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Biases in animal studies may differ from those in clinical trials, UCSF study finds

A new analysis of animal studies on cholesterol-lowering statins by UC San Francisco researchers found that non-industry studies had results that favored the drugs even more than studies funded by industry.

The analysis of 63 animal studies of statins, led by Lisa Bero, PhD, UCSF professor clinical pharmacy, was published online January 21, 2014, in the scientific journal PLoS Biology.

In previous studies, Bero determined that drug-company-sponsored clinical trials were associated with publication of outcomes that favor the sponsor. Bero's work has been cited as part of policy reform efforts that have led many journal publishers, agencies and institutions to require researchers to disclose funding sources and possible conflicts of interest when presenting their research.

The impetus for the current study, Bero said, was to explore whether or not industry-funded animal studies also would be likely to yield more positive outcomes for the companies' drug candidates.

But in their analysis the researchers found the opposite: Results of animal studies that had industry sponsorship were less likely to measure a benefit for statins in slowing or preventing arterial disease. Of the studies that disclosed funding, 9 of 19 industry-sponsored studies had results that favored statins, in comparison to 18 out of 28 studies that favored statins among studies not funded by industry.

The explanation may be, said Bero, that "the interests of the pharmaceutical industry might be best served by underestimating efficacy prior to clinical trials, and overestimating efficacy in clinical trials. By underestimating efficacy in preclinical studies, the pharmaceutical industry could reduce the money spent on clinical trials that did not lead to marketable products."

"Because demonstrating drug efficacy in human studies is linked to drug company profits, drug companies may have more incentive to publish favorable efficacy findings of human drug studies than animal studies."

However, the reason for the opposite findings obtained in analyzing animal and human studies merits additional investigation, Bero said. Selective reporting of study outcomes might play a role, she suggested.

Conclusions of all the studies tended to be favorable in Bero's PLoS Biology analysis. While the industry-sponsored animal studies had somewhat less favorable results, they nonetheless were more likely to present conclusions that favored the statin even when data were less favorable. This result highlights the role of "spin" in communicating research findings, Bero said.

The UCSF researchers also found methodological problems to be common, both in non-industry and industry-sponsored studies. Furthermore, Bero found that harmful side effects were not investigated.

"Not a single animal study we looked at assessed adverse events following the statin intervention," Bero said. "As toxicity data from animal studies must be submitted to drug regulatory authorities before a compound can proceed to testing in humans, it is surprising that so little data on harm appear in the published scientific literature."

In about half the studies analyzed, it appeared that animals were not assigned to treatment or placebo arms of the study randomly, a requirement of high-quality clinical trials. Furthermore, in about half the animal studies analyzed animals were identifiable to the person assigning treatment, a violation of the practice of "blinding."

Criteria for including or excluding animals from studies often were not included in published reports, the UCSF researchers found, and many studies also failed to account properly for changes in the assigned treatment arm that occurred during the course of treatment.

Most of the industry and non industry studies analyzed in Bero's PLoS Biology report were done using rabbits and mice. To gauge atherosclerosis, targeted by statins, researchers quantified blood vessel qualities such as number of damaged blood vessels, blood-vessel diameter, plaque severity, blockage to coronary and other arteries, and plaque rupture.

The study was funded by the National Institute of Environmental Health Sciences.

Co-authors are David Krauth, Andrew Anglemyer, PhD, Rose Philipps, all from the Department of Clinical Pharmacy at UCSF.

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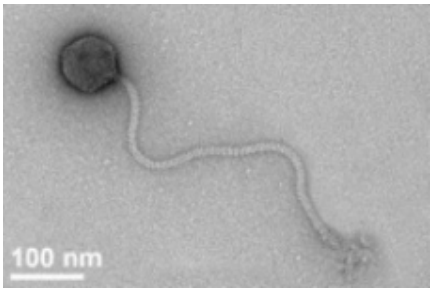
New, unusually large virus kills anthrax agent

From a zebra carcass on the plains of Namibia in Southern Africa, an international team of researchers has discovered a new, unusually large virus (or bacteriophage) that infects the bacterium that causes anthrax.

The novel bacteriophage could eventually open up new ways to detect, treat or decontaminate the anthrax bacillus and its relatives that cause food poisoning. The work is published Jan. 27 in the journal PLOS One.

The virus was isolated from samples collected from carcasses of zebras that died of anthrax in Etosha National Park, Namibia. The anthrax bacterium, Bacillus anthracis, forms spores that survive in soil for long periods.

Zebras are infected when they pick up the spores while grazing; the bacteria multiply and when the animal dies, they form spores that return to the soil as the carcass decomposes.
While anthrax is caused by a bacterium that invades and kills its animal host, bacteriophages, literally "bacteria eaters" are viruses that invade and kill bacterial hosts.
The first thing the team noticed was that the virus was a voracious predator of the anthrax bacterium, said Holly Ganz, a research scientist at the University of California, Davis Genome Center and first author on the paper.
They also noticed that the new virus, named Bacillus phage Tsamsa, is unusually large, with a giant head, a long tail and a large genome, placing it among the largest known bacteriophages.
Tsamsa infects not only B. anthracis but also some closely related bacteria, including strains of Bacillus cereus, which can cause food poisoning. Sequencing the genome allowed researchers to identify the gene for lysin, an enzyme that the virus uses to kill bacterial cells, that has potential use as an antibiotic or disinfecting agent.



Bacteriophages are often highly specific to a particular strain of bacteria, and when they were first discovered in the early 20th century there was strong interest in them as antimicrobial agents. But the discovery of penicillin and other antibiotics eclipsed phage treatments in the West, although research continued in the Soviet Union.
"With growing concerns about antibiotic resistance and superbugs, people are coming back to look at phages," said Ganz said.

The newly-isolated Tsamsa virus is a bacteriophage that infects and kills the anthrax bacterium and close relatives that cause food poisoning. It is one of the largest bacteriophages ever discovered. **Jochen Klumpp, ETH Zurich, Switzerland.**

One advantage of bacteriophages is that because they tend to be very specific, they can potentially target only "bad" bacteria while leaving beneficial bacteria unharmed.
Ganz began the work as a postdoctoral scientist on a team led by Wayne Getz, Professor of Environmental Science, Policy and Management at UC Berkeley and at the University of KwaZulu-Natal, South Africa.
Sequencing of the phage genome was conducted at UC Davis after Ganz joined the laboratory of Professor Jonathan Eisen.
Ganz said that she hoped the publication of the phage's sequence information would enable other researchers to investigate further and potentially develop applications for the phage and its proteins.
"You might use it to detect the anthrax Bacillus or B. cereus; use it as an alternative to antibiotics or as part of a decontaminant," she said.
Other authors on the study are: Wayne Getz, Christina Law and Richard Calendar, UC Berkeley; Martina Schmuki, Fritz Eichenseher, Martin Loessner and Jochen Klumpp at the Institute of Food, Nutrition and Health, ETH Zurich, Switzerland; Jonas Korlach, Pacific Biosciences, Menlo Park, Calif.; and Wolfgang Beyer, University of Hohenheim, Stuttgart, Germany. The work was supported by the NIH.

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University of Montreal study analyzes content of nightmares and bad dreams

Physical attacks are a recurring theme in nightmares

MONTREAL - According to a new study by researchers at the University of Montreal, nightmares have greater emotional impact than bad dreams do, and fear is not always a factor. In fact, it is mostly absent in bad dreams and in a third of nightmares. What is felt, instead, is sadness, confusion, guilt, disgust, etc. For their analysis of 253 nightmares and 431 bad dreams, researchers obtained the narratives of nearly 10,000 dreams.
"Physical aggression is the most frequently reported theme in nightmares. Moreover, nightmares become so intense they will wake you up. Bad dreams, on the other hand, are especially haunted by interpersonal conflicts," write Geneviève Robert and Antonio Zadra, psychology researchers at the Université de Montréal, in the last issue of Sleep.
"Death, health concerns and threats are common themes in nightmares," says Geneviève Robert, first author of the article, which formed part of her doctoral thesis. "But it would be wrong to think that they characterize all nightmares. "Sometimes, it is the feeling of a threat or a ominous atmosphere that causes the person to awaken. I'm thinking of one narrative, in which the person saw an owl on a branch and was absolutely terrified."
Nightmares in men were also more likely than those of women to contain themes of disasters and calamities such as floods, earthquakes and war while themes involving interpersonal conflicts were twice as frequent in the nightmares of women.
Why do we dream? What are nightmares? These questions are still unanswered, says Professor Zadra, who has focused on sleep disorders for 20 years (he is notably a specialist in sleepwalking). One hypothesis is that

dreams are a catharsis to the vicissitudes of daily life; another is that they reflect a disruption of the nervous system. Whatever they are, the scientific community generally agrees that everyone dreams, usually during the stage of sleep called REM sleep, which most people go through three to five times a night. Most sleepers forget their dreams right away; heavy dreamers remember them more easily. Five to six percent of the population report having nightmares.

Treatable

"Nightmares are not a disease in themselves but can be a problem for the individual who anticipates them or who is greatly distressed by their nightmares. People who have frequent nightmares may fear falling asleep – and being plunged into their worst dreams. Some nightmares are repeated every night. People who are awakened by their nightmares cannot get back to sleep, which creates artificial insomnia," says Zadra.

The source of a recurring nightmare may be a traumatic event. Returning soldiers sometimes, in their dreams, see the scenes that marked them. Consumption or withdrawal of alcohol or psychotropic drugs may also explain the frequency or intensity of nightmares. The Diagnostic Statistical Manual of Mental Disorders classifies nightmares in the category "parasomnias usually associated with REM sleep."

The good news is that nightmares are treatable. Through visualization techniques, patients learn to change the scenario of one or more of their dreams and repeat the new scenario using a mental imagery technique. It can be through a life-saving act (the dreamer confronts the attacker) or a supernatural intervention (Superman comes to the rescue). All in mid-dream!

The dream files

One of the research aims of Robert and Zadra, who were funded by the Social Sciences and Humanities Research Council of Canada, was to better understand the difference between bad dreams and nightmares, which seem to be in a continuum with "ordinary" dreams, along a sort of intensity scale.

For this first large-scale comparative study on the topic, the researchers asked 572 respondents to write a dream journal over two to five weeks instead of simply ticking off themes listed in a questionnaire, which is a quicker but less valid method. Some of these journals, stored in a large "dream repository" at the UdeM Department of Psychology, are quite rich.

One example: "I'm in a closet. A strip of white cloth is forcing me to crouch. Instead of clothes hanging, there are large and grotesquely shaped stuffed animals like cats and dogs with grimacing teeth and bulging eyes. They're hanging and wiggling towards me. I feel trapped and frightened."

Not all the narratives are as detailed, says Geneviève Robert, taking several folders from the filing cabinet. While some narratives are written on more than one page (the average is 144 words), some are briefer: one or two lines. Since the participants were asked to write their descriptions as soon as possible after awakening, some of the writing is almost stream-of-consciousness. One can only imagine the work of the research team who transcribed these thousands of narratives before classifying and analyzing them.

What more can we understand from dreams? "Almost everything," says Zadra. Through this research, we can better assert that dreams, bad dreams, and nightmares are part of the same emotional and neurocognitive process. How and which one? It remains to be determined.

Thematic and Content Analysis of Idiopathic Nightmares and Bad Dreams published in Sleep, Vol. 37, No. 2, 2014.
The research was funded by Social Sciences and Humanities Research Council of Canada.

http://www.eurekalert.org/pub_releases/2014-01/uol-ita012714.php

Is there an ocean beneath our feet?

Scientists at the University of Liverpool have shown that deep sea fault zones could transport much larger amounts of water from the Earth's oceans to the upper mantle than previously thought.

Seismologists at Liverpool have estimated that over the age of the Earth, the Japan subduction zone alone could transport the equivalent of up to three and a half times the water of all the Earth's oceans to its mantle.

Water is carried to the mantle by deep sea fault zones which penetrate the oceanic plate as it bends into the subduction zone. Subduction, where an oceanic tectonic plate is forced beneath another plate, causes large earthquakes such as the recent Tohoku earthquake, as well as many earthquakes that occur hundreds of kilometers below the Earth's surface.

Using seismic modelling techniques the researchers analysed earthquakes which occurred more than 100 km below the Earth's surface in the Wadati-Benioff zone, a plane of Earthquakes that occur in the oceanic plate as it sinks deep into the mantle.

Analysis of the seismic waves from these earthquakes shows that they occurred on 1 - 2 km wide fault zones with low seismic velocities. Seismic waves travel slower in these fault zones than in the rest of the subducting plate because the sea water that percolated through the faults reacted with the oceanic rocks to form serpentinite – a mineral that contains water.

Some of the water carried to the mantle by these hydrated fault zones is released as the tectonic plate heats up. This water causes the mantle material to melt, causing volcanoes above the subduction zone such as those that form the Pacific 'ring of fire'. Some water is transported deeper into the mantle, and is stored in the deep Earth.
"It has been known for a long time that subducting plates carry oceanic water to the mantle," said Tom Garth, a PhD student in the Earthquake Seismology research group led by Professor Rietbrock. "This water causes melting in the mantle, which leads to arc releasing some of the water back into the atmosphere. Part of the subducted water however is carried deeper into the mantle and may be stored there.
"We found that fault zones that form in the deep oceanic trench offshore Northern Japan persist to depths of up to 150 km. These hydrated fault zones can carry large amounts of water, suggesting that subduction zones carry much more water from the ocean down to the mantle than has previously been suggested. This supports the theory that there are large amounts of water stored deep in the Earth.
Understanding how much water is delivered to the mantle contributes to our knowledge of how the mantle convects and how it melts. This is important to understanding how plate tectonics began and how the continental crust was formed.
The research is published in Geology.

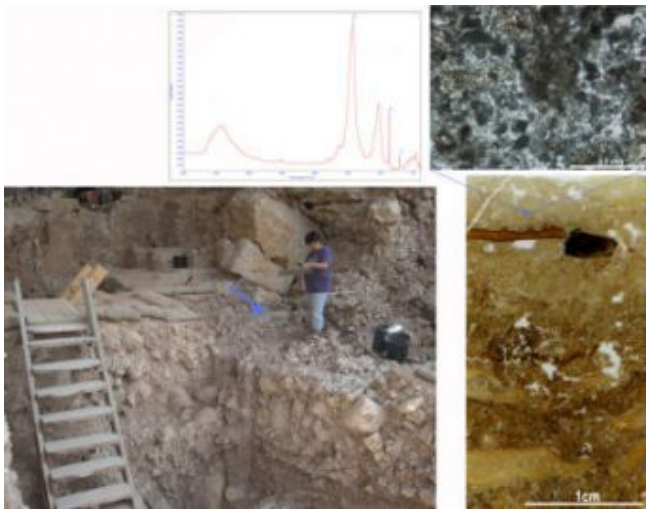
http://www.eurekalert.org/pub_releases/2014-01/wios-3hf012714.php

300,000-year-old hearth found

Microscopic evidence revealed in Weizmann Institute labs shows repeated fire use in the spot over time

Humans, by most estimates, discovered fire over a million years ago. But when did they really begin to control fire and use it for their daily needs? That question – one which is central to the subject of the rise of human culture – is still hotly debated. A team of Israeli scientists recently discovered in the Qesem Cave, an archaeological site near present-day Rosh Ha'ayin, the earliest evidence – dating to around 300,000 years ago – of unequivocal repeated fire building over a continuous period. These findings not only help answer the question, they hint that those prehistoric humans already had a highly advanced social structure and intellectual capacity.

Excavations in Qesem Cave have been ongoing since 2000. The team is headed by Profs. Avi Gopher and Ran Barkai of Tel Aviv University. Dr. Ruth Shahack-Gross of the Kimmel Center for Archeological Science at the Weizmann Institute has been involved in this archaeological research since excavations began, and she collects samples on-site for later detailed analysis in the lab. Shahack-Gross, whose expertise is in the identification of archaeological materials, identified a thick deposit of wood ash in the center of the cave. Using infrared spectroscopy, she and her colleagues were able to determine that mixed in with the ash were bits of bone and soil that had been heated to very high temperatures. This was conclusive proof that the area had been the site of a large hearth.



Upper left: This is an infrared spectrum of the grey sediments, right, showing that the dominant material is calcite, the mineral of which the wood ash is composed. Lower left: This is a photograph of the cave during excavation; arrow pointing to the hearth. Upper right: This is a micro-morphological image of the grey sediment showing dark grey particles and patches corresponding to the remains of wood ash. Lower right: This is a scan of a micro-morphological, thin section showing the layered burnt bones (yellow, brown and black fragments), intermixed with grey sediments.
Weizmann Institute of Science

Next, Shahack-Gross tested the micro-morphology of the ash. To do this, she extracted a cubic chunk of sediment from the hearth and hardened it in the lab. Then she sliced it into extremely thin slices – so thin they could be placed under a microscope to observe the exact composition of the materials in the deposit and reveal how they were formed. With this method, she was able to distinguish a great many micro-strata in the ash – evidence for a hearth that was used repeatedly over time. These findings were published in the Journal of Archaeological Science.
Around the hearth area, as well as inside it, the archaeologists found large numbers of flint tools that were clearly used for cutting meat. In contrast, the flint tools found just a few meters away had a different shape, designed for other activities. Also in and around the area were large numbers of burnt animal bones – further evidence for repeated fire use for cooking meat. Shahack-Gross and her colleagues have shown that this

organization of various "household" activities into different parts of the cave points to an organization of space – and thus a kind of social order – that is typical of modern humans. This suggests that the cave was a sort of base camp that prehistoric humans returned to again and again. "These findings help us to fix an important turning point in the development of human culture – that in which humans first began to regularly use fire both for cooking meat and as a focal point – a sort of campfire – for social gatherings," she says. "They also tell us something about the impressive levels of social and cognitive development of humans living some 300,000 years ago." The researchers think that these findings, along with others, are signs of substantial changes in human behavior and biology that commenced with the appearance in the region of new forms of culture – and indeed a new human species – about 400,000 years ago.

http://www.eurekalert.org/pub_releases/2014-01/mu-src_1012314.php

Scientists reveal cause of one of the most devastating pandemics in human history

Two of the world's most devastating plagues were caused by distinct strains of the same pathogen

An international team of scientists has discovered that two of the world's most devastating plagues – the plague of Justinian and the Black Death, each responsible for killing as many as half the people in Europe—were caused by distinct strains of the same pathogen, one that faded out on its own, the other leading to worldwide spread and re-emergence in the late 1800s. These findings suggest a new strain of plague could emerge again in humans in the future.

"The research is both fascinating and perplexing, it generates new questions which need to be explored, for example why did this pandemic, which killed somewhere between 50 and 100 million people die out?" questions Hendrik Poinar, associate professor and director of the McMaster Ancient DNA Centre and an investigator with the Michael G. DeGroote Institute for Infectious Disease Research.

The findings are dramatic because little has been known about the origins or cause of the Justinian Plague– which helped bring an end to the Roman Empire – and its relationship to the Black Death, some 800 years later. Scientists hope this could lead to a better understanding of the dynamics of modern infectious disease, including a form of the plague that still kills thousands every year.

The Plague of Justinian struck in the sixth century and is estimated to have killed between 30 and 50 million people— virtually half the world's population as it spread across Asia, North Africa, Arabia and Europe. The Black Death would strike some 800 years later with similar force, killing 50 million Europeans between just 1347 and 1351 alone.

Using sophisticated methods, researchers from many universities including McMaster University, Northern Arizona University and the University of Sydney, isolated miniscule DNA fragments from the 1500-year-old teeth of two victims of the Justinian plague, buried in Bavaria, Germany. These are the oldest pathogen genomes obtained to date. Using these short fragments, they reconstructed the genome of the oldest Yersinia pestis, the bacterium responsible for the plague, and compared it to a database of genomes of more than a hundred contemporary strains. The results are currently published in the online edition of The Lancet Infectious Diseases. They show the strain responsible for the Justinian outbreak was an evolutionary 'dead-end' and distinct from strains involved later in the Black Death and other plague pandemics that would follow.

The third pandemic, which spread from Hong Kong across the globe is likely a descendant of the Black Death strain and thus much more successful than the one responsible for the Justinian Plague.

"We know the bacterium Y. pestis has jumped from rodents into humans throughout history and rodent reservoirs of plague still exist today in many parts of the world. If the Justinian plague could erupt in the human population, cause a massive pandemic, and then die out, it suggest it could happen again. Fortunately we now have antibiotics that could be used to effectively treat plague, which lessens the chances of another large scale human pandemic" says Dave Wagner, an associate professor in the Center for Microbial Genetics and Genomics at Northern Arizona University.

The samples used in the latest research were taken from two victims of the Justinian plague, buried in a gravesite in a small cemetery in the German town of Aschheim. Scientists believe the victims died in the latter stages of the epidemic when it had reached southern Bavaria, likely sometime between 541 and 543.

The skeletal remains yielded important clues and raised more questions.

Researchers now believe the Justinian Y. pestis strain originated in Asia, not in Africa as originally thought. But they could not establish a 'molecular clock' so its evolutionary time-scale remains elusive. This suggests that earlier epidemics, such as the Plague of Athens (430 BC) and the Antonine Plague (165 -180 AD), could also be separate, independent emergences of related Y. pestis strains into humans.

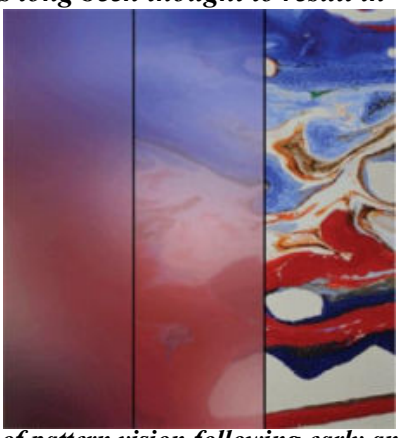
"The tick of the plague bacteria molecular clock is highly erratic. Determining why is an important goal for future research" says Edward Holmes, an NHMRC Australia Fellow at the University of Sydney.

Our response to modern infectious diseases is a direct outcome of lessons learned from ancestral pandemics, say the researchers.
"This study raises intriguing questions about why a pathogen that was both so successful and so deadly died out. One testable possibility is that human populations evolved to become less susceptible," says Holmes.
"Another possibility is that changes in the climate became less suitable for the plague bacterium to survive in the wild," says Wagner.
The research was funded in part by the Social Sciences and Humanities Research Council of Canada, Canada Research Chairs Program, U.S. Department of Homeland Security, U.S. National Institutes of Health and the Australian National Health and Medical Research Council.
Attention Editors: High definition clips, background video footage and high resolution photos are available to download at: https://www.dropbox.com/sh/ohlm782we03dxbb/DIgcm8Aqhw.

http://www.sciencedaily.com/releases/2014/01/140127112800.htm

Visual system can retain considerable plasticity after extended blindness

Deprivation of vision during critical periods of childhood development has long been thought to result in irreversible vision loss.



Now, researchers from the Schepens Eye Research Institute/Massachusetts Eye and Ear, Harvard Medical School (HMS) and Massachusetts Institute of Technology (MIT) have challenged that theory by studying a unique population of pediatric patients who were blind during these critical periods before removal of bilateral cataracts. The researchers found improvement after sight onset in contrast sensitivity tests, which measure basic visual function and have well-understood neural underpinnings. Their results show that the human visual system can retain plasticity beyond critical periods, even after early and extended blindness. Their findings were recently published in the Proceedings of the National Advancement of Science (PNAS) Early Edition.

Pictured are simulated views of an abstract painting to depict the development of pattern vision following early and extended blindness. Working with children who gained sight after several years of early onset blindness, Kalia et al., found that they had poor spatial resolution and impoverished contrast perception immediately after cataract surgery. This is simulated in the left panel. Follow-up assessments six months later revealed surprising enhancement of contrast sensitivity. The middle panel depicts the substantial improvements in perceptual quality this corresponds to. The right panel shows the original painting. These findings suggest that the visual system retains considerable plasticity beyond the early years believed to be critical for normal development. The painting (acrylics on canvas) was created by a child who gained sight after extended blindness. **Credit: Image courtesy of Luis Lesmes, Michael Dorr, Peter Bex, Amy Kalia and Pawan Sinha**

"Our research group has been studying the development of vision in children who were blind from birth because of congenital cataracts. We have been measuring if and how their vision develops after surgery in late childhood and adolescence to remove cataracts, which enables sight for the first time. Our results show remarkable plasticity and vision continues to improve in many children long after the surgery," said Senior Author Peter J. Bex, Ph.D., Senior Scientist, Schepens Eye Research Institute/Mass. Eye and Ear and Associate Professor, HMS Department of Ophthalmology.
The authors explain the research: Project Prakash is a joint scientific and humanitarian effort led by Pawan Sinha, Ph.D., full professor at MIT. The humanitarian part aims to address problems of treatable blindness in India by providing surgeries free of cost to children with cataracts. In the Western world, children born with cataracts typically are treated in the first year of life, but children with this condition in rural India often go untreated because their families lack the necessary financial resources. The project also aims to answer the questions: can children who suffer from extended congenital blindness develop vision after cataract surgery and if so, how does this process happen?
The "critical period" or the "critical window" is a traditional concept in the field of neuroscience that suggest that there is "plasticity," or potential for development, early in life. But as we grow older — and in the case of vision, pass the age of 7 or 8 — there is less and less plasticity in the visual system.
The concept of the critical period intersects with clinical care in the practice patterns for children with amblyopia: it was once thought that if you didn't treat amblyopia before age 8, then the window of opportunity for saving sight was lost. For these patients, one potential justification for not removing them during their adolescence was that "they'll just be blind anyway." However, this once accepted mantra has started to change in the last 10 years with new insights into plasticity and the potential impact of brain or sensory training following surgery.

The Schepens/Mass. Eye and Ear contribution to Project Prakash was an iPad-based assessment of the contrast sensitivity function developed in the Bex Laboratory. It is more precise and easier to apply than previous contrast sensitivity assessments.
"Given this background and past research, the most conservative hypothesis for our study would have been that children between 8 and 18 would show no changes in low-level vision, and no changes in their contrast sensitivity functions , when they were tested after their cataract surgery," said Dr. Bex. "With our test (which usually requires specialized laboratory equipment) and some analytics we developed, we showed that some patients developed substantial vision after 15 years of blindness. This visual change could not be accounted for by simple optical factors, either."
This research has important implications for potential treatments of congenital cataracts, in addition to the fundamental questions of development and plasticity in neuroscience, the researchers conclude.
A. Kalia, L. A. Lesmes, M. Dorr, T. Gandhi, G. Chatterjee, S. Ganesh, P. J. Bex, P. Sinha. Development of pattern vision following early and extended blindness. Proceedings of the National Academy of Sciences, 2014; DOI: 10.1073/pnas.1311041111

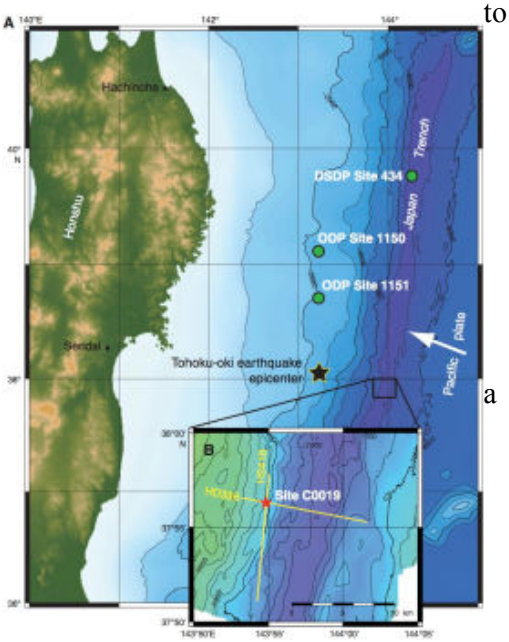
http://bit.ly/1iUejl8

Dead Plants Hold Earthquake Secrets

With a few tricks borrowed from the oil industry, scientists are hoping to one day better understand why earthquakes start and stop.

Jan 27, 2014 02:00 PM ET // by Becky Oskin, LiveScience

Geologists would love to know what controls earthquakes. But one of the best ways to answer that question - drilling into faults - is expensive and difficult. An easier alternative is to study faults exposed on Earth's surface, and look at "fossilized" earthquakes preserved along the faults.
But faults can be several feet wide and filled with crushed-up rock, or they can be inch-thick cracks. How does someone walk up to a crack, point a finger at it and determine an earthquake occurred there?
Sometimes, the tremendous heat created during an earthquake melts rock inside a fault. "That was the gold standard," said Heather Savage, a geophysicist at Lamont-Doherty Earth Observatory in New York. "When you get the melt, it means the fault slipped fast."
(Faults get hot because of friction. Just as rubbing your hands warms them on a winter's day, earthquakes heat the Earth when two sides of a fault slide past each other during a quake.)
But there are plenty of old faults exposed on Earth's surface and very little of this melted rock, called pseudotachylyte, Savage said. So, over the past few years, Savage and her colleagues have devised a new way to find old earthquakes. It turns out that earthquakes can "cook" dead plants and algae trapped in a fault, similar to how organic material transforms over eons into oil.



The drilling site offshore of Japan, where researchers pierced through the plate boundary that caused the 2011 Tohoku earthquake. **Credit: IODP/JAMSTEC**

And because heat from an earthquake is linked to fault strength, Savage is also testing whether this cooked organic matter reveals clues about fault strength during past earthquakes.
"Temperature rise during an earthquake says something about the strength of the fault when it was slipping, and that is a big unknown in earthquake science," Savage told LiveScience's OurAmazingPlanet. "These kinds of questions are really fundamental if we're ever going to get better at making accurate earthquake predictions."
The technique could prove especially handy at subduction zones — the source of the world's biggest earthquakes — which are often rich in organic material scraped off the ocean floor.
In Alaska, a 60-million-year old subduction zone between the Pacific and North American plates now sits exposed above shoreline at Pasagshak Point on Kodiak Island. This is one of the only places in the world where pseudotachylyte is found on a subduction zone. Savage and her colleagues tested their earthquake "biomarker" method here, comparing the temperature recorded by organic matter to that from the pseudotachylyte at one section of the fault.
The organic chemistry was borrowed from the oil industry, which has invested millions in measuring how rocks are heated based simply on the properties of organic matter in those rocks — though the cooking usually takes millions of years, not seconds and minutes, like earthquakes.

In Alaska, the biomarkers were diamondoids, carbon and hydrogen heated until they take on the same basic structure as diamonds. By modeling the heat needed to create diamondoids, Savage and her colleagues estimate the earthquake they found was about a magnitude 7 or magnitude 8, with a temperature rise of between 1,540 and 2,140 degrees Fahrenheit (840 to 1,170 degrees Celsius) and between 3 to 30 feet (1 to 9 meters) of movement. The findings were published Jan. 6 in the journal Geology.

"We're very excited; it's one of the first times we've been able to do this with a new method," Savage said.

Savage noted that this earthquake thermometer only works on faults in sedimentary rocks that carry organic material, and that not all earthquakes will generate a lot of heat. In California, along an ancient strand of the San Andreas Fault called the Punchbowl Fault, the team found a temperature rise of only 1,150 F (625 C), despite geologic evidence of past earthquakes.

The group has several new projects in the works. They're investigating rocks from Japan's JFAST drilling site, at the source of the 2011 Tohoku earthquake, and working on the San Andreas Fault deep drilling project, to see if the slow-moving part of the San Andreas Fault ever had large earthquakes. They are also running laboratory tests to customize those petroleum-industry chemical equations and to better understand the link between temperature on faults and organic matter. And someday, Savage would like to create a "heat map" of a fault.

"We're hoping that being able to walk up to an outcrop and fingerprint this kind of slip, which may help tell us how earthquakes get started, and maybe how they stop," Savage said.

"A fault plane is hundreds of kilometers long and tens of kilometers wide, and maybe the strength of that fault is determined by very small patches holding most of the resistance to sliding," Savage said. "Understanding how stress is distributed on faults is a very important question toward understanding when a fault is getting close to actually having an earthquake

http://www.bbc.co.uk/news/health-25913568

DDT: Pesticide linked to Alzheimer's

Exposure to a once widely used pesticide, DDT, may increase the chances of developing Alzheimer's disease, suggest US researchers.

By James Gallagher Health and science reporter, BBC News

A study, published in JAMA Neurology, showed patients with Alzheimer's had four times as much DDT lingering in the body as healthy people. Some countries still use the pesticide to control malaria. Alzheimer's Research UK said more evidence was needed to prove DDT had a role in dementia. DDT was a massively successful pesticide, initially used to control malaria at the end of World War Two and then to protect crops in commercial agriculture. However, there were questions about its impact on human health and wider environmental concerns, particularly for predators. It was banned in the US in 1972 and in many other countries. But the World Health Organization still recommends using DDT to keep malaria in check.

Not clear

DDT also lingers in the human body where it is broken down into DDE. The team at Rutgers University and Emory University tested levels of DDE in the blood of 86 people with Alzheimer's disease and compared the results with 79 healthy people of a similar age and background. The results showed those with Alzheimer's had 3.8 times the level of DDE. However, the picture is not clear-cut. Some healthy people had high levels of DDE while some with Alzheimer's had low levels. Alzheimer's also predates the use of DDT.

The researchers believe the chemical is increasing the chance of Alzheimer's and may be involved in the development of amyloid plaques in the brain, a hallmark of the disease, which contribute to the death of brain cells.

Prof Allan Levey, the director of the Alzheimer's Disease Research Centre at Emory, said: "This is one of the first studies identifying a strong environmental risk factor for Alzheimer's disease. "The magnitude of the effect is strikingly large, it is comparable in size to the most common genetic risk factor for late-onset Alzheimer's."

Fellow researcher Dr Jason Richardson added: "We are still being exposed to these chemicals in the United States, both because we get food products from other countries and because DDE persists in the environment for a long time," .

Dr Simon Ridley, the head of research at the charity Alzheimer's Research UK, said: "It's important to note that this research relates to DDT, a pesticide that has not been used in the UK since the 1980s. "While this small study suggests a possible connection between DDT exposure and Alzheimer's, we don't know whether other factors may account for these results. "Much more research would be needed to confirm whether this particular pesticide may contribute to the disease."

http://www.eurekalert.org/pub_releases/2014-01/esoc-aso012814.php

Aspirin still overprescribed for stroke prevention in AF

Aspirin is still overprescribed for stroke prevention in atrial fibrillation despite the potential for dangerous side effects, according to research published today

Sophia Antipolis Aspirin is still overprescribed for stroke prevention in atrial fibrillation (AF) despite the potential for dangerous side effects, according to research published today.

Professor Gregory Y.H. Lip, lead author of the European Society of Cardiology (ESC) study, said: "The perception that aspirin is a safe and effective drug for preventing strokes in AF needs to be dispelled. If anything, you could say that giving aspirin to patients with AF is harmful because it is minimally or not effective at stroke prevention, yet the risk of major bleeding or intracranial haemorrhage is not significantly different to well-managed oral anticoagulation."

He added: "All the contemporary guidelines1 say that aspirin should not be used for the prevention of stroke in patients with AF. And yet our study shows that aspirin is still overprescribed in these patients."

Stroke prevention is central to the management of patients with AF. As the most common cardiac rhythm disorder, AF occurs in 1.5-2% of the general population in the developed world and people over the age of 40 have a 1 in 4 lifetime risk of developing AF.2 Patients wit6h AF have a five-fold risk of stroke, and when they do have strokes they lead to more death and disability.3

Prevention of strokes in patients with AF is based on identification of risk factors.2 Patients with no stroke risk factors (ie. CHA2DS2-VASc score of 0 in males or 1 in females) are considered 'low risk' and do not need any antithrombotic drugs. Patients with one or more risk factors should be offered effective stroke prevention, and thus be given an oral anticoagulant (warfarin or one of the novel oral anticoagulants). The use of aspirin, either alone or in combination with an oral anticoagulant, is not recommended.

The study published online today in the American Journal of Medicine provides the most up-to-date picture of European cardiologists' prescribing of antithrombotic treatment, which includes oral anticoagulation therapy (warfarin and the novel oral anticoagulants) and antiplatelet drugs (mainly aspirin).4 The data are from the EORP Atrial Fibrillation General Pilot Registry of more than 3 100 patients in nine countries.5

Overall the study found that the use of oral anticoagulants has improved over the last decade since the last Euro Heart Survey was performed. Where oral anticoagulation was used, most patients (72%) were prescribed warfarin and just 8% were prescribed a new oral anticoagulant.

Professor Lip said: "Novel oral anticoagulant uptake is still a bit low, probably because of differences in regulatory approval, costs and access to drugs in different countries. But the main point is that overall oral anticoagulant uptake as a whole has improved in the last 10 years."

Aspirin was commonly prescribed, either alone or in combination with an oral anticoagulant, when patients had myocardial infarction or coronary artery disease. The strongest reason to prescribe both drugs was coronary artery disease, which increased the use of combined therapy by more than eight-fold.

Professor Lip said: "Aspirin is still overused for stroke prevention in AF. ESC guidelines say concomitant aspirin should not be given to anticoagulated AF patients with stable vascular disease. The combination of drugs does not reduce cardiovascular events and stroke but does increase the risk of bleeding."

Another worrying finding was that oral anticoagulants were underprescribed in elderly patients, with aspirin alone more commonly prescribed. Professor Lip said: "Elderly patients are at the highest risk for stroke and yet they are given aspirin which is not recommended and potentially harmful. There is a perception that elderly patients do not do well on anticoagulation. But a number of studies now, including BAFTA,6 have shown that in elderly patients warfarin is far superior to aspirin in preventing stroke."

Patients with paroxysmal AF were less likely to receive oral anticoagulation compared to patients with permanent AF. Professor Lip said: "Cardiologists are continuing to underprescribe anticoagulation in paroxysmal AF and the belief that these patients are at less risk is another myth. ESC guidelines say that AF patients with stroke risk factors should receive oral anticoagulation irrespective of the type of AF."

Professor Lip concluded: "Our study of antithrombotic prescribing by cardiologists reveals a positive trend of increasing oral anticoagulant use. But worrying misconceptions and practices remain regarding aspirin, treatment of the elderly and paroxysmal AF."

References and notes

1Guidelines which advocate oral anticoagulation therapy for stroke prevention in AF and do not recommend aspirin have been published by the ESC, the Asia Pacific Heart Rhythm Society and most recently the UK National Institute for Health and Care Excellence (NICE) (draft version – see http://guidance.nice.org.uk/CG/Wave0/638/Consultation/Latest). 22012 focused update of the ESC Guidelines for the management of atrial fibrillation. Eur Heart J. 2012;33:2719. 3Guidelines for the management of atrial fibrillation. Eur Heart J. 2010;31:2369.

4Lip GYH, Laroche C, Dan GA, Santini M, Kalarus Z, Rasmussen LH, Popescu MI, Tica O, Boriani G, Cimaglia P, Hellum CF, Mortensen B, Maggioni AP. Antithrombotic treatment in 'real-world' patients with atrial fibrillation: A report from the Euro Observational Research Programme Pilot survey on Atrial Fibrillation. American Journal of Medicine. http://www.sciencedirect.com/science/article/pii/S0002934314000692

http://www.eurekalert.org/pub_releases/2014-01/cp-brt012114.php

Brain regions thought to be uniquely human share many similarities with monkeys

New research suggests a surprising degree of similarity in the organization of regions of the brain that control language and complex thought processes in humans and monkeys.

The study, publishing online January 28 in the Cell Press journal Neuron, also revealed some key differences. The findings may provide valuable insights into the evolutionary processes that established our ties to other primates but also made us distinctly human.

The research concerns the ventrolateral frontal cortex, a region of the brain known for more than 150 years to be important for cognitive processes including language, cognitive flexibility, and decision-making. "It has been argued that to develop these abilities, humans had to evolve a completely new neural apparatus; however others have suggested precursors to these specialized brain systems might have existed in other primates," explains lead author Dr. Franz-Xaver Neubert of the University of Oxford, in the UK.

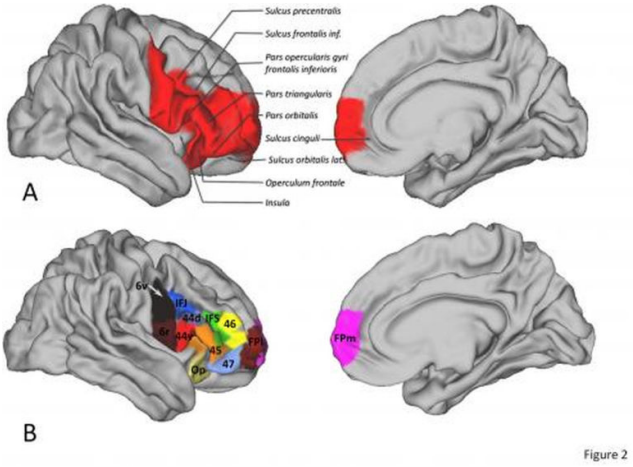


Figure 2

(A) The right vlFC ROI. Dorsally it included the inferior frontal sulcus and, more posteriorly, it included PMv; anteriorly it was bound by the paracingulate sulcus and ventrally by the lateral orbital sulcus and the border between the dorsal insula and the opercular cortex. (B) A schematic depiction of the result of the 12 cluster parcellation solution using an iterative parcellation approach. We subdivided PMv into ventral and dorsal regions (6v and 6r, purple and black). We delineated the IFJ area (blue) and areas 44d (gray) and 44v (red) in lateral pars opercularis. More anteriorly, we delineated areas 45 (orange) in the pars triangularis and adjacent operculum and IFS (green) in the inferior frontal sulcus and dorsal pars triangularis. We found area 12/47 in the pars orbitalis (light blue) and area Op (bright yellow) in the deep frontal operculum. We also identified area 46 (yellow), and lateral and medial frontal pole regions (FPl and FPm, ruby colored and pink). **Credit: Neuron, Neubert et al.**

By using non-invasive MRI techniques in 25 people and 25 macaques, Dr. Neubert and his team compared ventrolateral frontal cortex connectivity and architecture in humans and monkeys. The investigators were surprised to find many similarities in the connectivity of these regions. This suggests that some uniquely human cognitive traits may rely on an evolutionarily conserved neural apparatus that initially supported different functions. Additional research may reveal how slight changes in connectivity accompanied or facilitated the development of distinctly human abilities.

The researchers also noted some key differences between monkeys and humans. For example, ventrolateral frontal cortex circuits in the two species differ in the way that they interact with brain areas involved with hearing.

"This could explain why monkeys perform very poorly in some auditory tasks and might suggest that we humans use auditory information in a different way when making decisions and selecting actions," says Dr. Neubert.

A region in the human ventrolateral frontal cortex—called the lateral frontal pole—does not seem to have an equivalent area in the monkey. This area is involved with strategic planning, decision-making, and multi-tasking abilities.

"This might relate to humans being particularly proficient in tasks that require strategic planning and decision making as well as 'multi-tasking'", says Dr. Neubert.

Interestingly, some of the ventrolateral frontal cortex regions that were similar in humans and monkeys are thought to play roles in psychiatric disorders such as attention deficit hyperactivity disorder, obsessive compulsive disorder, and substance abuse. A better understanding of the networks that are altered in these disorders might lead to therapeutic insights.

Neuron, Neubert et al.: "Comparison of human ventral frontal cortex areas for cognitive control and language with areas in monkey frontal cortex."

http://www.eurekalert.org/pub_releases/2014-01/asfm-bta012314.php

Bacterial toxin a potential trigger for multiple sclerosis

Researchers from Weill Cornell Medical College have added to the growing body of evidence that multiple sclerosis may be triggered by a toxin produced by common foodborne bacteria.

They presented their research at the 2014 ASM Biodefense and Emerging Diseases Research Meeting.

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system characterized by blood brain (BBB) permeability and demyelination, a process in which the insulating myelin sheaths of neurons are damaged. The disease is thought to be triggered in a genetically susceptible individual by a combination of one or more environmental factors. The environmental trigger of MS, however, is still unknown. According to the National Multiple Sclerosis Society, the condition affects approximately 400,000 Americans and is, with the exception of trauma, the most frequent cause of neurological disability beginning in early to middle adulthood.

"We provide evidence that supports epsilon toxin's ability to cause BBB permeability and show that epsilon toxin kills the brain's myelin producing cells, oligodendrocytes; the same cells that die in MS lesions," says Jennifer Linden of Weill Cornell Medical College, who presented the research. "We also show that epsilon toxin targets other cells types associated with MS inflammation such as the retinal vascular and meningeal cells. Epsilon toxin may be responsible for triggering MS."

Epsilon toxin is produced by certain strains of Clostridium perfringens, a spore-forming bacterium that is one of the most common causes of foodborne illness in the United States. The U.S. Centers for Disease Control and Prevention estimates that non-epsilon toxin producing C. perfringens strains cause nearly a million cases of foodborne illness each year.

Previous studies have suggested that C. perfringens, and in particular epsilon toxin, may play a role in triggering MS. Late last year Linden and her colleagues discovered C. perfringens type B (a strain that is not known to infect humans and produces the epsilon toxin) in a 21-year-old woman who was experiencing a flare-up of her MS. To further test their hypothesis Linden and her colleagues studied the behavior of the toxin in mice, specifically which cells it targeted.

They discovered that the toxin did target the brain cells associated with MS pathology. But that was not all they found. "Originally, we only thought that epsilon toxin would target the brain endothelium cells and oligodendrocytes; we just happened to notice that it also bound to and killed meningeal cells. This was exciting because it provides a possible explanation for meningeal inflammation and subpial cortical lesions exclusively observed in MS patients, but not fully understood," says Linden.

They also tested samples of local foods for the presence of C. perfringens and the toxin gene. Of the 37 food samples, 13.5% were positive for bacteria and 2.7% were positive for the epsilon toxin gene.

Linden says these findings are important, because if it can be confirmed that epsilon toxin is indeed a trigger of MS, development of a neutralizing antibody or vaccine directed against epsilon toxin might stop the progression of the disease or prevent it from even developing.

http://planetearth.nerc.ac.uk/news/story.aspx?id=1596

Carbon dates cast doubt on Near East's singular role in modern human migration

Radiocarbon dating of human remains from one of the deepest prehistoric sites in the Near East throws into question widely-held ideas about how the first modern people spread across the world during the Palaeolithic era.

28 January 2014, by Tom Marshall

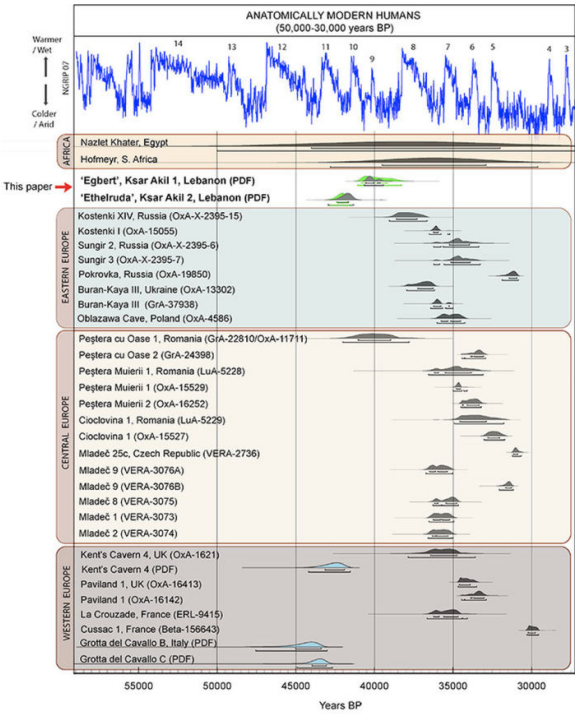
The traditional view is that the first humans with anatomy like ours evolved in Africa, then from about 50,000 years ago started to spread into the Near East before continuing into Asia and Europe.

But the new study suggests they may have settled the Near East a lot later than previously thought, and that therefore the region may not be the single vital crossroads through which early humans passed on their way to colonising the whole Eurasian landmass. If so, the story of our spread out of Africa may need to be rewritten. Instead of colonising the Levant then moving into Europe, our distant ancestors may have first settled in the central Asian steppes before turning west again.

'Since the 1930s, many prehistorians have believed the Levant was a major strategic point for people moving from Africa into the Middle East and Europe,' says Dr Katerina Douka of the University of Oxford, who led the research. 'It sounds a straightforward and obvious idea, but these early humans didn't necessarily follow the maps of today.' She adds that the region has received comparatively little attention from archaeologists, so theories tend to rest on a very small base of evidence - the Near East is the least-dated area of the Palaeolithic world. On top of this, the region's hot dry conditions make scientific archaeology difficult - for example, the climate tends to destroy the collagen on which radiocarbon dating of bones depends.

One of the most important sites in the region is Ksar Akil in modern-day Lebanon. Here, several fragments of ancient humans have been found over the years, crucially including a small part of a fossilised human known as Ethelruda, and another buried individual, whom archaeologists call Egbert. These have generally been seen as supporting the broader narrative of humans moving through the Near East into Asia and Europe. But until now, researchers hadn't used radiocarbon dating to check how long ago these people lived. The authors of a new study, published in PLoS ONE, set out to remedy that.

They used modern carbon-dating techniques on material found in the same archaeological layers as Egbert and Ethelruda at Ksar Akil - mostly beads made from sea shells, which were used as jewellery and are often considered a sign of complex symbolic behaviour akin to modern humans. They couldn't radiocarbon-date the remains themselves - for one thing, both went missing in the twentieth century, although part of Ethelruda's jawbone recently turned up again. For another, the collagen in the bones has degraded too far to be used in dating.



Comparison of the modelled ages obtained for Egbert and Ethelruda by the authors of the recent study with age estimates of anatomically-modern humans from other Palaeolithic sites between 50,000-30,000 years ago.

Analysis of the results shows the remains are considerably younger than archaeologists had assumed - between 40.8 and 39.2 thousand years ago for Egbert and between 42.4 and 41.7 thousand for Ethelruda. This means Egbert is about the same age as the oldest directly-dated human found in Europe, at the Pestera cu Oase in Romania, and younger than the oldest modern human teeth, found at Cavallo in Italy.

Douka says more research is needed on other possible routes by which humans could have dispersed into Europe and Asia. She's currently working on several projects in central Asia and Siberia - areas she thinks could form part of one such route.

'The traditional view is around the start of the Upper Palaeolithic, there was a movement out of Africa, through the Levant and into Europe,' she explains. 'But if you look further East, there's evidence for much earlier colonisation - sites that we can date as older than 50,000 years, which is the limit of how far back we can go with radiocarbon dating. My own view is that modern humans had probably already populated central Asia and modern-day Russia before colonising Europe in one or more waves of expansion.'

She's working on a European Research Council-funded project (PalaeoChron) that uses another technique, known as optically-stimulated luminescence dating, which can go much further back into history - around half a million years.

The radiocarbon dating work took place at the Oxford Radiocarbon Accelerator Unit; NERC provided financial support.

http://www.sciencedaily.com/releases/2014/01/140128153857.htm

Early rehabilitation important for recovery after severe traumatic brain injury

Early rehabilitation interventions seem to be essential for how well a patient recovers after a severe brain injury.

It might even increase the chances for long-term survival, according to researchers at the Sahlgrenska Academy. In a series of studies, Trandur Ulfarsson, doctoral student at the Sahlgrenska Academy, University of Gothenburg, has explored the long-term effects of traumatic brain injuries caused for example by accidents or violence. The studies, where 280 Swedish and Icelandic participants were followed up 1-11 years after the injury, show a clear association between how quickly patients get access to rehabilitation and how well they recover.

Functional activity improved

'We found that the functional activity -- for example how independent the patients are in their daily activities and how fast they can return to work -- is substantially improved among those who are admitted to inpatient rehabilitation care early,' says Ulfarsson, who presents the results in his doctoral thesis.

The studies also show that severe brain injury often leads to an impaired pituitary function, most often lack of growth hormone, which in turn may cause obesity.

Being unemployed or on sick leave prior to the injury also seems to be associated with worse functional activities performance and quality of life several years after the injury.

Higher risk of dying

Moreover, the Gothenburg studies show that men who suffer a severe traumatic brain injury have a five times higher risk of dying 10 years after the injury; for women, the risk is eight times higher. These results confirm a recent study from Karolinska Institutet. The increased risk can be attributed to illnesses and disabilities lingering on for several years after the injury. 'The participants reported lasting disability, and low quality of life, with a complex range of physical, cognitive, behavioral and emotional disturbance'.

Important information

Ulfarsson says that the studies provide important information for brain injury victims, their families and friends, and the healthcare sector. 'One conclusion is that a severe traumatic brain injury should be considered a chronic medical condition that requires professional care and support for a very long time. Our studies provide valuable information that will help us improve outcome predictions, optimize the rehabilitation process and evaluate treatment effects for these patients,' he says.

According to Ulfarsson, concrete factors that could increase long-term survival include admission to rehabilitation support at the right time, special interventions for patients who were unemployed or on sick leave prior to the injury, and assessment of pituitary function in overweight patients.

http://www.eurekalert.org/pub_releases/2014-01/uow-nle012914.php

Neanderthal lineages excavated from modern human genomes

A fossil-free method of sequencing archaic DNA may provide insight into human evolution

A substantial fraction of the Neanderthal genome persists in modern human populations. A new approach applied to analyzing whole-genome sequencing data from 665 people from Europe and East Asia shows that more than 20 percent of the Neanderthal genome survives in the DNA of this contemporary group, whose genetic information is part of the 1,000 Genomes Project.

Previous research proposes that someone of non-African descent may have inherited approximately 1 percent to 3 percent of his or her genome from Neanderthal ancestors. These archaic DNA sequences can vary from one person to another and were aggregated in the present study to determine the extent of the Neanderthal genome remaining in the study group as a whole. The findings are a start to identifying the location of specific pieces of Neanderthal DNA in modern humans and a beginning to creating a collection of Neanderthal lineages surviving in present-day human populations.

University of Washington scientists Benjamin Vernot and Joshua M. Akey, both population geneticists from the Department of Genome Sciences, report their results Jan. 29 in Science Express. Vernot is a graduate student and Akey is an associate professor. Their paper is titled, "Resurrecting Surviving Neanderthal Lineages from Modern Human Genomes."

To check the accuracy of their approach, Vernot ran their analysis before comparing the suspected Neanderthal sequences they found in modern humans to the recently mapped Neanderthal genome obtained from DNA recovered from bone. This genome came from the paleogenetics laboratory of Svante Paabo of the Max Planck Institute for Evolutionary Anthropology in Germany. "We wanted to know how well our predictions matched the Neanderthal reference genome," Akey said. "The analysis showed that, after more refinement of these methods, scientists might not need a reference genome from an archaic species to do this type of study."

The results suggest that significant amounts of population-level DNA sequences might be obtained from extinct groups even in the absence of fossilized remains, because these ancient sequences might have been inherited by other individuals from whom scientists can gather genomic data, according to Akey. Therein lies the potential to discover and characterize previously unknown archaic humans that bred with early humans.

"In the future, I think scientists will be able to identify DNA from other extinct hominin, just by analyzing modern human genomes," Vernot said. "From our end, this was an entirely computational project," he added, "I think it's really interesting how careful application of the correct statistical and computational tools can uncover important aspects of health, biology and human history. Of course, you need good data, too."

Neanderthals became extinct about 30,000 years ago. Their time on the earth, and some of their geographic range, overlapped with humans who anatomically resembled us. The two closely related groups mated and produced some fertile offspring, such that portions of Neanderthal DNA were passed along to the next generations. In a proposed model, this mixing of DNA could have occurred both before and after the evolutionary divergence of non-African modern humans from a common ancestral population.

It didn't necessarily take a lot of individual hybrid offspring to introduce Neanderthal genes into early human populations. Still, Akey said that it isn't known how many Neanderthal ancestors present-day humans have.

But past interactions between the groups, Akey noted, is probably more complicated than previously thought. "In addition, the analysis of surviving archaic lineages points to the possibility that there were fitness costs to the hybridization of Neanderthal and humans," Akey said.
"I think what was most surprising to me," Vernot noted, "is that we found evidence of selection. Last year, I would have bet that a Neanderthal/human hybrid would have been as fit as a fully modern human. This was mostly because we haven't been separated from them that long, on an evolutionary scale."
Nevertheless, the Neanderthals were also a probable source for at least a few genetic variations that were adaptive for their human descendants. Neanderthal DNA sequences are found in regions of the genome that have been linked to the regulation of skin pigmentation. The acquisition of these variants by mating with the Neanderthals may have proven to be a rapid way for humans to adapt to local conditions.
"We found evidence that Neanderthal skin genes made Europeans and East Asians more evolutionarily fit," Vernot said, "and that other Neanderthal genes were apparently incompatible with the rest of the modern human genome, and thus did not survive to present day human populations."
The researchers observed that certain chromosomes arms in humans are tellingly devoid of Neanderthal DNA sequences, perhaps due to mismatches between the two species along certain portions of their genetic materials. For example, they noticed a strong depletion of Neanderthal DNA in a region of human genomes that contains a gene for a factor thought to play an important role in human speech and language.
According to the scientists, the "fossil free" method of sequencing archaic genomes not only holds promise in revealing aspects of the evolution of now-extinct archaic humans and their characteristic population genetics, it also might provide insights into how interbreeding influenced current patterns of human diversity. Additionally, such studies might also help researchers hone in on genetic changes not found in any other species, and learn if these changes helped endow early people with uniquely human attributes.

http://www.eurekalert.org/pub_releases/2014-01/hhmi-wpc012914.php

When populations collide

The genomic landscape of Neanderthal ancestry in present-day humans

More than thirty thousand years ago, Homo sapiens migrating out of Africa began encountering Neanderthals, a lineage that had diverged from modern humans hundreds of thousands of years before. Despite their differences, Homo sapiens and Neanderthals mingled, and over time, produced children with genes from both lineages. Today, the biological remnants of that collision between two distinct populations remain alive in the genomes of humans with European and Asian ancestry.
Now, Howard Hughes Medical Institute (HHMI) researchers at Harvard Medical School have analyzed exactly which areas of the human genome retain segments of Neanderthal DNA, passed down throughout the generations. The findings were published January 29, 2014 in Nature.
"The goal was to understand the biological impact of the gene flow between Neanderthals and modern humans," says David Reich, an HHMI investigator at Harvard Medical School and the lead scientist on the new research. "We reasoned that when these two groups met and mixed, some new traits would have been selected for and remained in the human genome, while some incompatibilities would have been selected against and removed."
Reich has been interested in what happens when populations collide. "Throughout history, groups of humans have been on the move. Until recently, researchers did not have the ability to learn much about what happened when two populations met each other, and in particular whether they mixed or one replaced the other," Reich says. What really happens, he argues, is that populations mix, and that later people carry DNA from both ancestral groups.
In late 2013, Reich was one of the leaders of a team that published the complete genome of a Neanderthal woman, based on analysis of DNA isolated from a toe bone discovered in modern-day Siberia. To determine how the human-Neanderthal genetic mixing may have played out, Reich and his colleagues compared that completed Neanderthal genome with the genomes of 1,004 present-day humans from around the globe.
"If a gene variant is absent in Africans today, but present in modern day non-Africans as well as the Neanderthal genome, that's good evidence that it originates from Neanderthals," Reich says. Since humans met Neanderthals as they migrated out of Africa, those populations that remained in Africa had little contact or genetic mixing with Neanderthals. Reich's group also leveraged other genetic information, including the size of different gene fragments, to determine whether genes were inherited from Neanderthals or not.
The researchers found that today, humans in east Asia have, on average, more of their genome originating from Neanderthals than Europeans, and modern-day Africans have little or none. Those findings confirmed previous studies. But then, the scientists took their analysis a step further and examined which genes most often have

Neanderthal ancestry in present-day people. They found that some genes had variants of Neanderthal origin in more than sixty percent of Europeans or Asians, while other genes were never of Neanderthal heritage.
The scientists discovered that the genetic changes most often inherited from Neanderthals were disproportionately in genes related to keratin, a component of skin and hair.
"This suggests that as humans were adapting to the non-African environment they were moving into, they may have been able to exploit adaptations that Neanderthals had already achieved," Reich says. More work is needed, however, to show the exact biological implications of the Neanderthal keratin genes and how they differ from the versions of keratin related proteins that would have already been present in modern humans.
His group analyzed not only which Neanderthal genes remain in the human population today, but also which parts of today's genomes lack Neanderthal genes altogether.
"The most interesting findings were about the places in the genome that are devoid of Neanderthal genes – 'Neanderthal ancestry deserts'," says Reich. "At these locations, Neanderthal genetic material was not tolerated by modern humans and removed by the action of natural selection."
The most striking area of the human genome that lacked Neanderthal genes was the X chromosome—one of the sex chromosomes. In humans, women have two X chromosomes and men have an X and a Y chromosome. The team's observation that the X chromosome had very little Neanderthal ancestry suggested something the scientists hadn't predicted -- a biological phenomenon called hybrid sterility. When two organisms are distantly related, Reich explains, genes related to fertility, inherited on the X chromosome, can interact poorly with genes elsewhere in the genome. The interference between the pairs of genes can render males—who only have one X chromosome—infertile.
"When you have populations that have sufficiently diverged, this male-only sterility can occur," Reich says.
To confirm whether hybrid sterility could have occurred during the interbreeding between modern humans and Neanderthals, Reich's team looked at whether genes expressed in the testes were more or less enriched in Neanderthal DNA. Indeed, genes important for the functioning of the testes had a particularly low inheritance of Neanderthal ancestry. The combined evidence that both the testes and the X chromosome lack Neanderthal DNA, Reich says, suggests that modern human males who inherited a Neanderthal X chromosome often may have been unable to have children, and therefore pass along this X chromosome. Today, that translates into a near- absence of Neanderthal DNA on the X chromosomes of humans.
"It tells us that when Neanderthals and modern humans met and mixed, they were at the very edge of being biological compatible," he says.
Further studies on the legacy of Neanderthal genes in human biology could help shed light on not only human history, but the overall biological idea of hybrid sterility.
"The other direction we want to go is to use this information as a tool for understanding human disease genes," Reich adds. Already, the new study revealed that genetic changes that affect risk for lupus, diabetes, and Crohn's Disease likely originate from Neanderthals.

http://www.eurekalert.org/pub_releases/2014-01/miot-am012914.php

'Rogue' asteroids may be the norm

Rogue asteroids are actually more common than previously thought

Written by Jennifer Chu, MIT News Office

CAMBRIDGE, MA -- To get an idea of how the early solar system may have formed, scientists often look to asteroids. These relics of rock and dust represent what today's planets may have been before they differentiated into bodies of core, mantle, and crust.
In the 1980s, scientists' view of the solar system's asteroids was essentially static: Asteroids that formed near the sun remained near the sun; those that formed farther out stayed on the outskirts. But in the last decade, astronomers have detected asteroids with compositions unexpected for their locations in space: Those that looked like they formed in warmer environments were found further out in the solar system, and vice versa. Scientists considered these objects to be anomalous "rogue" asteroids.
But now, a new map developed by researchers from MIT and the Paris Observatory charts the size, composition, and location of more than 100,000 asteroids throughout the solar system, and shows that rogue asteroids are actually more common than previously thought. Particularly in the solar system's main asteroid belt — between Mars and Jupiter — the researchers found a compositionally diverse mix of asteroids.
The new asteroid map suggests that the early solar system may have undergone dramatic changes before the planets assumed their current alignment. For instance, Jupiter may have drifted closer to the sun, dragging with it a host of asteroids that originally formed in the colder edges of the solar system, before moving back out to its current position. Jupiter's migration may have simultaneously knocked around more close-in asteroids, scattering them outward.

"It's like Jupiter bowled a strike through the asteroid belt," says Francesca DeMeo, who did much of the mapping as a postdoc in MIT's Department of Earth, Atmospheric and Planetary Sciences. "Everything that was there moves, so you have this melting pot of material coming from all over the solar system."
DeMeo says the new map will help theorists flesh out such theories of how the solar system evolved early in its history. She and Benoit Carry of the Paris Observatory have published details of the map in Nature.

From a trickle to a river

To create a comprehensive asteroid map, the researchers first analyzed data from the Sloan Digital Sky Survey, which uses a large telescope in New Mexico to take in spectral images of hundreds of thousands of galaxies. Included in the survey is data from more than 100,000 asteroids in the solar system. DeMeo grouped these asteroids by size, location, and composition. She defined this last category by asteroids' origins — whether in a warmer or colder environment — a characteristic that can be determined by whether an asteroid's surface is more reflective at redder or bluer wavelengths.
The team then had to account for any observational biases. While the survey includes more than 100,000 asteroids, these are the brightest such objects in the sky. Asteroids that are smaller and less reflective are much harder to pick out, meaning that an asteroid map based on observations may unintentionally leave out an entire population of asteroids.
To avoid any bias in their mapping, the researchers determined that the survey most likely includes every asteroid down to a diameter of five kilometers. At this size limit, they were able to produce an accurate picture of the asteroid belt. The researchers grouped the asteroids by size and composition, and mapped them into distinct regions of the solar system where the asteroids were observed.
From their map, they observed that for larger asteroids, the traditional pattern holds true: The further one gets from the sun, the colder the asteroids appear. But for smaller asteroids, this trend seems to break down. Those that look to have formed in warmer environments can be found not just close to the sun, but throughout the solar system — and asteroids that resemble colder bodies beyond Jupiter can also be found in the inner asteroid belt, closer to Mars.
As the team writes in its paper, "the trickle of asteroids discovered in unexpected locations has turned into a river. We now see that all asteroid types exist in every region of the main belt."

A shifting solar system

The compositional diversity seen in this new asteroid map may add weight to a theory of planetary migration called the Grand Tack model. This model lays out a scenario in which Jupiter, within the first few million years of the solar system's creation, migrated as close to the sun as Mars is today. During its migration, Jupiter may have moved right through the asteroid belt, scattering its contents and repopulating it with asteroids from both the inner and outer solar system before moving back out to its current position — a picture that is very different from the traditional, static view of a solar system that formed and stayed essentially in place for the past 4.5 billion years.
"That [theory] has been completely turned on its head," DeMeo says. "Today we think the absolute opposite: Everything's been moved around a lot and the solar system has been very dynamic."
DeMeo adds that the early pinballing of asteroids around the solar system may have had big impacts - literally - on Earth. For instance, colder asteroids that formed further out likely contained ice. When they were brought closer in by planetary migrations, they may have collided with Earth, leaving remnants of ice that eventually melted into water. "The story of what the asteroid belt is telling us also relates to how Earth developed water, and how it stayed in this Goldilocks region of habitability today," DeMeo says.

http://www.eurekalert.org/pub_releases/2014-01/hfhs-soc012914.php

Study: Oropharyngeal cancer on the rise in young adults

A new study reveals an alarming increase in oropharyngeal cancers among young adults.

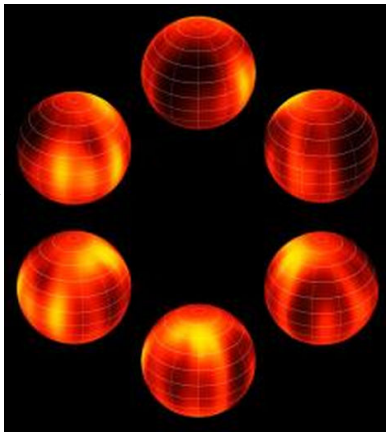
DETROIT - While the exact cause for this phenomenon is unknown, the human papillomavirus (HPV) may be to blame. According to researchers from Henry Ford Hospital in Detroit there was an overall 60 percent increase from 1973 and 2009 in cancers of the base of tongue, tonsils, soft palate and pharynx in people younger than age 45. Among Caucasians, there was a 113 percent increase, while among African-Americans the rate of these cancers declined by 52 percent during that period of time.
But compared to Caucasians and other races, the five-year survival rate remains worse for African Americans. The study is published online ahead of print in Otolaryngology-Head and Neck Surgery, the official journal of American Academy of Otolaryngology-Head and Neck Surgery.
"The growing incidence in oropharyngeal cancer has been largely attributed to the sexual revolution of the 1960s and 1970s, which led to an increased transmission of high-risk HPV," says study lead author Farzan

Siddiqui, M.D., Ph.D., director of the Head & Neck Radiation Therapy Program in the Department of Radiation Oncology at Henry Ford Hospital.
"We were interested in looking at people born during that time period and incidence of oropharyngeal cancer. Not only were we surprised to find a substantial increase in young adults with cancer of the tonsils and base of tongue, but also a wide deviation among Caucasians and African Americans with this cancer."
The American Cancer Society estimates about 36,000 people in the U.S. will get oral cavity and oropharyngeal cancers in 2013; an estimated 6,850 people will die of these cancers. Oropharyngeal cancers are more than twice as common in men as in women, and about equally common in African Americans and Caucasians.
Recent medical research has shown that HPV exposure and infection increases the risk of oropharyngeal squamous cell cancer independently of tobacco and alcohol use, two other important risk factors for the disease, according to the National Cancer Institute.
The incidence of oropharyngeal cancer has been growing in recent years due to increasing rates of HPV infection. This has been largely attributed to changes in sexual practices. Studies have shown, however, patients with HPV related head and neck cancer do have a better prognosis and survival.
For the Henry Ford study, Dr. Siddiqui and his colleagues used the SEER (Surveillance Epidemiology and End Results) database to gather information about adults younger than age 45 who had been diagnosed with invasive squamous cell oropharyngeal cancer between1973 and 2009. Since SEER does not record HPV information, the researchers used tumor grade as a surrogate indicator of HPV infection. Among the study group of more than 1,600 patients, 90 percent were ages 36-44 and the majority (73 percent) was Caucasian.
During the 36-year period, the majority of patients (50-65 percent) underwent surgical resection for their tumors. Patients who had both surgery and radiation therapy had the highest five-year survival rate.
"These patients have a favorable prognosis and are likely to live longer while dealing with treatment related side-effects that may impact their quality of life," notes Dr. Siddiqui.
The five-year survival for the study group was 54 percent. There was no difference in survival based on gender. African Americans, however, had significantly poor survival compared to other races. "The predominance of oropharyngeal cancer in this age group suggests either non-sexual modes of HPV transfer at a younger age or a shortened latency period between infection and development of cancer," says Dr. Siddiqui.
Along with Dr. Siddiqui, Henry Ford study co-authors are Omar H. Gayar, M.D.; Tamer Ghanem, M.D., Ph.D.; Francis Hall, M.D., and Mohamed Elshaikh, M.D.; along with Michele Cote, Ph.D., from Wayne State University, and Julie Ruterbusch from Karmanos Cancer Institute. Research funding: Henry Ford Hospital

http://www.eurekalert.org/pub_releases/2014-01/e-fwm012714.php

First weather map of brown dwarf

ESO's Very Large Telescope charts surface of nearest brown dwarf



ESO's Very Large Telescope has been used to create the first ever map of the weather on the surface of the nearest brown dwarf to Earth.
An international team has made a chart of the dark and light features on WISE J104915.57-531906.1B, which is informally known as Luhman 16B and is one of two recently discovered brown dwarfs forming a pair only six light-years from the Sun. The new results are being published in the 30 January 2014 issue of the journal Nature.
Brown dwarfs fill the gap between giant gas planets, such as Jupiter and Saturn, and faint cool stars. They do not contain enough mass to initiate nuclear fusion in their cores and can only glow feebly at infrared wavelengths of light. The first confirmed brown dwarf was only found twenty years ago and only a few hundred of these elusive objects are known.

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The closest brown dwarfs to the Solar System form a pair called Luhman 16AB [1] that lies just six light-years from Earth in the southern constellation of Vela (The Sail).
This pair is the third closest system to the Earth, after Alpha Centauri and Barnard's Star, but it was only discovered in early 2013. The fainter component, Luhman 16B, had already been found to be changing slightly in brightness every few hours as it rotated -- a clue that it might have marked surface features.

Now astronomers have used the power of ESO's Very Large Telescope (VLT) not just to image these brown dwarfs, but to map out dark and light features on the surface of Luhman 16B.
Ian Crossfield (Max Planck Institute for Astronomy, Heidelberg, Germany), the lead author of the new paper, sums up the results: "Previous observations suggested that brown dwarfs might have mottled surfaces, but now we can actually map them. Soon, we will be able to watch cloud patterns form, evolve, and dissipate on this brown dwarf -- eventually, exometeorologists may be able to predict whether a visitor to Luhman 16B could expect clear or cloudy skies."
To map the surface the astronomers used a clever technique. They observed the brown dwarfs using the CRIRES instrument on the VLT. This allowed them not just to see the changing brightness as Luhman 16B rotated, but also to see whether dark and light features were moving away from, or towards the observer. By combining all this information they could recreate a map of the dark and light patches of the surface.
The atmospheres of brown dwarfs are very similar to those of hot gas giant exoplanets, so by studying comparatively easy-to-observe brown dwarfs [2] astronomers can also learn more about the atmospheres of young, giant planets -- many of which will be found in the near future with the new SPHERE instrument that will be installed on the VLT in 2014.
Crossfield ends on a personal note: "Our brown dwarf map helps bring us one step closer to the goal of understanding weather patterns in other solar systems. From an early age I was brought up to appreciate the beauty and utility of maps. It's exciting that we're starting to map objects out beyond the Solar System!"
[1] This pair was discovered by the American astronomer Kevin Luhman on images from the WISE infrared survey satellite. It is formally known as WISE J104915.57-531906.1, but a shorter form was suggested as being much more convenient. As Luhman had already discovered fifteen double stars the name Luhman 16 was adopted. Following the usual conventions for naming double stars, Luhman 16A is the brighter of the two components, the secondary is named Luhman 16B and the pair is referred to as Luhman 16AB.
[2] Hot Jupiter exoplanets lie very close to their parent stars, which are much brighter. This makes it almost impossible to observe the faint glow from the planet, which is swamped by starlight. But in the case of brown dwarfs there is nothing to overwhelm the dim glow from the object itself, so it is much easier to make sensitive measurements.
This research was presented in a paper, "A Global Cloud Map of the Nearest Known Brown Dwarf", by Ian Crossfield et al. to appear in the journal Nature.

http://www.bbc.co.uk/news/uk-england-london-25862541

Joseph Lister's unknown operation uncovered

Fortuitous guess leads to archival record of his first surgery

By Beth Rose BBC News

A woman was stabbed in the early hours of Friday 27 June by her drunk husband in the streets of London. The year was 1851 and Jeremiah Sullivan, 59, had invited his wife Julia, a mother of eight, for a drink after she had moved to Camden Town to escape his violence. She was cautious, inviting a friend along and remaining sober as Sullivan had been overheard making threats against her life. As they walked along, Sullivan turned on her, lunging forward and stabbing her in the lower abdomen with a knife he had concealed up his sleeve.
Mrs Sullivan was bleeding heavily and is said to have told a policeman "my entrails are coming out".
She was taken to hospital on Gower Street and handed over to the doctor on duty.
That night that doctor was Joseph Lister, who would later go down in history for pioneering antiseptic surgery. But at that time he was a second-year medical student at University College London (UCL).
Using new internet databases and by trawling conventional archives, this previously-unknown operation was discovered by medical historian Dr Ruth Richardson who is connected to King's College London (KCL) and Lancaster-based orthopaedic surgeon Bryan Rhodes, who had both been researching Lister's career and had met at a conference at KCL.
"I was working on something else, and I don't know what made me do it but I looked him up on the Old Bailey online and this case came up," said Dr Richardson. "I mentioned it to Bryan Rhodes and I said to him, 'Is this unusual?', and his eyebrows went right up and he said, 'This is very unusual'. "The find was a fortuitous guess."
There is much written about Lister, mainly about his work on antiseptic surgery and his use of carbolic acid to sterilise surgical instruments and clean wounds, but less is known about his early career because the records have been lost.
What is known is that Lister enrolled as an arts student at UCL in 1844 at the age of 17, before turning to medicine as a graduate three years later. After a dangerous attack of smallpox and a nervous breakdown he took time out before returning to medicine in 1849 and took up the position of house surgeon under John Erichsen in 1851.

'Used common sense'

It was previously assumed he had started carrying out surgery much later in his career and none of his biographers seem to have known about this landmark operation.

On that night in June 1851, Lister, faced with Mrs Sullivan's dangerous injury, set about using a mixture of old and new techniques to clean the intestines with blood-warm water, before placing them back into the body.

He then put Mrs Sullivan on a strict diet, which included taking opium to make her constipated, in an attempt to give her intestine time to recover.

Dr Richardson said: "Erichsen was the consultant on call, but it would have taken him time to the get to the hospital. "The woman's bowels were hanging out and he decided to go for it. "Most patients with such a serious injury would have died, but Lister went at it with a mixture of ways he had read and using his own common sense and it worked."

Two months later Lister found himself at the centre of a trial at the Old Bailey giving evidence alongside Mrs Sullivan. Sullivan was tried for "feloniously stabbing, cutting, and wounding Julia Sullivan with intent to murder, disable or grievously harm her".

Giving evidence, Lister told the court: "I found a coil of intestine about eight inches across, comprehending, perhaps, about a yard of the small intestines, protruding from the lower part of the abdomen... no doubt all was done by one instrument and one stroke."

He added: "The injury she had received was excessively dangerous - she is now perfectly recovered."

Sullivan was found guilty of causing grievous bodily harm and sentenced to transportation for 20 years.

Lister's quick thinking not only saved his patient from death, but also her attacker from the gallows.

Using the online archives of The Lancet, Mr Rhodes and Dr Richardson found confirmation of Lister's early success with two articles relating to Mrs Sullivan whose recovery was attributable to Lister's "skill and judgement".

Mr Rhodes said: "He's one of my surgical heroes, but it's even more heroic in a way that he came back from his nervous breakdown, smallpox at a time when it was a killer, and then became a star medical student. "He became a house surgeon earlier than usual - it's like working as a doctor before you've actually qualified. Nowadays that would never happen."

Both historians consider the discovery of Lister's early operation as "fortuitous", but Lister may also have had some luck on his side. He probably witnessed hernia cases when he was on the wards that involved returning protrusions of the bowel, and he may also have read up on the subject after The Lancet announced in 1851 the topic for the Fothergillian Gold Medal was Wounds and Injuries of the Abdomen and their Treatment.

GJ Guthrie's lecture on Wounds and Injuries of the Abdomen had also been reprinted in The Lancet only a few weeks before the attack on Mrs Sullivan, but nonetheless it is considered a remarkable achievement for a surgical student.

Dr Richardson said: "Our discovery was fortuitous, a kind of conglomeration of old fashioned plodding documentary history and new internet databases - it's wonderful."

http://www.bbc.co.uk/news/health-25917270

Stem cell 'major discovery' claimed

Stem cell researchers are heralding a "major scientific discovery", with the potential to start a new age of personalised medicine.

By James Gallagher Health and science reporter, BBC News

Scientists in Japan showed stem cells can now be made quickly just by dipping blood cells into acid.

Stem cells can transform into any tissue and are already being trialled for healing the eye, heart and brain.

The latest development, published in the journal Nature, could make the technology cheaper, faster and safer.

The human body is built of cells with a specific role - nerve cells, liver cells, muscle cells - and that role is fixed.

However, stem cells can become any other type of cell, and they have become a major field of research in medicine for their potential to regenerate the body.

Embryos are one, ethically charged, source of stem cells. Nobel prize winning research also showed that skin cells could be "genetically reprogrammed" to become stem cells (termed induced pluripotent stem cells).

Acid bath

Now a study shows that shocking blood cells with acid could also trigger the transformation into stem cells - this time termed STAP (stimulus-triggered acquisition of pluripotency) cells. Dr Haruko Obokata, from the Riken Centre for Developmental Biology in Japan, said she was "really surprised" that cells could respond to their environment in this way. She added: "It's exciting to think about the new possibilities these findings offer us, not only in regenerative medicine, but cancer as well." The breakthrough was achieved in mouse blood cells, but research is now taking place to achieve the same results with human blood.

Chris Mason, professor of regenerative medicine at University College London, said if it also works in humans then "the age of personalised medicine would have finally arrived." He told the BBC: "I thought - 'my God that's a game changer!' It's a very exciting, but surprise, finding. "It looks a bit too good to be true, but the number of experts who have reviewed and checked this, I'm sure that it is. "If this works in people as well as it does in mice, it looks faster, cheaper and possibly safer than other cell reprogramming technologies - personalised reprogrammed cell therapies may now be viable."
For age-related macular degeneration, which causes sight loss, it takes 10 months to go from a patient's skin sample to a therapy that could be injected into their eye -and at huge cost. Prof Mason said weeks could be knocked off that time which would save money, as would cheaper components.

'Revolutionary'

The finding has been described as "remarkable" by the Medical Research Council's Prof Robin Lovell-Badge and as "a major scientific discovery" by Dr Dusko Ilic, a reader in stem cell science at Kings College London. Dr Ilic added: "The approach is indeed revolutionary. "It will make a fundamental change in how scientists perceive the interplay of environment and genome."
But he added: "It does not bring stem cell-based therapy closer. We will need to use the same precautions for the cells generated in this way as for the cells isolated from embryos or reprogrammed with a standard method."
And Prof Lovell-Badge said: "It is going to be a while before the nature of these cells are understood, and whether they might prove to be useful for developing therapies, but the really intriguing thing to discover will be the mechanism underlying how a low pH shock triggers reprogramming - and why it does not happen when we eat lemon or vinegar or drink cola?"

http://bit.ly/1aS6Znm

Why I'm sure human stem cell trial will be safe

The new kind of stem cell announced yesterday may be the future of regenerative medicine, but Masayo Takahashi's pilot safety study using a type of stem cell to treat age-related blindness is at the cutting edge

16:07 30 January 2014 by **Natasha Little**, Kobe, Japan

Later this year, you will make history when you begin the first ever human trial of induced pluripotent stem cells. Why is this such a big deal?

Stem cells have enormous medical potential because they can become any other type of cell. If we can use them to replace old or damaged cells, this could have huge implications for treating degenerative diseases.
Stem cells can be harvested from embryos, but this is ethically controversial. Despite this, there are several trials of these embryonic stem cells under way. Their use often requires drugs to stop the immune system from rejecting them, which can cause complications for elderly patients. Induced pluripotent stem (iPS) cells offer an alternative. These are made from a patient's own cells, removing the need for the immunosuppressant drugs. Plus there are no ethical issues.

How would treatment with iPS cells work?

iPS cells are made by injecting several "reprogramming" genes into adult cells that have been removed from the body. This makes them rewind to an embryonic state. Then, we can make iPS cells differentiate into the cell type we need by injecting proteins that instruct embryonic stem cells to become liver, retina or any other type of cell. The idea is that these reprogrammed cells can then be inserted in the body to replace damaged cells. We are at least 20 years from any clinical treatments, but the potential is exciting.

Are there any potential pitfalls with iPS cell treatments?

Yes, we have to be very careful because iPS cells multiply endlessly. This means that if any undifferentiated iPS cells were accidentally put into someone, they could cause tumours. That's why this study is so important. It is not a clinical trial, but a six-subject pilot study to confirm the safety of putting cells derived from iPS cells into humans.

Who are the participants in the study?

The six people all have age-related macular degeneration in their eyes. This weakens the vision in the central field, eventually leaving people with only peripheral vision. In the type of degeneration we are working with, this is caused by the deterioration of the retinal pigment epithelium (RPE) – the layer of cells that clears away extra-cellular debris that lands on the retina.
We aim to replace the damaged section of the RPE with cells created from skin taken from the patient's arm. The skin cells will be reprogrammed into iPS cells and then differentiated into RPE cells. It will take a year to grow enough RPE cells to introduce them to a damaged eye. Although I am excited to see if there is any improvement in sight, this study aims only to demonstrate the safety of RPE cells derived from IPS cells.

How confident are you that the pilot will be a success?

Very confident. We have trialled this intervention on mice, rats and monkeys, and observed no tumours. I chose

to work with RPE cells because of their characteristic brown pigment. This means we can avoid injecting tumour-causing iPS cells by selecting only the clumps of pure brown RPE cells. Of course, we do have to pick out around 50,000 RPE cells, so it can be a bit tough.
Another reason for optimism is that the retina is the safest place to try this out because we can watch the cells closely through the participant's dilated pupil.

What does the future hold for IPS cells?

Right now it takes a lot of time, money and labour to reprogram cells. In our study, each intervention costs 20 million yen ($200,000) per eye and will take 10 people a year to complete. However, my research uses "auto-transplantation", in which the iPS cells come from the patient. The possibility of "allogeneic" treatment, in which iPS cells from one person could be used in many people, could reduce the cost tenfold. Shinya Yamanaka [who won a Nobel prize in 2012 with John Gurdon, for discovering iPS cells] plans to create an iPS cell bank to store a number of genetically average iPS cell cultures – those that most easily integrate into people without immuno-rejection.
The greatest barrier to iPS cells being used to treat diseases of other organs is the difficulty of growing large quantities of cells. The retina only needs one dish of cells. To replace part of the liver or hip would require thousands of times as many.
However, there is no doubt this is a very exciting area with huge potential. My husband, Jun Takahashi, is planning on carrying out a safety trial of a treatment for Parkinson's disease based on IPS cells in two years time. I don't know if he can do it, but he says he can.

How important is the discovery announced this week that any adult cell can be rapidly reprogrammed just by putting it in a bath of acid?

The work is very exciting and will change many aspects of regenerative medicine in the future. I am looking forward to seeing where Haruku Obokata's [who carried out the work] research leads. I feel joyful that we are both working in this wonderful area of science.

Profile

Masayo Takahashi is at the Riken Center for Developmental Biology in Kobe, Japan, where she heads the Laboratory for Retinal Regeneration

http://www.bbc.co.uk/news/education-25947072

Catching the mother of all bed bugs

The ability of bed bugs to return so quickly after human attempts to get rid of them has been explained by University of Sheffield researchers.

By Sean Coughlan BBC News education correspondent

Genetic analysis has shown that a single pregnant bed bug that escapes detection can be responsible for an entire infestation, rapidly producing generations of offspring. It could create a colony of thousands of bed bugs, feeding on a single human. The study was based on London, which has seen a resurgence in bed bugs.
A DNA study showed that colonies of bed bugs in a house or hotel could all come from a common ancestor or a handful of female bed bugs.
The rapid expansion in numbers could take place over a matter of weeks - at which point there is usually human intervention to destroy the bugs.

Itch to travel

Bed bugs, which live on human blood, cannot fly and depend on their human carriers for travelling any distance.
There has been a rise in bed bug numbers and researchers wanted to know how they could suddenly appear in such large numbers after apparently being removed.
Researchers say bed bugs' ability to generate a new colony from such small numbers might be a "clue to their recent success". If a single pregnant bed bug manages to hide away, getting into a traveller's luggage for example, it is enough to begin a new infestation. Adult bed bugs can grow to about 5mm in length.
Prof Roger Butlin said bed bugs had almost disappeared from London by the middle of the 20th Century, but their numbers had risen since the 1980s.
Among the theories about the increase has been that they have followed transport routes and international travellers. They are also believed to have grown more resistant to chemicals used to get rid of them.
"The number of bed bugs in cities has risen dramatically, but there's no solid information why that is," said Prof Butlin, from Sheffield University's department of animal and plant sciences.
He added bed bugs could survive without feeding for a month, waiting for a human to arrive.
A property could have tens of thousands of bugs, he said, all trying to live on the human residents.
"If you just miss one, they can grow very quickly," he added.

http://bit.ly/1aSigEj

More harm than good? Antioxidants defend cancer in body

They may be marketed as a way to protect yourself against disease, but antioxidant supplements are increasingly thought of as more foe than friend.

20:18 29 January 2014 by Andy Coghlan

We now have an idea why: antioxidants may protect healthy cells from DNA damage but they also protect cancer cells from our bodies' defences.

Antioxidants are chemicals such as beta-carotene and vitamins C and E, which mop up destructive free radicals produced when our cells metabolise energy. The new finding could help explain why some research, particularly in smokers, has shown that antioxidants end up raising rather than reducing the risk of getting cancer. For example, in a prostate cancer prevention trial in 2011, men who took vitamin E for 5.5 years had a 17 per cent greater risk of developing the disease than men who took a placebo.

Now, research in mice has yielded a plausible explanation, at least for lung cancer. It seems antioxidants help early tumours survive and grow by protecting them and their DNA from damage from free radicals.

They do this by deactivating a gene called p53, dubbed the guardian of the genome, whose job is to destroy cells with defective DNA, including cancer cells. "Basically, the antioxidants shut off p53," which means the cancer cells can keep growing, says team leader Martin Bergö at the University of Gothenburg in Sweden.

To work out what was going on, Bergö and his colleagues triggered small lung cancers in mice and then gave some of them antioxidants. Of those receiving treatment, half got vitamin E and the other half an antioxidant called N-acetyl cysteine (NAC), a drug given to reduce mucus levels in people with chronic obstructive pulmonary disease (COPD).

Total knock-out

The results were dramatic. "The tumour number, size and aggressiveness increased threefold in the mice receiving either antioxidant, compared with non-recipients," says Bergö. "Also, survival was cut by at least 50 per cent." Further experiments on colonies of tumour cells from humans and mice showed that they grew faster after exposure to the antioxidants. Moreover, the activity of p53 fell dramatically, suggesting that the antioxidants switched off the gene's ability to sense and destroy defective cells. The effect of antioxidants on tumour growth was the same as knocking out p53 altogether, Bergö found.

Bergö says the results only suggest risks for people who already have small lung tumours, or are at risk of them. "Our study doesn't say anything about the use of antioxidants in healthy people, and their risk of cancer in the future," he says. "But if you have lung cancer, or increased risk of lung cancer because you smoke or you have COPD, our results suggest antioxidants would fuel the growth of any tumours, so use them with caution, or not at all."

Balanced diet

Concerns have also been raised that antioxidants may interfere with cancer treatments, says Emma Smith, a spokesperson for Cancer Research UK. "We recommend that people stick to a healthy balanced diet, which should provide all the nutrients needed without taking supplements," she says.

Shyam Biswal of Johns Hopkins Bloomberg School of Public Health in Baltimore says the next step will be to see if NAC and other antioxidants promote tumours in mice at high risk of cancer having been exposed to a carcinogen, as well as those bred to have the disease. "It also warrants more study in patients with COPD," he says. Bergö plans to perform some of this follow-up work, as well as investigating the effects of antioxidants on other cancers, including malignant melanomas and gut cancers.

Journal reference: Science Translational Medicine, DOI: 10.1126/scitranslmed.3007653

http://www.medscape.com/viewarticle/819957?src=rss

Peanut Allergy Effectively Countered With Oral Immunotherapy

Oral immunotherapy (OIT) for children's peanut allergy may be a safe and effective approach, a new study has shown.

Steven Fox

Findings from the phase 2 trial, published online January 29 in the Lancet, add to accumulating evidence that children can gradually build tolerance by ingesting increasing amounts of nut protein.

"To our knowledge, our findings provide the first well controlled and accurate estimate of the effect size, benefits, and risks of desensitisation with peanut OIT," write Katherine Anagnostou, PhD, from the Department of Medicine, Addenbrooke's Hospital, Cambridge, United Kingdom, and colleagues.

Previous results from small studies have suggested that peanut OIT might be an effective strategy for managing children with peanut allergy. However, until now, the approach had not been thoroughly evaluated in a sizable group of children.

Therefore, the investigators designed a 2-step, randomized controlled crossover trial testing OIT in 99 children aged 7 to 16 years. Children with all levels of peanut sensitivity were included in the trial.
In the first step, children were randomly assigned to 1 of 2 groups. One group received 26 weeks of OIT, which consisted of gradually increasing doses of peanut protein up to 800 mg daily. The other group was advised to avoid peanuts per usual, serving as controls. At the end of the 26 weeks, both groups underwent peanut challenge. In the second phase, children in the control group were offered the 26-week OIT treatment followed by challenge.
"OIT successfully induced desensitisation in most children within the study population with peanut allergy of any severity, with a clinically meaningful increase in peanut threshold," the researchers report. "Peanut OIT raises the reactive threshold at least 25-times so that 84–91% of participants can tolerate daily ingestion of 800 mg protein."
At the end of the first trial phase, 84% (95% confidence interval [CI], 70% - 93%) of the children in the active intervention group tolerated daily ingestion of 800 mg protein compared with none in the control group. In addition, 62% (95% confidence interval [CI], 45% - 78%) of the active intervention group had become desensitized, which was defined as having no reaction to ingestion of 1400 mg peanut protein (roughly equivalent to 10 peanuts).
After the second trial phase, 91% (95% CI, 79% - 98%) of children who had been assigned initially to the control group were able to tolerate ingestion of 800 mg protein daily, and 54% (95% CI, 35% - 72%) had become desensitized.
The authors point out that it would be unlikely for children to accidentally encounter 1400 mg of peanut protein. About a fifth of the patients reported adverse reactions to OIT. However most were mild, with oral itching being the most common, occurring after 6.3% of doses (76 children). Gastrointestinal symptoms were also common, with 31 children reporting nausea, 31 reporting vomiting, and 1 reporting diarrhea. In addition, 41 children developed wheeze (0.41% of doses) and 1 child required intramuscular adrenaline.
In an accompanying comment, Matthew J. Greenhawt, MD, from the University of Michigan Food Allergy Center, Division of Allergy and Clinical Immunology, Ann Arbor, stressed that although the results of the study are promising, more high-quality data are needed before recommending the therapy to all child and adolescent patients with peanut allergy.
"It is important to understand that OIT research cannot be rushed, and is years away from routine clinical use," Dr. Greenhawt notes. "Investigative groups need time to refine protocols, revalidate data, understand the mechanisms of OIT, and minimise adverse effects. This must be done without added pressure or heightened expectations to quickly produce a marketable therapy," he concludes.
Support for this study was received from the Medical Research Council, National Institute for Health Research, United Kingdom. Two coauthors are inventors on a patent application that covers the protocol described in this study. The remaining authors have disclosed no relevant financial relationships. Dr. Greenhawt has reported that he is a member of the Educational Advisory Council for the National Peanut Board and has served as a consultant for Deerfield Industries.
Lancet. Published online January 29, 2014.

http://www.eurekalert.org/pub_releases/2014-01/afps-ikp012914.php

Infants know plants provide food, but need to see they're safe to eat

Infants as young as six months old tend to expect that plants are food sources, but only after an adult shows them that the food is safe to eat, according to new research published in Psychological Science, a journal of the Association for Psychological Science.

The findings show that, after watching an adult put part of a plant and part of a man-made object in her mouth, infants at 6- and 18-months of age preferentially identify the plant as the food source.
"Plants are often peripheral to modern life, but they were central to fundamental problems of determining what is food and what is fatal across evolutionary time," says psychological scientist and study author Annie Wertz of Yale University. "Humans relied on gathered plant resources for food, but many plants are toxic and potentially deadly." So how do babies learn what's good to eat and what's not?
"Young children's decisions about what to eat are, famously, not determined by simply copying adult behavior," Wertz and co-author Karen Wynn note.
Wertz and Wynn hypothesized that, instead of imitating an adult's behavior outright, children tend to go for specific types of entities - in this case, plants -— but only when an adult does so first. They tested their hypothesis in four experiments.
Full-term 18-month-olds were presented with a realistic-looking artificial plant and an obviously man-made artifact, each of which had dried fruits attached. The infants watched an experimenter take one fruit off each object — the plant and the artifact — and place it in her mouth as if eating it.

The fruits were then taken off the plant and the artifact and the infants were asked, "Which one can you eat?" The infants showed a clear preference for the fruits that came from the plant, despite the fact that they saw the same social information — the experimenter "eating" the fruit — applied to both objects.
The experiments further showed that the eating action was crucial to this plant-based bias: When the experimenter placed the fruits behind the ear, or merely looked at the plant and artifact instead of performing an action, infants chose randomly.
Younger infants, who have little to no experience with solid food, also showed evidence of a plant-based bias: Six-month-old infants looked longer at in-mouth actions when they were performed with fruits from the artifact, suggesting that this violated their expectations for edibility.
"Together, these experiments show that infants use social information from adults to rapidly and selectively identify plants as food sources," says Wertz. "More broadly, this suggests that humans, unlike some other non-human primates, don't simply consider anything that goes into the mouth to be food. Instead, they also take the type of object into consideration."
Wertz notes that this social learning mechanism works in concert with other mechanisms, including sensitive periods for learning about food and aversions to certain tastes such as bitterness, which can signal something is poisonous. "Human food learning is complex, and we're only just starting to scratch the surface of these important questions," she says.
On a practical level, Wertz believes that parents of young children may be able to put these findings to use: "Knowing that infants may be biased to learn that fruits plucked from leafy green plants are edible suggests strategies for getting young children interested in eating novel fruits and vegetables, such as taking them to a 'pick-your-own' fruits and vegetables farm."
For more information about this study, please contact: Annie E. Wertz at annie.wertz@yale.edu.
This research was supported by National Science Foundation Grant BCS-0715557 and National Institutes of Health Grant R01 MH 081877 to Karen Wynn.
The article abstract is available online: http://pss.sagepub.com/content/early/2014/01/28/0956797613516145.abstract

http://www.eurekalert.org/pub_releases/2014-01/ifri-sua013014.php

Scientists unveil a molecular mechanism that controls plant growth and development

Researchers from Spain and the Netherlands reveal how auxin hormone-regulated proteins activate developmental genes in plants

Barcelona, Thursday 30 January, 2014.- A joint study published in Cell by the teams headed by Miquel Coll at the Institute for Research in Biomedicine (IRB Barcelona) and the Institute of Molecular Biology of CSIC, both in Barcelona, and Dolf Weijers at the University of Wageningen, in the Netherlands, unravels the mystery behind how the plant hormones called auxins activate multiple vital plant functions through various gene transcription factors.
Auxins are plant hormones that control growth and development, that is to say, they determine the size and structure of the plant. Among their many activities, auxins favor cell growth, root initiation, flowering, fruit setting and delay ripening. Auxins have practical applications and are used in agriculture to produce seedless fruit, to prevent fruit drop, and to promote rooting, in addition to being used as herbicides. The biomedical applications of these hormones as anti-tumor agents and to facilitate somatic cell reprogramming (the cells that form tissues) to stem cells are also being investigated.
The effects of auxins in plants was first observed by Darwin in 1881, and since then this hormone has been the focus of many studies. However, although it was known how and where auxin is synthesized in the plant, how it is transported, and the receptors on which it acts, it was unclear how a hormone could trigger such diverse processes.
At the molecular level, the hormone serves to unblock a transcription factor, a DNA-binding protein, which in turn activates or represses a specific group of genes. Some plants have more than 20 distinct auxin-regulated transcription factors. They are called ARFs (Auxin Response Factors) and control the expression of numerous plant genes in function of the task to be undertaken, that is to say, cell growth, flowering, root initiation, leaf growth etc.
Using the Synchrotron Alba, near Barcelona, and the European Synchrotron Radiation Facility, in Grenoble, Dr. Miquel Coll, a structural biologist and his team analyzed the DNA binding mode used by various ARFs. For this purpose, the scientists prepared crystals of complexes of DNA and ARF proteins obtained by Dolf Weijers team in Wageningen, and then shot the crystals with high intensity X-rays in the synchrotron to resolve their atomic structure. The resolution of five 3D structures has revealed why a given transcription factor is capable of activating a single set of genes, while other ARFs that are very similar with only slight differences trigger a distinct set.

"Each ARF recognizes and adapts to a particular DNA sequence through two binding arms or motifs that are barrel-shaped, and this adaptation differs for each ARF," explains Roeland Boer, postdoctoral researcher in Miquel Coll's group at IRB Barcelona, and one of the first authors of the study.
The ARF binding mode to DNA has never been described in bacteria or animals. "It appears to be exclusive to plants, but we cannot rule out that it is present in other kingdoms. Our finding is highly relevant because we have revealed the ultimate effect of a hormone that controls plant development on DNA, that is to say, on genes." says Miquel Coll.
Reference article: Structural basis for DNA binding specificity by the auxin-dependent ARF transcription factors
D. Roeland Boer, Alejandra Freire-Rios, Willy van den Berg, Terrens Saaki, Iain W. Manfield, Stefan Kepinski, Irene López-Vidrieo, Jose Manuel Franco, Sacco C. de Vries, Roberto Solano, Dolf Weijers, and Miquel Coll
Cell (2014) http://dx.doi.org/10.1016/j.cell.2013.12.027

http://www.eurekalert.org/pub_releases/2014-01/yu-ccs012714.php

Cell cycle speed is key to making aging cells young again

A fundamental axiom of biology used to be that cell fate is a one-way street — once a cell commits to becoming muscle, skin, or blood it always remains muscle, skin, or blood cell.

That belief was upended in the past decade when a Japanese scientist introduced four simple factors into skin cells and returned them to an embryonic-like state, capable of becoming almost any cell type in the body. Hopeful of revolutionary medical therapies using a patient's own cells, scientists rushed to capitalize on the discovery by 2012 Nobel Laureate Shinya Yamanaka. However, the process has remained slow and inefficient, and scientists have had a difficult time discovering a genetic explanation of why this should be.
In the Jan. 30 issue of the journal Cell, Yale School of Medicine researchers identified a major obstacle to converting cells back to their youthful state — the speed of the cell cycle, or the time required for a cell to divide. When the cell cycle accelerates to a certain speed, the barriers that keep a cell's fate on one path diminish. In such a state, cells are easily persuaded to change their identity and become pluripotent, or capable of becoming multiple cell types
"One analogy may be that when temperature increases to sufficient degrees, even a very hard piece of steel can be malleable so that you can give it a new shape easily," said Shangqin Guo, assistant professor of cell biology at the Yale Stem Cell Center and lead author of the paper. "Once cells are cycling extremely fast, they do not seem to face the same barriers to becoming pluripotent."
Guo's team studied blood-forming cells, which when dividing undergo specific changes in their cell cycle to produce new blood cells. Blood-forming progenitor cells normally produce only new blood cells. However, the introduction of Yamanaka factors sometimes — but not always — help these blood-forming cells become other types of cells. The new report finds that after this treatment blood-forming cells tend to become pluripotent when the cell cycle is completed in eight hours or less, an unusual speed for adult cells. Cells that cycle more slowly remain blood cells. "This discovery changes the way people think about how to change cell fate and reveals that a basic 'house-keeping' function of a cell, such as its cell cycle length, can actually have a major impact on switching the fate of a cell," said Haifan Lin, director of the Yale Stem Cell Center.
The study has other implications than explaining the bottleneck in reprogramming that makes it difficult to produce individualized pluripotent stem cells for research and therapy. Shangqin Guo noted that many human diseases are associated with abnormalities in establishing proper cell identity as well as abnormalities in cell cycle behavior.
Other Yale-affiliated authors are Xiaoyuan Zi, Vincent Schulz, Jijun Cheng, Mei Zhong, Sebastian H.J. Koochaki, Cynthia M. Megyola, Xinghua Pan, Kartoosh Heydari, Sherman M. Weissman, Patrick G. Gallagher, Diane S. Krause, Rong Fan, and Jun Lu.
The research was funded by the National Institutes of Health and the Connecticut Stem Cell Research Program.

http://www.eurekalert.org/pub_releases/2014-01/m-pgn013014.php

Parkinson gene: Nerve growth factor halts mitochondrial degeneration

New link discovered between processes associated with a Parkinson's-related gene defect

Neurodegenerative diseases like Parkinson's disease involve the death of thousands of neurons in the brain. Nerve growth factors produced by the body, such as GDNF, promote the survival of the neurons; however, clinical tests with GDNF have not yielded in any clear improvements. Scientists from the Max Planck Institute of Neurobiology in Martinsried and their colleagues have now succeeded in demonstrating that GDNF and its receptor Ret also promote the survival of mitochondria, the power plants of the cell. By activating the Ret receptor, the scientists were able to prevent in flies and human cell cultures the degeneration of mitochondria, which is caused by a gene defect related to Parkinson's disease. This important new link could lead to the development of more refined GDNF therapies in the future.

In his "Essay on the Shaking Palsy" of 1817, James Parkinson provided the first description of a disease that today affects almost 280,000 people in Germany. The most conspicuous symptom of Parkinson's disease is a slow tremor, which is usually accompanied by an increasing lack of mobility and movement in the entire body. These symptoms are visible manifestations of a dramatic change that takes place in the brain: the death of large numbers of neurons in the Substantia nigra of the midbrain.

Despite almost 200 years of research into Parkinson's, its causes have not yet been fully explained. It appears to be certain that, in addition to environmental factors, genetic mutations also play a role in the emergence of the disease. A series of genes is now associated with Parkinson's disease. One of these is PINK1, whose mutation causes mitochondrial dysfunction. Mitochondria are a cell's power plants and without them, a cell cannot function properly or regenerate. Scientists from the Max Planck Institute of Neurobiology and their colleagues from Munich and Martinsried have now discovered a hitherto unknown link that counteracts mitochondrial dysfunction in the case of a PINK1 mutation.

The PINK1 gene emerged at a very early stage in evolutionary history and exists in a similar form for example in humans, mice and flies. In the fruit fly Drosophila, a mitochondrial defect triggered by a PINK1 mutation manifests in the fraying of the muscles. Less visible, the flies' neurons also die. The scientists studied the molecular processes involved in these changes and discovered that the activation of the Ret receptor counteracts the muscle degeneration. "This is a really interesting finding which links the mitochondrial degeneration in Parkinson's disease with nerve growth factors," reports Rüdiger Klein, the head of the research study. Ret is not an unknown factor for the Martinsried-based neurobiologists: "We already succeeded in demonstrating a few years ago in mice that neurons without the Ret receptor die prematurely and in greater numbers with increasing age," says Klein.

The Ret receptor is the cells' docking site for the growth factor GDNF, which is produced by the body. Various studies carried out in previous years showed that the binding of GDNF to its Ret receptor can prevent the early death of neurons in the Substantia nigra. However, clinical studies on the influence of GDNF on the progression of Parkinson's in patients did not lead to any clear improvement in their condition.

The new findings from basic research suggest that the mitochondrial metabolism is boosted or re-established through Ret/GNDF. "Based on this finding, existing therapies could be refined or tailored to specific patient groups," hopes Pontus Klein, who conducted the study within the framework of his doctoral thesis. This hope does not appear to be completely unfounded: The scientists have already discovered a Ret/GDNF effect in human cells with a PINK1 defect similar to that observed in the fruit fly. It may therefore be possible to search for metabolic defects in the mitochondria of Parkinson's patients in future. A specially tailored GDNF therapy could then provide a new therapeutic approach for patients who test positively.

Pontus Klein, A. Kathrin Müller-Rischart, Elisa Motori, Cornelia Schönbauer, Frank Schnorrer, Konstanze F. Winklhofer, Rüdiger Klein Ret rescues mitochondrial morphology and muscle degeneration of Drosophila Pink1 mutants. The EMBO Journal. 29 January, 2014

http://www.eurekalert.org/pub_releases/2014-01/hzm--gei013014.php

Geranium extracts inhibit HIV-1

Scientists from the Helmholtz Zentrum München demonstrate that root extracts of the medicinal plant Pelargonium sidoides (PS) contain compounds that attack HIV-1 particles and prevent virus replication.

A team spearheaded by Dr. Markus Helfer and Prof. Dr. Ruth Brack-Werner from the Institute of Virology and Prof. Dr. Philippe Schmitt-Kopplin from the Analytical BioGeoChemistry research unit (BGC) performed a detailed investigation of the effects of PS extracts on HIV-1 infection of cultured cells. They demonstrated that PS extracts protect blood and immune cells from infection by HIV-1, the most widespread type of HIV. PS extracts block attachment of virus particles to host cells and thus effectively prevent the virus from invading cells. Chemical analyses revealed that the antiviral effect of the PS extracts is mediated by polyphenols. Polyphenol mixtures isolated from PS extracts retain high anti-HIV-1 activity but are even less toxic for cells than the crude extract.

Safety of PS-extracts has been established in several clinical trials. In Germany PS extracts are licensed as a herbal medicine and used to reduce symptoms of acute bronchitis. Research group leader Brack-Werner says, "PS-extracts are a very promising lead for the development of the first scientifically validated phytomedicine against HIV-1. PS extracts attack HIV-1 with a mode-of-action that is different from all anti-HIV-1 drugs in clinical use. Therefore a PS-based phytomedicine may be a valuable supplement for established anti-HIV therapies. Furthermore, PS extracts are attractive candidates for increasing anti-HIV-1 therapy options in resource-limited settings, since they are easy to produce and do not require refrigeration. The results of our study and the proven safety of PS extracts encourages their testing in HIV-1 infected individuals as next step."

According to the World Health Organisation (WHO), more than 35 million people in the world are infected with HIV, the majority with HIV-1. Without treatment, HIV destroys the immune system and causes the acquired immunodeficiency syndrome (AIDS), which is a life-threatening disease. HIV/AIDS is one of the 10 leading causes of death worldwide.
The goal of research at the Helmholtz Zentrum München is to develop new approaches to diagnosing, treating and preventing common diseases. In the interest of translational research, the acquired knowledge is to be applied to humans as quickly as possible in order to provide concrete benefits for society.
Helfer, M. et al. (2014), The root extract of the medicinal plant Pelargonium sidoides is a potent HIV-1 attachment inhibitor. Plos One, DOI: 10.1371/journal.pone.0087487
http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0087487;jsessionid=45989588E197E4F67E74FC14365E554A

http://bit.ly/1gDuUcI

First brain map of speech units could aid mind-reading

"He moistened his lips uneasily." It sounds like a cheap romance novel, but this line is actually lifted from quite a different type of prose: a neuroscience study.

19:00 30 January 2014 by Aviva Rutkin

Video: How speech sounds activate the brain

Along with other sentences, including "Have you got enough blankets?" and "And what eyes they were", it was used to build the first map of how the brain processes the building blocks of speech – distinct units of sound known as phonemes.
The map reveals that the brain devotes distinct areas to processing different types of phonemes. It might one day help efforts to read off what someone is hearing from a brain scan.
"If you could see the brain of someone who is listening to speech, there is a rapid activation of different areas, each responding specifically to a particular feature the speaker is producing," says Nima Mesgarani, an electrical engineer at Columbia University in New York City.

Snakes on a brain

To build the map, Mesgarani's team turned to a group of volunteers who already had electrodes implanted in their brains as part of an unrelated treatment for epilepsy. The invasive electrodes sit directly on the surface of the brain, providing a unique and detailed view of neural activity.
The researchers got the volunteers to listen to hundreds of snippets of speech taken from a database designed to provide an efficient way to cycle through a wide variety of phonemes, while monitoring the signals from the electrodes. As well as those already mentioned, sentences ran the gamut from "It had gone like clockwork" to "Junior, what on Earth's the matter with you?" to "Nobody likes snakes".
This showed that there are distinct areas in a brain region called the superior temporal gyrus that are dedicated to different types of sounds – the STG is already known to be involved in filtering incoming sound.
One cluster of neurons responded only to consonants, while another responded only to vowels. These two areas then appeared to divide into even smaller groups. For example, some of the consonant neurons responded only to fricatives – sounds that force air through a narrow channel, like the s sound at the beginning of "scientist". Others responded only to plosives – sounds that block airflow, like the b in "brain".
Other scientists have used neural activity in attempts to recreate what people are looking at or capture people's thoughts in the form of their inner voice.

Mystery of meaning

Mesgarani thinks that the phoneme map may make it easier to figure out what someone is hearing from nothing but brain signals. He has tried to do this before by analysing neural responses to sound in ferrets and in people. The map should make relating the brain activity to specific sounds much easier.
Sophie Scott at the Institute of Cognitive Neuroscience at University College London cautions that the way we hear language is more complicated than just lining up different phonemes. Sounds change in subtle ways when they come together, so the brain must analyse the sequence as a whole.
"I think it's a shame that they haven't taken a more realistic approach to what we know actually happens when people listen to speech," Scott said. "Information isn't located at the level of the segments, it's actually extending over the sequence."
Mesgarani agrees that how the brain turns phonemes into meaning is still unknown. "How the brain takes these basic units, and puts them together to form sub-word and words, and ultimately meaning, remains a mystery," he says. He hopes the phoneme map will one day help answer this question, too.
Journal reference: Science, DOI: 10.1126/science.1245994

http://www.bbc.co.uk/news/science-environment-25968755

Michael Mosley infests himself with tapeworms

BBC TV presenter Dr Michael Mosley has infected himself with a number of parasites in an effort to understand how they affect the human body.

By James Morgan Science reporter, BBC News

He swallowed tapeworm cysts, stuck a leech on his arm, and tried to infest himself with lice, in a new BBC Four documentary programme. The worms lived in his body for several weeks - and he felt no ill effects. The stool samples he gave while infected will be used by scientists studying signs of parasitic infection. Dr Mosley is known for his "gonzo" medical journalism - he has previously taken "truth serum", trialled magic mushrooms, and undergone the fasting 5:2 diet.

'Delightful' discovery

In this latest film, he swallows three tapeworm cysts (larvae) which he obtained from infected cattle in Kenya. Several weeks later, he swallows a "pill camera" which travels into his gut and broadcasts live pictures to his iPad.

He discovers three worms - "triplets" - attached to the lining of his intestine, about a metre in length.

"When I first saw the worms, I was in an Indian restaurant. I shouted out: 'Blimey! There's a tapeworm in me!' The other diners looked very surprised." "I was delighted, but at the same time, it was rather horrible. "My wife wasn't too keen on the idea, either. But I told her not to worry - this particular tapeworm is relatively innocuous."

The beef tapeworm, Taenia saginata, is transmitted from cows to humans via infected meat. It can grow more than 10m long in the intestine, and reproduces by passing new eggs out in the faeces. The worm is usually asymptomatic - and Dr Mosley suffered no obvious effects, although he did put on about 1kg (2.2lbs) in weight.

"It could be that the parasite increased my appetite. I ate a lot of chocolate," he explained. "So anyone who is thinking of popping parasites as a weight-loss device should think twice."

While that idea may seem absurd, there is growing evidence that parasites may have health benefits in certain cases. They are being considered as treatments for allergies and auto-immune diseases, as they appear to dampen the body's inflammatory responses.

Dr Mosley himself has "mild" hay fever, but was disappointed to find that the worms made no difference to his symptoms. By documenting his experiences, he hopes to help scientists at Salford University, who are searching for early warning signs of worm infections. "There are other tapeworms that are very nasty in humans - especially the pork tapeworm. It can get into your brain and eyes and causes cysts," he said.

'Blood everywhere'

If scientists could spot these infections early, they have a chance of treating patients. But in most cases the first clue that a person is infected comes much later - such as when they pass out eggs in their faeces.

In the programme, which will air in February, Dr Mosley also attempted to infest himself with head lice.

"I was unsuccessful - they didn't take to me," he said.

However, a blood-sucking leech that he stuck to his forearm made itself perfectly at home. "They told me it drank eight times its body weight in blood. There was blood everywhere when I took it off," Dr Mosley said.

The main conclusion of his experiments, he said, was that "parasites on the whole, are not crazy about me".

His other conclusion: don't try this at home.

"I wouldn't recommend buying something on the internet and infecting yourself. Heaven knows where it's been," he said. "Some people get better, some get worse, it appears. And we never seem to hear from the people who get worse."

'Michael Mosley: Infested! Living with parasites' will be broadcast in BBC Four's natural history season, starting in February.

http://www.eurekalert.org/pub_releases/2014-01/cwru-ssa013114.php

Study shows autistic brains create more information at rest

Possible explanation for 'withdrawal into self,' a characteristic of the disorder

New research from Case Western Reserve University and University of Toronto neuroscientists finds that the brains of autistic children generate more information at rest – a 42% increase on average. The study offers a scientific explanation for the most typical characteristic of autism – withdrawal into one's own inner world. The excess production of information may explain a child's detachment from their environment.

Published at the end of December in Frontiers in Neuroinformatics, this study is a follow-up to the authors' prior finding that brain connections are different in autistic children. This paper determined that the differences account for the increased complexity within their brains.

"Our results suggest that autistic children are not interested in social interactions because their brains generate more information at rest, which we interpret as more introspection in line with early descriptions of the disorder," said Roberto Fernández Galán, PhD, senior author and associate professor of neurosciences at Case Western Reserve School of Medicine.
The authors quantified information as engineers normally do but instead of applying it to signals in electronic devices, they applied it to brain activity recorded with magnetoencephalography (MEG). They showed that autistic children's brains at rest generate more information than non-autistic children. This may explain their lack of interest in external stimuli, including interactions with other people.
The researchers also quantified interactions between brain regions, i.e., the brain's functional connectivity, and determined the inputs to the brain in the resting state allowing them to interpret the children's introspection level.
"This is a novel interpretation because it is a different attempt to understand the children's cognition by analyzing their brain activity," said José L. Pérez Velázquez, PhD, first author and professor of neuroscience at University of Toronto Institute of Medical Science and Department of Pediatrics, Brain and Behavior Center. "Measuring cognitive processes is not trivial; yet, our findings indicate that this can be done to some extent with well-established mathematical tools from physics and engineering."
This study provides quantitative support for the relatively new "Intense World Theory" of autism proposed by neuroscientists Henry and Kamila Markram of the Brain Mind Institute in Switzerland, which describes the disorder as the result of hyper-functioning neural circuitry, leading to a state of over-arousal. More generally, the work of Galán and Pérez Velázquez is an initial step in the investigation of how information generation in the brain relates to cognitive/psychological traits and will begin to frame neurophysiological data into psychological aspects. The team now aims to apply a similar approach to patients with schizophrenia.

http://www.eurekalert.org/pub_releases/2014-01/uovm-tyw013114.php

Teaching young wolves new tricks

Wolves were domesticated more than 15,000 years ago and it is widely assumed that the ability of domestic dogs to form close relationships with humans stems from changes during the domestication process.

But the effects of domestication on the interactions between the animals have not received much attention. The point has been addressed by Friederike Range and Zsófia Virányi, two members of the University of Veterinary Medicine, Vienna (Vetmeduni Vienna) who work at the Wolf Science Center (WSC) in Ernstbrunn, Niederösterreich.

Wolves copy other wolves solving problems

The scientists found that wolves are considerably better than dogs at opening a container, providing they have previously watched another animal do so. Their study involved 14 wolves and 15 mongrel dogs, all about six months old, hand-reared and kept in packs. Each animal was allowed to observe one of two situations in which a trained dog opened a wooden box, either with its mouth or with its paw, to gain access to a food reward. Surprisingly, all of the wolves managed to open the box after watching a dog solve the puzzle, while only four of the dogs managed to do so. Wolves more frequently opened the box using the method they had observed, whereas the dogs appeared to choose randomly whether to use their mouth or their paw.

Watch closely …

To exclude the possibility that six-month old dogs fail the experiment because of a delayed physical or cognitive development, the researchers repeated the test after nine months. The dogs proved no more adept at opening the box than they were at a younger age. Another possible explanation for the wolves' apparent superiority at learning is that wolves might simply be better than dogs at solving such problems.
To test this idea, the researchers examined the animals' ability to open a box without prior demonstration by a dog. They found that the wolves were rarely successful. "Their problem-solving capability really seems to be based on the observation of a dog performing the task," says Range. "The wolves watched the dog very closely and were able to apply their new knowledge to solve the problem. Their skill at copying probably relates to the fact that wolves are more dependent on cooperation with conspecifics than dogs are and therefore pay more attention to the actions of their partners."
The researchers think that it is likely that the dog-human cooperation originated from cooperation between wolves. During the process of domestication, dogs have become able to accept humans as social partners and thus have adapted their social skills to include interactions with them, concomitantly losing the ability to learn by watching other dogs.

The article „Wolves are better imitators of conspecifics than dogs", by Friederike Range und Zsófia Virányi was published in the Online Journal PlOS ONE. http://dx.plos.org/10.1371/journal.pone.0086559

http://bit.ly/1lusLC3

Too much sugar in food? Follow the salt solution

ANYONE who worries about their diet must have had a few anxious moments about sugar in recent weeks.

The media has been full of stories about its effects on health, from obesity and diabetes to liver disease. Some stories were exaggerated, but many got it right (see "Sugar on trial: What you really need to know").

It's hardly news that sugar is bad for you, so why the sudden interest? One underappreciated reason is the success of a public health battle against another white crystalline powder.

Around 20 years ago a small group of cardiovascular specialists in the UK decided to do something about the large amounts of salt being added to processed food. As a result of their campaign, people in the UK now eat around 15 per cent less salt than they used to, preventing thousands of deaths a year from strokes and heart attacks.

How did they do it? The answer was to work with the food industry, not against it. The campaigners persuaded manufacturers to gradually reduce the amount of salt in processed foods. The aim was to wean people off salt.

It worked: people in the UK now prefer foods with less salt. That success is being replicated worldwide.

Salt is still a problem, but the salt campaigners have made enough progress to turn their attention to sugar.

There are reasons to believe that the anti-salt tactics will work again. Like salt, sugar leads to habituation. The more you eat, the less sensitive your taste buds become to it, so gradual weaning should work.

Salt reduction has shown that the food industry can do the right thing for public health. Sugar is a problem on a similar scale. The industry can – and should – help to solve it.

http://phys.org/news/2014-01-climate-heatnot-coldis-real-killer.html

Climate change's heat—not cold—is the real killer

Chill with impunity through this winter's extreme cold – and brace for the next summer heat wave, when fiery temperatures and air pollution conspire to fill hospitals and morgues.

Phys.org - That's the advice from a team of climate-change researchers who studied 170 million hospital admissions and 8 million deaths (season by season, day by day, for 10 years) in Germany before issuing a report with global implications.

"We show that extreme heat events have a highly significant and largely adverse impact on both hospitalizations and deaths, whereas extreme cold seems to have a negligible real-world impact on population health," said Nicolas Ziebarth, assistant professor of policy analysis and management in Cornell's College of Human Ecology.

Ziebarth published "The Short-term Population Health Effects of Weather and Pollution: Implications of Climate Change" in the December 2013 Journal of Economic Literature with Maike Schmitt, Darmstadt Technical University, and Martin Karlsson, University of Duisburg-Essen. Ziebarth is also affiliated with the German Institute for Economic Research and the Institute for the Study of Labor (IZA).

The researchers gathered a decade's worth (1999-2008) of health, temperature and air-pollution data from a variety of sources – including 1,044 weather stations and 1,314 air quality monitors across Germany and all 17 million hospital admissions and 800,000 deaths that occur in Germany per year. They were particularly interested in deaths from respiratory, infectious or metabolic causes that might be linked to heat stress and pollution.

An extreme "cold day," for study purposes, had temperatures below 14 degrees F, and a "cold wave" was four days of such temperatures. A "hot day" had temperatures above 86 degrees F, and a "heat wave" was four consecutive hot days.

Severe air pollution days had alert-level amounts of ozone, nitrate and particulate matter in the air (according to EU standards, which have much lower alert thresholds than the United States).

The analysis found temperature-and-pollution spikes tended to increase hospital admissions and deaths by 2 percent to 5 percent the first day. Adverse health effects and mortality mounted with each day of a heat wave. But extreme cold events typically had no effect on hospitalization and death numbers. In some cases, hospital admissions actually decreased during extreme cold days – probably, researchers speculate, because people have trouble traveling to hospitals on icy roads.

Their analysis of heat waves (averaging about one per year in Germany between 1999 and 2006) took into account the grimly named "harvesting effect," when the gravely ill, whose deaths were imminent, died during the first day or two of extreme heat.

"We showed that extremely high temperatures do not lead to a permanent increase in hospitalizations and deaths – just an 'instantaneous heat-health relationship' in the short term," Ziebarth noted.

Distributed across the entire population of a country like Germany or the United States, Ziebarth estimated, the cost of a hot day is between 10 cents and 68 cents per resident in health care and lost productivity.
Looking ahead, other researchers link the melting arctic sea ice to colder winters (and occasional, atypically chilly summer days) in North America and Europe. Climate change is leading to more frequent, more severe heat and cold events in the mid-latitudes, and that trend is probably unstoppable, they say.
But, the researchers said, one factor in the heat/pollution/health connection could be controlled by national and municipal governments: air quality. "Lower pollution-alert levels would be beneficial for population health," they conclude in the report, "and would save lives."
More information: The paper, "The Short-term Population Health Effects of Weather and Pollution: Implications of Climate Change," is available online: ftp.iza.org/dp7875.pdf

http://bit.ly/MoUAfg

Dog Family Tree Traced Back 2 Million Years

A new cache of extremely well preserved, prehistoric canine fossils is shedding light on dog and wolf ancestors from 2 million years ago to today.

Jan 31, 2014 07:00 AM ET // by Jennifer Viegas

The fossils, described in the latest issue of the Journal of Mammalian Evolution, date to that early period and belonged to a scrappy canine carnivore known as Canis etruscus that lived near Rome, Italy.
"Canis etruscus appeared approximately 2 million years ago and is the oldest European species referred to in the genus Canis," lead author Marco Cherin told Discovery News, adding that this species "was considerably smaller than the modern wolf."
Dog owners have been saying it for years: "Dogs are really just four-legged, furry humans."
"We can suppose that it was a social dog, as most of the living species of similar size," continued Cherin, who is a researcher at Perugia University's Department of Earth Sciences. "Hunting in packs, Canis etruscus could have preyed on small to medium-sized animals."
The prey of this carnivore, which looked like a cross between a German shepherd and a wolf, would have included animals such as ancient relatives of deer and pigs. They were all common at the site: Pantalla, Italy.
This apparent mother of all dogs in Europe likely gave rise to another member of the dog/wolf family tree, Canis mosbachensis, about 1 million years ago. Canis mosbachensis, in turn, is considered to be a direct ancestor of modern wolves.
Until recently, it was thought that dogs were domesticated from the gray wolf, but a separate study earlier this month countered that popular belief.
"The common ancestor of dogs and wolves was a large, wolf-like animal that lived between 9,000 and 34,000 years ago," Robert Wayne of UCLA, who was co-senior author of the study, told Discovery News.
That animal went extinct thousands of years ago and, as of now, remains unknown.
What is known about dog history is that the first canines came from North America, Cherin said. The earliest documented species from the genus Canis was Canis lepophagus, aka the "hare-eating wolf." Like the prehistoric canine from Italy, it was relatively small and had a narrow head.
Canines spread to Asia and then to Europe. It was in Eurasia at least 780,000 years ago that a dog relative might have encountered a member of our genus.
Eudald Carbonell, a professor at the University of Rovira and Virgili, told Discovery News that fossils of Homo antecessor -- an extinct human that looked a lot like us -- were found with fossils of Canis mosbachensis in Spain.
Could this very early human have enjoyed the companionship of the dog/wolf relative, or was the latter considered to be good eats or a predator? The fossil record so far, unfortunately, does not have those answers.
Carbonell and his team did find evidence for cannibalism -- for nutritional purposes -- among Homo antecessor individuals, so it's likely that this early, hungry human hunted the dog and wolf relative.
As the human population continued to expand and evolve in Europe and Asia, people discovered how valuable canines could be for security, hunting, companionship and more, resulting over time in the domestication of dogs. That moment of doggy revelation might have even happened in Italy, since recent DNA evidence suggests the first domesticated dogs were from Europe.
Marina Sotnikova of the Geological Institute of Russian Academy of Sciences told Discovery News that the fossils discovered in Italy are "very interesting" and "allow for a more detailed study of this group of carnivores."

http://www.sciencedaily.com/releases/2014/01/140131101205.htm

Forensic experts compile guide on how to ID child abuse, starvation

Forensic science experts from North Carolina State University are publishing a comprehensive overview of forensic research that can be used to identify child abuse and starvation.

"By pulling all of this information together in one place, we hope that we can save the lives of some children and find justice for others," says Dr. Ann Ross, a professor of anthropology at NC State and lead author of the paper. Ross is also co-editor of the book "The Juvenile Skeleton in Forensic Abuse Investigations."

"For example, we looked at issues of neglect in which children are starved to death," Ross says. "These are supposedly rare, but I've unfortunately seen this a few times in my capacity as an advisor to medical examiners. In this paper we offer some guidelines on how to use the mineral density of bones to determine whether a child was being starved."

Proving that a child was starved to death is difficult; it's essentially impossible to assess normal indicators of starvation once a body has decomposed. But the paper explains that forensic investigators can use a DXA scan, like those used to assess osteoporosis in older adults, to assess bone density and determine whether a child was severely malnourished.

Also, because teeth are not as affected by malnutrition as bones are, investigators can compare the development of an individual's teeth and bones. Stunted growth of a child's tibia can be a strong indicator of starvation, for example.

"These techniques are well-established but are not in widespread use in the United States," Ross says.

"We also combed the existing literature to focus on skeletal injuries that are indicators of abuse and that are unlikely or impossible to be caused by accident," says Dr. Chelsey Juarez, an assistant professor of anthropology at NC State and co-author of the paper.

For example, rib fractures are very rare in accidental trauma, so the presence of rib fractures in children is highly suggestive of abuse.

The paper also offers broader advice, such as noting that forensic investigators should determine whether the story they're getting from a child's caregiver is consistent with the injuries they see on the child.

"The portion of the paper dealing with injuries is particularly important," Juarez says. "Because while it can be used for post-mortem assessment, it can also be used to examine X-rays of living children who can still be saved from abuse."

Ann H. Ross, Chelsey A. Juarez. A brief history of fatal child maltreatment and neglect. Forensic Science, Medicine, and Pathology, 2014; DOI: 10.1007/s12024-014-9531-1

http://bit.ly/1n5Y81f

Give the gift of life by donating your medical records

There are huge benefits to using confidential records in England for research purposes

15:14 31 January 2014 by Sharmila Nebhrajani

Those of us who work with medical research charities already know how generous the public is when it comes to helping others. Those charities are now asking supporters to consider making a new gift – one that requires no opening of the wallet or giving of blood or other tissue. They want you to donate the information in your medical records.

Pictures of a young boy appeared in adverts in the press with the caption: "Hello, I'm Peter. We haven't met before but one day you could save my life." It was an emotive campaign by a group of medical charities, and it was designed to encourage the public to find out more about the power of sharing their data – but the message is true.

For example, large medical data sets enabled the link between smoking and cancer to be proven and the supposed link between autism and MMR vaccines to be debunked.

The charities are acting now because an opportunity to decide what to do with medical records is fast approaching.

The National Health Service in England has the ambitious plan of opening up of all records held by family doctors in an anonymised form from April. Leaflets are going out to all homes in England this month explaining the scheme. The result should be a huge data set, spanning the population and going back decades, which will allow important research questions to be answered.

Success stories

For those not yet persuaded about the power of this approach, there are other good examples. A recent British Heart Foundation funded project reviewed 370,000 patients, almost half of the people living with heart failure in the UK, and showed that fears that drugs for high blood pressure might increase the risk of cancer were

unfounded. This study simply would not have been possible without access to the 5 million anonymised records already in the General Practice Research Database.
A similar project analysed data stretching back 50 years to assess the effect of taking the contraceptive pill for a long time and, by linking to mortality data sets, improved prescribing guidance.
How could anyone object to the principle of sharing? It is clear the value of the data held by family doctors, also known as general practitioners (GPs), is immense, so they must be willing partners in this.
There are reports of some reservations among doctors who are fearful that a long tradition of protecting medical records in their surgeries is under threat. But it is clear that this is overwhelmingly what the public want. Polls tell us that most people feel the same: a 2011 IPSOS Mori survey of about 1000 people showed that 80 per cent of the public were happy for researchers to have access to confidential medical records.
Additionally, the value of this data is multiplied by the ability to link it to other sources, as in the contraceptive pill study that linked GP records to databases of cancer and mortality.

Re-identification

This is not risk free, however. Privacy campaigners are worried about re-identification.
These records are some of our most personal and sensitive information, so it goes without saying that they must be stored carefully and used with care and respect. The planned database will strip data of all identifiers and make sure that researchers only have de-identified data.
The planned safeguards seem strong. But no system can be risk free – there may be rare cases in the future when the codes will be breached. We need to weigh that theoretical possibility against the immense gains to research now. If we wanted to eliminate risk completely from our lives, humans would do nothing.
That is not to say, though, that the information from the NHS in England to help the public reach a decision has been perfect. I would like to see the supporting information be clearer about who will and, crucially, who will not have access to this data.

No surprises

We should not be afraid, for example, that commercial researchers might use the data for ethically approved medical research projects, but it must not be a surprise to us when they do. New drugs and devices need the involvement of pharmaceutical and biotech companies.
And the leaflet should be clear that insurance companies and government departments that aren't involved in medical research or providing care will not have access to the data as a matter of right.
There is great potential benefit here. Charities are asking us to consider those benefits, the proposed safeguards and our own personal instincts before coming to a view. It is clear that people feel a strong sense of altruism to the cause of medical research. If the NHS can demonstrate that they will use it wisely, the overwhelming majority of the public will generously donate their data too.

PROFILE: *Sharmila Nebhrajani is chief executive of the Association of Medical Research Charities, based in London*

http://www.medscape.com/viewarticle/819685?src=rss

Marijuana Medical Silliness, Be Gone!

One of the advantages of growing old -- and trust me, there are not many -- is to observe how observations you have made and positions you have taken over the years play out. Now is such a time for me and marijuana.

George D. Lundberg, MD

Hello and welcome. I am Dr. George Lundberg and this is At Large at Medscape.
I am not a user, but I have been a loud proponent for science and justice to supersede ignorance and ideological bias against cannabis since at least September 21, 1970, [1] when I wrote in JAMA that, in contrast to alcohol and tobacco, which kill Americans every day, there appears "...never to have been an authenticated case of marijuana killing anyone..."; and in the journal called California Medicine in May 1971, [2] "...Marijuana is noteworthy for the absence of recognized harmful physical effects...."
Needless to say, I have tried to move the issue only incrementally to blunt the effect of the anticipated and realized harsh criticism on my career.
Finally, crowd-sourced science is winning; justice should not be too far behind. Justice Brandeis was right: The states are the laboratories. The people are leading the leaders, who trail badly and now must play catch-up.
Because the nonresponsive federal government's repression of research is the main reason we know so little medically about cannabis, the federal coffers (Francis Collins at NIH, Peggy Hamburg at FDA, Nora Volkow at NIDA, and Michele Leonhart at DEA, take note) should now be opened wide to support serious marijuana research in the community as well as in the clinic and laboratory.

The people have chosen to become the guinea pigs in real life. Study them clinically, Colorado and Washington. Study them medically, you 20 states (plus the District of Columbia) where medical marijuana is legal.
For the marijuana users: It ain't harmless. Be careful because there is much we do not yet know, largely as a result of the long-term "federal foolishness" that has prevented most serious research from being done.
We do know this:
• Developing brains (at least to age 21 or later) are more vulnerable to drug damage. [3] ***Delay using cannabis as long as possible, if ever.***
• It is dangerous to drive automobiles (or tractors or motorcycles, or fly airplanes) while stoned. Don't drug and drive.
• DO NOT mainline pot potions. Intravenous injection of crude cannabis extracts makes one very sick. We also reported that in JAMA in 1971. [4]
For the criminal justice system: Decriminalize marijuana possession and use. Empty the prisons of nonviolent marijuana offenders, who should never have been there in the first place. Overturn Richard Nixon's Southern strategy of disenfranchising black voters by incarceration. Save tons of public money even while resisting the lobbying of the American for-profit prison system. Reverse 21st century Jim Crow.
For the US Congress: Revise the Controlled Substances Act. Either delete cannabis from any schedule or move it way down from Schedule I. My old friend Roger Egeberg (Assistant Secretary for Health and Scientific Affairs in the Department of Health, Education, and Welfare during the Nixon administration) was seriously wrong in 1970 when he advised you to make cannabis a Schedule I drug.
For journal editors: Invite papers describing reality as recorded by the observant and inquisitive local physician-scientist authors. JAMA: Plan a theme issue on medical and public health/policy aspects of cannabis.
I have included a lot of topics in this brief column, some without building background for the reader. I have the references and will make them available at your request.
That's my opinion. I am Dr. George Lundberg, At Large at Medscape.
Lundberg GD. Drug abuse in the Western world. JAMA. 1970;213:2082.
Lundberg GD. Complications of drug abuse. Calif Med. 1971;114:77-78.
Smith MJ, Cobia DJ, Wang L, et al. Cannabis-related working memory deficits and associated subcortical morphological differences in healthy individuals and schizophrenia subjects. Schizophr Bull. 2013 Dec 15. [Epub ahead of print]
Lundberg GD, Adelson J, Prosnitz EH. Marihuana-induced hospitalization. JAMA. 1971;215:121.

http://bit.ly/1bkrWFt

Hemp Gets High Five for Heart-Health Benefits

An outlawed plant could help fight America's top killer, heart disease, which ended the lives of nearly 600,000 in the United States in 2010, according to the Centers for Disease Control.

Jan 31, 2014 02:12 PM ET // by Tim Wall

A recent analysis identified several potentially heart-healthy chemicals in hemp, marijuana's hard-working, non-intoxicating cousin.
In particular, oil from hemp seeds contained high levels of alpha-linolenic acid, according to the study published by Spanish pharmacologists in the Journal of Agriculture and Food Chemistry. Alpha-linolenic acid is an omega-3 fatty acid that research suggests could reduce the risk of coronary heart disease.
Hemp seed oil's high polyunsaturated fat content -- compared to saturated fats -- could help reduce people's cholesterol levels and treat atherosclerosis, or the buildup of materials on the inside of arteries, wrote the researchers from the University of Seville, Spain.
The hemp oil also held gamma-linolenic acid. This chemical improved the condition of mice suffering from fibromyalgia syndrome, a chronic degenerative disease, in an experiment published in the Journal of Functional Foods. The hemp seed used in the study grew in western Canada. Canada legalized industrial hemp in 1998 for the production of fiber, vegetable oil and other products.
Since 1958, hemp has remained illegal in much of the United States, but change recently sprouted.
The Farm Bill currently working through the Senate would allow industrial hemp pilot projects on American farms.
Seeking a head start in the reemergent hemp business, some state governments moved early in anticipation of the passage of the bill. For example, Kentucky's General Assembly voted to legalize hemp last year and recently began moving forward with a test project, reported USA Today.
Botanists classify hemp and marijuana as different varieties of one plant, Cannabis sativa. Sturdy fibers from the stems of hemp have been used for thousands of years to make rope, fabric and other materials, yet contain very little tetrahydrocannabinol (THC), one of the main intoxicating chemicals that gives the flowers of the female marijuana plant her illegal potency.

http://bit.ly/1afBu6f

Threatwatch: Mother virus of China's deadly bird flu

Exactly 10 years after H5N1 bird flu exploded across south-east Asia, the virus is still widespread, and has been joined by new killer types of bird flu. Human cases of H7N9 flu are surging in south-east China, and a new type of bird flu, H10N8, has claimed its second human victim, in the same region.

17:28 31 January 2014 by Debora MacKenzie

Now it seems that all of these viruses stem from a single, mother virus. Targeting it might stop it from spawning new, deadly viruses in the future. Few people have heard of H9N2, but this virus was crucial in giving rise to the three dangerous bird flu viruses that have emerged so far in China – H5N1, H7N9 and H10N8. None of these viruses has yet evolved the ability to spread readily in people and potentially trigger a pandemic – although we know H5N1 can, and H7N9 and H10N8 seem similar. But even if those viruses never go rogue, their cousins might, because the real problem is their common ancestor, which endowed them with the genes that make them dangerous.

The enabler

"H9N2 is the enabler, the one to worry about," Robert Webster of St. Jude Children's Research Hospital in Memphis, Tennessee, told New Scientist. Bird flu is usually a gut infection in ducks, but H9N2 has evolved into a benign respiratory virus in chickens that has spread across Eurasia. When multiple flu viruses infect the same host, they can swap genes. They may be named for their various H and N surface proteins, but H5N1, H7N9 and H10N8 all got some or all of their "internal" genes from H9N2.

Those genes – for the enzymes that replicate the viral genome, for example, or a protein that confuses a host's immune system – can make these viruses dangerous, says Webster. Any of them might become pandemic if they acquire the right mutations to spread in people – or hybridise with a normal human flu.

Closing Asia's ubiquitous live poultry markets would be the key to controlling N9N2, says Webster, as this is where H9N2 and its spin-off viruses spread, mingle and evolve – and where humans catch them.

That is just what China is trying to do. As millions celebrate Lunar New Year this week with home-slaughtered poultry, Shanghai and three other cities have shut their live markets and officials are urging people to eat pre-slaughtered, frozen birds. The continued threat from China's bird flu may depend on whether that catches on. "It's the Year of the Horse in China," says Webster. "I hope they can get the stable door closed before the horse has bolted."

Back with a vengeance

H7N9 emerged in south-east China last spring, infecting 136 people, a third of whom died. In response, Chinese flu scientists called for live poultry markets to be shut last April. Some were – but they were re-opened when flu cases dropped in the following months.

The virus returned with a vengeance at the end of last year, however. So far 131 more infections have been reported since October last year. Caitlin Rivers of Virginia Tech in Blacksburg, Virginia, has modelled the spread of H7N9, and says she is convinced that poultry markets are a primary driver of the outbreak.

Now the affected area is growing and south-east China is reporting some half dozen new cases per day, so the call to close markets is strengthening. China's National Health and Family Planning Commission announced this week that live markets should close if they harbour H7N9, after the country's Ministry of Agriculture confirmed that the virus is mainly found in these markets, rather than on farms.

Killer in the family

But H7N9 is not the only problem. The latest killer in the family, H10N8, took the life of a 73-year-old woman in December last year, and now a 55-year-old woman is critically ill with it after visiting a live poultry market. "We know very little about H10 viruses," says Richard Webby, also at St. Jude, and there may be other new viruses that have not been detected yet.

Meanwhile, H5N1 still circulates in Chinese poultry – silently, because it can spread in vaccinated birds without causing obvious disease. A Canadian woman died of H5N1 flu this month after flying home from a visit to Beijing, even though the city has not reported a case of H5N1 in years.

Shanghai and three cities in Zhejiang Province, the hardest hit by the current outbreak of H7N9, have now temporarily shut their live markets. Officials from one of these cities, Hangzhou, say they want to make the closure permanent, and switch to frozen, centrally slaughtered poultry. Zhang Yonghui, head of the Guangdong Centre for Disease Prevention and Control, told China's official news service Xinhua this week that the government should switch the country to such industrial chicken slaughter.

That will not be easy. Hopes that the temporary market closures of last spring would become permanent were dashed when consumers demanded their re-opening. "I can understand the difficulty," says Webster. "Culturally, the Chinese must eat freshly slaughtered poultry on New Year's Day," and they tend to prefer it at any time.

But the risks, he says, have become too high. The world now waits to see what the future holds for China's chickens.

http://www.eurekalert.org/pub_releases/2014-02/embl-myb013114.php

Making your brain social

Failure to eliminate links between neurons produces autistic-like mice

In many people with autism and other neurodevelopmental disorders, different parts of the brain don't talk to each other very well. Scientists have now identified, for the first time, a way in which this decreased functional connectivity can come about. In a study published online today in Nature Neuroscience, scientists at the European Molecular Biology Laboratory (EMBL) in Monterotondo, Italy, and collaborators at the Istituto Italiano di Tecnologia (IIT), in Rovereto, and La Sapienza University in Rome, demonstrate that it can be caused by cells called microglia failing to trim connections between neurons.

"We show that a deficit in microglia during development can have widespread and long-lasting effects on brain wiring and behaviour," says Cornelius Gross, who led the study. "It leads to weak brain connectivity, decreased social behaviour, and increased repetitive behaviour, all hallmarks of autism."

The findings indicate that, by trimming surplus connections in the developing brain, microglia allow the remaining links to grow stronger, like high-speed fibre-optic cables carrying strong signals between brain regions. But if these cells fail to do their job at that crucial stage of development, those brain regions are left with a weaker communication network, which in turn has lifelong effects on behaviour.

Yang Zhan, a postdoctoral fellow in Gross' lab at EMBL, analysed the strength of connections between different areas of brain in mice that were genetically engineered to have fewer microglia during development. Working with Alessandro Gozzi's lab at IIT and Davide Ragozzino at La Sapienza University, the EMBL scientists combined this approach with high-resolution fMRI (functional Magnetic Resonance Imaging) scans of the mice's brains, taking full advantage of a novel technique developed at IIT, which enables scientists to obtain detailed, three-dimensional maps of the brain's functional connections. The team found that mice with fewer microglia had weaker connections between neurons, and less cross-talk between different brain regions.

When Rosa Paolicelli, a PhD student in Gross' lab, studied the mice's behaviour, she discovered that mice with fewer microglia and decreased connectivity displayed behaviours commonly associated with autism spectrum disorders. These mice spent more time repeatedly grooming themselves, and avoided social interactions.

"This is an exciting time to be studying microglia," Gross concludes: "they're turning out to be major players in how our brain gets wired up."