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Mystery of the pandemic flu virus of 1918 solved by University of Arizona researchers

University of Arizona researcher Michael Worobey and his team have discovered the key to understanding influenza pandemics may lie in previous flu exposure during childhood

A study led by Michael Worobey at the University of Arizona in Tucson provides the most conclusive answers yet to two of the world's foremost biomedical mysteries of the past century: the origin of the 1918 pandemic flu virus and its unusual severity, which resulted in a death toll of approximately 50 million people.

Worobey's paper on the flu, to be published in the early edition of the Proceedings of the National Academy of Sciences (PNAS) on April 28, not only sheds light on the devastating 1918 pandemic, but also suggests that the types of flu viruses to which people were exposed during childhood may predict how susceptible they are to future strains, which could inform vaccination strategies and pandemic prevention and preparedness.

"Ever since the great flu pandemic of 1918, it has been a mystery where that virus came from and why it was so severe, and in particular, why it killed young adults in the prime of life," said Worobey, a professor in the UA Department of Ecology and Evolutionary Biology. "It has been a huge question what the ingredients for that calamity were, and whether we should expect the same thing to happen tomorrow, or whether there was something special about that situation."

Worobey and his colleagues developed an unprecedentedly accurate molecular clock approach and used it to reconstruct the origins of the 1918 pandemic H1N1 influenza A virus (IAV), the classical swine H1N1 influenza virus and the post-pandemic seasonal H1N1 lineage that circulated from 1918 until 1957.

Surprisingly, they found no evidence for either of the prevailing hypotheses for the origin of the 1918 virus – that it jumped directly from birds or involved the swapping of genes between existing human and swine influenza strains. Instead, the researchers inferred that the pandemic virus arose shortly before 1918 upon the acquisition of genetic material from a bird flu virus by an already circulating human H1 virus – one that had likely entered the human population 10-15 years prior to 1918.

The researchers found a remarkable overlap between death rates in various age groups in 1918 and childhood exposure to an H3 influenza virus mismatched in its major antigenic protein to the H1 virus of 1918: age groups with the highest percentage of individuals exhibiting H3 antibodies fared the worst in 1918, and the death-by-age curve closely tracks the peaks and valleys of H3 antibodies in cohorts born before, during and after the 1889 H3 pandemic.
Michael Worobey

"It sounds like a modest little detail, but it may be the missing piece of the puzzle," Worobey said. "Once you have that clue, many other lines of evidence that have been around since 1918 fall into place."

If these individuals had been already been exposed to an H1 virus, it could explain why they experienced much lower rates of death in 1918 than those who died in greatest numbers, a cohort centered on those about 29 years of age in 1918.

IAV typically kills primarily infants and the elderly, but the pandemic virus caused extensive mortality in those ages 20 to 40, primarily from secondary bacterial infections, especially pneumonia. The authors suggest that this is likely to be because many young adults born from about 1880 to 1900 were exposed during childhood to a putative H3N8 virus circulating in the population, which featured surface proteins distinct to both the major antigenic proteins of the H1N1 virus.

The authors compared the virus' genetic history with the types of antibodies present in people from different generations alive in 1918 and with death-by-birth-year patterns not only in 1918 but also in later years. The combined lines of evidence suggest that this small wedge of the population may have been uniquely susceptible to severe disease in 1918, whereas most individuals born earlier or later than between 1880 and 1900 would have had better protection against the 1918 H1N1 virus due to childhood exposure to N1 and/or H1-related antigens.

The authors speculate that long-term protection, for example the perplexingly low mortality in very elderly people in 1918 who may have been exposed in youth to an H1N1-like virus, might be mediated by immune responses to relatively slowly evolving regions of the viral HA protein. "Imagine a soccer ball studded with lollipops," Worobey explained. "The candy part of the lollipop is the globular part of the HA protein, and that is by far the most potent part of the flu virus against which our immune system can make antibodies. If antibodies cover all the lollipop heads, the virus can't even infect you."

The part of the protein that represents the stem of the lollipop in this analogy is less exposed to the immune system's responses. "Antibodies binding the HA stalk might not prevent infection altogether, but they can get in

the way enough to prevent the virus from multiplying as much as it otherwise would, which protects you from severe disease and death," Worobey said.
"But a person with an antibody arsenal directed against the H3 protein would not have fared well when faced with flu viruses studded with H1 protein," Worobey said, "And we believe that that mismatch may have resulted in the heightened mortality in the age group that happened to be in their late 20s during the 1918 pandemic."
The authors note that childhood exposure to mismatched viral proteins may nevertheless have been better than nothing: isolated populations on islands where many individuals might have had no prior exposure to IAV before 1918 suffered mortality rates many times higher than the "H3N8" cohort of young adults worldwide.
The authors suggest that immunization strategies that mimic the often impressive protection provided by initial childhood exposure to influenza virus variants encountered later in life might dramatically reduce mortality due to both seasonal and novel IAV strains.
Worobey said the new perspective does not just apply to the pandemic of 1918, but might also explain patterns of seasonal flu mortality and the mysterious patterns of mortality from highly pathogenic avian origin H5N1. H5N1causes higher mortality rates in young people and H7N9 causes higher mortality in the elderly. In both cases, the more susceptible age groups were exposed initially, as children, to viruses with a mismatched HA, and may suffer severe consequences similar to young adults faced with a mismatched virus in 1918.
"What seems to be the decisive factor is prior immunity," Worobey said. "Our study takes a variety of observations that have been difficult to explain and reconciles and places them into a logical chain able to explain many patterns of influenza mortality over the last 200 years. What we need to do now is to attempt to validate these hypotheses and determine the exact mechanisms involved, then apply that knowledge directly to *better prevent people from dying from seasonal flu and future pandemic strains."*
The study, "The genesis and pathogenesis of the 1918 pandemic influenza A virus," was co-authored by Guan-Zhu Han at the UA Department of Ecology and Evolutionary Biology and Andrew Rambaut at the Centre for Infection, Immunity and Evolution at the University of Edinburgh and the National Institutes of Health in Bethesda, Md.

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Stanford scientists create circuit board modeled on the human brain

The Neurogrid circuit board can simulate orders of magnitude more neurons and synapses than other brain mimics on the power it takes to run a tablet computer.

Stanford scientists have developed a new circuit board modeled on the human brain, possibly opening up new frontiers in robotics and computing. For all their sophistication, computers pale in comparison to the brain. The modest cortex of the mouse, for instance, operates 9,000 times faster than a personal computer simulation of its functions.
Not only is the PC slower, it takes 40,000 times more power to run, writes Kwabena Boahen, associate professor of bioengineering at Stanford, in an article for the Proceedings of the IEEE. "From a pure energy perspective, the brain is hard to match," says Boahen, whose article surveys how "neuromorphic" researchers in the United States and Europe are using silicon and software to build electronic systems that mimic neurons and synapses.
Boahen and his team have developed Neurogrid, a circuit board consisting of 16 custom-designed "Neurocore" chips. Together these 16 chips can simulate 1 million neurons and billions of synaptic connections. The team designed these chips with power efficiency in mind. Their strategy was to enable certain synapses to share hardware circuits. The result was Neurogrid – a device about the size of an iPad that can simulate orders of magnitude more neurons and synapses than other brain mimics on the power it takes to run a tablet computer.
The National Institutes of Health funded development of this million-neuron prototype with a five-year Pioneer Award. Now Boahen stands ready for the next steps – lowering costs and creating compiler software that would enable engineers and computer scientists with no knowledge of neuroscience to solve problems – such as controlling a humanoid robot – using Neurogrid. Its speed and low power characteristics make Neurogrid ideal for more than just modeling the human brain. Boahen is working with other Stanford scientists to develop prosthetic limbs for paralyzed people that would be controlled by a Neurocore-like chip.
"Right now, you have to know how the brain works to program one of these," said Boahen, gesturing at the $40,000 prototype board on the desk of his Stanford office. "We want to create a neurocompiler so that you would not need to know anything about synapses and neurons to able to use one of these."

Brain ferment

In his article, Boahen notes the larger context of neuromorphic research, including the European Union's Human Brain Project, which aims to simulate a human brain on a supercomputer. By contrast, the U.S. BRAIN Project – short for Brain Research through Advancing Innovative Neurotechnologies – has taken a tool-building

approach by challenging scientists, including many at Stanford, to develop new kinds of tools that can read out the activity of thousands or even millions of neurons in the brain as well as write in complex patterns of activity.
Zooming from the big picture, Boahen's article focuses on two projects comparable to Neurogrid that attempt to model brain functions in silicon and/or software.
One of these efforts is IBM's SyNAPSE Project – short for Systems of Neuromorphic Adaptive Plastic Scalable Electronics. As the name implies, SyNAPSE involves a bid to redesign chips, code-named Golden Gate, to emulate the ability of neurons to make a great many synaptic connections – a feature that helps the brain solve problems on the fly. At present a Golden Gate chip consists of 256 digital neurons each equipped with 1,024 digital synaptic circuits, with IBM on track to greatly increase the numbers of neurons in the system.
Heidelberg University's BrainScales project has the ambitious goal of developing analog chips to mimic the behaviors of neurons and synapses. Their HICANN chip – short for High Input Count Analog Neural Network – would be the core of a system designed to accelerate brain simulations, to enable researchers to model drug interactions that might take months to play out in a compressed time frame. At present, the HICANN system can emulate 512 neurons each equipped with 224 synaptic circuits, with a roadmap to greatly expand that hardware base.
Each of these research teams has made different technical choices, such as whether to dedicate each hardware circuit to modeling a single neural element (e.g., a single synapse) or several (e.g., by activating the hardware circuit twice to model the effect of two active synapses). These choices have resulted in different trade-offs in terms of capability and performance. In his analysis, Boahen creates a single metric to account for total system cost – including the size of the chip, how many neurons it simulates and the power it consumes. Neurogrid was by far the most cost-effective way to simulate neurons, in keeping with Boahen's goal of creating a system affordable enough to be widely used in research.

Speed and efficiency

But much work lies ahead. Each of the current million-neuron Neurogrid circuit boards cost about $40,000. Boahen believes dramatic cost reductions are possible. Neurogrid is based on 16 Neurocores, each of which supports 65,536 neurons. Those chips were made using 15-year-old fabrication technologies.
By switching to modern manufacturing processes and fabricating the chips in large volumes, he could cut a Neurocore's cost 100-fold – suggesting a million-neuron board for $400 a copy. With that cheaper hardware and compiler software to make it easy to configure, these neuromorphic systems could find numerous applications.
For instance, a chip as fast and efficient as the human brain could drive prosthetic limbs with the speed and complexity of our own actions – but without being tethered to a power source. Krishna Shenoy, an electrical engineering professor at Stanford and Boahen's neighbor at the interdisciplinary Bio-X center, is developing ways of reading brain signals to understand movement. Boahen envisions a Neurocore-like chip that could be implanted in a paralyzed person's brain, interpreting those intended movements and translating them to commands for prosthetic limbs without overheating the brain. A small prosthetic arm in Boahen's lab is currently controlled by Neurogrid to execute movement commands in real time. For now it doesn't look like much, but its simple levers and joints hold hope for robotic limbs of the future.
Of course, all of these neuromorphic efforts are beggared by the complexity and efficiency of the human brain. In his article, Boahen notes that Neurogrid is about 100,000 times more energy efficient than a personal computer simulation of 1 million neurons. Yet it is an energy hog compared to our biological CPU.
"The human brain, with 80,000 times more neurons than Neurogrid, consumes only three times as much power," Boahen writes. "Achieving this level of energy efficiency while offering greater configurability and scale is the ultimate challenge neuromorphic engineers face."

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The power of protein at breakfast; higher amounts may deliver more benefits

A higher-protein breakfast provides better appetite and glucose control when compared to lower-protein breakfasts, suggests new research

CHICAGO - Many consumers are aware they should make protein a priority at breakfast, but it may be equally important for them to choose an optimal amount of protein to maximize its benefits, suggests new research presented at the American Society for Nutrition's Experimental Biology conference this week. Researchers found that when comparing common breakfasts with varying amounts of protein, a commercially prepared turkey-sausage and egg bowl, cereal and milk, and pancakes with syrup, choosing the higher-protein commercially prepared turkey-sausage and egg bowl provided increased feelings of fullness and lesser calorie intake at lunch, when compared to the lower-protein breakfasts.1

"There is great value in understanding protein's true power when optimal amounts are consumed. Protein is top of mind, but consumers should be more informed about how much protein they need at each meal occasion so they can maximize benefits, like hunger control," said Dr. Kristin Harris, head of nutrition research at Hillshire Brands. "Hillshire Brands expects to continue to leverage clinical research to drive innovation, which includes delivering consumer-preferred products that meet health and wellness needs."

Greater satiety through morning and fewer calories consumed at lunch

Dr. Melinda Karalus, lead researcher, tested the short-term satiety effects of six breakfast meals similar in calories, fat and fiber and varied in protein; three turkey-sausage and egg-based breakfast bowls containing 40, 23 and 9 grams of protein, respectively, a cereal and milk breakfast containing eight grams of protein, a pancake and syrup breakfast with three grams of protein or no breakfast.

Participants were asked to rate their level of hunger before breakfast and at 30-minute intervals for four hours. After four hours, a pasta lunch was served and test subjects were asked to eat until comfortably full.

Participants who ate the higher-protein breakfasts had improved appetite ratings throughout the morning, and they also consumed fewer calories during lunch, compared with the lower-protein cereal and pancake and syrup breakfasts, or no breakfast at all.

Blood glucose stability

Other research presented at Experimental Biology further supports the benefits of optimal amounts of protein at breakfast. A different team of researchers found that a commercially prepared sausage and egg breakfast containing 39 grams of protein better stabilized blood glucose levels after eating when compared to a commercially prepared sausage and egg breakfast containing 30 grams of protein and a pancake and syrup breakfast containing 3 grams of protein.2

The abstracts entitled, "The effect of commercially prepared breakfast meals with varying levels of protein on acute satiety in non-restrained women" and "Acute Effects of High Protein, Sausage and Egg-based Convenience Breakfast Meals on Postprandial Glucose Homeostasis in Healthy, Premenopausal Women" were sponsored and funded by Hillshire Brands, Chicago.

1 Karalus, M, et al.The effect of commercially prepared breakfast meals with varying levels of protein on acute satiety in non-restrained women. Abstract presented at Experimental Biology, 2014.

2 Leidy H, et al. Acute Effects of High Protein, Sausage and Egg-based Convenience Breakfast Meals on Postprandial Glucose Homeostasis in Healthy, Premenopausal Women. Abstract presented at Experimental Biology, 2014.

http://www.eurekalert.org/pub_releases/2014-04/f-sf-tbc042814.php#rssowlmlink

Two breath compounds could be associated with larynx cancer

Concentrations of certain molecules, mainly ethanol and 2-butanone, are higher in individuals with carcinoma

Researchers at the Rey Juan Carlos University and the Alcorcón Hospital (Madrid) have compared the volatile substances exhaled by eleven people with cancer of larynx, with those of another twenty healthy people. The results show that the concentrations of certain molecules, mainly ethanol and 2-butanone, are higher in individuals with carcinoma, therefore they act as potential markers of the disease.

Human breath contains thousands of volatile organic compounds (VOC) and some of them can be used as non-invasive biomarkers for various types of head and neck cancers as well as cancer of the larynx.

This was shown in the experiment carried out by scientists from the Rey Juan Carlos University (URJC) with 31 volunteers: 20 healthy subjects (half of which are smokers) and 11 with cancer of the larynx in various phases of the disease and who are being treated in the Alcorcón Hospital in Madrid.

The results, published in the journal 'Chromatographia', reveal that the air exhaled by the more seriously ill patients – in a stage called T3 – contains different concentrations of seven compounds compared with the levels of healthy people or even those with a less developed tumour (T1). Specifically, in the graphics of individuals with advanced cancer, the peaks that represent ethanol (C2H6O) and 2-butanone (C4H8O) are particularly significant. These two compounds therefore become potential markers of laryngeal carcinoma.

"At the moment it is still a preliminary study and a wider sample has to be obtained," Rafael García, professor of Chemical Engineering at the URJC and co-author of the study told SINC, "but it is a step in the right direction, an alternative with regard to identifying biomarkers, not only for this type of cancer but for other more prevalent and serious ones such as lung cancer, where early detection is key".

As part of the experiment, the researchers asked the participants to breathe into tedlar bags after fasting for at least eight hours so there was no leftover food or drink on their breath. The samples were then analysed with solid phase micro-extraction, gas chromatography and mass spectrometry techniques, which enable very small amounts of a substance to be separated and identified. The concentrations are around or slightly above the equipment's detection limits (40 nanograms/mL), which is equivalent to 40 ppb or parts per billion.

The ultimate aim of the research is to "create an electronic nose that can be used in hospitals and health centres for the early detection of these types of diseases," concluded Rafael García. This team, together with other Spanish and foreign research groups, is working hard to develop sensors capable of detecting diseases through breath analysis.
Head and neck cancers represent between 5% and 10% of all malignant tumours currently diagnosed in Spain. Every year nearly half a million new cases are detected worldwide, mainly attributed to tobacco and alcohol use and approximately 90% are laryngeal cancer. The study also identified four markers in the exhaled breath that are typical of smokers, such as benzene and furfural.
Rafael A. García, Victoria Morales, Sergio Martín, Estela Vilches, Adolfo Toledano. "Volatile Organic Compounds Analysis in Breath Air in Healthy Volunteers and Patients Suffering Epidermoid Laryngeal Carcinomas". Chromatographia 77 (5-6): 501-509, 2014.

http://www.eurekalert.org/pub_releases/2014-04/tju-oct042814.php#rssowlmlink

One cell type may quash tumor vaccines

A single cell type could explain why cancer vaccines have a tough time stimulating the immune system to fight tumors

PHILADELPHIA - Most cancer vaccines have not lived up to their promise in clinical trials. The reason, many researchers suspect, is that the immune cells that would help the body destroy the tumor – even those reactions boosted by cancer vaccines – are actively suppressed. Now, researchers at Thomas Jefferson University have found that a single cell type is actively suppressed in several experimental cancer vaccines, paving the way toward methods to break suppression and improve the effectiveness of cancer vaccines. The work was published this week online in the European Journal of Immunology.
"The conventional wisdom is that the body knocks out all of the cells that can mount an immune response to the cancer," says first author Adam Snook, PhD, a Research Instructor at Thomas Jefferson University. "In fact, our work shows that it's only one cell type that is affected. But that cell, the T-helper cell, acts as the lynchpin."
Cancer vaccines are designed to boost the body's natural defenses against cancer. They work by training the immune system to recognize and attack specific tumor peptides, which are a kind of identification tag for tumors. These peptide "tags" help the immune system find and attack cancer cells. There are three types of cells that can "see" and react to these tags: T-helper cells, cytotoxic T cells, and B cells, and researchers thought that all three were trained, or tolerized, to ignore the tags on cancer cells.
Dr. Snook and colleagues tested which cell was involved by inoculating mice with a cancer vaccine they developed for colorectal cancer using a tumor peptide called guanylyl cyclase C (GUCY2C). Normally, GUCY2C-vaccinated mice would not produce much of an immune response, from either T cell type or B cells. However, when the researchers boosted the GUCY2C vaccine by linking it to another peptide called S1 that efficiently activates T-helper cells, they were able to see a vigorous activation of cytotoxic T cells and B cells directed at GUCY2C. In fact, the GUCY2C vaccine-S1 combo improved the survival time of mice with cancer by months compared to only days with GUCY2C vaccine alone. In fact, many mice were cured of their disease.
When Dr. Snook tested two other cancer peptides, one for breast cancer (Her2) and one for melanoma (Trp2), he saw similar results, suggesting that selective inactivation of T helper cells occurs for peptides found in many cancer types. "The results make a lot of sense," says Dr. Snook. "T-helper cells, as their name suggests, provide help to both cytotoxic T cells and to B cells. The entire peptide-specific immune response can be taken out by tolerizing this one cell type."
In addition, T-helper cells are also essential for creating immunological memory. Boosting T-helper cell activation also protected mice from challenge with cancer months after the initial vaccination, increasing their survival and decreasing tumor number.
The next step is to test whether a T helper peptide-linked GUCY2C vaccine could help fight colorectal cancer in humans. Dr. Snook and colleagues are currently enrolling patients in a clinical trial aimed at reducing the rate *of cancer recurrence in patients who had their primary tumors removed.*
The work was funded by NIH (R01 CA75123, R01 CA95026, RC1 CA146033, P30 CA56036, R01 CA170533; F31 CA171672); Targeted Diagnostic and Therapeutics Inc.; and a Measey Foundation Fellowship. Scott Waldman is the Samuel M.V. Hamilton Professor of Thomas Jefferson University. This project was funded, in part, by grants from the Pennsylvania Department of Health (SAP #4100059197, SAP #4100051723). The Department specifically disclaims responsibility for any analyses, interpretations or conclusions. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.
Scott Waldman was the Chair of the Data Safety Monitoring Board for the C-Cure Trial sponsored by Cardio Biosciences, and the Chair (uncompensated) of the Scientific Advisory Board to Targeted Diagnostics and Therapeutics, Inc. which provided research funding that, in part, supported this work and has a license to commercialize inventions related to this work. All other authors declare no financial or commercial conflict of interest.

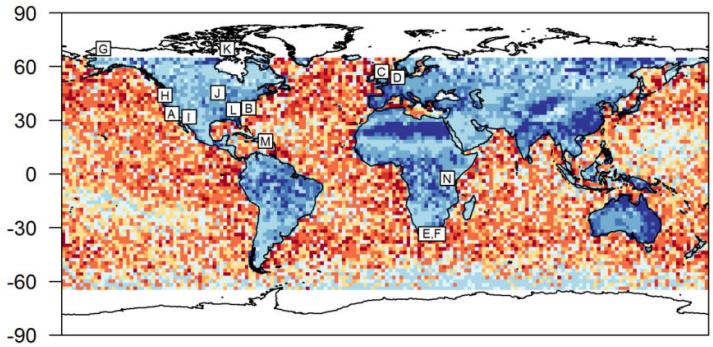
http://phys.org/news/2014-04-scientist-life-earth.html#rssowlmlink

Scientist helps create the first computer model of all life on Earth

A Sussex ecologist is among a team of scientists who have created a pioneering computer model that can predict the futures of all of the Earth's ecosystems and could help to address key environmental concerns.

Phys.org - Dr Jörn Scharlemann and his colleagues at Microsoft Research and the United Nations Environment Programme World Conservation Monitoring Centre (UNEP-WCMC) have spent three years developing the world's first General Ecosystem Model, or GEM, the results of which are published this week (22 April) in the journal *PloS Biology*.

The mathematical model incorporates the biological life cycle and fundamental ecological processes of all species, simulating the millions of trillions of the planet's organisms and is able to reproduce characteristics of ecosystems we see in the real world.



Dr Jorn Sharlemann co-led the development of the Madingley Model, which can predict the futures of all the Earth's ecosystems. The image shows the total biomass of animals (red colours indicate high biomass levels and blue low levels of biomass per area).

Dubbed the 'Madingley Model', after the village in Cambridgeshire, UK, where the scientists first hatched the idea, it addresses central questions in ecology about how interactions among plants and animals create the planet's many different ecosystems, and could help answer key environmental issues, such as the long term outcome of deforestation or the introduction of invasive species on the health and functioning of ecosystems.

Dr Scharlemann, Reader in Ecology and Conservation at Sussex, who co-led the development of the model, said: "The Madingley Model offers decision-makers for the first time an interactive tool to explore and quantify the impacts of their decisions on the global environment.

"The model brings together current ecological understanding to create a virtual world that simulates the impacts of human activities on the planet, analogous to early General Circulation Models that predict our impacts on the climate system. It's an exciting development for scientists."

More information: *Harfoot MBJ, Newbold T, Tittensor DP, Emmott S, Hutton J, et al. (2014) "Emergent Global Patterns of Ecosystem Structure and Function from a Mechanistic General Ecosystem Model." PLoS Biol 12(4): e1001841. DOI: 10.1371/journal.pbio.1001841*

The Madingley Model is being released as open source code to allow other scientists to inspect the model and develop it further. The code can be downloaded from www.madingleymodel.org

http://www.scientificamerican.com/article/many-prisoners-on-death-row-are-wrongfully-convicted

Many Prisoners on Death Row are Wrongfully Convicted

Researchers estimate that more than 340 U.S. inmates that could have been exonerated were sentenced to death since 1973

Apr 28, 2014 |By Dina Fine Maron

Just how many individuals on death row are incorrectly convicted? The question has dogged attorneys and civil rights advocates for years, but a simple answer is almost impossible because few wrongful cases are ever overturned. A new analysis is adding a level of much-needed detail, and it concludes that more than twice as many inmates were wrongly convicted and sentenced to death than have been exonerated and freed.

Borrowing a statistical method often used to evaluate whether new medical therapies help patients survive, a team of researchers has concluded that about 4.1 percent of criminal defendants who are sentenced to death are falsely convicted. The approach allows researchers to “actually come up with a valid estimate of the rate of false convictions—knowing something that people say [in criminal justice] is not knowable,” says study author Samuel Gross, a law professor at the University of Michigan Law School and editor of the National Registry of Exonerations, a U.S.-focused exoneration database. What makes the analysis possible is that data on the potential need for exoneration from death penalty cases come to light more often than it does for other types of criminal proceedings. All death sentences in the U.S. are based on crimes that include homicide.

The study, led by a team of lawyers and statisticians, examined data on both 7,482 defendants who were given death sentences between 1973 and 2004 and death row exonerations during that time. By applying survival analysis—a statistical method often used to calculate how well new treatments help patients survive—they determined how often a prisoner under threat of execution was exonerated. The method usually tracks patients to see if a new therapy prolongs the period of time until a person dies from the illness in question but it can also

be applied to policy questions that have clear end points. In this study the end point of tracking was exoneration (being found innocent and freed) or the actual execution. “Survival” was defined as remaining in prison. The “therapy” here would be removal of the threat of execution.

Here’s how their analysis works. It says that if all death-sentenced defendants remained under this sentence indefinitely, as opposed to being taken off death row due to being resentenced to life in prison or their fate being artificially cut off by the study ending, then 4.1 percent of those prisoners would have otherwise been exonerated. (And being exonerated and freed by legal action here is used as the best proxy for innocence.) The analysis also takes into account other occurrences such as suicide or death of a prisoner from natural causes. The number of false convictions among the death-sentenced has been particularly hard to estimate, Gross says, because many prisoners who are on death row are eventually moved off of it but remain in prison, which often reduces their chances of exoneration.

The issue affects a significant number of people. Since 1973 144 death-sentenced defendants have been exonerated in the U.S. But Gross says that the analysis indicates that at least 340 people would have been put to death unjustly in that same time period. “There are no other reliable estimates of the rate of false conviction in any context,” the researchers wrote in the study, published online on April 28 in Proceedings of the National Academy of Sciences.

The researchers also note that a 4.1 percent rate of false conviction is conservative, given that separate calculations gauging the accuracy of the assumptions that took an even more conservative stance—assuming that people who were executed had zero chance of false conviction and that the chances of exoneration after retrial would be twice that of people on death row—would still produce a larger figure than their 4.1 percent estimate. Although their analysis does not include data after 2004, the researchers note that they doubt that the use of DNA identification technology would have much impact on false conviction rates—because DNA evidence is primarily used in cases such as rape rather than homicide. Only about 13 percent of death row exonerations have resulted from DNA testing.

http://www.eurekalert.org/pub_releases/2014-04/uon-mi042914.php#rssowlmlink

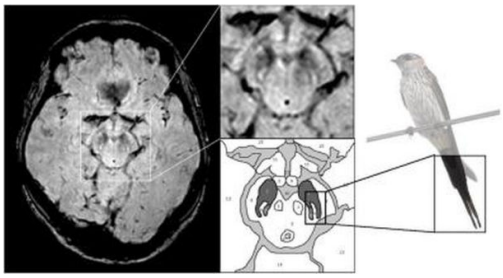
'Tell-tail' MRI image diagnosis for Parkinson's disease

An image similar in shape to a Swallow's tail has been identified as a new and accurate test for Parkinson's disease.

The image, which depicts the healthy state of a group of cells in the sub-region of the human brain, was singled out using 3T MRI scanning technology – standard equipment in clinical settings today. The research was led by Dr Stefan Schwarz and Professor Dorothee Auer, experts in neuroradiology in the School of Medicine at The University of Nottingham and was carried out at the Queen's Medical Centre in collaboration with Dr Nin Bajaj, an expert in Movement Disorder Diseases at the Nottingham University Hospitals NHS Trust. The findings have been published in the open access academic journal PLOS one.

The work builds on a successful collaboration with Professor Penny Gowland at the Sir Peter Mansfield Magnetic Resonance Centre at The University of Nottingham.

'The 'Swallow Tail' Appearance of the Healthy Nigrosome – A New Accurate Test of Parkinson's Disease: A Case-Control and Retrospective Cross-Sectional MRI Study at 3T' – describes how the absence of this imaging sign can help to diagnose Parkinson's disease using standard clinical Magnetic Resonance Scanners.



This is a 'Swallow tale' image from 3T MRI scan. **Dr Stefan Schwarz**

Parkinson's disease is a progressive neurodegenerative disorder which destroys brain cells that control movement. Around 127,000 people in the UK have the disease. Currently there is no cure but drugs and treatments can be taken to manage the symptoms.

The challenges of diagnosing Parkinson's

Until now diagnosing Parkinson's in clinically uncertain cases has been limited to expensive nuclear medical techniques. The diagnosis can be challenging early in the course of the condition and in tremor dominant cases. Other non-licensed diagnostic techniques offer a varying range of accuracy, repeatability and reliability but none of them have demonstrated the required accuracy and ease of use to allow translation into standard clinical practice.

Using high resolution, ultra high filed 7T magnetic resonance imaging the Nottingham research team has already pinpointed the characteristic pathology of Parkinson's with structural change in a small area of the mid brain known as the substantia nigra. The latest study has shown that these changes can also be detected using 3T MRI technology which is accessible in hospitals across the country. They subsequently coined the phrase

the 'swallow tail appearance' as an easy recognizable sign of the healthy appearing substantia nigra which is lost in Parkinson's disease. A total of 114 high-resolution scans were reviewed and in 94 per cent of cases the diagnosis was accurately made using this technique.

New findings give new hope

Dr Schwarz said: "This is a breakthrough finding as currently Parkinson's disease is mostly diagnosed by identifying symptoms like stiffness and tremor. Imaging tests to confirm the diagnosis are limited to expensive nuclear medical techniques which are not widely available and associated with potentially harmful ionizing radiation. "Using Magnetic Resonance Imaging (no ionizing radiation involved and much cheaper than nuclear medical techniques) we identified a specific imaging feature which has great similarity to a tail of a swallow and therefore decided to call it the 'swallow tail sign'. This sign is absent in Parkinson's disease."

The research was funded by The University of Nottingham, the Sarah Matheson Trust, and the Medical Research Council. Dr Schwarz's Academic Clinical Lectureship is funded by the National Institute for Health Research UK.
The funders had no role in study design, data collection and analysis.

http://www.eurekalert.org/pub_releases/2014-04/uoe-srr042914.php#rssowlmlink

Stroke risk reduced if brain blood vessel disorder is left alone

Treating patients who suffer from a common condition that affects blood vessels in the brain increases their risk of stroke, a study has found.

People with a condition known as arteriovenous malformation (AVM) – which causes blood vessels in the brain to tangle – have a better outcome if doctors treat their symptoms only and not the AVM. A team of doctors looked at the long-term outcome of patients with the condition, which is caused by abnormal connections between the arteries and veins in the brain. They found that, over a 12 year period, patients who chose not to be treated for their condition were less likely to have a stroke or die from related causes. These patients were also less likely to suffer sustained disability compared with those who opted for an intervention to treat the tangles. This is the first study to compare the risks and benefits of treatment for AVM in the long term. The findings build on previous research that reported an increased risk of stroke in the first three years after treatment for AVM.

AVM affects around 1 in 2000 people. Although most people with the condition can lead relatively normal lives, they live with the risk that the tangles can burst and bleed into the brain at any time, causing a stroke. Around one in every hundred AVM patients suffers a stroke each year. In some cases doctors can surgically remove the tangle or block the blood vessels involved to reduce the risk of bleeding. However, treatment can sometimes increase the chances that the tangle will burst and bleed into the brain, resulting in a stroke.

Professor Rustam Al-Shahi Salman, MRC Senior Clinical Fellow at the University of Edinburgh and a consultant neurologist, said: "Many patients feel that living with AVM is like living with a time bomb in your head that could explode at any time. Patients and their doctors face difficult choices when deciding whether or not to pursue treatment. We have found that, for most people whose AVM has not caused a bleed, the risks of treatment exceed the risks of leaving it alone over 12 years."

The study was led by researchers at the University of Edinburgh and is published in the Journal of the American Medical Association.

http://www.eurekalert.org/pub_releases/2014-04/aaft-mlr042414.php#rssowlmlink

Major lung resection safer than ever, especially at the busiest hospitals

According to New study presented at the 94th Annual AATS Meeting

Toronto, ON, Canada – A major new study using data from the National Cancer Data Base details the impact of annual hospital volume on 30- and 90-day mortality rates. Investigators found that major lung surgery has become progressively safer over the last few decades, although higher death rates at low-volume hospitals and an unexpected increase in mortality at 90 days compared to 30 days were observed. The study further suggests that choosing a center that performs major lung surgery regularly can have a strong impact on survival.

Lung cancer is the leading cause of death from cancer in both men and women in the U.S. The best chance to cure lung cancer after it develops involves a combination of early detection at an "operable" stage, followed by surgery to remove the portion of the lung where the cancer developed. The number of operations for lung cancer is likely to increase with lung cancer screening.

The study used the National Cancer Data Base (NCDB) cancer treatment and outcomes database, which is a joint project co-sponsored by the American Cancer Society and the American College of Surgeons. The NCDB captures more than 80% of all new lung cancer cases treated in the U.S. each year, and evaluated data for 121,099 patients who underwent major pulmonary resection for lung cancer at more than 1,200 Commission on Cancer-accredited hospitals across the U.S. between 2007 and 2011. Survival at 30 days and 90 days after surgery and numerous risk factors for dying after the surgery were evaluated.

Analysis revealed that at all 1,200+ hospitals combined, 2.8% of patients who underwent major lung surgery (93% of which were lobectomies or bi-lobectomies) died within 30 days after their surgery during this five-year time period. This rate was lower than reported from the busiest hospitals with the highest volume of surgeries just a decade ago. Further analysis showed that annual hospital volume of major lung operations for cancer had a significant impact on both 30-day and 90-day mortality rates. The chance of death was twice as high at hospitals where less than 10 major lung cancer resections per year were performed (3.7%), compared to mortality at the busiest hospitals performing more than 90 such operations per year (1.7%). More than 10,000 of these operations took place at these lowest volume hospitals.

The researchers were surprised that the number of deaths by 90 days after surgery climbed to 5.4% overall, nearly double the rate at 30 days. "This increase in the number of deaths between 30 days and 90 days after surgery was not expected and has not been extensively reported in the past, as mortality rates after surgery are traditionally examined at 30 days. The reasons for this ongoing mortality beyond 30 days are not yet clear, but deserve further investigation," says lead author Christopher M. Pezzi, MD, Department of Surgery, Abington Health, Abington PA. The ongoing deaths between 30 and 90 days occurred at both low volume and high volume hospitals, although remained less likely at the busiest hospitals.

Other factors associated with mortality after lung surgery were anticipated, and included older age, male gender, socioeconomic factors, more advanced tumors, and a number of serious medical conditions present before the surgery. Having private insurance coverage was also associated with low (1.8%) 30-day mortality rates.

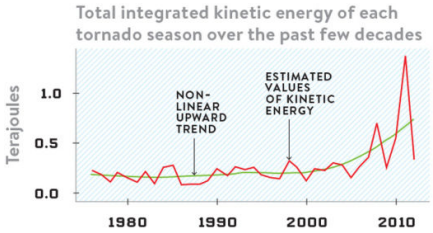
The Commission on Cancer of the American College of Surgeons has the ability to directly report to more than 1,500 accredited hospitals in the U.S. regarding their annual volume of these operations as well as the mortality rate at their hospital compared to national data. This information is part of a new national Cancer Quality Improvement Program (CQIP), which was launched in February 2014 and will be updated annually.

http://www.wired.com/2014/04/tornado-strength/#rssowlmlink

Yes, Tornadoes Are Getting Stronger

On May 20, 2013, a mass of swirling wind gouged a path of destruction across Oklahoma, killing 24 people and causing $2 billion in damage.

By Kate Greene



And earlier this week a deadly cluster of tornadoes ripped through the midwest and the south, killing more than dozen people and injuring hundreds. This kind of destruction would seem to indicate that tornadoes are getting worse. But with the way we currently measure twisters, it's nearly impossible to know. Now James Elsner, a geographer from Florida State University, has a fix.

See, meteorologists use the Enhanced Fujita Scale, which looks at damage to buildings and vegetation to rank a storm from EF0 to EF5. But that's subjective, and it doesn't work well in areas with few structures or trees. And you can't look inside the categories to see if one EF5 storm is stronger than another.

A tornado-power equation that actually gauges a twister's kinetic energy would be more useful to scientists who are also examining the effects of climate change, so that's what Elsner built. He looked at the length and width of a storm's damage path, correlated that to the amount of damage, and then used the result to estimate wind 1.0 speed. A little more crunching and bam!—integrated kinetic energy of a storm. Non-linear upward trend estimated values of kinetic energy Elsner's analysis suggests that since the turn of the century, tornadoes have packed a more powerful punch. Which, if you live in Tornado Alley, totally blows.

http://bit.ly/1lGLrMN

Pharma megadeals do nothing for neglected medicines

Big may not necessarily mean better if Pfizer, the world's largest pharmaceutical company, buys UK giant AstraZeneca.

17:30 29 April 2014 by Andy Coghlan

The announcement that the company is to pursue AstraZeneca, despite being rebuffed in January, comes a week after Swiss firm Novartis and GSK of the UK, swapped assets. The deal strengthened Novartis's already pre-eminent position in cancer drug development, and reinforced GSK's dominance in vaccines. "By doing that, they both played to their strengths," says John Carroll from the online industry bulletin, FierceBiotech.

Frank Orthbandt of FitchRatings in London, a global agency assessing the value of deals, says that this kind of asset swapping is now the industry norm. "It's too capital intensive to invest across many areas, so it's better to be a leader in a specific area, but you need to be sure you're going to be world class if you're going to swap or buy major assets," he says.

By contrast, there seems to be less scope for Pfizer to improve its standing by gobbling up AstraZeneca, says Carroll, because neither is dominant in fields where they overlap.

No love for antibiotics

There is little hope that pharma megadeals will do much for neglected medicines, such as new antibiotics and drugs for tropical diseases such as malaria. "Companies don't make much money from antibiotics, although some smaller biotechnology companies are developing them," says Carroll.

Disease-wise, cancer is definitely the hottest area of investment, and this is one area where Pfizer hopes to boost its prospects by buying AstraZeneca. "Cancer is the big one, as people understand the biology much better and there are startling new drugs coming through," says Carroll.

At the other end of the spectrum, companies are shying away from areas like depression. "People don't fully understand the biology, it's very hard to tackle in the clinic with high failure rates, and there are large placebo effects," he says.

http://phys.org/news/2014-04-girls-higher-grades-boys-school.html#rssowlmlink

Girls make higher grades than boys in all school subjects, analysis finds

Despite the stereotype that boys do better in math and science, girls have made higher grades than boys throughout their school years for nearly a century, according to a new analysis published by the American Psychological Association.

"Although gender differences follow essentially stereotypical patterns on achievement tests in which boys typically score higher on math and science, females have the advantage on school grades regardless of the material," said lead study author Daniel Voyer, PhD, of the University of New Brunswick, Fredericton, Canada. "School marks reflect learning in the larger social context of the classroom and require effort and persistence over long periods of time, whereas standardized tests assess basic or specialized academic abilities and aptitudes at one point in time without social influences."

Based on research from 1914 through 2011 that spanned more than 30 countries, the study found the differences in grades between girls and boys were largest for language courses and smallest for math and science. The female advantage in school performance in math and science did not become apparent until junior or middle school, according to the study, published in the APA journal Psychological Bulletin. The degree of gender difference in grades increased from elementary to middle school, but decreased between high school and college.

The researchers examined 369 samples from 308 studies, reflecting grades of 538,710 boys and 595,332 girls. Seventy percent of the samples consisted of students from the United States. Other countries or regions represented by more than one sample included Norway, Canada, Turkey, Germany, Taiwan, Malaysia, Israel, New Zealand, Australia, Sweden, Slovakia, United Kingdom Africa and Finland. Countries represented by one sample included Belgium, Czech Republic, Estonia, Mexico, Hong Kong, India, Iran, Jordan, the Netherlands, Portugal, Saudi Arabia, Serbia and Slovenia.

All studies included an evaluation of gender differences in teacher-assigned grades or official grade point averages in elementary, junior/middle or high school, or undergraduate and graduate university. Studies that relied on self-report and those about special populations, such as high-risk or mentored students, were excluded. The studies also looked at variables that might affect the students' grades, such as the country where students attended school, course material, students' ages at the time the grades were obtained, the study date and racial composition of the samples.

The study reveals that recent claims of a "boy crisis," with boys lagging behind girls in school achievement, are not accurate because girls' grades have been consistently higher than boys' across several decades with no significant changes in recent years, the authors wrote. "The fact that females generally perform better than their male counterparts throughout what is essentially mandatory schooling in most countries seems to be a well-kept secret, considering how little attention it has received as a global phenomenon," said co-author Susan Voyer, MASc, also of the University of New Brunswick.

As for why girls perform better in school than boys, the authors speculated that social and cultural factors could be among several possible explanations. Parents may assume boys are better at math and science so they might encourage girls to put more effort into their studies, which could lead to the slight advantage girls have in all courses, they wrote. Gender differences in learning styles is another possibility. Previous research has shown girls tend to study in order to understand the materials, whereas boys emphasize performance, which indicates a focus on the final grades. "Mastery of the subject matter generally produces better marks than performance emphasis, so this could account in part for males' lower marks than females," the authors wrote.

More information: "Gender Differences in Scholastic Achievement: A Meta-Analysis," Daniel Voyer, PhD, and Susan D. Voyer, MASc, University of New Brunswick, Psychological Bulletin, online April 28, 2014.

http://www.medscape.com/viewarticle/824310?src=rss#1

'Low-Risk' Kidney Stone Removal May Be Risky and Costly

After low-risk procedures to remove urinary stones, 1 in 7 patients need an unplanned emergency visit at substantial cost, according to a study published in the May issue of Surgery.

Laurie Barclay, MD

"Emergency department care is an all-too-common side effect for patients undergoing kidney stone removal surgery, when it should be a routine, outpatient procedure," lead author Charles Scales, MD, a surgeon at Duke University Medical Center in Durham, NC, said in a news release. "No one should have to roll the dice when it comes to the risk and overall cost of follow-up care for a very common procedure."

Although the Affordable Care Act has recently imposed financial penalties for unplanned follow-up care, unplanned postsurgical care for patients with kidney stones is not well-understood. The goal of this study was to examine the frequency, variation, and costs of unplanned, high-urgency follow-up visits for privately insured patients undergoing percutaneous nephrostolithotomy, ureteroscopy, or shockwave lithotripsy for stones.

The researchers searched the Marketscan database for individuals who underwent a procedure for kidney stones between 2003 and 2011. The Marketscan database covers 170 million United States residents who are covered by private health insurance.

Among 93,523 initial procedures for stone fragmentation or removal, 1 in 7 (n=12,478; 13%) was followed by an unplanned visit or hospital admission within 30 days of the procedure. This included 12% of patients who had undergone shockwave lithotripsy, 15% of those who underwent ureteroscopy, and 15% of those who underwent percutaneous nephrostolithotomy.

The authors note that the most common reasons for the unplanned follow-up visit were pain (16%), infection (10%), bleeding (1.5%), and renal failure (1.4%). "An estimated 70 percent of follow-up procedures occurred in the emergency room," Dr. Scales said in the release. "Additional, unexpected care after a common procedure places an undue cost burden on both the patient and an overtaxed health care system."

Unplanned Visits Less Likely After Procedures at High-Volume Facilities

Multivariate analyses showed that unplanned visits were significantly less likely after procedures at high-volume facilities (odds ratio [OR], 0.80; 95% confidence interval [CI], 0.74 - 0.87; $P < .001$), suggesting that some unplanned follow-up care may be preventable. Most patients in the study were relatively healthy, but older patients with more comorbidities were more likely to need unplanned follow-up treatment.

Among patients who had an unplanned postprocedural visit, adjusted incremental costs per episode were greater after shockwave lithotripsy ($32,156; 95% CI, $30,453 - $33,859) than after ureteroscopy ($23,436; 95% CI, $22,281 - $24,590). The potential financial effect of each unplanned follow-up episode ranged from just over $23,000 to more than $47,000. Limitations of this study include use of claims-based analysis lacking important clinical details and possible misclassification bias.

"Our results suggest that unplanned, high-acuity visits after procedures are not uncommon in this patient population and can be quite costly," the authors conclude. "Furthermore, the identification of a volume-outcome relationship suggests that mutable factors, such as processes of care, may influence the risk of unplanned post-procedure visits. These results should prompt efforts to identify preventable causes of unplanned care, and design interventions to reduce the occurrence of this complication of stone surgery."

The National Institute of Diabetes and Digestive and Kidney Diseases and the Urologic Diseases in America Project supported this study. Dr. Scales was supported by the Robert Wood Johnson Foundation Clinical Scholars program and the US Department of Veterans Affairs.

http://bit.ly/1i5ytTr

Fukushima Radioactivity Found in Tuna Off Oregon and Washington

A sample of albacore tuna caught off the shores of Oregon and Washington state have small levels of radioactivity from the 2011 Fukushima nuclear disaster in Japan, researchers said on Tuesday.

By Shelby Sebens

PORTLAND Ore. (Reuters) - But authors of the Oregon State University study say the levels are so small you would have to consume more than 700,000 pounds of the fish with the highest radioactive level to match the amount of radiation the average person is annually exposed to in everyday life through cosmic rays, the air, the ground, X-rays and other sources. Still, the findings shed some light about the impact of the meltdown on the Pacific Ocean following the March 2011 tsunami and subsequent power plant disaster, said Delvan Neville, a graduate research assistant at OSU and lead author of the study. “I think people would rather have an answer on what is there and what isn’t there than have a big question mark,” Neville said.

At the most extreme, radiation levels tripled from fish tested before Fuskushima and fish tested after. That level was 0.1 percent of the level set by the U.S. Food and Drug Administration for concern. “The levels were way

too small to really be a food safety issue, but we still want to tell people about it so they know what's there." Neville said.
Jason Phillips, a research associate in OSU's College of Earth, Ocean, and Atmospheric Sciences and co-author of the study, said he did not expect to find high levels of radiation in the fish, but rather thought it would be a way to track the migratory patterns of the albacore.
He said that thanks to continued support from the Oregon Sea Grant, the research will continue and they will expand the pilot program to look at fish from California and other parts of the North Pacific.
Their study looked at 26 Pacific albacore from 2008 to 2012. Phillips said the albacore tuna was a good species to study because it migrates as far as Japan.
"If we were going to see it in something, we would see it in albacore' or other high level predators," he added.

http://www.eurekalert.org/pub_releases/2014-04/aaft-cit042414.php#rssowlmlink

CT in the operating room allows more precise removal of small lung cancers

Procedure helps spare healthy lung tissue, according to presentation at 94th AATS Annual Meeting

Toronto, ON, Canada - A new technique that brings CT imaging into the operating room will allow surgeons to precisely demarcate and remove small sub-centimeter lung nodules, leaving as much healthy tissue as possible, according to Raphael Bueno, MD, of Brigham and Women's Hospital in Boston. His team is presenting the results of this late-breaking research at the 94th AATS Annual Meeting in Toronto, ON, Canada on April 30, 2014.
Lung cancer remains the deadliest cancer and a recent study, the National Lung Cancer Screening Trial, indicated that screening with low-dose computed tomography (CT) scans in smokers, who have certain risk factors, may decrease the number of deaths. Lung cancer screening with CT can detect many small lung lesions that can potentially be cancerous and should be removed surgically. The goal is to remove these small lung cancers but at the same time spare as much healthy lung as possible. To do so requires being able to precisely determine the exact location of the nodule and its margins.
"These results are exciting and promising, indicating that image-guided lung surgery could play a significant role in the treatment of lung cancer," says Dr. Bueno. "This surgical approach has the potential to increase accuracy and reduce errors. It is like using GPS to navigate to the destination and perform a true surgical strike."
In this phase I/II clinical study conducted in conjunction with researchers from the Siemens Corporation, 20 patients were identified who had small pulmonary nodules in the outer half of the lung. Previous CT scans showed that the lesions were very small, ranging from 0.6 to 1.8 cm. The nodules were so small that they could not be easily palpated or seen.
Using a CT scanner in the operating room, surgeons first marked the location of the lung nodules by inserting two small markers (T-bars) through the skin and placing them next to the nodule. The markers have attached wires that make them visible to surgeons during the resection process. This technique is safe and successful for nodule localization and all patients underwent complete removal of the lesions with minimal removal of healthy lung tissue.
"We propose that image-guided video assisted thoracic surgery (IVATS) can be used to improve the ability to precisely identify small pulmonary nodules and allow for resections of sub-centimeter nodules," says Dr. Bueno.

http://phys.org/news/2014-04-ancient-egyptians-pyramid-stones-sand.html#rssowlmlink

Ancient Egyptians transported pyramid stones over wet sand

Physicists from the FOM Foundation and the University of Amsterdam have discovered that the ancient Egyptians used a clever trick to make it easier to transport heavy pyramid stones by sledge.

The Egyptians moistened the sand over which the sledge moved. By using the right quantity of water they could halve the number of workers needed. The researchers published this discovery online on 29 April 2014 in Physical Review Letters.
For the construction of the pyramids, the ancient Egyptians had to transport heavy blocks of stone and large statues across the desert. The Egyptians therefore placed the heavy objects on a sledge that workers pulled over the sand. Research from the University of Amsterdam has now revealed that the Egyptians probably made the desert sand in front of the sledge wet. Experiments have demonstrated that the correct amount of dampness in the sand halves the pulling force required.

Firm sand

The physicists placed a laboratory version of the Egyptian sledge in a tray of sand. They determined both the required pulling force and the stiffness of the sand as a function of the quantity of water in the sand. To

determine the stiffness they used a rheometer, which shows how much force is needed to deform a certain volume of sand.
Experiments revealed that the required pulling force decreased proportional to the stiffness of the sand. Capillary bridges arise when water is added to the sand. These are small water droplets that bind the sand grains together. In the presence of the correct quantity of water, wet desert sand is about twice as stiff as dry sand. A sledge glides far more easily over firm desert sand simply because the sand does not pile up in front of the sledge as it does in the case of dry sand.

Wall painting

The Egyptians were probably aware of this handy trick. A wall painting in the tomb of Djehutihotep clearly shows a person standing on the front of the pulled sledge and pouring water over the sand just in front of it.
Besides revealing something about the ancient Egyptians, the results are also interesting for modern-day applications. We still do not fully understand the behaviour of granular material like sand. Granular materials are, however, very common. Other examples are asphalt, concrete and coal. The research results could therefore be useful for examining how to optimise the transport and processing of granular material, which at present accounts for about ten percent of the worldwide energy consumption.
The research was supervised by FOM group leader professor Daniel Bonn and is part of the FOM programme 'Fundamental aspects of friction'.

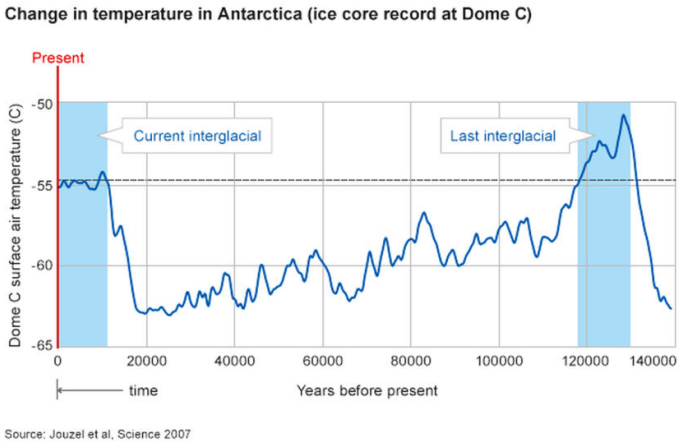
http://www.bbc.com/news/science-environment-27110880##rssowlmlink

Scientists probe Earth's last warm phase

Scientists now have a fuller picture of what happened at the poles during the last warm phase on Earth.

By Jonathan Amos Science correspondent, BBC News, Vienna

Known as the Eemian, this time period extended from roughly 129,000 years ago to about 116,000 years before present. The poles were known to have been a few degrees warmer than they are today. But by pulling together more than 40 ice core and marine sediment records, researchers, led by the British Antarctic Survey (BAS), have obtained the most comprehensive assessment yet. It confirms that the Antarctic emerged from Ice Age conditions first. The Northern Hemisphere followed.
"Interglacial conditions, warm conditions, were in place earlier in the Southern Hemisphere than in the Northern Hemisphere," explained Dr Emilie Capron from BAS. "Eventually, the Northern Hemisphere catches up and then both poles are warmer than they are today. "It's something we knew looking at a few records, but now we have more records showing exactly the same pattern," she told BBC News.
The researcher was speaking here in Vienna at the European Geosciences Union General Assembly.
The data synthesis has been completed as part of the UK iGlass programme and the Past4Future project - initiatives that seek clues about what will happen to the Earth's climate in the decades ahead from an understanding of its past behaviour.



Scientists will now use the information to test their computer models. If their simulations can reproduce the variation in temperatures across the land and ocean surfaces during the Eemian there will be greater confidence in the models as they look forward in time. This has already been done for one model, "and its simulations are on the right track," confirms Dr Capron. For her analysis, the BAS researcher combined five ice cores and 39 marine sediment records.
These can be used to infer past temperatures. For example, by studying the ratio of light to heavy molecules of water in the layers of the ice cores, it is possible to gauge the likely precipitation conditions, and therefore the prevailing temperatures, during the ancient snowfalls on Antarctica and Greenland.
And something similar can be done using the mud layers of marine sediments. These contain the skeletons of microscopic organisms called foraminifera, and the chemistry of their hard parts is heavily influenced by the temperature of the surface waters in which they swam.
"But having the temperatures is not enough," explained Dr Capron. "If you are going to compare the climate from one place to another, you need a common chronology for all the different records. And this was the great challenge in this study - to try to transfer all the palaeoclimatic records on to just one chronology, because we are working beyond the time where we can use radiocarbon dating."

One way to line up these types of records is to look for distinctive markers such as ash layers from major volcanic eruptions. A set of marine sediment records that came too late to be included in the study is the newly retrieved cores that were drilled from the Baltic Sea at the end of last year.
Under the International Ocean Discovery Program, scientists took cores from seven locations that trace the history of the Baltic Sea back in time from the present, all the way to, and through, the Eemian.
Preliminary study of these cores reveals extremely fine layers that should throw up fascinating new insights on the climate history of the region.
"The sediments of the Baltic basin provide a link between the continental and marine records," Dr Thomas Andren, the expedition's co-chief scientist, reported here at the EGU meeting.
"The Baltic is complicated because it reflects both the inputs of freshwater precipitation over land and also the inflow of marine water. These new cores will allow us to pull apart these signals, to see the climate history of the Baltic in unprecedented detail."

http://www.eurekalert.org/pub_releases/2014-04/uoc--dcr042814.php#rssowlmlink

Damage control: Recovering from radiation and chemotherapy

Protein discovery could boost efficacy of bone marrow replacement treatments

Researchers at the University of California, San Diego School of Medicine report that a protein called beta-catenin plays a critical, and previously unappreciated, role in promoting recovery of stricken hematopoietic stem cells after radiation exposure.
The findings, published in the May 1 issue of Genes and Development, provide a new understanding of how radiation impacts cellular and molecular processes, but perhaps more importantly, they suggest new possibilities for improving hematopoietic stem cell regeneration in the bone marrow following cancer radiation treatment.
Ionizing radiation exposure – accidental or deliberate – can be fatal due to widespread destruction of hematopoietic stem cells, the cells in the bone marrow that give rise to all blood cells. A number of cancer treatments involve irradiating malignancies, essentially destroying all exposed blood cells, followed by transplantation of replacement stem cells to rebuild blood stores. The effectiveness of these treatments depends upon how well the replacement hematopoietic stem cells do their job.
In their new paper, principal investigator Tannishtha Reya, PhD, professor in the department of pharmacology, and colleagues used mouse models to show that radiation exposure triggers activation of a fundamental cellular signaling pathway called Wnt in hematopoietic stem and progenitor cells.
"The Wnt pathway and its key mediator, beta catenin, are critical for embryonic development and establishment of the body plan," said Reya. "In addition, the Wnt pathway is activated in stem cells from many tissues and is needed for their continued maintenance."
The researchers found that mice deficient in beta-catenin lacked the ability to activate canonical Wnt signaling and suffered from impaired hematopoietic stem cell regeneration and bone marrow recovery after radiation. Specifically, mouse hematopoietic stem cells without beta-catenin could not suppress the production of oxidative stress molecules that damage cell structures. As a result, they could not recover effectively after radiation or chemotherapy.
"Our work shows that Wnt signaling is important in the mammalian hematopoietic system, and is critical for recovery from chemotherapy and radiation," Reya said. "While these therapies can be life-saving, they take a heavy toll on the hematopoietic system from which the patient may not always recover."
The findings have significant clinical implications.
"There are two major reasons why accelerating regeneration is important clinically," said Reya. "One is that after cancer patients are irradiated and transplanted with stem cells, the rate and extent of recovery is often not sufficient to protect the patient from anemia or infections, which can be difficult to treat and sometimes deadly. Identifying signals that can boost regeneration after the bone marrow is severely damaged may help improve outcomes after transplantation.
"Second, doses of chemotherapy and radiation used to treat cancer are often limited by the collateral damage they cause to normal tissues. Although higher doses might kill more cancer cells more effectively, they can't be used because they kill normal cells too. If we can improve and accelerate recovery, we might be able to use higher doses of radiation or chemotherapy and reduce the risk of cancer relapse."
Reya said post-therapy hematopoietic stem cell regeneration could be accelerated by modulating the Wnt pathway, either by delivering additional Wnt proteins directly to patients or through drugs that activate the pathway. Further studies will be needed to determine if these approaches may be clinically useful to mitigate the damage caused by radiation and chemotherapy.

Co-authors include William Lento, UCSD Department of Pharmacology, Sanford Consortium for Regenerative Medicine (SCRM) and Duke University departments of Pharmacology and Medicine; Takahiro Ito, UCSD Department of Pharmacology and SCRM; Chen Zhao, Duke University Department of Pharmacology; Jeffrey R. Harris, Wei Huang, Sadhna Piryani and Nelson Chao, Duke University Department of Medicine; Chen Jiang and Kouros Owzar, Duke University Department of Biostatistics and Bioinformatics; Luigi Racioppi, University of Naples Federico II.
Funding for this research came, in part, from National Institutes of Health grants T32CA059365, U19AI067798, DK63031, HL097767 and DP1CA174422, the California Institute for Regenerative Medicine and the Leukemia and Lymphoma Society.

http://www.eurekalert.org/pub_releases/2014-04/vuot-fdt043014.php#rssowlmlink

Faster dental treatment with new photoactive molecule

A new dental filling material, developed at the Vienna University of Technology, is easier to harden; It makes dental treatment faster and easier

In modern dentistry, amalgam fillings have become unpopular. Instead, white composite materials are more commonly used, which at first glance can hardly be distinguished from the tooth. The majority of these composites are based on photoactive materials that harden when they are exposed to light. But as the light does not penetrate very deeply into the material, the patients often have to endure a cumbersome procedure in which the fillings are applied and hardened in several steps. The Vienna University of Technology in collaboration with the company Ivoclar Vivadent have now developed a new generation of photoactive materials based on the element Germanium. Simply put, improved photoreactivity is good news for everyone who wants to spend as little time as possible in the dental chair.

Hardening With Light

Similar to natural tooth enamel, modern dental composites consist of a mixture of different material components. In addition to inorganic fillers they can also contain photoactive organic resins which react to light of a particular wavelength and readily solidify.

Professor Robert Liska and his team at the Vienna University of Technology (TU Vienna) have been working with such photoactive substances for a long time. Similar photoactive substances are used for additional applications including protective coatings and modern 3d-printing.

The penetration depth of the light depends on its wavelength. "Usually, light in the violet and ultraviolet region is used", says Robert Liska. It is also possible to use light with longer wavelengths, which penetrates deeper into the material, but then the polymerization process is less efficient. If the filling cannot be hardened in one step, the procedure has to be repeated several times. If the cavity is large, this can be rather uncomfortable.

Germanium-based Compound Initiates Chain Reaction

This problem can now be solved with a new Germanium-based molecule. It only makes up 0.04% of the composite material, but it plays a crucial role. The molecule is split into two parts by blue light, creating radicals, which initiate a chain reaction: molecular compounds, which are already present in the filling, assemble into polymers, and the material hardens.

The Germanium-based photo initiator was created at the Vienna University of Technology and then extensively tested by Ivoclar Vivadent. At Graz University of Technology, the physicochemical mechanism was investigated further. Using this new compound, the hardening depth could be increased from 2 mm to 4 mm, which considerably reduces the duration of the medical procedure.

Based on these excellent results, the Vienna University of Technology and Ivoclar Vivadent have made additional strides to further extend their collective research insterests in dental materials. Already in 2012, the Institute for Applied Synthetic Chemistry together with the Institute for Materials Science and Technology with collective funding from Ivoclar Vivadent and the Christian Doppler Research Association put into place a Laboratory for "Photopolymers in digital and restorative dentistry". Since its inception the laboratory has Goals for the laboratory include the development of improved photosensitive substances for dentistry with additional research efforts placed on 3D-printing of ceramic implants.

http://www.eurekalert.org/pub_releases/2014-04/jhu-wp043014.php#rssowlmlink

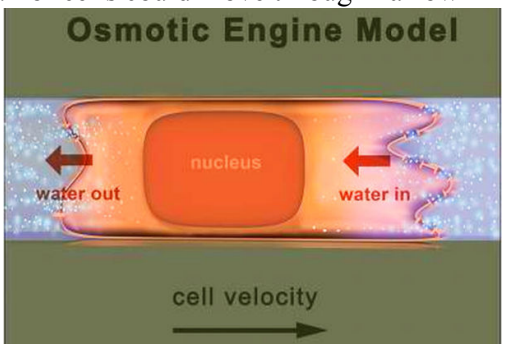
Water-based 'engine' propels tumor cells through tight spaces in the body

Johns Hopkins researchers have discovered a new mechanism that explains how cancer cells spread through extremely narrow three-dimensional spaces in the body by using a propulsion system based on water and charged particles.

The finding, reported in the April 24 issue of the journal Cell, uncovers a novel method the deadly cells use to migrate through a cancer patient's body. The discovery may lead to new treatments that help keep the disease in check. The work also points to the growing importance of studying how cells behave in three dimensions, not just atop flat two-dimensional lab dishes. Based on such lab dish studies, cancer researchers had concluded that tumor cells require actin and other proteins to form arm-like extensions to "crawl" across the flat surfaces. This

type of travel was believed to be the primary means of how cancer spreads within a patient, a process called metastasis. Based on this conclusion, researchers have been working on ways to disable actin and its molecular helpers, hoping this can keep cancer from spreading.

But in a study published in 2012, a Johns Hopkins team led by Konstantinos Konstantopoulos, chair of the Department of Chemical and Biomolecular Engineering, found that tumor cells could move through narrow spaces without using actin and its biochemical partners. "That was a stunning discovery, not in line with the prevailing beliefs about how cells migrate," Konstantopoulos said. "So we wanted to figure out exactly how the tumor cells were able to move through these spaces without relying on actin." He collaborated with Sean X. Sun, a Johns Hopkins associate professor of mechanical engineering with experience in math modeling and physics at microscopic levels. "The mystery we needed to solve," Sun said, "was how the cells in these confined spaces could still move when you took away their usual 'engine,' the actin."



This is an illustration of the newly discovered mechanism by which cancer cells are able to spread disease throughout the body. **Martin Rietveld/JHU**

Kostantopoulos said Sun and Hongyuan Jiang, a postdoctoral fellow working in Sun's lab, "came up with a phenomenal mathematical model that provided insights into how the cells might use a different system to travel." Then Konstantopoulos and other team members, including Kimberly Stroka, a postdoctoral fellow in his own lab, used a microfluidic lab-on-a-chip and imaging techniques to conduct experiments establishing the new mechanism of migration proposed by Sun and Jiang's model. The tests utilized human and animal cancer cells. Stroka and Jiang were designated co-lead authors of the resulting journal article.

As reported in the article, the tumor cells' new "engine" turned out to be a combination of sodium-hydrogen ions, cell membrane proteins called aquaporins, and water. The researchers found that within tight spaces, cancer cells create a flow of liquid that takes in water and ions at a cell's leading edge and pumps them out the trailing edge, propelling the cell forward. In the actin-dependent migration model, the cell is pushed forward by the biochemical equivalent of a boat engine. The water-based mechanism, the researchers said, more closely resembles the way a sailboat is thrust ahead by gusts of wind. The team called this mechanism the Osmotic Engine Model.

"This discovery is important because it reveals one reason why some diseases like cancer don't always respond to certain treatments," Konstantopoulos said. Sun added, "It's because these diseases have redundant mechanisms—more than one method—for migrating through the body."

The Johns Hopkins researchers are applying for funds to conduct further research into physical and biological aspects of the Osmotic Engine Model. Their hope is that the work will uncover a way to shut down this biochemical engine and keep it from spreading tumor cells.

The multidisciplinary research at Johns Hopkins was conducted within the university's Institute for NanoBioTechnology and its Physical Sciences-Oncology Center. These organizations and the departments of Chemical and Biomolecular Engineering and Mechanical Engineering are based in the Whiting School of Engineering. Co-lead author of the Cell article Stroka will join the faculty of the University of Maryland College Park as an assistant professor later this year. Whiting School postdoctoral fellow Jiang, the other lead author, is now a professor at the University of Science and Technology of China. Kostantopoulos and Sun supervised the research and served as senior authors of the paper. Other co-authors, all from Johns Hopkins, were Shih-Hsun Chen, Ziqiu Tong and Denis Wirtz.

This work was supported by National Science Foundation grant NSF-1159823, National Cancer Institute grants U54-CA143868, RO1GM075305, RO1CA174388, T32-CA130840 and F32-CA177756, a Kleberg Foundation grant and National Natural Science Foundation of China grant NSFC 11342010.

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Study questions Neandertal inferiority to early modern humans

Neandertal demise may be the result of interbreeding, assimilation, not early modern human superiority

The embargo has been lifted for the article, 'Neandertal Demise: An Archaeological Analysis of the Modern Human Superiority Complex.'

An analysis of the archaeological records of Neandertals and their modern human contemporaries has found that complex interbreeding and assimilation may have been responsible for Neandertal disappearance 40,000 years ago, in contrast to many current theories, according to results published April 30, 2014, in the open access journal PLOS ONE by Paola Villa from the University of Colorado Museum and Wil Roebroeks from Leiden University in the Netherlands.

Neandertals thrived in Eurasia for more than 300,000 years but vanished around 40,000 years ago, around the same time that modern humans entered Europe. Archaeologists have developed many theories to explain their disappearance, and many of these suggest that modern-day humans were superior in a wide range of ways, including weaponry and subsistence strategies. This superiority may have eventually led to the demise of Neandertals. However, new evidence, including genetic data, suggest that differences between Neandertals and modern humans in Africa may not be so clear as previously thought.

In this study, scientists systematically tested the strength of some of the archaeologically derived explanations for Neandertal extinction, such as the Neandertals' supposed lack of complex language, inferior capacity for innovation, inferior hunting ability, and smaller social networks, as well as other environmental explanations, including harsh climate or volcanic eruptions that occurred at the time of their decline.

If the Neandertal record is compared to that of African Middle Stone Age human contemporaries, instead of the modern humans that succeeded them, the differences between them and humans in their capacities, like weaponry, subsistence, and use of symbols are too small to explain their demise in terms of cognitive or behavioral inferiority. Instead, the authors argue, genetic data recently obtained from Neandertal skeletal remains suggest that complex and drawn-out processes of interbreeding and assimilation may have been responsible for the disappearance of the specific Neandertal morphology from the fossil record.

Citation: Villa P, Roebroeks W (2014) Neandertal Demise: An Archaeological Analysis of the Modern Human Superiority Complex. PLoS ONE 9(4): e96424. doi:10.1371/journal.pone.0096424

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Mini-stroke dismissed as 'funny turn'

Those who ignore symptoms of a TIA (transient ischaemic attack) or mini-stroke are running the risk of having a major stroke, the Stroke Association warns.

TIA causes similar symptoms to a stroke, such as speech problems, but may last only a few minutes. A survey of TIA patients found more than one in three had dismissed their symptoms as just a "funny turn". About 10,000 strokes could be prevented if TIAs were treated, said the charity.

• The symptoms of TIAs usually come on suddenly

• Mini-stroke symptoms are the same as for stroke but last no longer than 24 hours

• Symptoms include facial weakness, such as drooping mouth or eyes, arm weakness, and speech problems

The greatest risk of having a major stroke was within the first few days after a TIA, said chief executive Jon Barrick.

For many people "it doesn't feel like an emergency because the symptoms are brief or mild", he said.

"There's nothing small about mini-stroke," he added.

"It's a medical emergency. When the symptoms start, you should call 999 and say you may be having a stroke."

The Fast test

Facial weakness - Can the person smile? Has their mouth or eye drooped?

Arm weakness - Can the person raise both arms?

Speech problems - Can the person speak clearly and understand what you say?

Time to call 999 - If you see any one of these signs, seek immediate medical attention.

Source: Stroke Association

'Simple ignorance'

Each year about 46,000 people in the UK suffer from a TIA for the first time.

One in 20 people will have a major stroke within two days of a mini-stroke and this figure rises to one in 12 within a week of a TIA.

BBC TV presenter Andrew Marr, who has recovered from a stroke, said: "I had two mini-strokes before going on to have a major stroke. "I was one of the thousands of people who dismissed the warning signs - simple ignorance."

'I had a TIA at 24'

Peter Tugwell from Essex was only 24 when he suddenly became ill.

"I was normal one minute, then I got pins and needles from the top of my shoulder down to my hand - I had no grip," he told BBC News.

"I slid down the wall into a heap on the floor."

His mother called an ambulance, but when paramedics arrived they thought he was too young for a TIA.

"They thought it was a 'funny turn'," he said.

He was eventually taken to hospital for treatment.

"TIA can happen at any age - take it seriously," said Mr Tugwell, now 25.

http://www.eurekalert.org/pub_releases/2014-04/uos-gbt043014.php#rssowlmlink

Groundbreaking technique offers DNA 'sat nav' direct to your ancestor's home 1,000 years ago

Geographic Population Structure can locate the village your ancestors lived 1,000 years ago

Tracing where your DNA was formed over 1,000 years ago is now possible due to a revolutionary technique developed by a team of international scientists led by experts from the University of Sheffield.

The ground breaking Geographic Population Structure (GPS) tool, created by Dr Eran Elhaik from the University of Sheffield's Department of Animal and Plant Sciences and Dr Tatiana Tatarinova from the University of Southern California, works similarly to a satellite navigation system as it helps you to find your way home, but not the one you currently live in – but rather your actual ancestor's home from 1,000 years ago.

Previously, scientists have only been able to locate where your DNA was formed to within 700kms, which in Europe could be two countries away; however this pioneering technique has been 98 per cent successful in locating worldwide populations to their right geographic regions, and down to their village and island of origin.

The breakthrough of knowing where the gene pools that created your DNA were last mixed has massive implications for life-saving personalised medicine, advancing forensic science and for the study of populations whose ancestral origins are under debate, such as African Americans, Roma gypsies and European Jews.

Genetic admixture occurs when individuals from two or more previously separated populations begin interbreeding. This results in the creation of new gene pools representing a mixture of the founder gene pool. Such processes are extremely common in history during migrations and invasions, for example, when the Vikings invaded Britain and Europe in the 11th Century and settled with locals some of them formed a new Viking-Anglo-Saxon gene pool, but some married other Vikings and maintained their original gene pool, allowing GPS to trace their Scandinavian origins.

Dr Eran Elhaik said: "If we think of our world as being made up of different colours of soup – representing different populations - it is easy to visualise how genetic admixture occurs. If a population from the blue soup region mixes with a population from the red soup region their off-springs would appear as a purple soup.

"The more genetic admixture that takes place, the more different colours of soup are introduced which makes it increasingly difficult to locate your DNA's ancestry using traditional tools like Spatial Ancestry analysis (SPA) which has an accuracy level of less than two per cent."

He added: "What we have discovered here at the University of Sheffield is a way to find not where you were born – as you have that information on your passport – but where your DNA was formed up to 1,000 years ago by modelling these admixture processes.

"What is remarkable is that, we can do this so accurately that we can locate the village where your ancestors lived hundreds and hundreds of years ago – until now this has never been possible."

To demonstrate how accurate GPS predictions are, Dr Elhaik and his colleagues analysed data from 10 villages in Sardinia and over 20 islands in Oceania. The research published today in the journal Nature Communications shows that Dr Elhaik and his team were able to place a quarter of the residents in Sardinia directly to their home village and most of the remaining residents within 50km of their village. The results for Oceania were no less impressive with almost 90 per cent success of tracing islanders exactly to their island.

"This is a significant improvement compared to the alternative SPA tool that placed Oceanians in India," said Elhaik.

"In his third book, children's author L. Frank Baum revealed that Oz resided around Australia. It always troubled me that if I ever met anyone claiming to be from the wonderful world of Oz, I would like to be able to verify their origins and now we can!

"This technique also means that we can no longer easily classify people's ethnic identities with one single label. It is impossible for any of us to tick one box on a form such as White British or African as we are much complex models with our own unique identities. The notion of races is simply not plausible."

Tracing our ancestry is now a major social trend and genealogy is the number one hobby in America. An estimated one million people in the USA have already had their DNA genotyped. People can explore their DNA by simply taking a swab from inside their mouth and sending it to a company such as 23andme or ancestry.com for costs ranging from $99-$200.

Dr Elhaik's co-author, Dr Tatiana Tatarinova, developed a website making GPS accessible to the public.

"To help people find their roots, I developed a website that allows anyone who has had their DNA genotyped to upload their results and use GPS to find their ancestral home," said Dr Tatarinova, who is also an Associate Professor of Research Paediatrics at the Keck School of Medicine of the University of Southern California.

"We were surprised by the simplicity and precision of this method. People in a given geographical area are more likely to have similar genetics. When they also have genetic traits typically found in other, distant regions, the geographical origin of those traits is generally the closest location where those traits can be found."
According to the researchers, in ethnically-diverse regions like the UK or US, where many people know only a few generations of their descendants, this kind of screening has huge, important medical implications. Discovery of a certain genotype might indicate the potential for a genetic disease and suggest that diagnostic testing be done. Also, as scientists learn more about personalized medicine, there is evidence that specific genotypes respond differently to medications—making this information potentially useful when selecting the most effective therapy and appropriate dosage. The investigators are currently designing a study to correlate pharmacokinetics - the time course of drug metabolism - with genotype.

http://www.eurekalert.org/pub_releases/2014-04/uoc--aa043014.php#rssowlmlink

Algae 'see' a wide range of light

Aquatic algae can sense an unexpectedly wide range of color, allowing them to sense and adapt to changing light conditions in lakes and oceans.

The study by researchers at UC Davis was published earlier this year in the journal Proceedings of the National Academy of Sciences.
Phytochromes are the eyes of a plant, allowing it to detect changes in the color, intensity, and quality of light so that the plant can react and adapt. "They control all aspects of a plant's life," said Professor Clark Lagarias, senior author on the study. Typically about 20 percent of a plant's genes are regulated by phytochromes, he said. Phytochromes use bilin pigments that are structurally related to chlorophyll, the molecule that plants use to harvest light and use it to turn carbon dioxide and water into food.
Lagarias' laboratory in the Department of Molecular and Cellular Biology at UC Davis studies these phytochromes and their properties. Phytochromes from land plants, Lagarias said, respond to red light — plants absorb red and reflect green light, which is why they look green. Red light does not penetrate far into water, and some marine and shore-dwelling algae lack phytochrome genes. But others do not, so Lagarias and colleagues looked at the properties of phytochromes from a variety of algae. They found that phytochromes from algae, unlike those of land plants, are able to perceive light across the visible spectrum — blue, green, yellow, orange, red and far-red.
This broad spectral coverage likely helps algae make use of whatever light they can in the ocean, Lagarias said — whether adjusting their light-harvesting chemistry for changing conditions, or rising and sinking in the water column as light levels at the surface change. Because different colors of light penetrate to different depths in water, algae face challenges in light harvesting that land plants do not. This work from the Lagarias lab shows one way that algae can rise to the occasion.
Phytochromes themselves have a long evolutionary history and likely arose from the interaction between oxygen and bilins, pigment molecules closely tied to chlorophyll and the oxygen-carrying heme pigment in hemoglobin, Lagarias said. The ancestral form appears to be sensitive to red light, similar to phytochromes of modern land plants. But between the origin and today, phytochromes went through a stage of massive diversity when they could detect a much wider range of wavelengths.
"It's a molecule that has been there and back again," Lagarias said.
The discoveries help researchers better understand the role of light and response to light in shaping ecology, as well as a model for how living cells react to light. They could also help in breeding of aquatic crops that could take advantage of different light conditions.
Coauthors on the paper are: at UC Davis, Nathan Rockwell, Deqiang Duanmu, and Shelley Martin; Alexandra Worden and Charles Bachy at the Monterey Bay Aquarium Research Institute and Canadian Institute for Advanced Research; Dana Price and Debashish Bhattacharya, Rutgers University. The work was supported by multiple agencies including the NIH, NSF, US Department of Agriculture, Department of Defense, the Packard Foundation and the Gordon and Betty Moore Foundation.

http://bit.ly/1iYiUlB

Why did evolution stall during the 'boring billion'?

LONG before evolution on Earth kicked in with a vengeance, it seemed to stall completely.

01 May 2014 by Jeff Hecht

From 1.7 billion years ago, for a billion boring years, Earth remained a slimy, near-static world of algae and microbes. The pace picked up 750 million years ago: glaciers spread, complex animals appeared, and by 520 million years ago the Cambrian revolution – an explosion of varied life – was under way. The reason for that long stasis has been a mystery.
We may now have the answer: the gradual cooling of the planet's interior. Just as turning down a stove burner slows the boiling of a stew pot, cooling of the mantle allowed the "scum" on top to thicken, says Peter Cawood

at the University of St Andrews, UK. The resulting surface stability slowed geological change, seemingly stalling evolution for a billion years, until the planet was cool enough for tectonic activity to shift up a gear. Cawood and Chris Hawkesworth, also at St Andrews, analysed studies of continental motions and geologic processes to see how they lined up with the boring period.

About 1.8 billion years ago, the cores of modern North America, Baltic Europe and Siberia collided and went on to form part of a supercontinent called Rodinia, which accounted for most of the planet's land mass. They found that Rodinia was surprisingly stable, and that it stayed largely in tropical and temperate zones before breaking up 750 million years ago (Geology, doi.org/sj7).

What caused such a long period of tectonic stability? Taras Gerya at the Swiss Federal Institute of Technology in Zurich reviewed studies that modelled Earth's early formation and found that the process changed as the mantle cooled.

On the hot young Earth, the outer layer was too weak and soft for plate tectonics to operate until the upper mantle cooled enough to allow sections of crust to slip under each other, or subduct, at collision zones some 3.2 to 2.5 billion years ago. However, the mantle remained so hot that it softened the subducting oceanic crust too much for it to pull large areas of continental crust down behind it, as it does today. Only when the mantle cooled further did that modern-style subduction start, about 750 million years ago. Rodinia was duly ripped apart and the boring billion ended (Geology, doi.org/sjq).

Cawood and Hawkesworth also found more big differences between the boring billion and other times. Major ice ages occurred before and after but not during the boring billion. Oxygen levels were also stable during, but varied widely before and after.

Cawood says all these systems are linked. "The atmosphere, the oceans, and the crust of the Earth were acting as a stable, interlinked system." The start of modern-style plate tectonics that tore up Rodinia also brought other changes, and complex life evolved to meet the new challenges.

Martin Brasier at the University of Oxford says the stable period may also have been vital for the evolution of eukaryotic cells – cells with a nucleus of genetic material. "I argue that the boring billion was the anvil on which the eukaryote cell was forged. If so, then modern eukaryote cells could be the product of geologically rare conditions."

http://bit.ly/SouIUh

Antibiotic-resistant superbug arose in northern Manhattan

Its spread is happening not through hospitals but through households.

by Kausik Datta May 1 2014, 10:59pm TST

Human skin is a garden of microbes that is home to about 1,000 bacterial species. Most are benign, but some invade the skin and cause illness—of these, antibiotic-resistant bacteria are particularly dangerous.

We normally associate these resistant bugs with hospitals, but new research finds that they could be living and spreading in households and within communities, too. For one notoriously resistant bug, scientists have also been able to pinpoint where and when it first began spreading. The hope is that this knowledge will allow a better way of controlling infection and stopping epidemics.

The Staph of nightmares

About one in five humans carries the disease-causing bacteria Staphylococcus aureus, or Staph, on their skin without any problem. However, breached skin, surgical wounds, or low immunity (often caused by HIV infection or cancer treatments) may allow Staph to cause diseases ranging from minor skin ailments to catastrophic infections.

The spread of methicillin-resistant Staphylococcus aureus (MRSA) is well known. Originally associated with infections in hospitals and nursing homes, MRSA is now known to colonize the skin of otherwise healthy individuals—these infections are called "community-associated" (CA-MRSA).

CA-MRSA spreads by contact with an infected individual. That's why the spread of CA-MRSA can occur in households, where the contact between house members is difficult to control. This also results in high rates of recurrent infection due to contaminated household objects such as shared razors, towels, and door knobs.

Global epidemic

While the presence of Staph on skin has always put people at risk for infection, two features make CA-MRSA riskier. It can cause severe disease in previously healthy people. In about one in every ten cases, CA-MRSA infections lead to deadly pneumonia, severe sepsis, or the dreaded "flesh-eating disease" (aka necrotizing fasciitis). They also have the ability to spread rapidly, which has helped propel them to a global epidemic.

The global epidemic has been attributed to a single CA-MRSA microbe known as USA300. In the US, it is responsible for outbreaks in 38 states, and it has spread to Canada and several European countries. Studies of

USA300 have found molecular evidence that suggests it has the ability to readily evolve into more harmful versions.
USA300's invasion of community households is less well understood. To change that, Anne-Catrin Uhlemann at Columbia University Medical Center and her colleagues have used whole-genome sequencing to reconstruct USA300's evolutionary history. The results have been published in PNAS.
Whole-genome sequencing takes a snapshot of an organism's complete genetic makeup. Uhlemann obtained Staph cells from 161 CA-MRSA-infected residents in New York City and combined their genome data with health statistics to gain insights into USA300's spread during a period covering 2009-2011.
They looked for small changes in the genome, which often give clues about how the cell evolved. After investigating more than 12,000 small changes in the USA300 genome, the authors reconstructed its genetic history. This helped them determine that USA300 first arose around 1993. The molecular signatures allowed them to also home in on the geographic location where this happened, which they determined to be right in Columbia's neighborhood: northern Manhattan.

Sneaky bug

Detailed study of USA300's genome showed it acquired antibiotic resistant genes from viruses that infect bacteria. The authors also discovered a smaller subgroup of USA300 resistant to another antibiotic class, fluoroquinolones, which appeared to evolve around the time when fluoroquinolone prescription rates had soared in the US.
All this information put together shows that USA300 originally evolved and spread in households and communities in New York City before going global. The occurrence of different antibiotic-resistant bugs highlights the effects of overuse of antibiotics. But working out how CA-MRSA spread within households and inside communities may help researchers devise an infection control strategy that can break this pattern of spread and reduce the possibility of another large-scale outbreak.
PNAS, 2014. DOI: 10.1073/pnas.1401006111 (About DOIs).

http://bit.ly/1iPsQPb

Human Sexual Responses Boosted by Bodily Scents

Two human steroidal compounds may help scientists make sense of how bodily scents affect sexual arousal

May 1, 2014 |By Daisy Yuhas

Could men and women rely on smell to find potential mates? Birds do, bees do—and now scientists have some reason to think that humans do, too.
Growing evidence suggests that bodily odors carry chemical signals that affect moods and menstrual cycles, but isolating the specific compounds that elicit these effects, called pheromones, has proved difficult. Wen Zhou, a psychologist and olfaction researcher at the Chinese Academy of sciences, and her colleagues looked at two compounds found in bodily fluids that, according to earlier studies, are good candidates for human pheromones: androstadienone, associated with men, and estratetraenol, from women. The two steroids were found to elicit markedly different responses in male and female test subjects.
Neither steroid has any discernible fragrance, but it is believed that the human nose picks up these chemicals. Earlier research suggests that androstadienone boosts women's mood and cortisol levels whereas estratetraenol enhances men's arousal and mood in certain circumstances.
Zhou and her colleagues worked with 96 subjects, half female and half male. Half of the men and women self-identified as heterosexual and the other half as either homosexual or, in the case of female participants, bisexual. The researchers presented each subject with moving dots on a screen that simulate the outline of a walking human figure. By changing the position of the dots, Zhou and colleagues could make the figure appear more masculine, feminine or androgynous. The subjects responded by judging each figure as either a man or a woman.
After the researchers recorded how each participant labeled the figures, the subjects watched more walking figures while being exposed to a solution that smelled like cloves. This mixture contained estratetraenol, androstadienone or just the cloves scent.
Zhou and her colleagues discovered that when heterosexual subjects viewed gender-neutral walkers, being exposed to the male or female steroid biased their responses. Heterosexual men were more likely to identify the figure as female when exposed to estratetraenol and heterosexual women tended to call the walkers male in the presence of androstadienone.
Homosexual men responded to androstadienone much as heterosexual women did.Homosexual or bisexual women, by contrast, showed no bias to either steroid. Taken together, the findings suggest that humans could use chemical signals to detect an individual with romantic potential, and that these cues work in a sex- and orientation-specific way. The work was published in Current Biology on May 1. (Researchers at the Chinese

Academy's State Key Laboratory of Brain and Cognitive Sciences and the University of Minnesota also participated.)
Psychologist and olfaction researcher Johan Lundström, of the Monell Chemical Senses Center, who was not involved in this study, calls the work "the most elegant" findings yet for androstadienone and estratetraenol's behavioral effects. "I think they are bringing the field forward," Lundström says.
Zhou isn't ready to declare that these two steroids are human pheromones. For one thing, their test subjects were exposed to steroids in much higher concentrations than people naturally secrete. "It is very important to examine the effects of steroids at more ecologically relevant concentrations," Zhou says. In addition, the underlying mechanism by which people would receive and respond to these steroids remains a mystery.
The source of these compounds is also problematic. Androstadienone can be found in women as well as men and estratetraenol has only been found in pregnant women's urine and placentas. More study is needed to investigate how sex or gender specific these signals are.
Finally, it's possible that instead of true chemical signaling, this is simply a case of learned association, in which people become familiar with certain chemicals from men and women through repeated exposure to intimate partners. Zhou tried to control for this by repeating their procedure with isovaleric acid, a strong smelling fatty acid that men have in abundance, instead of the two steroids. Because the acid exposure did not bias subjects toward recognizing male walkers, Zhou concluded that the response is not learned. Lundström, however, is more skeptical. The lack of bias may reflect subjects' exposure to isovaleric acid in food: It is the compound that imbues stinky cheese with the odor of dirty socks.
Although many questions remain, it is clear that even chemicals we cannot consciously detect could have a complex effect on human sexual behavior, perhaps as strong as a handsome face or "come hither" glance.

http://www.eurekalert.org/pub_releases/2014-05/ps-aef050114.php#rssowlmlink

Antimicrobial edible films inhibit pathogens in meat

Antimicrobial agents incorporated into edible films applied to foods to seal in flavor, freshness and color can improve the microbiological safety of meats, according to researchers in Penn State's College of Agricultural Sciences.

Using films made of pullulan -- an edible, mostly tasteless, transparent polymer produced by the fungus Aureobasidium pulluns -- researchers evaluated the effectiveness of films containing essential oils derived from rosemary, oregano and nanoparticles against foodborne pathogens associated with meat and poultry.
The results demonstrate that the bacterial pathogens were inhibited significantly by the use of the antimicrobial films, said Catherine Cutter, professor of food science. She hopes that the research will lead to the application of edible, antimicrobial films to meat and poultry, either before packaging or, more likely, as part of the packaging process. In the study, which was published online in the April issue of the Journal of Food Science, researchers determined survivability of bacterial pathogens after treatment with 2 percent oregano essential oil, 2 percent rosemary essential oil, zinc oxide nanoparticles or silver nanoparticles.
The compounds then were incorporated into edible films made from pullulan, and the researchers determined the antimicrobial activity of these films against bacterial pathogens inoculated onto petri dishes.
Finally, the researchers experimentally inoculated fresh and ready-to-eat meat and poultry products with bacterial pathogens, treated them with the pullulan films containing the essential oils and nanoparticles, vacuum packaged, and then evaluated for bacterial growth following refrigerated storage for up to three weeks.
"The results from this study demonstrated that edible films made from pullulan and incorporated with essential oils or nanoparticles have the potential to improve the safety of refrigerated, fresh or further-processed meat and poultry products," said Cutter. "The research shows that we can apply these food-grade films and have them do double duty -- releasing antimicrobials and imparting characteristics to protect and improve food we eat."
Working in Cutter's laboratory in the Department of Food Science, Mohamed Morsy, a doctoral student at Benha University in Egypt, conducted the research. Morsy was at Penn State as a Borlaug Fellow through a grant provided by the USDA-Foreign Agricultural Service.
The edible films are a novel but effective way to deliver antimicrobial agents to meats, Cutter explained, because the bacteria-killing action is longer lasting. Liquid applications run off the surface, are not absorbed and are less effective. The pullulan films adhere to the meat, allowing the incorporated antimicrobials to slowly dissolve, providing immediate and sustained kill of bacteria. In addition, the microorganisms do not have the opportunity to regrow.
Cutter conceded that pullulan films are not as oxygen-impermeable as plastic packaging now used to package meats, so the edible films are not likely to replace that material.

"The meat industry likes the properties of the polyethylene vacuum packaging materials that they are using now," she said. "However, the one thing I really want to be able to do in the next few years is to figure out a way to co-extrude antimicrobial, edible films with the polyethylene so we have the true oxygen barrier properties of the plastic with the antimicrobial properties of the edible film."
Knowing that edible films can release antimicrobials slowly over time and keep bacteria in meat at bay, further research will be aimed at creating what Cutter referred to as "active packaging" -- polyethylene film with antimicrobial properties. "Right now, we have two different packaging materials that are not necessarily compatible, leading to a two-step process. I keep thinking there's a way to extrude edible, antimicrobial film in one layer with polyethylene, creating all-in-one packaging.
"The chemistry of binding the two together is the challenge, but we need to find a way to do it because marrying the two materials together in packaging would make foods -- especially meat and poultry -- safer to eat."
The U.S. Department of Agriculture-Foreign Agriculture Service, Borlaug Fellows Program and the Center for Food Manufacturing, Department of Food Science, Penn State supported this research.

http://www.eurekalert.org/pub_releases/2014-05/cu-trd050114.php#rssowlmlink

The real difference between how men and women choose their partners

New Concordia University research points to surprising evidence about how we select our mates

In Concordia's study, men responded more strongly to the "framing effect" when physical attractiveness was described.
A hamburger that's 90 per cent fat-free sounds a lot better than one with 10 per cent fat. And even when the choices are the same, humans are hard-wired to prefer the more positive option.
This is because of what's known as the "framing effect," a principle that new research from Concordia has proved applies to mate selection, too.
The study — co-authored by Concordia marketing professor Gad Saad and Wilfrid Laurier University's Tripat Gill, and published in the journal *Evolution and Human Behavior* — shows that when we choose a partner, the framing effect is even stronger in women than it is for men.
"When it comes to mate selection, women are more attuned to negatively framed information due to an evolutionary phenomenon called 'parental investment theory,'" says Saad, who has done extensive research on the evolutionary and biological roots of consumer behavior.
"Choosing someone who might be a poor provider or an unloving father would have serious consequences for a woman and for her offspring. So we hypothesized that women would naturally be more leery of negatively framed information when evaluating a prospective mate."
To prove this, Saad and Gill called on hundreds of young men and women to take part in their study.
Participants were given positively and negatively framed descriptions of potential partners. For example:
"Seven out of 10 people who know this person think that this person is kind." *[positive frame*] versus
"Three out of 10 people who know this person think that this person is not kind." *[negative frame]*
The researchers tested the framing effect using six key attributes, two of which are more important to men and women respectively, and two that are considered as necessities by both sexes:

- ***Attractive body (more important to men)***
- ***Attractive face (more important to men)***
- ***Earning potential (more important to women)***
- ***Ambition (more important to women)***
- ***Kindness (equally important to both)***
- ***Intelligence (equally important to both)***

Participants evaluated both high-quality (e.g. seven out of 10 people think this person is kind) and low-quality (e.g. three out of 10 people think this person is kind) prospective mates for these attributes, in the context of a short-term fling or a long-term relationship.
More often than not, women said they were far less likely to date the potential mates described in the negatively framed descriptions — even though in each instance, they were being presented with exactly the same information as in the positively framed descriptions.
Women also proved more susceptible to framing effects in attributes like ambition and earning potential, while men responded more strongly to framing when physical attractiveness was described.
This research highlights how an evolutionary lens could help explain the biologicial origins of seemingly "irrational" decision-making biases like the framing effect.
"The Framing Effect When Evaluating Prospective Mates: an Adaptationist Perspective"

http://www.eurekalert.org/pub_releases/2014-05/ehs-ifs050114.php#rssowlmlink

Investigators find something fishy with classical evidence for dietary fish recommendation

New study in the Canadian Journal of Cardiology questions the validity of original Bang and Dyerberg study; finds Eskimos have coronary artery disease at the same rate as other populations

Philadelphia - Oily fish are currently recommended as part of a heart healthy diet. This guideline is partially based on the landmark 1970s study from Bang and Dyerberg that connected the low incidence of coronary artery disease (CAD) among the Eskimos of Greenland to their diet, rich in whale and seal blubber. Now, researchers have found that Eskimos actually suffered from CAD at the same rate as their Caucasian counterparts, meaning there is insufficient evidence to back Bang and Dyerberg's claims. Their findings are published in the Canadian Journal of Cardiology.

Using 40 years of new information and research, a team of investigators set out to reexamine Bang and Dyerberg's study of Greenland Eskimos and CAD. This study is still widely cited today when recommending the dietary addition of fish oil supplements (like omega-3 fatty acids) or oily fish to help avoid cardiovascular problems. However, the new review of information has determined that Bang and Dyerberg failed to actually investigate the cardiovascular health of the Eskimo population, meaning that the cardioprotective effects of their diet are unsubstantiated.

"Bang and Dyerberg's seminal studies from the 1970s are routinely invoked as 'proof' of low prevalence of CAD in Greenland Eskimos ignoring the fact that these two Danish investigators did not study the prevalence of CAD," notes lead investigator George Fodor, MD, PhD, FRCPC, FAHA. "Instead, their research focused on the dietary habits of Eskimos and offered only speculation that the high intake of marine fats exerted a protective effect on coronary arteries."

Bang and Dyerberg relied mainly on annual reports produced by the Chief Medical Officer of Greenland to ascertain CAD deaths in the region. The 2014 study has identified a number of reasons that those records were likely insufficient, mainly that the rural and inaccessible nature of Greenland made it difficult for accurate records to be kept and that many people had inadequate access to medical personnel to report cardiovascular problems or heart attacks. In fact, researchers have now found that concerns about the validity of Greenland's death certificates have been raised by a number of different reports and that at the time, more than 30% of the population lived in remote outposts where no medical officer was stationed. This meant that 20% of the death certificates were completed without a doctor having examined the body.

The data collected through this new investigation shows that Eskimos do have a similar prevalence of CAD to non-Eskimo populations, and in fact, they have very high rates of mortality due to cerebrovascular events (strokes). Overall, their life expectancy is approximately 10 years less than the typical Danish population and their overall mortality is twice as high as that of non-Eskimo populations.

"Considering the dismal health status of Eskimos, it is remarkable that instead of labeling their diet as dangerous to health, a hypothesis has been construed that dietary intake of marine fats prevents CAD and reduces atherosclerotic burden," remarks Dr. Fodor.

Many recent large and well-designed studies have shown ambiguous or negative results regarding the cardioprotective properties of omega-3 fatty acids and fish oil supplements, and yet partly based on the work of Bang and Dyerberg, they are still widely recommended as part of a heart healthy diet plan.

"Publications still referring to Bang and Dyerberg's nutritional studies as proof that Eskimos have low prevalence of CAD represent either misinterpretation of the original findings or an example of confirmation bias," concludes Dr. Fodor. "To date, more than 5000 papers have been published studying the alleged beneficial properties of omega-3 fatty acids, not to mention the billion dollar industry producing and selling fish oil capsules based on a hypothesis that was questionable from the beginning."

http://www.eurekalert.org/pub_releases/2014-05/ehs-ens050114.php#rssowlmlink

Electronic nose sniffs out prostate cancer using urine samples

Novel noninvasive technique successfully discriminates between prostate cancer and benign disease in proof of principle study, paving the way for easy and early diagnosis, reports the Journal Of Urology

New York, NY - We may soon be able to make easy and early diagnoses of prostate cancer by smell. Investigators in Finland have established that a novel noninvasive technique can detect prostate cancer using an electronic nose. In a proof of principle study, the eNose successfully discriminated between prostate cancer and benign prostatic hyperplasia (BPH) by "sniffing" urine headspace (the space directly above the urine sample). Results using the eNose are comparable to testing prostate specific antigen (PSA), reports the Journal of Urology®.

Prostate cancer is the second most common cancer in males and one of the leading causes of cancer death. The heterogeneity of prostate cancer makes it difficult to diagnose and predict tumor progression. Both of the

current cornerstones of diagnosis, i.e. digital rectal examination (DRE) and PSA have limitations, while ultrasound guided biopsies are costly, uncomfortable for the patient, and have a risk of infection. Additionally, significant numbers of diagnosed prostate cancers are of low grade and will not cause symptoms or disease-specific mortality. Therefore, aggressive treatment can lead to decreased quality of life without extending the patient's life. Thus, there is a need for novel diagnostic tools.

In the 1980s incidental reports of dogs that detected cancer in their owners sparked a number of experimental studies that have since confirmed that trained sniffer dogs can detect cancer. However, variations in the performance of dogs during and between studies have meant that these findings are of limited application. A more promising development is the growth of sensor technology (generally referred to as artificial olfaction) that has led to the invention of numerous new types of olfactory electronic sensors.

eNoses are best suited for qualitative analysis of complex gaseous mixtures of molecules, and are routinely used in food and agricultural quality control and military applications. The eNose used in the current study is a device that consists of a cluster of nonspecific sensors. When the device is exposed to the sample, it produces a profile or a "smell print."

"eNoses have been studied in various medical applications, including early detection of cancer, especially from exhaled air," says lead investigator Niku KJ. Oksala, MD, PhD, DSc, of the Department of Surgery, School of Medicine, University of Tampere and Department of Vascular Surgery, Tampere University Hospital, Finland. "However, exhaled air is a problematic sample material since it requires good cooperation and technique from the patient and immediate analysis, while urine is simple to attain and store, and is therefore more feasible in clinical practice. Preliminary data suggested that detection of urologic malignancies from urine headspace was possible. Our own preliminary results on prostate cancer cells encouraged us to launch this prospective clinical study."

The ChemPro® 100–eNose (Environics Inc., Mikkeli, Finland) was tested on 50 patients who had been diagnosed with prostate cancer confirmed by biopsy, and 15 patients with BPH. Both groups were scheduled for surgery. The patients provided urine samples before surgery and those with benign disease also provided samples three months after surgery to be used as a pooled control sample population. Patients with prostate cancer underwent robotic assisted laparoscopic radical prostatectomy, while the benign disease group underwent transurethral resection of prostate.

Results with the eNose confirmed that using urine headspace, the eNose is able to discriminate prostate cancer from BPH. The eNose achieved a sensitivity of 78%, specificity of 67% and AUC of 42.0.

"The performance with the eNose matches that of PSA results in previous literature and the results are achieved rapidly and in a completely noninvasive manner," comments Dr. Oksala. "PSA is known to correlate positively with prostate volume, which is a potential source of diagnostic error when comparing prostate cancer with benign disease. According to our current analysis, prostate volume did not affect the eNose results, potentially indicating high specificity of our sensor array to cancer. We also studied whether eNose signal correlates with the size of the tumor. No such correlation was found. Further studies are now warranted to enhance current technology and to identify the molecules behind the distinct odors."

http://bit.ly/1niiFlw

Jurassic predator had surprisingly sensitive snout

Pliosaurs had massive jaws, crushing teeth – and sensitive snouts. That is the conclusion of a study on an exceptionally preserved 2-metre-long fossil skull.

15:51 01 May 2014 by Jeff Hecht

Pliosaurs were the top marine predators of the Jurassic, growing up to 12 metres long, but their biology is poorly understood because nothing quite like them is alive today. Davide Foffa at the University of Bristol, UK, may now have added an important piece to the puzzle of how they detected prey. He has found channels in a pliosaur skull that probably contained nerves and blood vessels, suggesting that it had a well-developed sensory system extending to the tip of the snout. Palaeontologists have long recognised that pliosaur skulls, like those of many other vertebrates, have small holes called foramina leading into the interior. In living species these connect to nerves. However, this is the first time anyone has been able to trace the networks inside a fossil.

Crocodile-like senses?

Using a custom-built CT scanner, Foffa traced channels filled with sediment and pyrite in a pliosaur skull unearthed in Dorset, UK. From the shape of the channels inside the skull, Foffa identified them as containing both the maxillary artery and the trigeminal nerve. These carry signals to and from the upper jaw and snout – including the skin and face.

It's unclear what the nerves sensed, but they may have responded to pressure like crocodile snouts, or to electrical fields, like sharks, says Foffa. "This kind of sensing system would have complemented the animals' vision in turbid water," he adds. The most conservative interpretation is that the channels supplied blood and nerve connections to skin and soft tissue in the snout, says Adam Smith of the Nottingham Natural History Museum, UK, who wasn't involved in the research. "It is quite likely the skull had sensitive and somewhat fleshy lip-like structures," he says, so pliosaur snouts had a sense of touch, and might also have responded to pressure or chemicals in the water.

Sensitive snout **(Image: Nobumichi Tamura/Stocktrek Images/Getty)**

"Pliosaurs didn't have any other appendages to manipulate food or other items in their environment," he says, so a sensitive snout could help them hunt prey and manipulate food in the water.

"To get this much resolution out of the data is incredible," says Gareth Dyke of the University of Southampton, UK, who wasn't involved in the study but is using the scanner to study the shape of the pliosaur's brain.

Journal reference: Naturwissenschaften, DOI: 10.1007/s00114-014-1173-3

http://www.medscape.com/viewarticle/824462?src=rss#1

Improved Survival in Cancer Patients With High Vitamin D Levels

Researchers have again found that higher levels of circulating vitamin D on diagnosis of cancer are associated with significantly better survival and remission rates.

Pam Harrison

The new findings come from a comprehensive meta-analysis involving more than 17,000 cancer patients, published online in the April 29 issue of the *Journal of Clinical Endocrinology and Metabolism.*

Mian Li, PhD, graduate student, University of the Chinese Academy of Sciences, Shanghai, China, and multicenter colleagues found that overall survival for colorectal and breast cancer patients in the highest quartile of circulating 25-hydroxyvitamin D [25(OH)D] levels was significantly better than it was for those in the lowest quartile of 25(OH)D levels. Overall survival was also significantly better for lymphoma patients in the highest 25(OH)D quartile compared with those in the lowest quartile.

Higher circulating levels of vitamin D were also significantly associated with lower cancer-specific mortality rates among patients with both colorectal cancer and lymphoma, and disease-free survival rates were also significantly improved for patients with breast cancer and those with lymphoma.

"This study could be considered as the most confirmatory evidence to date supporting an association between circulating 25(OH)D levels and cancer outcomes," senior author Hui Wang, MD, PhD, professor at the Institute for Nutritional Sciences, Chinese Academy of Sciences, told *Medscape Medical News.*

"Considering that vitamin D deficiency is widespread around the world, our suggestion is to ensure everyone has sufficient levels of this important nutrient - that is, circulating 25(OH)D levels - greater than 75 nmol/L."

Robust Evidence

For the meta-analysis, the authors included 25 studies involving a total of 17,732 patients with cancer.

The evidence supporting a protective effect from high circulating 25(OH)D levels on diagnosis was most robust for colorectal cancer, breast cancer, and lymphoma.

Table. Cancer Outcomes Between Those in the Highest vs the Lowest 25(OH)D Quintiles

	Overall Survival ***[Highest vs Lowest 25(OH)D Quintiles]***	**Cancer-Specific Mortality** ***[Highest vs Lowest 25(OH)D Quintiles]***	**Disease-Free Survival** ***[Highest vs Lowest 25(OH)D Quintiles]***
Colorectal cancer	45% reduction (HR = .55; *P* = .02)	35% reduction (HR = .65; *P* = .005)	
Breast cancer	37% reduction (HR = .63; *P* < .001)	35% reduction (HR = .65; *P* = .04)	58% improvement (HR = .42; *P* < .001)
Lymphoma	52% reduction (HR = .48; *P* < .001)	50% reduction (HR = .50; *P* < .001)	

HR, hazard ratio

Limited — but favorable — evidence for a protective effect from high circulating 25(OH)D levels on diagnosis was also observed for patients with lung cancer, gastric cancer, prostate cancer, leukemia, melanoma, and Merkel cell carcinoma. Indeed, when investigators compared 25(OH)D levels in the range of 40 to 70 nmol/L to levels <19 nmol/L, they found that a 10-nmol/L increase in circulating vitamin D levels upon cancer

diagnosis was associated with a 4% reduction in all-cause mortality among all cancer patients in whom a dose-response relationship was assessed.

Chemopreventive Agent

As Dr. Wang told *Medscape Medical News*, researchers tend to consider vitamin D as a cancer chemopreventive agent. "A lot of laboratory studies have suggested that vitamin D might inhibit the progression of cancers by acting on tumor cells and modulating the tumor microenvironment," he explained. In addition, the biological effects of vitamin D on both bone health and the immune system may help cancer patients better weather difficult treatment regimens and help alleviate adverse reactions.

More Aggressive Prostate Cancer

In a separate study published in *Clinical Cancer Research*, vitamin D deficiency was associated with more aggressive prostate cancer in both European American and African American men. These men were undergoing their first biopsy because of an abnormal prostate-specific antigen (PSA) or digital rectal examination (DRE) test.

Results showed that a 25(OH)D level of <12 ng/ml was positively associated with a higher Gleason grade (≥ 4 + 4) and a higher clinical stage (tumor stage ≥ cT2b) in both groups of men but that the association between more aggressive prostate cancer and vitamin D deficiency was stronger among African Americans.

This study also found an association between lower 25(OH)D levels and men at high and very high risk for prostate cancer according to National Comprehensive Cancer Network (NCCN) criteria.

"In our study, vitamin D deficiency seemed to be a predictor of aggressive forms of prostate cancer diagnosis in European American and African American men," lead author Adam B. Murphy, MD, assistant professor in the Department of Urology at the Northwestern University Feinberg School of Medicine in Chicago, commented in a statement.

"The stronger associations in African American men imply that vitamin D deficiency is a bigger contributor to prostate cancer in African American men compared with European American men," Dr. Murphy added.

"Vitamin D supplementation may be a relevant strategy for preventing prostate cancer incidence and/or tumor progression in prostate cancer patients," he suggested.

The study by Dr. Li and colleagues was supported by a number of grants, including a grant from the Ministry of Science and Technology of China, the National Nature Science Foundation, and the Science and Technology Commission of Shanghai Municipality. The study by Dr. Murphy and colleagues was funded by the National Institutes of Health and the US Department of Defense. The authors of both studies have disclosed no relevant financial relationships.

Clin Endocrinol Metab. Published online April 29, 2014. Abstract Clin Cancer Res. 2014;20:2289-2299.

http://arstechnica.com/science/2014/05/win-at-rock-paper-scissors-by-knowing-thy-opponent/#rssowlmlink

Scientists find a winning strategy for rock-paper-scissors

A new study applies statistics, probability, and psychology to RPS.

by Casey Johnston - May 2 2014, 5:56am TST

A group of researchers from Chinese universities have written a paper about the role of psychology in winning (or losing) at rock-paper-scissors. After studying how players change or keep their strategies during multiple-round sessions, they figured out a basic rule that people tend to play by that could potentially be exploited.

The researchers took 360 students, broke them into groups of six, and had them play 300 rounds of rock-paper-scissors in random pairings. The students received small amounts of money each time they won a round. As they played, the researchers observed how the players rotated through the three play options as they won or lost. What they found was that "if a player wins over her opponent in one play, her probability of repeating the same action in the next play is considerably higher than her probabilities of shifting actions." If a player has lost two or more times, she is likely to shift her play, and more likely to shift to the play that will beat the one that has just beaten her than the same one her opponent just used to beat her. For instance, if Megan loses by playing scissors to Casey's rock, Megan is most likely to switch to paper, which would beat Casey's rock. Per the research, this is a sound strategy, since Casey is likely to keep playing the hand that has been winning. The authors refer to this as the "win-stay, lose-shift" strategy.

Therefore, this is the best way to win at rock-paper-scissors: if you lose the first round, switch to the thing that beats the thing your opponent just played. If you win, don't keep playing the same thing, but instead switch to the thing that would beat the thing that you just played. In other words, play the hand your losing opponent just played. To wit: you win a round with rock against someone else's scissors. They are about to switch to paper. You should switch to scissors. Got it? Good.

This should work unless your opponent has read this article, in which case, you both are in trouble, because you're now living on a plane of RPS strategy the likes of which we can only imagine.

http://phys.org/news/2014-05-superheavy-element.html#rssowlmlink

Superheavy element 117 confirmed

Team creates atoms of element 117, matching the heaviest atoms ever observed

Phys.org - The stage is set for a new, super-heavy element to be added to the periodic table following research published in the latest Physics Review Letters. Led by researchers at Germany's GSI laboratory, the team created atoms of element 117, matching the heaviest atoms ever observed, which are 40 per cent heavier than an atom of lead.

The periodic table of the elements is to get crowded towards its heaviest members. Evidence for the artificial creation of element 117 has recently been obtained at the GSI Helmholtz Centre for Heavy Ion Research, an accelerator laboratory located in Darm-stadt, Germany.

The experiment was performed by an international team of chemists and physicists headed by Prof. Christoph Düllmann, who holds positions at GSI, Johannes Gutenberg University Mainz (JGU), and the Helmholtz Institute Mainz (HIM). The team included 72 scientists and engineers from 16 institutions in Australia, Finland, Germany, India, Japan, Norway, Poland, Sweden, Switzerland, the United Kingdom, and the United States.

Elements beyond atomic number 104 are referred to as superheavy elements. The most long-lived ones are expected to be situated on a so-called 'island of stability', where nuclei with extremely long half-lives should be found. Although superheavy elements have not been found in nature, they can be produced by accelerating beams of nuclei and shooting them at the heaviest possible target nuclei. Fusion of two nuclei – a very rare event – occasionally produces a superheavy element. Those currently accessible generally only exist for a short time. Initial reports about the discovery of an element with atomic number 117 were released in 2010 from a Russia-U.S. collaboration working at the Joint Institute for Nuclear Research in Dubna, Russia.

In a powerful example of international collaboration, this new measurement required close coordination between the accelerator and detection capabilities at GSI in Germany and the unique actinide isotope production and separation facilities at Oak Ridge National Laboratory (ORNL) in the U.S. The special berkelium target material, essential for the synthesis of element 117, was produced over an 18-month-long campaign. This required intense neutron irradiation at ORNL's High Flux Isotope Reactor, followed by chemical separation and purification at ORNL's Radiochemical Engineering Development Center.

Approximately 13 milligrams of the highly-purified isotope Bk-249, which itself decays with a half-life of only 330 days, were then shipped to Mainz University. There, the facilities and expertise are available to transform the exotic radioisotope into a target, able to withstand the high-power calcium-ion beams from the GSI accelerator. Atoms of element 117 were separated from huge numbers of other nuclear reaction products in the TransActinide Separator and Chemistry Apparatus (TASCA) and were identified through their radioactive decay. These measured chains of alpha-decays produced isotopes of lighter elements with atomic numbers 115 to 103, whose registration added to the proof for the observation of element 117.

In the decay chains, both a previously unknown alpha-decay pathway in Db-270 (dubnium – element 105) and the new isotope Lr-266 (lawrencium – element 103) were identified. With half-lives of about one hour and about 11 hours, respectively, they are among the longest-lived superheavy isotopes known to date. As unwanted background events are present in all superheavy element experiments, the longer-lived an isotope is, the harder is its reliable identification. The present experiment, for which TASCA was significantly upgraded to better separate unwanted background products and thus to allow more sensitive identification of superheavy nuclei, proved that their reliable identification is now possible.

"This is of paramount importance as even longer-lived isotopes are predicted to exist in a region of enhanced nuclear stability", explains Christoph Düllmann.

Prof. Horst Stöcker, Scientific Director of GSI, adds: "The successful experiments on element 117 are an important step on the path to the production and detection of ele-ments situated on the 'island of stability' of superheavy elements."

"This is an important scientific result and a compelling example of international cooperation in science, advancing superheavy element research by leveraging the special capabilities of national laboratories in Germany and the U.S.," said ORNL Director Thom Mason.

Element 117 is yet to be named: a committee comprising members of the International Unions of Pure and Applied Physics and Chemistry will review these new findings, along with the original ones, and decide whether further experiments are needed before acknowledging the element's discovery. Only after such final acceptance, a name may be proposed by the discoverers.

More information: Paper: Phys. Rev. Lett. 112, 172501 – Published 1 May 2014, journals.aps.org/prl/abstract/10.1103/PhysRevLett.112.172501 www.superheavies.de/

http://wrd.cm/RgCSxd

This Marsupial Has Marathon Sex Until It Goes Blind and Drops Dead

In the forests of Australia, every year just before spring, there erupts a sexual frenzy unlike any other on Earth.

By Matt Simon

It's bigger than an ultra-romantic Neil Diamond concert, bigger even than spring break in Cancun. Here a tiny hyperactive marsupial called antechinus sprints around mating almost non-stop for an exhausting three weeks, with single romps lasting as long as 14 straight hours. Males relentlessly bound from partner to partner, as massive hormone releases in their bodies cause their immune systems to crash and their fur to fall out. They bleed internally. Some males even go blind, yet still stumble around the leaf litter hoping for one last tryst. In a few short weeks, every single male lies dead, leaving the females to raise their offspring. And so it seems that in perpetually dangerous Australia, even the sex can kill you.

For these three weeks of sexual kamikaze, antechinus males are concerned with nothing–absolutely nothing–other than mating with as many females as they possibly can. Ecologist Andrew Baker of Australia's Queensland University of Technology, who studies these critters' astonishing habits, has even picked up a copulating pair, who ignored him entirely and went about their business in his hands. "It's pretty frenzied," said Baker. "There's no courtship or anything like that. The males basically just grab the females and go for it."

Driving males to such feats are astronomical levels of testosterone. Think of an MMA fight wrapped in an Insane Clown Posse concert wrapped in the Insane Clown Posse playing during an MMA fight. While the hormone mobilizes all the sugars in the antechinus' body so it doesn't need to feed for the three-week orgy, it also glitches the mechanism responsible for regulating the production of cortisol, a stress hormone that in small amounts results in bursts of energy and higher pain tolerances.

With runaway levels of cortisol, though, the males' bodies literally begin to fall apart. Bone density plummets and blood-sugar levels go nuts. Their immune systems essentially degrade to worthlessness, as open sores form and never heal. Of course, females are also quite stressed during all of this, but they don't produce anywhere near the same levels of testosterone, so their cortisol regulation remains normal.

The whole affair is one of nature's most striking manifestations of the true meaning of life: At a very basic level, all critters, including you and me, are on this planet to pass along their genes, even if it means an early demise. Antechinus males, after all, were only born after the previous year's mating season. Not a single one reaches 12 months old, while females live up to three years.

A rare picture of antechinus on top of something other than another antechinus. **Gary Cranitch, Queensland Museum**

And while it may not seem like anything other than strange hedonism, the males, with their mass suicide, in a way help guarantee the success of the offspring they'll never get to enlighten with what would have been a truly epic sex talk. (You see, son, when a man loves a woman very much, it's not long before he goes blind and dies.)

"It's all geared toward the young being born when spring starts," said Baker, "so there will be a big flush of insects in spring. The female will give birth to the young and then she'll have plenty of food available because the population has been halved, because all the males are dead."

In the eight to 12 weeks leading up to the mating season, though, males are taking more than their fair share of food, scurrying around frantically and hoovering up insects. "They're spending all of their time building up food and fat stores," said Baker, "because they know they're going to need it across that intensive mating block." Plus, the more weight you pack on, the more energy you can devote to producing sperm, which males store in enormous quantities before the mating season begins. Bigger males will also beat out smaller ones for the right to mate–Baker has found individuals that are twice the weight of others (MMA enthusiasts, obviously).

In the end, though, females find themselves alone in a forest of dead males, carrying an incredible amount of sperm from perhaps dozens of different potential fathers. But this seems to be problematic for one of evolution's most basic principles: sexual selection. Typically, females pick only the most fit of males, so they can better guarantee offspring with strong genetics. But antechinus ladies aren't exactly picky–it's not like they roll up to a sperm bank and studiously flip through catalogs of donors. So aren't they inevitably stuck with sub-par sperm?

Well, sure, she's carrying sperm from smaller, less fit males. But larger males produce more sperm, boosting the chance that theirs will win out in the fertilization game. And obviously, with that many partners the competition is fierce. Indeed, a single brood will consist of young from several different fathers.

She'll actually give birth to up to three times as many young as she has teats. This, too, is where good genes from their fathers benefit the diminutive, barely developed young. "They haven't got much going for them except for a really strong mouth and sucking mechanism and some little hands and arms to crawl their way up," said Baker. "They'll crawl up and attach to a teat and then once all the teats are occupied all the other extras that were born will die within an hour or two."

So right from birth, natural selection favors only the strongest young from the strongest fathers. The ones that survive settle into a kind of pouch, though it's nowhere near as luxurious as a baby kangaroo's digs. This is more of a depression in the lower abdomen, with raised and slightly enclosed walls, where the young hole up even while the mother hunts.

And the female must feed ravenously, for milk production in marsupials is extremely energy-intensive. In placentals, most of the energy in rearing young is spent in utero, as you mothers out there can attest (that's not to say that significant energy isn't eventually spent on the uniquely human duties of keeping kids from tumbling down stairs and eating crayons). "But marsupials are born small and immature," said Baker, "and most of the energy is driven toward milk production. So when she's producing milk for the growing young, it's an incredible imposition on her energetics."

After six weeks, the young have become too large for their mother to schlep around, so they'll detach and hang tight in the nest and resume suckling when the mother returns. After another six weeks, they're large enough for the female to evict entirely. And so the tiny critters scurry toward their fates: for males, certain death–for females, a male-free paradise of boundless food. Ah, la petite mort.

http://phys.org/news/2014-05-game-changing-gas-membrane.html#rssowlmlink

Researchers develop "game-changing" gas separation membrane

Refining, whether oil or natural gases, can be a costly process because of the need to remove impurities found when extracting them from the ground. Currently expensive materials are used to handle this process.

Phys.org - Texas A&M engineering professors Jaime C. Grunlan and Benjamin A. Wilhite have developed a completely new "game-changing" gas separation membrane that will make the process of extracting these impurities easier, and more importantly, less expensive. Their work was published recently in the journal Advanced Materials with the title "Highly size-selective ionically crosslinked multilayer polymer films for light gas separation." They have also filed a patent for this technology due to its commercial potential.

"We use a simple polymer-based film to remove the impurities and it has the promise of a less expensive method for producing purer oil," said Wilhite, associate professor in the Artie McFerrin Department of Chemical Engineering. "It is all polymer and we are able to get performances comparable to really expensive materials such as mixed matrix membranes and zeolites."

"The technology is separating gases," added Grunlan, associate professor in the Department of Mechanical Engineering. "Gas where they mine it is impure and contains different poison gases you don't want. If you run gas through this membrane what comes out is much purer than what went in on the other side."

The membrane that Grunlan and Wilhite have developed is a layer-by-layer polymer coating that is comprised of alternating individual layers of common, low-cost polyelectrolytes.

The coating can be made by dipping or spraying, making it very easy to apply to existing gas separation systems. These films separate molecules based on size, the smaller ones such as hydrogen pass through, while larger ones such as carbon dioxide and nitrogen are slowed down.

"You can have multiple membranes in a row and it would keep getting purer and purer each time it went through the membranes," said Grunlan. "Except for a sheet of metal, nothing has higher selectivity than our coating. This cheap easy coating is the best thing after a pure sheet of metal. The processing is easier and the materials are cheaper."

The oil and gas industry could stand to be one of the main benefactors of the new technology. Both oil and gas contain impurities that have to be filtered. For example, crude oil comes out of the ground with sulfur. If the amount of sulfur is greater than 0.5 percent the crude is considered "sour." Crude with less than 0.5 percent sulfur is considered "sweet," and is commonly used for processing into gasoline, kerosene and high-quality diesel.

"Traditionally we have operated just off sweet crudes," said Wilhite. "As all the sweet stuff is pretty much gone now, we are increasingly having to tap the holes in the ground we didn't want 50 to 100 years ago."

In order for the "sour" crude to be refined into gasoline, the sulfur has to be removed, which is currently done through hydro treating, an expensive process that in turn leads to higher-priced gasoline.

"You need hydrogen in order to sweeten crudes," Wilhite said. "We can use our membrane right now as a hydrogen purifier, which is valuable because hydrogen is extremely useful in the refining industry."

http://www.eurekalert.org/pub_releases/2014-05/ifhm-mdo050214.php#rssowlmlink

Maternal deaths on the rise in the United States

US falls behind most high-income countries, and is one of only eight worldwide showing disturbing trend

SEATTLE - The United States is among just eight countries in the world to experience an increase in maternal mortality since 2003 - joining Afghanistan and countries in Africa and Central America, according to a new study by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington. The study, "Global, regional, and national levels and causes of maternal mortality during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013," published May 2 in The Lancet, ranked the United States number 60 in the list of 180 countries on maternal deaths, compared to its rank of 22 in 1990, demonstrating how it has fallen behind globally. By contrast, China rose to number 57, up from number 116 in 1990.

In the US, 18.5 mothers died for every 100,000 live births in 2013, more than double the figures for maternal mortality in Saudi Arabia (7) and Canada (8.2), and more than triple that for the United Kingdom (6.1).

The biggest increase in maternal mortality by age group occurred in women 20-24. In 1990, 7.2 women in this age group died for every 100,000 live births and in 2013, 14 died for every 100,000 live births.

The study findings focus on measuring the trends in maternal mortality, but the researchers offer a range of possible explanations for the disparities between the US and other countries, including lack of access to prenatal care and other health services, high rates of caesarian section deliveries, and pregnancies complicated by obesity, diabetes, and other conditions.

"For American women, high-risk pregnancies and the number of women with inadequate access to preventive and maternal health care are just two potential causes of this trend," said study author Dr. Nicholas Kassebaum, Assistant Professor at IHME. "The good news is that most maternal deaths are preventable, and we can do better."

The first installment in IHME's new updates to the Global Burden of Disease (GBD) study finds that globally, maternal deaths fell significantly between 1990 and 2013, but 293,000 women still died in 2013 from pregnancy-related causes. In the US, 796 women died in 2013. The vast majority of countries have seen accelerated reductions in maternal mortality – with maternal deaths declining by 2.7% per year since 2003.

The leading cause of maternal death globally is medical complications of childbirth and the period post-delivery. Approximately one-quarter of maternal deaths were found to occur during childbirth and the 24 hours following. Another quarter happen during pregnancy, and the remaining deaths occur up to one year after delivery.

A separate study also released on May 2 in The Lancet examined child survival rates and found that 28,000 children under age 5 died in the United States in 2013. Child death rates in the US declined throughout 1990-2013, but the pace of the declines has slowed. During the 1990s, child mortality declined 3.2% annually, and after 2000, the rate slowed to 1.7%. The results appeared in "Global, regional, and national levels of neonatal, infant, and under-5 mortality during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013." The study finds that child death rates dropped by 48% globally between 1990 and 2013. However, 6.3 million children still died before their fifth birthday in 2013. Most countries have seen faster declines in child deaths – with child deaths declining by 3.5% per year since 2000.

The study on child mortality shows that maternal education and income growth have had a significant impact in reducing child deaths. In addition, there is a strong trend in rich and poor countries that appears to be related to technological and other advances, such as vaccine and drug innovations.

A separate IHME study found that donor spending on maternal and child health grew substantially since 2000, indicating that the decline in deaths comes at a time of increased investment.

"There's no reason that a country with the resources and the medical expertise that the US has should see maternal deaths going up," said Dr. Christopher Murray, Director of IHME and a co-founder of the Global Burden of Disease. "The next step would be to examine local-level differences in maternal deaths to look for patterns and the drivers behind those patterns." For children, the data show that the earliest days of life are the most dangerous. In 2013, nearly 42% of global child deaths occurred in infants less than one month old. The 10 countries with the lowest child survival rates were all in sub-Saharan Africa. The studies also present scenarios to forecast the under-5 mortality rate and maternal mortality in 2030.

The trends show that it's possible for millions of children's lives to be saved in a short amount of time. If current trends persist, there would be 3.8 million child deaths worldwide in 2030. Under the most ambitious child mortality scenario, though – if all countries saw declines as strong as the countries that saw the fastest declines – there would be 2.4 million child deaths in 2030. The expected number of maternal deaths by 2030 globally is 184,000, and 53 countries will still have maternal mortality ratios over 100.

http://bit.ly/RgGOhl

Elephant Seals Reveal Anti-Inflammatory Secrets of Carbon Monoxide

The gas appears to protect the deep-diving seals from cell damage after periods of restricted blood flow

May 2, 2014 |By Jessica Marshall and Nature magazine

Blood samples from elephant seals may help to explain how carbon monoxide — a poison — can stop inflammation, researchers have found.The seals routinely dive to depths of 500 meters and stay underwater for 25 minutes at a time, surfacing for just a few minutes between plunges. During these forays, blood flow to nonessential tissues and organs is restricted, but the tissues are not damaged. Researchers at the Scripps Institution of Oceanography in San Diego, California, suggest that high levels of carbon monoxide in the seals' blood has a protective effect — echoing laboratory research on rats and mice that has found the gas has anti-inflammatory properties and can lead to better outcomes after organ transplant.

This unusual physiology was first observed in the mid-1950s by Lewis Pugh of the National Institute for Medical Research in London. Pugh monitored carbon monoxide levels in the blood of the men living in an Antarctic base to ensure that their stoves were not poisoning them. While there, Pugh also found surprisingly high carbon monoxide concentrations in the blood of Weddell seals killed to feed sled dogs, .

In the 1960s, researchers discovered that mammals produce carbon monoxide when haemoglobin and myoglobin proteins in their cells degrade. Decades later, in the early 1990s, scientists realized that the gas — previously thought of only as a toxin — can be therapeutic at some concentrations. Experiments in animals including rats and mice have shown that inhaling carbon monoxide improves outcomes after organ transplants and heart attacks, and carbon monoxide treatments for organ transplants are beginning human clinical trials. Yet the mechanism behind the gas's benefits remains unknown. Now, in research presented this week at the Experimental Biology 2014 meeting in San Diego, California, seals return to the picture.

When Michael Tift, a comparative physiologist at Scripps, analysed blood samples from 24 elephant seals on a California beach, he found high levels of haemoglobin. In adult seals, up to 10% of that haemoglobin was bound to carbon monoxide, implying high levels of carbon monoxide in the blood. The levels of carbon monoxide in the seals' blood was comparable to that of "someone who is smoking more than 40 cigarettes a day," Tift says. In nonsmoking humans, just 1–1.5% of haemoglobin is bound to carbon monoxide.

Tift thinks that the seals' carbon monoxide levels and the gas's therapeutic benefits in medical studies have a common explanation. Just as elephant seals restrict blood flow to their nonessential tissues during deep dives, blood flow is interrupted in humans during organ transplantation, stroke, heart attack and other injuries. In humans, when oxygen-rich blood floods back into tissues, it prompts an onslaught of chemical reactions that cause inflammation, cell death and even tissue necrosis. The seals have none of these effects.

"These animals are constantly holding their breath," Tift says, "but they don't have any injuries." He proposes that elevated carbon monoxide may prevent damage from the returning blood flow.

"Carbon monoxide seems to slow the metabolism of the tissue," says Leo Otterbein, a physiologist at Harvard Medical School in Boston, Massachusetts, who pioneered therapeutic uses of carbon monoxide. Slowing metabolism — and thus oxygen use — would delay or eliminate the formation of molecules that cause inflammation and cell death, he says.

The seals may provide a useful system to better understand how carbon monoxide works in the body to prevent problems, says Roberto Motterlini, a vascular biologist at the French medical research agency (INSERM) in Paris. Carbon monoxide may stimulate mitochondria production, he notes, something researchers could test in elephant seals.

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Nightmares may signal a child is being bullied

Study finds victims of bullying are at increased risk of experiencing sleep disturbances

Vancouver, British Columbia – Many children who are bullied suffer in silence. The trauma can lead to anxiety, depression, psychotic episodes and even suicide. There may be a way to identify victims of bullying before they experience serious mental health problems, according to a study to be presented Saturday, May 3, at the Pediatric Academic Societies (PAS) annual meeting in Vancouver, British Columbia, Canada.

Researchers from the University of Warwick in the United Kingdom found that nightmares or night terrors were more common in 12-year-olds who had reported being bullied when they were 8 and 10 years old.

"Nightmares are relatively common in childhood, while night terrors occur in up to 10 percent of children," said lead author Suzet Tanya Lereya, PhD, research fellow at University of Warwick. "If either occurs frequently or over a prolonged time period, they may indicate that a child/adolescent has or is being bullied by peers. These arousals in sleep may indicate significant distress for the child."

Dr. Lereya and Dieter Wolke, PhD, analyzed data from the Avon Longitudinal Study of Parents and Children, which examined the determinants of development, health and disease during childhood and beyond. Children were enrolled at birth, and 6,438 were interviewed at ages 8 and 10 years about bullying and at age 12 about parasomnias, including nightmares, night terrors and sleep walking.

Survey results showed that at age 12 years, 1,555 (24.2 percent) of children had nightmares, 598 (9.3 percent) had night terrors, 814 (12.6 percent) reported sleep walking and 2,315 (36 percent) had at least one type of parasomnia (nightmares, night terrors and sleep walking).

After adjusting for confounders (e.g., any psychiatric diagnosis, family adversity, IQ, internalizing and externalizing problems, sexual or physical abuse, domestic violence, and nightmares before 8 years), children who were victimized at 8 or 10 years were significantly more likely to have nightmares, night terrors or sleep walking at age 12. Moreover, those who were both a victim and a bully were much more likely to have any parasomnia, but bullies were not at increased risk of a sleep disturbance.

"Our findings indicate that being bullied is a significant stress/trauma that leads to increased risk of sleep arousal problems, such as nightmares or night terrors," said Dr. Wolke, professor of developmental psychology and individual differences at University of Warwick. "It is an easily identifiable indicator that something scary is being processed during the night. Parents should be aware that this may be related to experiences of being bullied by peers, and it provides them with an opportunity to talk with their child about it.

"General practitioners also should consider peer bullying as a potential precursor of nightmares or night terrors in children," Dr. Wolke added.

This study was supported by a grant from the Economic and Social Research Council in the United Kingdom (ES/K003593/1).

http://www.eurekalert.org/pub_releases/2014-05/cchm-sss050114.php#rssowlmlink

Study shows steroids ineffective, possibly harmful in pediatric liver disease

A multi-center study concludes that treating infants with high doses of steroids fails to improve medical outcomes in the end-stage pediatric liver disease biliary atresia and leads to earlier onset of serious adverse events.

CINCINNATI – Researchers say the clinical trial involving 14 sites provides new evidence on a growing controversy in the medical community – whether treating infants with steroids to augment surgery improves outcomes. Results for the study will be published May 7 in the Journal of the American Medical Association. The data are being released early to coincide with the Pediatric Academic Societies Annual Meeting.

"The results from this clinical trial differ from previous reports of a benefit from steroid therapy on bile drainage or survival in biliary atresia," said Jorge Bezerra, MD, a lead investigator on the study and physician in the division of Gastroenterology, Hepatology and Nutrition at Cincinnati Children's Hospital Medical Center. "Although we cannot exclude some small potential benefit from steroid treatment, we observed no statistical differences in two-year survival between patients receiving steroid treatment after surgery and those receiving placebo," Bezerra said. "Children receiving steroids during the study also developed serious adverse events more quickly, raising a potential increase in risks associated with steroid therapy."

Biliary atresia is the leading cause of pediatric liver transplantation in the world. The disease accounts for about 50 percent of transplants in children and 10 percent of transplants at any age. It results from inflammation and rapid accumulation of connective tissues that obstruct and restrict bile ducts from draining. The condition then manifests as cholestatic jaundice in the first few weeks after birth.

At diagnosis, the primary treatment is the hepatoportoenterostomy (HPE, the Kasai procedure) – a surgical procedure that removes the diseased bile ducts and gallbladder and connects an intestinal loop directly to the liver to restore bile drainage. Study authors point out that some clinicians suggest steroid treatment after surgery may help prevent additional fibrosis and improve bile drainage. The current study – called START (Steroids in Biliary Atresia Randomized Trial) – was designed to provide rigorous medical data to help answer that question.

The study involved 140 infants with a median age of 2.3 months. The initial study was conducted between September 2005 and February 2011, with follow up ending in January 2013.

Researchers report that in 70 children treated with steroids, bile drainage was not significantly different six months post-surgery compared to 70 children who received placebo after surgery. Of the 70 who received steroids, 41 of 70 patients (58.6 percent) had improved bile drainage. Of 70 patients who did not receive steroids, 34 of 70 (48.6 percent) had improved bile drainage.

When researchers compared survival rates between the steroid/non-steroid groups at age 24 months, 58.7 percent of children in the steroid group survived compared to 59.4 percent in the placebo group.

The percent of children who experienced serious safety events was relatively the same between the steroid group (81.4 percent) and non-steroid group (80 percent), but children who received steroids had an earlier time

to onset for those events. Serious safety events occurred with 30 days post-surgery in 37.2 percent of children who received steroid treatment, versus 19 percent in the placebo group.
Potential serious safety events the authors pointed to included complications such as immunosuppression, associated risk of infection, poor wound healing, hyperglycemia, gastrointestinal bleeding, poor growth, and inadequate response to routine immunizations.
Funding support for the study came from grants provided by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK grant numbers DK62497, 62503, 62436, 62453, 62445, 62481, 62466, 62500, 62452, 62470, 84538, DK84585, 62470, 84536, 62456). Formula and medications for the study were provided by – in coordination through the NIDDK – by support GlaxoSmithKline, Axcan Pharma US, Inc., and Mead Johnson Nutrition.
Other institutions collaborating on the study included: the NIDDK; the University of Michigan, Ann Arbor, Mich.; Children's Hospital of Pittsburgh/University of Pittsburgh Medical Center; University of California San Francisco/Benioff Children's Hospital; Children's Hospital Los Angeles and University of Southern California; Children's Hospital of Philadelphia; Baylor College of Medicine and Texas Children's Hospital, Houston; Emory University School of Medicine and Children's Healthcare of Atlanta; Mount Sinai School of Medicine, New York, NY; Indiana University School of Medicine and Riley Hospital for Children, Indianapolis, IN; Seattle Children's Hospital, Seattle; Johns Hopkins University School of Medicine, Baltimore, MD.

http://www.eurekalert.org/pub_releases/2014-05/hu-foa050214.php#rssowlmlink

Functioning of aged brains and muscles in mice made younger

More progress with GDF 11, anti-aging protein

Cambridge, MA - Harvard Stem Cell Institute (HSCI) researchers have shown that a protein they previously demonstrated can make the failing hearts in aging mice appear more like those of young health mice, similarly improves brain and skeletal muscle function in aging mice.
In two separate papers given early online release today by the journal Science – which is publishing the papers this coming Friday, Professors Amy Wagers and Lee Rubin, of Harvard's Department of Stem Cell and Regenerative Biology (HSCRB), report that injections of a protein known as GDF11, which is found in humans as well as mice, improved the exercise capability of mice equivalent in age to that of about a 70-year-old human, and also improved the function of the olfactory region of the brains of the older mice – they could detect smell as younger mice do.
Rubin and Wagers each said that, baring unexpected developments, they expect to have GDF11 in initial human clinical trials within three to five years. Postdoctoral fellow Lida Katsimpardi is the lead author on the Rubin group's paper, and postdocs Manisha Sinha and Young Jang are the lead authors on the paper from the Wagers group.
Both studies examined the effect of GDF11 in two ways. First, by using what is called a parabiotic system, in which two mice are surgically joined and the blood of the younger mouse circulates through the older mouse. And second, by injecting the older mice with GDF11, which in an earlier study by Wagers and Richard Lee, of Brigham and Women's Hospital who is also an author on the two papers released today, was shown to be sufficient to reverse characteristics of aging in the heart.
Doug Melton, co-chair of HSCRB and co-director of HSCI, reacted to the two papers by saying that he couldn't "recall a more exciting finding to come from stem cell science and clever experiments. This should give us all hope for a healthier future. We all wonder why we were stronger and mentally more agile when young, and these two unusually exciting papers actually point to a possible answer: the higher levels of the protein GDF11 we have when young. There seems to be little question that, at least in animals, GDF11 has an amazing capacity to restore aging muscle and brain function," he said.
Melton, Harvard's Xander University Professor continued, saying that the ongoing collaboration between Wagers, a stem cell biologist whose focus has been on muscle, Rubin, whose focus is on neurodegenerative diseases and using patient generated stem cells as targets for drug discover, and Lee, a practicing cardiologist and researcher, "is a perfect example of the power of the Harvard Stem Cell Institute as an engine of truly collaborative efforts and discovery, bringing together people with big, unique ideas and expertise in different biological areas."
As Melton noted, GDF11 is naturally found in much higher concentration in young mice than in older mice, and raising its levels in the older mice has improved the function of every organ system thus far studied.
Wagers first began using the parabiotic system in mice 14 years ago as a post doctoral fellow at Stanford University, when she and colleagues Thomas Rando, of Stanford, Irina Conboy, of UC Berkley, and Irving Weissman, of Stanford, observed that the blood of young mice circulating in old mice seemed to have some rejuvenating effects on muscle repair after injury.
Last year she and Richard Lee published a paper in which they reported that when exposed to the blood of young mice, the enlarged, weakened hearts of older mice returned to a more youthful size, and their function improved. And then working with a Colorado firm, the pair reported that GDF11 was the factor in the blood

apparently responsible for the rejuvenating effect. That finding has raised hopes that GDF11 may prove, in some form, to be a possible treatment for diastolic heart failure, a fatal condition in the elderly that now is irreversible, and fatal. "From the previous work it could have seemed that GD11 was heart specific," said Wagers, "but this shows that it is active in multiple organs and cell types… Prior studies of skeletal muscle and the parabiotic effect really focused on regenerative biology. Muscle was damaged and assayed on how well it could recover," Wagers explained.

She continued: "The additional piece is that while prior studies of young blood factors have shown that we achieve restoration of muscle stem cell function and they repair the muscle better, in this study, we also saw repair of DNA damage associated with aging, and we got it in association with recovery of function, and we saw improvements in unmanipulated muscle. Based on other studies, we think that the accumulation DNA damage in muscle stem cells might be reflect an inability of the cells to properly differentiate to make mature muscle cells, which is needed for adequate muscle repair.

Wagers noted that there is still a great deal to be learned about the mechanics of aging in muscle, and its repair. "I don't think we fully understand how this happening or why. We might say that the damage is modification to the genetic material; the genome does have breaks in it. But whether it's damaging, or a necessary part of repair, we don't know yet."

Rubin, whose primary research focus is on developing treatment for neurodegenerative diseases, particularly in children, said that that when his group began its GDF11 experiments, "we knew that in the old mouse things were bad in the brain, there is a reduced amount of neurogenesis (the development of neurons), and it's well known that cognition goes down. It wasn't obvious to me that those things that can be repaired in peripheral tissue could be fixed in the brain."

Rubin said that post doctoral fellow Lida Katsimpardi, the lead author on his group's paper, was taught the parabiotic experimental technique by Wagers, but conducted the Rubin group's experiments independently of the Wagers group, and "she saw an increase in neural stem cells, and saw increased development of blood vessels in the brain." Rubin said that 3D reconstruction of the brain, and magnetic resonance imaging (MRI) of the mouse brain showed "more new blood vessels and more blood flow," both of which are normally associated with younger, healthier brain tissue." Younger mice, Rubin said, "have a keen sense of olfactory discrimination," they can sense fine differences in odor. "When we tested the young mice, they avoided the smell of mint; the old mice didn't. But the old mice exposed to the blood of the young mice, and those treated with GDF11 did.

"We think an effect of GDF 11 is the improved vascularity and blood flow, associated with increased neurogenesis," Rubin said. "This should have other more widespread effect on other areas of the brain. We do think that, at least in principal, there will be a way to reverse some of the decline of aging with a single protein. It could be that a molecule like GDF 11, or GDF 11 itself, could" reverse the damage of aging.

"It isn't out of question that GDF11," or a drug developed from it, "might be worthwhile in Alzheimer's Disease," Rubin said. "You might be able to separate out the issues of treating the plaque and tangles associated with the disease, and the decline in cognition, and perhaps improve cognition." Wagers said that the two research groups are in discussions with a venture capital group to obtain funding to "be able to do the additional pre-clinical work" necessary before moving GDF 11 into human trials.

"I would wager that the results of this work, together with the other work, will translate into a clinical trial and a treatment," said the stem cell biologist. "but of course that's just a wager."

"We think an effect of GDF 11 is the improved vascularity and blood flow, which is associated with increased neurogenesis," Rubin said. "However, the increased blood flow should have more widespread effects on brain function. We do think that, at least in principle, there will be a way to reverse some of the cognitive decline that takes place during aging, perhaps even with a single protein. It could be that a molecule like GDF 11, or GDF 11 itself, could" reverse the damage of aging.

"It isn't out of question that GDF11," or a drug developed from it, "might be capable of slowing some of the cognitive defects associated with Alzheimer's Disease, a disorder whose main risk factor is aging itself," Rubin said. It is even possible that this could occur without directly changing the "plaque and tangle burden" that are the pathological hallmarks of Alzheimer's. Thus, a future treatment for this disease might be a combination of a therapeutic that reduces plaques and tangles, such as an antibody directed against the β-amyloid peptide, with a potential cognition enhancer like GDF-11.

Wagers said that the two research groups are in discussions with a venture capital group to obtain funding to "be able to do the additional preclinical work" necessary before moving GDF 11 into human trials.

"I would wager that the results of this work, together with the other work, will translate into a clinical trial and a treatment," said the stem cell biologist. "but of course that's just a wager."

http://nyti.ms/1kOfxNo

Polio Spreading at Alarming Rates, World Health Organization Declares

Alarmed by the spread of polio from conflict zones in three continents, the Wolrd Health Organization on Monday declared the spread of the disease an international health emergency.

By RICK GLADSTONEMAY 5, 2014

The United Nations health body said it was taking the step in an effort to slow the further spread of the disease, a paralyzing virus once thought to be nearly eradicated.

An emergency committee convened by the organization announced in Geneva that three countries — Pakistan, Syria and Cameroon — had allowed the spread of the virus and should take extraordinary measures to stop it.

The committee announced via a telephone news conference from its Geneva headquarters that all children in these countries should be inoculated or reinoculated and all travelers from these countries should be reinoculated and should carry proof in the form of an internationally recognized document.

The emergency committee said it was alarmed that polio had spread recently from Pakistan to Afghanistan, Syria to Iraq, and Cameroon to Equatorial Guinea. It said there was "increasing evidence that adult travelers contributed to this spread."

The committee said the spread of the virus, which primarily affects children five years and younger, "stands in stark contrast to the near-cessation" of the spread of the virus in recent years.

"If unchecked, this situation could result in failure to eradicate globally once of the world's most serious vaccine-preventable diseases," the committee said in a statement.

The committee's decision partly reflected the inability to battle polio's spread in conflict zones where inoculation efforts have been severely impaired. In Syria, where the virus reappeared last year for the first time in more than a decade, health workers have not been able to reach children in areas isolated by the fighting in that country's civil war.

In Pakistan's tribal areas, where the government has been battling a Taliban insurgency, health workers seeking to inoculate children have been attacked, and some have been killed.