led a team that surveyed 1,041 women diagnosed with cancer between the ages of 18 and 40 years. Five cancer types were included: leukemia, Hodgkin's disease, Non-Hodgkin Lymphoma, breast cancer, and gastrointestinal cancer. The women were randomly sampled from the California Cancer Registry from 1993 to 2007. A total of 918 women were treated with therapies that could negatively affect their fertility (chemotherapy, pelvic radiation, pelvic surgery, or bone marrow transplant).

The investigators found that 61 percent of women received counseling on the risks of cancer treatment to their fertility from their doctors or other clinicians. Overall, only four percent of women pursued fertility preservation, but rates increased over time. (Only one percent pursued fertility preservation in 1993, compared with between six percent and 10 percent in 2005 to 2007.) Also, certain groups of women were more likely to receive important information about their reproductive health at the time of their cancer diagnosis and were also more likely to preserve their fertility than others.

Women who are childless, younger, Caucasian, heterosexual, and who graduated from college are more likely than women of other backgrounds to be counseled about the risks of cancer treatment to fertility or to preserve fertility before cancer treatment.

"Although more women are getting counseled regarding reproductive health risks, many women are still not receiving adequate information about their options at the time of cancer diagnosis," said Dr. Rosen. "Routine counseling regarding reproductive health risk and options for preserving reproductive potential will improve the quality of life among survivors, and the overall quality of care."

The authors concluded that socio-demographic health disparities likely affect access to fertility preservation services. "An opportunity lies ahead to explore educational and policy interventions to ameliorate health disparities that may exist in the growing use of fertility preservation," said Dr. Rosen.