

http://www.eurekalert.org/pub_releases/2014-05/uops-sci052314.php

Sex-specific changes in cerebral blood flow begin at puberty, Penn study finds

Could give hints about male versus female risk for certain psychiatric disorders

PHILADELPHIA – Puberty is the defining process of adolescent development, beginning a cascade of changes throughout the body, including the brain. Penn Medicine researchers have discovered that cerebral blood flow (CBF) levels decreased similarly in males and females before puberty, but saw them diverge sharply in puberty, with levels increasing in females while decreasing further in males, which could give hints as to developing differences in behavior in men and women and sex-specific pre-dispositions to certain psychiatric disorders. Their findings are available in Proceedings of the National Academy of Science (PNAS). "These findings help us understand normal neurodevelopment and could be a step towards creating normal 'growth charts' for brain development in kids. These results also show what every parent knows: boys and girls grow differently. This applies to the brain as well," says Theodore D. Satterthwaite, MD, MA, assistant professor in the Department of Psychiatry in the Perelman School of Medicine at the University of Pennsylvania. "Hopefully, one day such growth charts might allow us to identify abnormal brain development much earlier before it leads to major mental illness." Studies on structural brain development have shown that puberty is an important source of sex differences. Previous work has shown that CBF declines throughout childhood, but the effects of puberty on properties of brain physiology such as CBF, also known as cerebral perfusion, are not well known. "We know that adult women have higher blood flow than men, but it was not clear when that difference began, so we hypothesized that the gap between women and men would begin in adolescence and coincide with puberty," Satterthwaite says.

The Penn team imaged the brains of 922 youth ages 8 through 22 using arterial spin labeled (ASL) MRI. The youth were all members of the Philadelphia Neurodevelopmental Cohort, a National Institute of Mental Health-funded collaboration between the University of Pennsylvania Brain Behavior Laboratory and the Center for Applied Genomics at the Children's Hospital of Philadelphia. They found support for their hypothesis.

Age related differences were observed in the amount and location of blood flow in males versus females, with blood flow declining at a similar rate before puberty and diverging markedly in mid-puberty. At around age 16, while male CBF values continue to decline with advanced age, females CBF values actually increased. This resulted in females having notably higher CBF than males by the end of adolescence. The difference between males and females was most notable in parts

of the brain that are critical for social behaviors and emotion regulation such as the orbitofrontal cortex. The researchers speculate that such differences could be related to females' well-established superior performance on social cognition tasks. Potentially, these effects could also be related to the higher risk in women for depression and anxiety disorders, and higher risk of flat affect and schizophrenia in men.

Additional Penn authors include ; Russell T. Shinohara of Biostatistics and Epidemiology; Raquel E. Gur, Ruben C. Gur, Daniel H. Wolf, Ryan Hopson, Simon Vandekar, Kosha Ruparel, Monica E. Calkins, David Roalf, Efstathios Gennatas, Chad Johnson, Karthik Prabhakaran of the department of Psychiatry; Mark A. Elliott and Christos Davatzikos, department of Radiology; John A. Detre of the department of Neurology; Hakon Hakonarson of the Center for Applied Genomics at the Children's Hospital of Philadelphia.

This work was funded by RC2 grants from the National Institute of Mental Health MH089983 and MH089924, as well as T32 MH019112. Dr. Satterthwaite was supported by K23MH098130 and the Mar Rapport family Investigator grant through the Brain and Behavior Foundation.

<http://phys.org/news/2014-05-incredible-dinosaur.html>

The incredible shrinking dinosaur

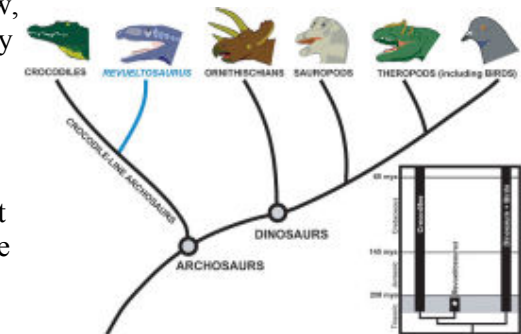
How dinosaurs re-sized.

Dinosaurs still roam the Earth - only now, according to researchers at the University of Oxford, they rule the air. At least, according to this landmark study, their miniaturized forms do.

"Dinosaurs aren't extinct," said Dr. Robert Benson, vertebrate paleontologist at Oxford University, England, "there are about 10,000 species alive today in the form of birds."

An evolutionary tree demonstrating the dinosaur clade and the bird clade that descended from it. Image Credit: Randall Irmis / Andrew Lee / Nick Pyenson

In an ambitious attempt to uncover the root of diversity in animals still alive today, Benson, along with Dr. David Evans of the Royal Ontario Museum and several others, assembled hundreds of evolutionary trees representing birds/dinosaurs from the Mesozoic era. The Mesozoic era ran roughly from 250 million to 65 million years ago. The "meso-" or middle era of life on Earth saw the rise of dinosaurs and mammals. It later saw the fall of almost all of the dinosaurs on land. The evolutionary trees showed that one solitary group managed to walk, or rather fly, away from the disaster. Birds were, and are, the one group of dinosaur that never stopped evolving.



In their recently published paper in PLOS Biology, Benson et al describe how at first dinosaurs rapidly diversified into different species, assuming a large variety of shapes and sizes. Each morphology, or permutation of appearance and function, reflected to some environmental niche, or resource area, that the dinosaur adapted to fill.

Once they adapted to fill those niches, most of the dinosaur species "became conservative," or stopped exploring new ecologies through their evolution. Every part of the dinosaur group, that is, except the branch of the evolutionary tree that evolved into what later became birds.

Since the 1970's evolutionary biology has proceeded largely on the assumption that modern birds are descended from non-bird dinosaurs.

What's new about this study is that the lineage is traced out by body mass. It showed for the first that when the Mesozoic chapter of Earth's history came to an abrupt end 65 million years ago, large body mass was not conducive to survival, whereas small-very small-was. - See more at: <http://www.astrobio.net/news-brief/the-incredible-shrinking-dinosaur/#sthash.5jlaLpbi.dpuf>

This is why: the enormous impact that triggered a rapid, prolonged winter decimated the food sources for large animals. According to the fossil record, those birds/dinosaurs that survived and evolved into modern times could have been as small as modern sparrows, which weigh around 15 grams, and are considerably lighter than the smallest non-bird dinosaurs, which weighed about 600 grams. Because of their small size, these Mesozoic birds had a wide-enough selection food sources to make it to modern times.

"If you are a small organism, ecologically you are capable of exploiting microhabitats," said Benson, "We find the greatest ecological diversity [today] in mammals and birds at around 100 grams."

The mass extinction that took place 65 million years ago provided an unprecedented opportunity for tiny dinosaurs that survived to take over wherever the larger dinosaurs couldn't find food: which was nearly everywhere.

With most other land animals extinct, the niches of the world now belonged to the birds.

Having achieved basic survival by shrinking, and having thrived by eating what others could not, the next step for small dinosaurs/birds was staking a permanent claim to each newly exploited niche. The key success in the recently remodeled world was rapid transformation or adaptive radiation.

"Adaptive radiation is the idea that evolution sometimes allows organisms to do something new for the first time," said Benson.

In this model of adaptive radiation, the clade of dinosaurs radiated a clade of birds. The bird clade then rapidly diversified, radiating branches for each of the many

species that filled the Earth. After every land dinosaur weighting over a kilogram died the birds took over their niches, adaptively radiating as they went.

In this way, adaptive radiation allows species to take advantage of ecologic diversity it exists in the world, and at the same time become ecologically diverse themselves.

Furthermore, according to this hypothesis, the dinosaurs that became birds didn't just go small and diverse: they continued to do so for the next 170 million years.

"Birds owe their success not just to recent adaptive radiation, they owe their evolutionary success to a long-term history of finding new niches over hundreds of millions of years," said Benson, "The rates of [bird] evolution never slowed down. They continued to find and exploit new niches throughout their ecologic history." Fast-forward to the present: birds are the most successful land vertebrate by a long shot.

Today there are 300 times more species of birds than species of crocodiles, even though both are descended from a dinosaur-like ancestor that lived 250 million years ago. The birds branched out because the land changed, whereas crocodiles lurked in freshwater, and seem to have lacked the evolutionary potential to change further, with no new niches to expand into. As a result the birds, said Benson, "are doing all kinds of things in the environment, whereas crocodiles are doing basically one thing."

Benson and Evans' model of continuous niche-filling on the part of the birds explains much of what we see in the world today including the dinosaur-descendant double-standard that exists between crocodiles and birds, how birds became the most successful land vertebrates, and why most birds are small and why ostriches and emus are the exception rather than the rule.

Their hypothesis draws a line, or rather a long series of lines, that outline the relationship between species extinct since the Mesozoic and the diversity of those still alive today.

According to their hypothesis, the mechanism behind dinosaurs surviving to the present as 10,000 bird species was miniaturization followed by adaptive radiation: leaving no useful ecological niche unfilled. If there was a place to move into with something to eat, birds moved there and adapted. Then they kept moving, kept adapting and kept surviving. Here, not just evolvability, but maintenance of evolvability, is the key.

In other words: re-sizing matters.

More information: Benson RBJ, Campione NE, Carrano MT, Mannion PD, Sullivan C, et al. (2014) Rates of Dinosaur Body Mass Evolution Indicate 170 Million Years of Sustained Ecological Innovation on the Avian Stem Lineage. PLoS Biol 12(5): e1001853. DOI: 10.1371/journal.pbio.1001853

<http://bit.ly/1wyOtiQ>

Ethiopia's blue volcano burns deadly sulphuric gas

IT'S a volcano, but not as we know it.

27 May 2014 by Clare Wilson

This cerulean eruption takes place in the Danakil Depression, a low-lying plain in Ethiopia. The volcano's lava is the usual orange-red – the blue comes from flames produced when escaping sulphuric gases burn.

French photographer Olivier Grunewald creates such images without using colour filters or digital enhancement, which is no simple task. To get this shot he had to wait until dusk, when the electric blue flames were visible, but before all the daylight had ebbed away. Then the wind had to be blowing away from him so he could get close enough. Photographing the similarly sulphurous Kawah Ijen volcano in Indonesia, where he worked inside the crater, was even more treacherous. "We have to take care when the winds push the flames close to us," he says. "In Danakil it is easier to escape as the land is flat."



(Image: Olivier Grunewald)

Grunewald works in a gas mask to avoid breathing in the deadly fumes – but photographing Kawah Ijen still left him with peeling skin and clothes smelling of rotten eggs for weeks afterwards.

Another drawback of Grunewald's subject matter is that the acidic gases don't agree with his cameras. But it's worth it, he says. "The phenomenon is so uncommon – we really feel like we are on another planet."

http://www.eurekalert.org/pub_releases/2014-05/tum-utt052614.php

Using thoughts to control airplanes

TUM researchers demonstrate: Brain controlled flight is possible

The pilot is wearing a white cap with myriad attached cables. His gaze is concentrated on the runway ahead of him. All of a sudden the control stick starts to move, as if by magic. The airplane banks and then approaches straight on towards the runway. The position of the plane is corrected time and again until the landing gear gently touches down. During the entire maneuver the pilot touches neither pedals nor controls.

This is not a scene from a science fiction movie, but rather the rendition of a test at the Institute for Flight System Dynamics of the Technische Universität München

(TUM). Scientists working for Professor Florian Holzapfel are researching ways in which brain controlled flight might work in the EU-funded project "Brainflight." "A long-term vision of the project is to make flying accessible to more people," explains aerospace engineer Tim Fricke, who heads the project at TUM. "With brain control, flying, in itself, could become easier.

This would reduce the work load of pilots and thereby increase safety. In addition, pilots would have more freedom of movement to manage other manual tasks in the cockpit."

Surprising accuracy

The scientists have logged their first breakthrough: They succeeded in demonstrating that brain-controlled flight is indeed possible – with amazing precision. Seven subjects took part in the flight simulator tests. They had varying levels of flight experience, including one person without any practical cockpit experience whatsoever.

The accuracy with which the test subjects stayed on course by merely thinking commands would have sufficed, in part, to fulfill the requirements of a flying license test. "One of the subjects was able to follow eight out of ten target headings with a deviation of only 10 degrees," reports Fricke. Several of the subjects also managed the landing approach under poor visibility. One test pilot even landed within only few meters of the centerline.

The TU München scientists are now focusing in particular on the question of how the requirements for the control system and flight dynamics need to be altered to accommodate the new control method.

Normally, pilots feel resistance in steering and must exert significant force when the loads induced on the aircraft become too large. This feedback is missing when using brain control. The researchers are thus looking for alternative methods of feedback to signal when the envelope is pushed too hard, for example.

Electrical potentials are converted into control commands

In order for humans and machines to communicate, brain waves of the pilots are measured using electroencephalography (EEG) electrodes connected to a cap. An algorithm developed by scientists from the Department of Biological Psychology and Neuroergonomics at the Berlin Institute of Technology allows the program to decipher electrical potentials and convert them into useful control commands.

Only the very clearly defined electrical brain impulses required for control are recognized by the brain-computer interface. "This is pure signal processing," emphasizes Fricke. Mind reading is not possible.

The researchers will present their results end of September at the "Deutscher Luft- und Raumfahrtkongress."

http://www.eurekalert.org/pub_releases/2014-05/au-smt052714.php

Scientists map the worst times of day for people allergic to grass pollen

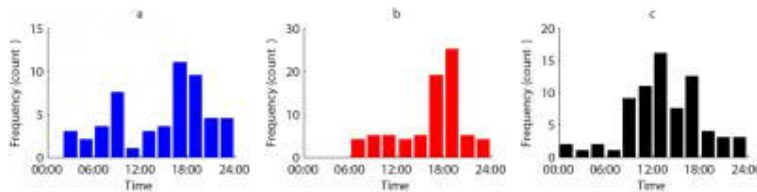
Based on their results, the researchers provide new advices to allergy sufferers

Atishoo! Help, there are flowering grasses around, please stay indoors – while your friends enjoy the nice summer weather! Traditionally, people allergic to grass pollen are advised to be aware of high pollen concentrations during the day, and to reduce their outdoor activities during this period.

A new study led by researchers from Aarhus University shows that it is considerably more complicated to avoid grass pollen. Based on a three-year study with intensive measurements at three different locations in Aarhus, they divide the grass pollen season into three periods, as shown in the graph below: a twin peak profile during the early season, a single evening profile in the middle season and a single midday profile during the late season.

How should people react to these complicated patterns? Dr. Robert Peel, Aarhus University, explains:

"People should avoid being outdoors during the peak hours in periods one and two, especially between 16 and 20. Later in the summer, allergy sufferers should avoid being outdoor in the middle of the day."



Diurnal concentration of grass pollen for periods one-three is shown. The graph shows peak-time distributions for (a) Period 1 (early season), (b) Period 2 (mid-season) and (c)

Period 3 (late season). Please note the different scales: Period two has the highest concentrations of pollen. These ideal profiles are based on 37, 58 and 62 basic profiles, respectively. Credit: Robert G. Peel

Different species have different patterns

Concentrations of grass pollen are influenced by many factors, the most important being the weather and the emissions, which again depends on the grass species. In Denmark alone, 230 species of grass (atishoo!) have been recorded, of which around 20 species are likely to be particularly common in urban environments. The emission of pollen from the individual species is driven by different weather parameters, e.g. the temperature on the previous day or on the current day, some emissions stop when it is raining, others release their pollen in response to rain. Each species flowers intensively for approximately one-two weeks, and the total season is around two months. So no wonder, the patterns of grass pollen are

complicated. But in general, people react more or less in the same manner to the pollen of all grasses growing in Denmark – and you cannot distinguish the species when counting pollen under a microscope.

Even though the information of the exact species present in the monitored area and pollen release patterns of the individual species are far from complete, Peel and his colleagues conclude that the best way to explain the three concentration patterns is to look at the succession of different grass species with different diurnal flowering patterns which dominate the atmospheric pollen loads as the season progresses.

The study was performed in collaboration with colleagues from the universities of Worcester, Vienna, Roskilde and the Astma-Allergy Association Denmark.

Seasonal variation in diurnal atmospheric grass pollen concentration profiles. R.G. Peel et al., Biogeosciences 11 (2014), 821-832. Doi:10.5194/bg-11-821/2014,

http://www.biogeosciences.net/11/821/2014/bg-11-821-2014-metrics.ht

http://www.eurekalert.org/pub_releases/2014-05/agu-aep052714.php

AGU: Experts publish new view of zone where Malaysia Airlines flight 370 might lie

A new illustration of the seafloor details underwater terrain where the missing Malaysia Airlines flight might be located

WASHINGTON, D.C. -- A new illustration of the seafloor, created by two of the world's leading ocean floor mapping experts that details underwater terrain where the missing Malaysia Airlines flight might be located, could shed additional light on what type of underwater vehicles might be used to find the missing airplane and where any debris from the crash might lie.

The seafloor topography map illustrates jagged plateaus, ridges and other underwater features of a large area underneath the Indian Ocean where search efforts have focused since contact with Malaysia Airlines flight MH370 was lost on March 8. The image was published today in Eos, the weekly newspaper of the Earth and space sciences, published by the American Geophysical Union.

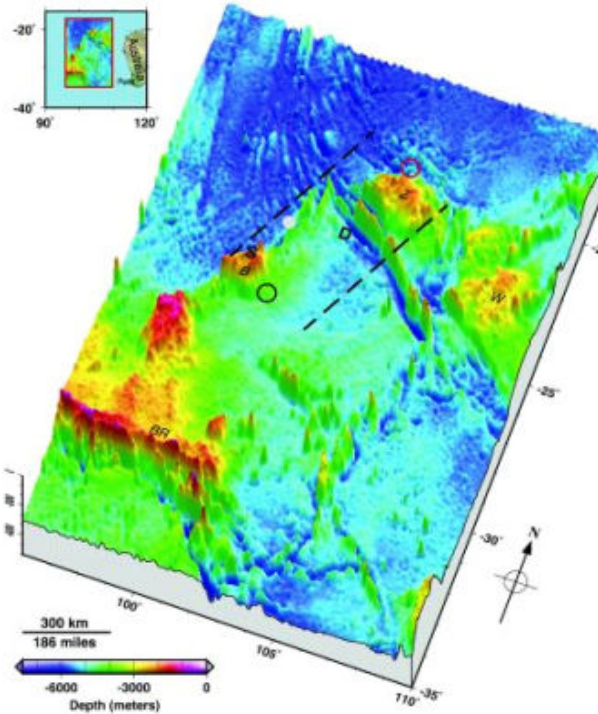
The new illustration of a 2,000 kilometer by 1,400 kilometer (1,243 miles by 870 miles) area where the plane might be shows locations on the seafloor corresponding to where acoustic signals from the airplane's black boxes were reportedly detected at the surface by two vessels in the area. It also shows the two plateaus near where these "pings" were heard.

It points out the deepest point in the area: 7,883 meters (about five miles) underneath the sea in the Wallaby-Zenith Fracture Zone – about as deep as 20 Empire State buildings stacked top to bottom. Undersea mountains and plateaus rise nearly 5,000 meters (about three miles) above the deep seafloor, according to the map.

The illustration, designated as Figure 1 of the Eos article, was created by Walter H.F. Smith and Karen M. Marks, both of the National Oceanic and Atmospheric Administration's Laboratory for Satellite Altimetry in College Park, Maryland, and the former and current chairs, respectively, of the Technical Sub-Committee on Ocean Mapping of the General Bathymetric Chart of the Oceans, or GEBCO. GEBCO is an international organization that aims to provide the most authoritative publicly available maps of the depths and shapes of the terrain underneath the world's oceans.

Satellite altimetry has made it possible to depict the topography of vast regions of the seafloor that would otherwise have remained unmapped, Smith said. To illustrate the topography of the search area, Smith and Marks used publicly available data from GEBCO and other bathymetric models and data banks, along with information culled from news reports.

This is the seafloor topography in the Malaysia Airlines flight MH370 search area. Dashed lines approximate the search zone for sonar pings emitted by the flight data recorder and cockpit voice recorder popularly called black boxes. The first sonar contact (black circle) was reportedly made by a Chinese vessel on the east flank of Batavia Plateau (B), where the shallowest point in the area (S) is at an estimated depth of 1637 meters. The next reported sonar contact (red circle) was made by an Australian vessel on the north flank of Zenith Plateau (Z). The deepest point in the area (D) lies in the Wallaby-Zenith Fracture Zone at an estimated depth of 7883 meters. The Wallaby Plateau (W) lies to the east of the Zenith Plateau. The shallowest point in the entire area shown here is on Broken Ridge (BR). Deep Sea Drilling Project (DSDP) site 256 is marked by a gray dot. The inset in the top left shows the area's location to the west of Australia. Seafloor depths are from the General Bathymetric Chart of the Oceans [2010].



Walter H.F. Smith and Karen M. Marks

Smith said the terrain and depths shown in the map could help searchers choose the appropriate underwater robotic vehicles they might use to look for the missing

plane. Knowing the roughness and shape of the ocean floor could also help inform models predicting where floating debris from the airplane might turn up. Smith cautions that the new illustration is not a roadmap to find the missing airplane. Nor does the map define the official search area for the aircraft, he added. "It is not 'x marks the spot'," Smith said of their map. "We are painting with a very, very broad brush."

Search efforts for the missing airplane have focused on an area of the southern Indian Ocean west of Australia where officials suspect that the plane crashed after it veered off course. After an initial air and underwater search failed to find any trace of the airplane, authorities announced this month that they will expand the search area and also map the seabed in the area.

Smith pointed out that the search for the missing plane is made more difficult because so little is understood about the seafloor in this part of the Indian Ocean. In the southeast Indian Ocean, only 5 percent of the ocean bottom has been measured by ships with echo soundings. Knowledge of the rest of the area comes from satellite altimetry, which provides relatively low-resolution mapping compared to ship-borne methods.

"It is a very complex part of the world that is very poorly known," Smith said. A lack of good data about Earth's seafloors not only hinders search efforts, it also makes it harder for scientists to accurately model the world's environment and climate, Smith noted. Today, our knowledge of our planet's undersea topography is "vastly poorer than our knowledge of the topographies of Earth's Moon, Mars and Venus," Smith and Marks write in Eos. This is because these other planetary bodies have no oceans, making their surfaces relatively easy to sense from space. Smith said he hoped that "the data collected during the search for MH370 will be contributed to public data banks and will be a start of greater efforts to map Earth's ocean floor."

http://www.eurekalert.org/pub_releases/2014-05/bu-ahe052714.php

A habitable environment on Martian volcano?

Slopes of Arsia Mons, once covered in glacial ice, may have been home to one of the most recent habitable environments yet found on the Red Planet

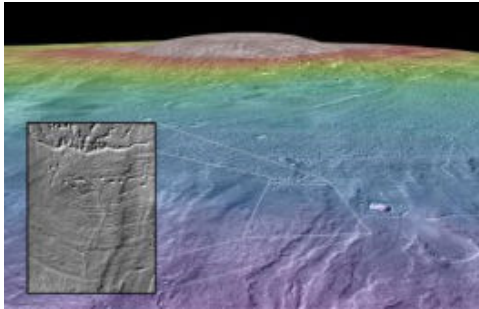
PROVIDENCE, R.I. [Brown University] - The slopes of a giant Martian volcano, once covered in glacial ice, may have been home to one of the most recent habitable environments yet found on the Red Planet, according to new research led by Brown University geologists.

Nearly twice as tall as Mount Everest, Arsia Mons is the third tallest volcano on Mars and one of the largest mountains in the solar system. This new analysis of the landforms surrounding Arsia Mons shows that eruptions along the volcano's northwest flank happened at the same time that a glacier covered the region around

210 million years ago. The heat from those eruptions would have melted massive amounts of ice to form englacial lakes - bodies of water that form within glaciers like liquid bubbles in a half-frozen ice cube.

The ice-covered lakes of Arsia Mons would have held hundreds of cubic kilometers of meltwater, according to calculations by Kat Scanlon, a graduate student at Brown who led the work. And where there's water, there's the possibility of a habitable environment. "This is interesting because it's a way to get a lot of liquid water very recently on Mars," Scanlon said.

While 210 million years ago might not sound terribly recent, the Arsia Mons site is much younger than the habitable environments turned up by Curiosity and other Mars rovers. Those sites are all likely older than 2.5 billion years. The fact that the Arsia Mons site is relatively young makes it an interesting target for possible future exploration.



Arsia Mons, the third-largest volcano on Mars may have been home to a habitable environment in Mars's relatively recent past. The rippled terrain in the foreground shows where a glacier once clung to the foothills of the mountain. Brown University researchers show that eruptions occurred under that ice sheet, which would have created lakes of liquid water. Where there was water, there's the possibility of past life. (Colors indicate elevation.) NASA/Goddard Space Flight Center/Arizona State University/Brown University

"If signs of past life are ever found at those older sites, then Arsia Mons would be the next place I would want to go," Scanlon said.

A paper describing Scanlon's work is published in the journal *Icarus*. Scientists have speculated since the 1970s that the northwest flank of Arsia Mons may once have been covered by glacial ice. That view got a big boost in 2003 when Brown geologist Jim Head and Boston University's David Marchant showed that terrain around Arsia Mons looks strikingly similar to landforms left by receding glaciers in the Dry Valleys of Antarctica. Parallel ridges toward the bottom of the mountain appear to be drop moraines - piles of rubble deposited at the edges of a receding glacier. An assemblage of small hills in the region also appears to be debris left behind by slowly flowing glacial ice.

The glacier idea got another boost with recently developed climate models for Mars that take into account changes in the planet's axis tilt. The models suggested that during periods of increased tilt, ice now found at the poles would have migrated toward the equator. That would make Mars's giant mid-latitude mountains -

Ascraeus Mons, Pavonis Mons and Arsia Mons - prime locations for glaciation around 210 million years ago.

Fire and ice

Working with Head, Marchant, and Lionel Wilson from the Lancaster Environmental Centre in the U.K., Scanlon looked for evidence that hot volcanic lava may have flowed in the region the same time that the glacier was present. She found plenty.

Using data from NASA's Mars Reconnaissance Orbiter, Scanlon found pillow lava formations, similar to those that form on Earth when lava erupts at the bottom of an ocean. She also found the kinds of ridges and mounds that form on Earth when a lava flow is constrained by glacial ice. The pressure of the ice sheet constrains the lava flow, and glacial meltwater chills the erupting lava into fragments of volcanic glass, forming mounds and ridges with steep sides and flat tops. The analysis also turned up evidence of a river formed in a jökulhlaup, a massive flood that occurs when water trapped in a glacier breaks free.

Based on the sizes of the formations, Scanlon could estimate how much lava would have interacted with the glacier. Using basic thermodynamics, she could then calculate how much meltwater that lava would produce. She found that two of the deposits would have created lakes containing around 40 cubic kilometers of water each. That's almost a third of the volume of Lake Tahoe in each lake. Another of the formations would have created around 20 cubic kilometers of water.

Even in the frigid conditions of Mars, that much ice-covered water would have remained liquid for a substantial period of time. Scanlon's back-of-the-envelope calculation suggests the lakes could have persisted for hundreds or even a few thousand years.

That may have been long enough for the lakes to be colonized by microbial life forms, if in fact such creatures ever inhabited Mars.

"There's been a lot of work on Earth - though not as much as we would like - on the types of microbes that live in these englacial lakes," Scanlon said. "They've been studied mainly as an analog to [Saturn's moon] Europa, where you've got an entire planet that's an ice covered lake."

In light of this research, it seems possible that those same kinds of environs existed on Mars at this site in the relatively recent past.

There's also possibility, Head points out, that some of that glacial ice may still be there. "Remnant craters and ridges strongly suggest that some of the glacial ice remains buried below rock and soil debris," he said. "That's interesting from a scientific point of view because it likely preserves in tiny bubbles a record of the atmosphere of Mars hundreds of millions of years ago. But an existing ice deposit might also be an exploitable water source for future human exploration."

http://www.eurekalert.org/pub_releases/2014-05/p-ieo052114.php

Intertwined evolution of human brain and brawn

New study suggests that human muscle may be as unique as our cognition

The cognitive differences between humans and our closest living cousins, the chimpanzees, are staggeringly obvious. Although we share strong superficial physical similarities, we have been able to use our incredible mental abilities to construct civilisations and manipulate our environment to our will, allowing us to take over our planet and walk on the moon while the chimps grub around in a few remaining African forests.

But a new study suggests that human muscle may be just as unique. Scientists from Shanghai's CAS-MPG Partner Institute for Computational Biology, together with teams from German Max Planck Institutes, investigated the evolution of metabolites – small molecules like sugars, vitamins, amino acids and neurotransmitters that represent key elements of our physiological functions. Their study found that metabolite concentrations evolved rapidly over the course of human evolution in two tissues: in the brain and, more surprisingly, in muscle. An article describing their findings will be published on May 27th in the open-access journal PLOS Biology.

Genomes, including the human genome, accumulate changes steadily over time.

Among the genetic changes that have happened over the course of human evolution, only a few might be responsible for the rise of distinct human features. To determine what other molecules played a role in human evolution, scientists began to look beyond the genome. The international team of scientists, led by Dr Philipp Khaitovich from Shanghai, examined for the first time the evolution of the human metabolome – the compendium of metabolites present in human tissues.

"Metabolites are more dynamic than the genome and they can give us more information about what makes us human", says Khaitovich. "It is also commonly known that the human brain consumes way more energy than the brains of other species; we were curious to see which metabolic processes this involves."

Indeed, it turned out that unlike the uniformly-paced evolution of the genome, the metabolome of the human brain has evolved four times faster than that of the chimpanzee. What was more surprising, however, is that human muscle accumulated an even higher amount of metabolic change – ten times that of the chimpanzee!

To rule out the possibility that this change simply reflects our couch potato lifestyle, the scientists performed additional measurements in specially treated macaque monkeys. These macaques were moved from a spacious countryside facility to small indoor enclosures and served fatty and sugary food for several weeks, to imitate the environment of many contemporary humans. These lifestyle changes

had only a small effect on the macaque muscle metabolome. "For a long time we were confused by metabolic changes in human muscle", says Dr Kasia Bozek, the lead author of the study, "until we realized that what other primates have in common, in contrast to humans, is their enormous muscle strength." Dr Josep Call, from the Wolfgang Kohler Primate Research Center in Leipzig, Germany, concurs: "This is common knowledge to all the zoo keepers, but it was never tested systematically." To prove their point, researchers involved several chimpanzees, macaques, university students, and even professional athletes in a pulling strength competition. Despite their sweat and determination, all of the human participants of the experiment were outcompeted by their primate opponents by more than two-fold.

A tantalizing hypothesis suggested by the scientists is that the metabolic roles of human brain and brawn are intertwined. "Our results suggest a special energy management in humans, that allows us to spare energy for our extraordinary cognitive powers at a cost of weak muscle", summarizes Dr Kasia Bozek. "The world of human metabolomics is just starting to open up its secrets to us", adds Dr Patrick Giavalisco, who led the metabolome measurement effort at the Max Planck Institute for Molecular Plant Physiology in Golm. "Such human-specific metabolic features we find could be related not only to physical or cognitive performance but also to common human metabolic diseases".

<http://www.plosbiology.org/article/info:doi/10.1371/journal.pbio.1001871>

Citation: Bozek K, Wei Y, Yan Z, Liu X, Xiong J, et al. (2014) Exceptional Evolutionary Divergence of Human Muscle and Brain Metabolomes Parallels Human Cognitive and Physical Uniqueness. PLoS Biol 12(5): e1001871. doi:10.1371/journal.pbio.1001871
Funding: This study was supported by the National Natural Science Foundation of China (grant numbers 31171232, 31250110071, Y23DC41301) and Ministry of Science and Technology of China (grant number 2012DFG31940), National Science Foundation (grant BCS-0824531) and James S. McDonnell Foundation (grants 22002078 and 220020293). PK was supported by the Foreign Expert 1000 Talents Plan program; KB was supported by a Chinese Academy of Sciences fellowship (2011Y1SB06). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. Competing Interests: The authors have declared that no competing interests exist.

<http://www.medscape.com/viewarticle/825514?>

Prostate Cancer Screening: It Ain't Dead Yet

Data suggest that infrequent screening with PSA levels may help to reduce the overdiagnosis of prostate cancer

Charles P. Vega, MD

Prostate Cancer

Prostate cancer is the second leading cancer killer in the United States, yet 2 large randomized trials of screening for prostate cancer provided mixed, and generally

unfavorable, results.^[1,2] New research continues to underscore the dichotomy between the results of screening programs in Europe and the United States. However, new and highly interesting data also suggest that infrequent screening with prostate-specific antigen (PSA) levels may help to reduce the overdiagnosis of prostate cancer. This review examines the state of the art in prostate cancer screening.

Screening for Prostate Cancer

There are few areas more controversial in clinical medicine than screening for prostate cancer. The high prevalence of prostate cancer, especially in light of an increasingly older male population, and its impact on personal and public health, cannot be denied. In 2012, more than 240,000 new cases of prostate cancer were diagnosed in the United States, and prostate cancer accounted for 28,170 deaths.^[3] Prostate cancer is the number-two cancer killer among US men, trailing only lung cancer. Overall, the lifetime risk for prostate cancer among men in the United States is 16.5%.

Nonetheless, the tools promoted to screen men for asymptomatic prostate cancer are clearly flawed. In its 2012 recommendation against routine screening for prostate cancer, the US Preventive Services Task Force cites 2 major trials in influencing its decision.^[4]

Results from the Prostate, Lung, Colon, and Ovarian (PLCO) Cancer Screening Trial in the United States failed to detect any benefit associated with prostate cancer screening in preventing prostate cancer-specific mortality after 7-10 years.^[1] In the European Randomized Study of Screening for Prostate Cancer (ERSPC), 162,000 men between the ages of 55 and 69 years underwent randomization to PSA screening at an average of once every 4 years, or no screening.^[2] Screening was associated with an overall reduction in the risk for death from prostate cancer of 20% -- a significant result but modest, considering that 1410 men would have to be invited to screening to prevent 1 additional death from prostate cancer.

This recommendation and other articles highlighting the limitations of PSA screening have led to a profound change in clinical practice. In a study evaluating PSA screening performed in multiple centers between 2008 and 2012, PSA testing increased until March 2009, when the PLCO and ERSPC trial results were published.^[5] Afterward, there was a steady decline overall in the number of screening PSA tests ordered, with the most substantial reductions occurring in urology practices and among men aged 50-59 years.

But are we being too hasty in dismissing prostate cancer screening as ineffective and wasteful? New research on the large cohorts randomly assigned to screening vs usual care in the European trial suggest that the relative value of earlier prostate

cancer detection may increase as men grow older. Other studies suggest smarter, more efficient ways to use PSA to identify men at high risk for prostate cancer.

Does Prostate Cancer Screening, Like a Fine Wine, Improve With Age?

A follow-up study of the ERSPC cohort evaluated men who were 55-74 years of age at the time of prostate cancer screening.^[6] Researchers found that the benefit of screening increased as men grew older. After a median of 12.8 years, the relative risk reduction for prostate cancer mortality among men between the ages of 55-69 years was 31.6. The number of men needed to invite to screen to prevent an additional case of prostate cancer fell to 565 in those 55-74 years of age and 392 for those 65-69 years of age, a substantial reduction compared with the previous analysis from 2009.

This follow-up research suggests that the benefits of prostate cancer screening increase with time. However, data from PLCO again contradict the results of ERSPC. In a follow-up study 13 years after randomization of the PLCO cohort to prostate cancer screening or usual care, the screening cohort still did not experience a benefit in prostate cancer-specific mortality.^[7]

A Practical Solution: Can Less Testing Identify High-Risk Patients?

Currently, men at high risk for prostate cancer are identified by family history or, often too late, symptoms. However, infrequent screening begun in early middle age may be another efficient means to identify patients at risk for prostate cancer while reducing the number of false-positive tests.

In a study of more than 21,000 men in Sweden, 44% of all deaths from prostate cancer occurred among men in the highest 10th percentile of PSA values between 45 and 49 years of age.^[8] In contrast, a PSA value below the median for age among men aged 45-49 or 51-55 years was associated with a 15-year risk for prostate cancer metastasis of only 0.09%. The study investigators concluded that a longer screening interval is appropriate for men with PSA values below the median during early middle age.

Another recent study examined the value of PSA levels obtained at age 60 years.^[9] Among men with a PSA level less than 2 ng/mL, which comprised 71.7% of the study sample, PSA screening vs no screening was associated with a moderate increase in the number of prostate cancer diagnoses, without a concomitant effect on prostate cancer mortality.

However, men with a baseline PSA level of 2 ng/mL experienced a substantial prostate cancer-specific mortality benefit associated with PSA screening. Only 23 men needed to be screened among this higher-risk group to prevent 1 additional death from prostate cancer.

The researchers concluded that men with a PSA level less than 1 ng/mL at age 60 years require no further screening. In contrast, a PSA level of 2 ng/mL or more

should prompt continued screening beyond age 60 years. Levels of 1-2 ng/mL fall in a gray area in which patients and clinicians should consider the benefits vs risks of further screening more closely.

Implications for Practice

The controversy regarding prostate cancer screening is far from over. The lack of clarity on the issue is sure to be frustrating for patient and provider alike.

It appears that routine annual testing with PSA is not substantially beneficial overall. A recent Cochrane Collaboration meta-analysis confirmed no benefit in terms of prostate cancer-specific mortality with screening, and screening has not been demonstrated to improve overall mortality in any trial.^[10] At the same time, the Cochrane report focuses on the potential danger of overdiagnosis of prostate cancer, suggesting that up to 50% of cancers discovered as part of the ERSPC trial were not clinically relevant to the patient's morbidity or mortality risk.

There is reason for hope among patients and clinicians who believe in prostate cancer screening, and it comes in the form of these highly constructive analyses of large prevention studies from Europe. Shared decision-making with patients with respect to prostate cancer screening remains critical. Patients can be told that PSA levels obtained at 1 or 2 time points in the life cycle may direct further screening in a meaningful and highly efficient way. Specifically, average-risk men with low PSA levels at the ages of 45-55 and 60 years are unlikely to benefit from further screening for prostate cancer, which reduces the risk for overdiagnosis and frees the patient and provider to pursue other preventive health goals.

Further research will certainly enlighten screening practices, but the current data allow for a range of choices in detecting prostate cancer in the general population. The choice of a screening plan should be informed by this most recent analysis, with the patient's beliefs and preferences paramount in that decision-making process.

Clinical Pearls

- The lifetime risk for prostate cancer in the United States exceeds 16%.
- Clinical trials of screening for prostate cancer have had mixed results in terms of reducing prostate cancer-specific mortality, and screening does not improve overall mortality.
- New data updated for a longer follow-up period from the large prostate cancer screening trials continue to provide conflicting results about the mortality benefits of screening.
- However, recent studies examining the value of infrequent PSA screening for prostate cancer suggest that testing between the ages of 45 and 55 years and at age 60 years could identify a large group of men at low risk for prostate cancer. These men would no longer need routine screening.
- Shared decision-making with patients is still critically important in decisions on whether and how to screen for prostate cancer.

References

1. Andriole GL, Crawford ED, Grubb RL 3rd, et al; PLCO Project Team. Mortality results from a randomized prostate-cancer screening trial. *N Engl J Med.* 2009;360:1310-1319. [Abstract](#)
2. Schröder FH, Hugosson J, Roobol MJ, et al; ERSPC Investigators. Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med.* 2009;360:1320-1328. [Abstract](#)
3. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J Clin.* 2012;62:10-29. [Abstract](#)
4. Moyer VA; U.S. Preventive Services Task Force. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2012;157:120-134. [Abstract](#)
5. Aslani A, Minnillo BJ, Johnson B, Cherullo EE, Ponsky LE, Abouassaly R. The impact of recent screening recommendations on prostate cancer screening in a large health care system. *Urology.* 2014;191:1737-1742.
6. Roobol MJ, Kranse R, Bangma CH, et al; ERSPC Rotterdam Study Group. Screening for prostate cancer: results of the Rotterdam section of the European randomized study of screening for prostate cancer. *Eur Urol.* 2013;64:530-539. [Abstract](#)
7. Andriole GL, Crawford ED, Grubb RL 3rd, et al; PLCO Project Team. Prostate cancer screening in the randomized Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial: mortality results after 13 years of follow-up. *J Natl Cancer Inst.* 2012;104:125-132. [Abstract](#)
8. Vickers AJ, Ulmert D, Sjoberg DD, et al. Strategy for detection of prostate cancer based on relation between prostate specific antigen at age 40-55 and long term risk of metastasis: case-control study. *BMJ.* 2013;346:f2023.
9. Carlsson S, Assel M, Sjoberg D, et al. Influence of blood prostate specific antigen levels at age 60 on benefits and harms of prostate cancer screening: population based cohort study. *BMJ.* 2014;348:g2296.
10. Ilic D, Neuberger MM, Djulbegovic M, Dahm P. Screening for prostate cancer. *Cochrane Database Syst Rev.* 2013;CD004720.

<http://bit.ly/1keaqZ5>

California to Issue Driving Licenses to Robots

California, eager to retain its role as legal arbiter to the auto world, in July will begin taking applications for driving licenses for self-driving cars.

By Philip E. Ross

The licenses take effect in September.

The car will merely have to bring along a sane, sober, attentive, insured, licensed human driver to sit behind the wheel and quickly take over if need be. And the license will cost US \$150 a pop. And the insurance policy must be for \$5 million. It's almost as if the law were crafted only for those who want to experiment with robocars. By the way, companies will be allowed to take out 10 licenses apiece. Also, the person sitting behind the wheel must have been suitably trained by the car's manufacturer.

That means nobody will be able to sleep his way to work or sleep off a night of heavy drinking on his way back. But this rule is a first, and a certain amount of initial caution is well founded, certainly more than was the case in the earliest days of the automobile (which itself means "self-driving").

Back then, in some places - as an expert recalled in a book published in 1939 - "a man with a red flag had to walk in front of the car, and that might easily have developed into a very strenuous job had not those who drafted the law seen this possibility and fixed the legal speed limit at four miles per hour."

It's all part of a forward-looking package that the California state legislature has stipulated must be turned into law by the end of the year. And what's law today in California often molds what companies and governments do tomorrow.

<http://bit.ly/U5b6pd>

European Invasion Changed Peru's Coastline

Sections of Peru's coastline were stabilized by the activities of indigenous people, the demise of whom following the Spanish invasion led to an alteration of the geography. Cynthia Graber reports

[Download MP3](#)

The Spanish arrival in South America changed many things - including, it seems, even the Peruvian coastline.

In dry northwestern Peru, unusual 19-mile-long sandy coastal ridges were formed through tectonic activity, El Niño storms and natural sediment deposit.

The nine ridges still standing appear to have formed from 5,100 years ago until about 400 years ago. And they're topped with deposits of shells, rocks from fire pits and other human artifacts.

Scientists studying the region found that the shells are from mollusks and barnacles, and primarily of species still fished there today.

They thus concluded that the shells were left by native communities who long called the region home.

The researchers also found that the clamshell and fire deposits stabilized the ridges and protected them from erosion.

No such stable ridges exist along the coast from the past 400 years, after the local people died from disease or war, or were pushed inland. Any incipient ridges since were easily toppled by wind and storms.

The research is in the Proceedings of the Natural Academy of Sciences. [\[Daniel F. Belknap and Daniel H. Sandweiss, Effect of the Spanish Conquest on coastal change in Northwestern Peru\]](#)

Visitors now see what they may think is a natural landscape. But its formation depended on thousands of years of human activity.

<http://bit.ly/1mFeej9>

Drug users switch to heroin because it's cheap, easy to get

A nationwide survey indicates that heroin users are attracted to the drug not only for the "high" but because it is less expensive and easier to get than prescription painkillers.

Researchers at Washington University School of Medicine in St. Louis published the survey's results May 28 in the journal JAMA Psychiatry.

"In the past, heroin was a drug that introduced people to narcotics," said principal investigator Theodore J. Cicero, PhD. "But what we're seeing now is that most people using heroin begin with prescription painkillers such as OxyContin, Percocet or Vicodin, and only switch to heroin when their prescription drug habits get too expensive."

Cicero and his colleagues analyzed data gathered from more than 150 drug treatment centers across the United States. More than 9,000 patients dependent on narcotic painkillers, or opioids, completed the surveys from 2010 to 2013. Of those, almost 2,800 reported heroin as their primary drug of abuse.

The researchers noted three key factors in the decision to use heroin: accessibility, including lower cost; enjoyment of the high; and the ease with which the drug could be snorted or injected. To get even more detail about those who use heroin, the researchers zeroed in on 54 patients who participated in unstructured interviews about drug use.

"The price on the street for prescription painkillers, like OxyContin, got very expensive," Cicero said. "It has sold for up to a dollar per milligram, so an 80 milligram tablet would cost \$80. Meanwhile, they can get heroin for \$10."

In 2010, the often-abused prescription painkiller OxyContin was reformulated to make the pills more difficult to crush or dissolve. In a 2012 letter to The New England Journal of Medicine, Cicero noted that the reformulation had made it more difficult for users to snort or inject OxyContin but that the change had led some users to switch to other drugs, including heroin.

"If you make abuse-deterrent formulations of these drugs and make it harder to get high, these people aren't just going to stop using drugs," said Cicero, a professor of neuropharmacology in psychiatry. "As we made it more difficult to use one drug, people simply migrated to another. Policymakers weren't ready for that, and we certainly didn't anticipate a shift to heroin."

Today's heroin users are older - 23, on average - when they first try the drug. Most got high with prescription drugs acquired illegally before switching to heroin. They tend to live in suburban or rural areas rather than the inner city, and more than 90 percent of the study subjects who began using heroin in the past decade are white.

Previous research had reported that in the 1960s and 1970s, more than 80 percent of heroin users were young male minorities who lived in inner cities and began using the drug at about age 16.

"Our earlier studies showed that people taking prescription painkillers thought of themselves as different from those who used heroin," Cicero said. "We heard over and over again, 'At least I'm not taking heroin.' Obviously, that's changed."

Cicero said it's surprising that a drug like heroin is becoming more acceptable in suburban and rural settings. But he believes that more studies of people in treatment programs may shine light on the problem.

"The overdose deaths and hospitalizations are symptoms of a problem that we really need to deal with," he said. "You can't effectively treat people or prevent addiction unless you know why they are taking drugs, and we don't really have a handle on that yet. Unfortunately, the problem with heroin is it's the most powerful opiate ever created, and even if people think they are being careful, it can kill."

The data was collected as part of the SKIP program, a component of the RADARS System, funded through an unrestricted research grant sponsored by the Denver Health and Hospital Authority, which collects subscription fees from 14 pharmaceutical firms.

Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: A retrospective analysis of the past 50 years. JAMA Psychiatry, published online May 28, 2014. doi:10.1001/jamapsychiatry.2014.366

<http://bit.ly/1oJtEYH>

Most physicians would forgo aggressive treatment for themselves at the end of life

Most physicians would choose a do-not-resuscitate or "no code" status for themselves when they are terminally ill

STANFORD, Calif. - Most physicians would choose a do-not-resuscitate or "no code" status for themselves when they are terminally ill, yet they tend to pursue aggressive, life-prolonging treatment for patients facing the same prognosis, according to a study from the Stanford University School of Medicine to be published May 28 in PLOS ONE. It's a disconnect that needs to be better understood, said VJ Periyakoil, MD, clinical associate professor of medicine and lead author of the study.

"Why do we physicians choose to pursue such aggressive treatment for our patients when we wouldn't choose it for ourselves?" said Periyakoil, director of the Stanford Palliative Care Education and Training Program. "The reasons likely are multifaceted and complex."

In the study, Periyakoil and her colleagues set out to determine how physicians' attitudes have changed toward advance directives since passage of the Self-Determination Act in 1990, a law designed to give patients more control over

determining end-of-life-care decisions. Advance directives are documents that patients can use to indicate end-of-life care preferences.

The study involved two sets of subjects: One comprised 1,081 physicians who in 2013 completed a web-based advanced directive form and a 14-item advance directive attitude survey at Stanford Hospital & Clinics and the Veterans Affairs Palo Alto Health Care System; the other comprised 790 physicians from Arkansas who were asked the same 14 survey questions - but did not complete an advance directive form - in a 1989 study published in the Journal of the American Medical Association.

Surprisingly, results showed that doctors' attitudes toward advance directives have changed little in 25 years. "The needle has not moved very much," Periyakoil said, who is also associate director of palliative care services at the Palo Alto VA center. The lack of change in physicians' attitudes toward advance directives mirrors what the study describes as the medical system's continued focus on aggressive treatment at the end of life, despite the fact that most Americans now say they would prefer to die at home without life-prolonging interventions.

"A big disparity exists between what Americans say they want at the end of life and the care they actually receive," the study said. "More than 80 percent of patients say that they wish to avoid hospitalizations and high-intensity care at the end of life, but their wishes are often overridden."

In fact, the type of treatments they receive depends not on the patients' care preferences or on their advance directives, but rather on the local health-care system variables, such as institutional capacity and individual doctors' practice style, according to the study. "Patients' voices are often too feeble and drowned out by the speed and intensity of a fragmented health-care system," Periyakoil said.

Other results from the study showed that because of the Self-Determination Act, doctors now feel they are less likely to be sued for not providing the most aggressive care if a patient has an advance directive. The law requires hospitals to inform patients about advance directives, but it doesn't ensure that the directives be followed.

Physicians' attitudes toward end-of-life care also differed depending on their ethnicity and gender. Emergency physicians, pediatricians, obstetrician-gynecologists and those in physical medicine and rehabilitation had more favorable attitudes toward advance directives. Radiologists, surgeons, orthopaedists and radiation oncologists were less favorable. Caucasian and African American doctors were the most favorable; Latino physicians were the least favorable.

An overwhelming percentage of the 2013 doctors surveyed - 88.3 percent - said they would choose "no-code" or do-not-resuscitate orders for themselves.

As a geriatrics and palliative care physician who sits at the bedside of sick patients herself, Periyakoil said she understands the disconnect between the type of care doctors want for themselves at the end of life and what they actually do for their patients. It's not because doctors are trying to make more money or because they are intentionally insensitive to their patients' desires. At the core of the problem is a biomedical system that rewards doctors for taking action, not for talking with their patients.

"Our current default is 'doing,' but in any serious illness there comes a tipping point where the high-intensity treatment becomes more of a burden than the disease itself," said Periyakoil, who trains physicians in palliative medicine. "It's tricky, but physicians don't have to figure it out by themselves. They can talk to the patients and their families and to the other interdisciplinary team members, and it becomes much easier. "But we don't train doctors to talk or reward them for talking. We train them to do and reward them for doing. The system needs to be changed."

Other Stanford authors included analyst Eric Neri; Ann Fong, critical care pharmacist at Stanford Hospital & Clinics; and Helena Karemer, PhD, professor emerita of psychiatry and behavioral sciences.

The research was supported by the National Institutes of Health (grants R01CA115562 and R25MD006857) and the Department of Veterans Affairs.

<http://bit.ly/T3s0n6>

Study affirms value of epigenetic test for markers of prostate cancer

Test designed to rule out the presence of genetic biomarkers of prostate cancer may be accurate enough to exclude the need for most repeat prostate biopsies

A multicenter team of researchers report that a commercial test designed to rule out the presence of genetic biomarkers of prostate cancer may be accurate enough to exclude the need for repeat prostate biopsies in many - if not most - men.

"Often, one biopsy is not enough to definitively rule out prostate cancer," says study researcher Jonathan Epstein, M.D., director of the Division of Surgical Pathology and a professor of pathology, urology and oncology at the Johns Hopkins University School of Medicine. "Our research finds that by looking for the presence or absence of cancer in a different way, we may be able to offer many men peace of mind without putting them through the pain, bleeding and risk of infection that can come with a repeat biopsy."

The new research, called the Detection of Cancer Using Methylated Events in Negative Tissue (DOCUMENT) study, suggests that an initial biopsy complemented with an epigenetic diagnostic test accurately rules out the existence of cancer up to 88 percent of the time. The test, developed by MDxHealth, which paid for the study, was described online in April in *The Journal of Urology*.

The test specifically captures the presence of chemical modifications to non-nuclear DNA sequences within cells that commonly appear when prostate cancer is present. These so-called epigenetic changes, which add a methyl group to the biochemical makeup of the DNA, alter the way genes function without changing their foundational DNA sequence. The researchers analyzed tissue from biopsies from 320 men with elevated prostate-specific antigen (PSA) levels whose results were negative for prostate cancer. The men were patients at The Johns Hopkins Hospital; the University of California, Los Angeles; the Cleveland Clinic; Eastern Virginia Medical School; and Lahey Hospital & Medical Center.

The epigenetic biomarkers the test detects reflect a process called DNA hypermethylation, in which a methyl group is chemically attached to DNA - in this case, to genes called GSTP1, APC and RASSF1. These genes are known to play prominent tumor suppressive roles in key cancer-related pathways. When these genes are hypermethylated, they are commonly silenced, which can lead to a loss of this tumor-suppressing function and the emergence of cancer.

Specifically, the GSTP1 gene acts as a detoxifying agent, preventing genomic damage by carcinogens. Studies find that GSTP1 is methylated in up to 90 percent of prostate cancer cases, making it a strong indicator of the disease.

For the study, pathologists compared methylation levels between the subjects' initial tissue biopsies and later tissue samples taken from each man done within 24 months of the first biopsy. They found that average levels of APC and RASSF1 were about twice as high in the 92 subjects whose second biopsies yielded positive results, as compared to the 228 with two negative biopsies. For GSTP1, the levels were more than eight times higher in the cancerous biopsies.

"It turns out as many as 20 percent of men have prostate cancer, even if their first biopsy results are negative," says Epstein, the Rose-Lee and Keith Reinhard Professor of Urologic Pathology. Approximately 40 percent of men with a negative biopsy go on to receive a second biopsy. Many high-risk men fear sampling errors in their initial biopsy, which often leads to a high rate of follow-up procedures to merely confirm the absence of the disease.

Initial biopsies are typically performed when men receive abnormal results on PSA screenings or digital rectal exams. But an initial biopsy can sometimes miss cancer if none of the biopsy needles pass through the cancer, leading to the false-negative results.

"With prostate biopsies, there is often very little cancer, which makes it difficult to perform molecular prognostic and predictive tests," says Epstein. "The DOCUMENT study overcomes this problem, because it looks at benign tissue, not just the cancer. There is a lot of benign tissue, which is why we think it performs so well."

"Overall, if there is an absence of methylation in all three biomarkers, there is an 88 percent likelihood you don't have cancer," Epstein says. "The test isn't 100 percent of an assurance, but it is a major step forward."

Jonathan Epstein, M.D., and Alan Partin, M.D., Ph.D., of Johns Hopkins contributed to the research, as well as researchers from Maastricht University Medical Center, the Glickman Urological and Kidney Institute, the UCLA Urology Department, Lahey Hospital & Medical Center, Eastern Virginia Medical School, MDxHealth Inc. and Ghent University. Lead researcher Leander Van Neste, Ph.D., a consultant for MDxHealth, may have stock or stock options. **Related stories:**

http://www.hopkinsmedicine.org/news/publications/johns_hopkins_health/fall_2010/second_opinions_second_chances

http://www.hopkinsmedicine.org/news/media/releases/chronic_inflammation_linked_to_high_grade_prostate_cancer

<http://www.hopkinsmedicine.org/profiles/results/directory/profile/0002004/jonathan-epstein>

<http://bit.ly/1pwMXV9>

Suspect strep throat? Re-check negative rapid test results with lab culture

Accurate diagnosis essential for appropriate use of antibiotics

Clinical guidelines conflict on testing teens and adults whose symptoms point to a possible strep throat. A chief contention is whether negative tests results from a rapid analysis of a throat swab, done in a doctor's office, should be confirmed through a follow-up laboratory culture.

The rapid test detects certain antigens, one of the body's efforts to fight off strep bacteria. Attempting to grow bacteria from a throat specimen double checks for the presence or absence of Group A Streptococcus bacteria, as well as a few other bacterial infections.

A study published May 27 in *Clinical Infectious Diseases* indicates that performing a laboratory culture could help doctors and patients avoid both under-treating and over-treating sore throats.

Several guidelines on diagnosing and treating Group A Streptococcus sore throats in adults have been published by medical and scientific professional societies, including the College of American Pathologists and the Infectious Diseases Society of America.

The study findings call into serious question clinical guidelines that rely only on the rapid test, according to Dr. Ferric Fang, professor of microbiology and laboratory medicine at the University of Washington, and senior author of the paper.

Fang said, "Each year nearly seven million Americans seek medical attention for a sore throat, making it one of the most common reasons to see a doctor."

About one in 10 of these patients has a strep throat. The rest are due to viruses or other causes. Although most cases of strep throat heal on their own, antibiotic

treatment reduce symptoms decrease transmission to others, and can prevent rare but serious complications such as damage to heart valves.

Accurately diagnosing that the sore throat is not bacterial is also important, Fang said. Antibiotics for a strep throat don't work against a viral sore throat, and can produce harmful side effects not outweighed by benefits. Unnecessary use of antibiotics also contributes to antibiotic-resistance.

Fang explained that rapid tests, while convenient, miss up to 1 out of 4 cases of strep throat. Some physicians will recommend a throat culture even when the rapid test is negative, if the patient's symptoms seem to warrant it.

Doctors check a patient with a suspected strep throat for tender glands in the neck below the ears, lack of a cough, difficulty opening the jaw, painful swallowing; oozing, swollen, tonsils; fever and a high white blood cell count.

Despite the constellation of suspicious symptoms in the Centor score for strep throat likelihood, it is still difficult to distinguish a viral sore throat from a strep throat. However, if doctors depend simply on symptom presentation to diagnose, without any testing, the tendency is to over-prescribed antibiotics. Doctors who rely just on the rapid test may end up undertreating strep throat.

The controversy on diagnosing strep throat prompted Fang and his UW colleagues, Dr. Tanis Dingle, senior fellow in laboratory medicine, and Dr. April Abbot, assistant professor of laboratory medicine and director of clinical microbiology at UW Medicine, to review the anonymous records of more than 25,000 teens and adults seen for sore throats at Harborview Medical Center and University of Washington Medical Center in Seattle. The records went back 11 years. The researchers found that more than 1,000 patients whose rapid throat cultures were negative actually turned out to have strep in their laboratory throat cultures.

"These cases would have been undetected if their doctors hadn't performed cultures," Fang said.

Most of these patients had moderate to severe symptoms; a very few had serious complications such as a tonsil abscess or rheumatic fever. Most of the patients were given antibiotics. The throat cultures, Fang said, helped guide treatment decisions in half of the cases.

From their results, the researchers extrapolated that, each year in the United States more than 250,000 patients with strep throat would not receive beneficial treatment if doctors followed those clinical guidelines that advise relying on the rapid test alone. The findings support those guidelines that mandate back-up lab cultures.

The researchers concluded, "Appropriate use of rapid and culture-based diagnostic tests can reduce inappropriate use of antibiotics for sore throats, while avoiding under-treatment of patients who can benefit from antibiotics."

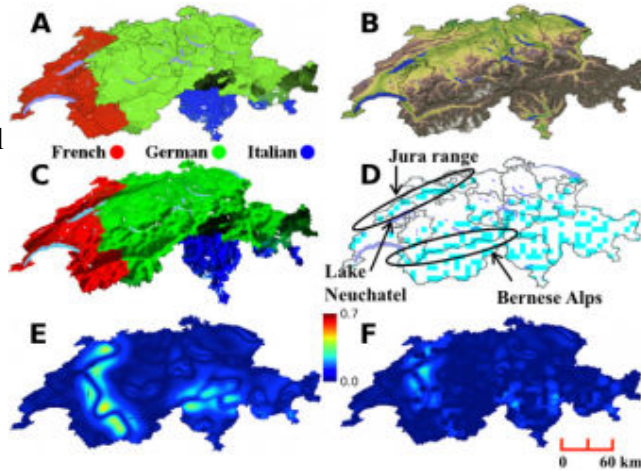
<http://bit.ly/1u4cPYc>

Using science to avoid ethnic violence

What if we could use science to understand, accurately predict, and ultimately avoid, ethnic violence?

A new study published in PLOS ONE does just that. The key to peace, the theory argues, is to either completely integrate or completely separate people based on cultural, linguistic, and ethnical differences.

Researchers at New England Complex Systems Institute (NECSI) analyzed two countries that both have boundaries separating cultural and linguistic groups, and found that the violence in both cases matched the theory's predictions, but in very different ways. Switzerland, a model of success when it comes to peace, contains boundaries within it that align with people ethnicities, and has almost no violence.



Linguistic groups and topographical boundaries in Switzerland. Maps of Switzerland showing (A) proportion of linguistic groups according to the 2000 census, (B) elevation within Switzerland, (C) overlay of linguistic groups onto a digital elevation model, and (D) topographical features including lakes (blue) and ridges extracted using edge detection (cyan). Comparison of calculated propensity (color bar) to violence between linguistic groups without (E) and with (F) the inclusion of topographical features as boundaries using a characteristic length scale of 24 km. Mercator projection, except C which is the Europe Albers projection. The distance scale is approximate.

In fact, the only area of violence occurs in Jura, precisely where NECSI's theory predicts that the boundaries between groups are insufficient. In Yugoslavia on the other hand, the boundaries do not actually align with people's differences and, as predicted, there is violence at the points of friction. This shows that there are right ways and there are wrong ways to set up boundaries to achieve peace within a country. Knowing that can help us make informed decisions and design for peace. "We've seen that the ways borders and boundaries between groups are arranged really can prevent violence. When I think of the suffering and the lives lost, and I

see those results, the findings just can't be ignored," said Andreas Gros, one of the authors.

"Conflicts rooted in ethnic strife are tearing countries apart today," said Bar-Yam. "Scientists who focus on predictive models cannot help but raise the question: 'What, if any, conditions are identifiable for peaceful coexistence among multiple groups with linguistic and religious differences?'"

The paper shows that Switzerland can be used as a model for many places in the world that are diverse and struggle with maintaining peace. This study shows that it is not necessary to create separate countries; groups with boundaries that delineate local autonomy will live peacefully together. The theory and the data also show that people who are in fully integrated societies will also successfully live in peace.

More information: The paper is available online: necsi.edu/research/social/peace_PLoS_f.pdf

<http://nyti.ms/1ohLle8>

Climate Change Doomed the Ancients

THIS month, a report issued by a prominent military advisory board concluded that climate change posed a serious threat to America's national security.

By ERIC H. CLINE

The authors, 16 retired high-ranking officers, warned that droughts, rising seas and extreme weather events, among other environmental threats, were already causing global "instability and conflict." But Senator James M. Inhofe of Oklahoma, the ranking Republican on the Senate Armed Services Committee and a stalwart believer that global warming is a "hoax," dismissed the report as a publicity stunt. Perhaps the senator needs a history lesson, because climate change has been leading to global conflict - and even the collapse of civilizations - for more than 3,000 years. Drought and famine led to internal rebellions in some societies and the sacking of others, as people fleeing hardship at home became conquerors abroad. One of the most vivid examples comes from around 1200 B.C. A centuries-long drought in the Aegean and Eastern Mediterranean regions, contributed to - if not caused - widespread famine, unrest and ultimately the destruction of many once prosperous cities, according to four recent studies.

The scientists determined the length and severity of the drought by examining ancient pollen as well as oxygen and carbon isotope data drawn from alluvial and mineral deposits. All of their conclusions are corroborated by correspondence, inscribed and fired on clay tablets, dating from that time.

Ancient letters from the Hittite kingdom, in what is now modern-day Turkey, beseech neighboring powers for shipments of grain to stave off famine caused by the drought. (The drought is thought to have affected much of what is now Greece, Israel, Lebanon and Syria for up to 300 years.) One letter, sent from a Hittite king, pleads for help: "It is a matter of life or death!"

Another letter, sent from the city of Emar, in what is now inland Syria, states simply, "If you do not quickly arrive here, we ourselves will die of hunger." The kingdom of Egypt, as well as the city of Ugarit, on the coast of what is now Syria, responded with food and supplies, but it is not clear if they were able to provide enough relief.

It certainly created problems of national security for the great powers of the time. Correspondence between the Egyptians, Hittites, Canaanites, Cypriots, Minoans, Mycenaeans, Assyrians and Babylonians - effectively, the Group of 8 of the Late Bronze Age - includes warnings of attacks from enemy ships in the Mediterranean. The marauders are thought to have been the Sea Peoples, possibly from the western Mediterranean, who were probably fleeing their island homes because of the drought and famine and were moving across the Mediterranean as both refugees and conquerors.

One letter sent to Ugarit advised the king to "be on the lookout for the enemy and make yourself very strong!" The warning probably came too late, for another letter dating from the same time states: "When your messenger arrived, the army was humiliated and the city was sacked. Our food in the threshing floors was burned and the vineyards were also destroyed. Our city is sacked. May you know it! May you know it!"

While sea levels may not have been rising then, as they are now, changes in the water temperature may have been to blame for making life virtually unlivable in parts of the region.

A 2012 study published in the *Journal of Archaeological Science* found that the surface temperatures of the Mediterranean Sea cooled rapidly during this time, severely reducing precipitation over the coasts. The study concluded that agriculture would have suffered and that the conditions might have influenced the "population declines, urban abandonments and long-distance migrations associated with the period."

To top it off, catastrophic events, in the form of a series of earthquakes, also rocked many ancient cities in these areas from around 1225 to 1175 B.C. These, together with the famines and droughts, would have further undermined the societies of the time, most likely leading to internal rebellions by the underclass and peasant populations who were facing severe food shortages, as well as invasions by migrating peoples.

We still do not know the specific details of the collapse at the end of the Late Bronze Age or how the cascade of events came to change society so drastically. But it is clear that climate change was one of the primary drivers, or stressors, leading to the societal breakdown.

The era that followed is known as the first Dark Ages, during which the thriving economy and cultures of the late second millennium B.C. suddenly ceased to exist. It took decades, and even hundreds of years in some areas, for the people in these regions to rebuild.

We live in a world that has more similarities to that of the Late Bronze Age than one might suspect, including, as the British archaeologist Susan Sherratt has put it, an "increasingly homogeneous yet uncontrollable global economy and culture" in which "political uncertainties on one side of the world can drastically affect the economies of regions thousands of miles away."

But there is one important difference. The Late Bronze Age civilizations collapsed at the hands of Mother Nature. It remains to be seen if we will cause the collapse of our own.

Eric H. Cline, a professor of classics and anthropology at George Washington University, is the author of "1177 B.C.: The Year Civilization Collapsed."

<http://www.medscape.com/viewarticle/825808?>

Vedolizumab (Entyvio) Approved in Europe for Crohn's, Ulcerative Colitis

The European Commission has approved vedolizumab for adults with moderate to severe Crohn's disease or ulcerative colitis

Megan Brooks

The European Commission (EC) has approved vedolizumab (*Entyvio*, Takeda Pharmaceuticals) for adults with moderate to severe Crohn's disease or ulcerative colitis who do not respond to or cannot tolerate corticosteroids, immunosuppressants, or tumor necrosis factor- α antagonists, the company announced May 27.

The approval follows a [positive opinion](#) on vedolizumab in March by the European Medicines Agency Committee for Medicinal Products for Human Use.

The US Food and Drug Administration [approved vedolizumab](#) last week.

Crohn's disease and ulcerative colitis are the 2 most common types of inflammatory bowel disease, affecting more than 4 million people worldwide, including roughly 2.2 million in Europe, Takeda noted in a [statement](#) announcing European approval.

Crohn's disease and ulcerative colitis can have a "devastating impact on patients, many of whom are in early adulthood when they receive a diagnosis," Paul Rutgeerts, MD, PhD, FRCP, emeritus professor of medicine, Catholic University of Leuven, Belgium, noted in the Takeda statement.

"As physicians, our aim is to help patients achieve and maintain remission and disease control. The approval of vedolizumab in Europe is an important step forward in the treatment of ulcerative colitis and Crohn's disease. It is the first gut-selective, biologic agent for this condition to be approved in Europe and provides

us with a new therapeutic option to help us to tackle these challenging diseases," Dr. Rutgeerts said.

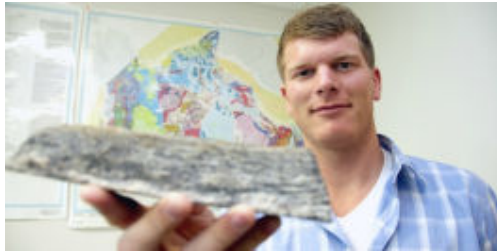
The efficacy of vedolizumab was demonstrated in 2 randomized, double-blind, placebo-controlled trials [published](#) in August 2013 in the *New England Journal of Medicine*. Vedolizumab is a humanized IgG1 monoclonal antibody that binds exclusively to the $\alpha 4\beta 7$ integrin, a key mediator of gastrointestinal inflammation.

<http://phys.org/news/2014-05-ancient-yield-clues-earth-earliest.html>

Ancient rocks yield clues about Earth's earliest crust

It looks like just another rock, but what Jesse Reimink holds in his hands is a four-billion-year-old chunk of an ancient protocontinent that holds clues about how the Earth's first continents formed.

Phys.org - The University of Alberta geochemistry student spent the better part of three years collecting and studying ancient rock samples from the Acasta Gneiss Complex in the Northwest Territories, part of his PhD research to understand the environment in which they formed.



"The timing and mode of continental crust formation throughout Earth's history is a controversial topic in early Earth sciences," says Reimink, lead author of a new study in *Nature Geoscience* that points to Iceland as a solid comparison for how the earliest continents formed.

Continents today form when one tectonic plate shifts beneath another into the Earth's mantle and cause magma to rise to the surface, a process called subduction. It's unclear whether plate tectonics existed 2.5 billion to four billion years ago or if another process was at play, says Reimink.

One theory is the first continents formed in the ocean as liquid magma rose from the Earth's mantle before cooling and solidifying into a crust.

Iceland's crust formed when magma from the mantle rises to shallow levels, incorporating previously formed volcanic rocks. For this reason, Reimink says Iceland is considered a theoretical analogue on early Earth continental crust formation.

Ancient rocks 3.6 to four billion years old

Working under the supervision of co-author Tom Chacko, Reimink spent his summers in the field collecting rock samples from the Acasta Gneiss Complex, which was discovered in the 1980s and found to contain some of the Earth's oldest rocks, between 3.6 and four billion years old. Due to their extreme age, the rocks

have undergone multiple metamorphic events, making it difficult to understand their geochemistry, Reimink says.

Fortunately, a few rocks - which the research team dubbed "Idiwhaa" meaning "ancient" in the local Tlicho dialect - were better preserved. This provided a "window" to see the samples' geochemical characteristics, which Reimink says showed crust-forming processes that are very similar to those occurring in present-day Iceland. "This provides the first physical evidence that a setting similar to modern Iceland was present on the early Earth."

These ancient rocks are among the oldest samples of protocontinental crust that we have, he adds, and may have helped jump-start the formation of the rest of the continental crust.

Reimink, who came to the U of A to work with Chacko, says the university's lab resources are "second to none," particularly the Ion Microprobe facility within the Canadian Centre for Isotopic Microanalysis run by co-author Richard Stern, which was instrumental to the discovery. "That lab is producing some of the best data of its kind in the world. That was very key to this project."

More information: "Earth's earliest evolved crust generated in an Iceland-like setting." Jesse R. Reimink, et al. Nature Geoscience (2014). DOI: 10.1038/ngeo2170. Received 24 September 2013 Accepted 16 April 2014 Published online 25 May 2014

http://www.eurekalert.org/pub_releases/2014-05/iu-spi052714.php

Study: Performance improved even after athletes learned of deception

Indiana University researchers say a little deception caused cyclists in their 4-kilometer time trial to up their performance even after they realized they had been tricked.

The findings support the idea that the brain plays a powerful role in how hard athletes push their bodies.

"The idea is that there's some sort of governor in your brain that regulates exercise intensity so you don't overheat, or run out of gas, so to speak," said Ren-Jay Shei, a doctoral student in the IU School of Public Health-Bloomington. "In this case, the governor was reset to a higher upper limit, allowing for improved performance." For the study, 14 trained, competitive male cyclists participated in four time trials. For each session, they rode cycle ergometers, which are stationary bikes that measure such variables as speed and power output and display the readings on computer monitors on the handlebars.

The first time trial was designed to familiarize the cyclists with the procedures. The second was considered the baseline session. In the third and fourth, two avatars and their corresponding stats appeared side by side on the computer monitors. In the session involving deception, the stats for the avatar on the right were programmed

to be 102 percent of the baseline performance of the cyclist, yet the cyclist was told the stats were based on his actual baseline results.

Not only did most of the cyclists improve during the deception round, but the group improved by an average of 2.1 percent over baseline even when they knew they had been tricked.

"This helps us understand how the body protects itself during exercise," Shei said.

Shei will discuss the findings during the behavioral aspects of sport session at 3:30 p.m.

Thursday, May 29. Co-authors include Robert F. Chapman, John S. Raglin and Timothy D.

Mickleborough, all in the Department of Kinesiology in the IU School of Public Health-Bloomington; and Kevin G. Thompson, Research Institute for Sport and Exercise, University of Canberra, Canberra, Australia.

http://www.eurekalert.org/pub_releases/2014-05/osu-adi052914.php

Amber discovery indicates Lyme disease is older than human race

Ticks fossilized in amber show that the bacteria which cause it may have been lurking around for 15 million years

CORVALLIS, Ore. – Lyme disease is a stealthy, often misdiagnosed disease that was only recognized about 40 years ago, but new discoveries of ticks fossilized in amber show that the bacteria which cause it may have been lurking around for 15 million years – long before any humans walked on Earth.

The findings were made by researchers from Oregon State University, who studied 15-20 million-year-old amber from the Dominican Republic that offer the oldest fossil evidence ever found of *Borrelia*, a type of spirochete-like bacteria that to this day causes Lyme disease. They were published in the journal *Historical Biology*.



This tick trapped in ancient amber from the Dominican Republic can carry the type of bacteria that causes lyme disease. George Poinar, Jr., courtesy of Oregon State University

In a related study, published in *Cretaceous Research*, OSU scientists announced the first fossil record of Rickettsial-like cells, a bacteria that can cause various types of spotted fever. Those fossils from Myanmar were found in ticks about 100 million years old.

As summer arrives and millions of people head for the outdoors, it's worth considering that these tick-borne diseases may be far more common than has been historically appreciated, and they've been around for a long, long time.

"Ticks and the bacteria they carry are very opportunistic," said George Poinar, Jr., a professor emeritus in the Department of Integrative Biology of the OSU College of

Science, and one of the world's leading experts on plant and animal life forms found preserved in amber. "They are very efficient at maintaining populations of microbes in their tissues, and can infect mammals, birds, reptiles and other animals. "In the United States, Europe and Asia, ticks are a more important insect vector of disease than mosquitos," Poinar said. "They can carry bacteria that cause a wide range of diseases, affect many different animal species, and often are not even understood or recognized by doctors.

"It's likely that many ailments in human history for which doctors had no explanation have been caused by tick-borne disease."

Lyme disease is a perfect example. It can cause problems with joints, the heart and central nervous system, but researchers didn't even know it existed until 1975. If recognized early and treated with antibiotics, it can be cured. But it's often mistaken for other health conditions. And surging deer populations in many areas are causing a rapid increase in Lyme disease – the confirmed and probable cases of Lyme disease in Nova Scotia nearly tripled in 2013 over the previous year.

The new research shows these problems with tick-borne disease have been around for millions of years.

Bacteria are an ancient group that date back about 3.6 billion years, almost as old as the planet itself. As soft-bodied organisms they are rarely preserved in the fossil record, but an exception is amber, which begins as a free-flowing tree sap that traps and preserves material in exquisite detail as it slowly turns into a semi-precious mineral.

A series of four ticks from Dominican amber were analyzed in this study, revealing a large population of spirochete-like cells that most closely resemble those of the present-day *Borrelia* species. In a separate report, Poinar found cells that resemble *Rickettsia* bacteria, the cause of Rocky Mountain spotted fever and related illnesses. This is the oldest fossil evidence of ticks associated with such bacteria.

In 30 years of studying diseases revealed in the fossil record, Poinar has documented the ancient presence of such diseases as malaria, leishmania, and others. Evidence suggests that dinosaurs could have been infected with Rickettsial pathogens.

Humans have probably been getting diseases, including Lyme disease, from tick-borne bacteria as long as there have been humans, Poinar said. The oldest documented case is the Tyrolean iceman, a 5,300-year-old mummy found in a glacier in the Italian Alps.

"Before he was frozen in the glacier, the iceman was probably already in misery from Lyme disease," Poinar said. "He had a lot of health problems and was really a mess."

http://www.eurekalert.org/pub_releases/2014-05/ps-dod052914.php

Domestication of dogs may explain mammoth kill sites and success of early modern humans

Surge in killings of mammoths may have been due to early modern humans working with the earliest domestic dogs

A new analysis of European archaeological sites containing large numbers of dead mammoths and dwellings built with mammoth bones has led Penn State Professor Emerita Pat Shipman to formulate a new interpretation of how these sites were formed. She suggests that their abrupt appearance may have been due to early modern humans working with the earliest domestic dogs to kill the now-extinct mammoth -- a now-extinct animal distantly related to the modern-day elephant. Shipman's analysis also provides a way to test the predictions of her new hypothesis. Advance publication of her article "How do you kill 86 mammoths?" is available online through Quaternary International.



A fragment of a large bone, probably from a mammoth, Pat Shipman reports, was placed in this dog's mouth shortly after death. This finding suggests the animal was accorded special mortuary treatment, perhaps acknowledging its role in mammoth hunting. The fossil comes from the site of Predmosti, in the Czech republic, and is about 27,000 years B.P. old. This object is one of three canid skulls from Predmosti that were identified as dogs based on analysis of their morphology. Anthropos Museum, Brno, the Czech Republic, courtesy of Mietje Germonpre

Spectacular archaeological sites yielding stone tools and extraordinary numbers of dead mammoths -- some containing the remains of hundreds of individuals -- suddenly became common in central and eastern Eurasia between about 45,000 and 15,000 years ago, although mammoths previously had been hunted by humans and their extinct relatives and ancestors for at least a million years. Some of these mysterious sites have huts built of mammoth bones in complex, geometric patterns as well as piles of butchered mammoth bones.

"One of the greatest puzzles about these sites is how such large numbers of mammoths could have been killed with the weapons available during that time," Shipman said. Many earlier studies of the age distribution of the mammoths at these sites found similarities with modern elephants killed by hunting or natural disasters, but Shipman's new analysis of the earlier studies found that they lacked

the statistical evaluations necessary for concluding with any certainty how these animals were killed.

Surprisingly, Shipman said, she found that "few of the mortality patterns from these mammoth deaths matched either those from natural deaths among modern elephants killed by droughts or by culling operations with modern weapons that kill entire family herds of modern elephants at once." This discovery suggested to Shipman that a successful new technique for killing such large animals had been developed and its repeated use over time could explain the mysterious, massive collections of mammoth bones in Europe.

The key to Shipman's new hypothesis is recent work by a team led by Mietje Germonpré of the Royal Belgian Institute of Natural Sciences, which has uncovered evidence that some of the large carnivores at these sites were early domesticated dogs, not wolves as generally had been assumed. Then, with this evidence as a clue, Shipman used information about how humans hunt with dogs to formulate a series of testable predictions about these mammoth sites.

"Dogs help hunters find prey faster and more often, and dogs also can surround a large animal and hold it in place by growling and charging while hunters move in. Both of these effects would increase hunting success," Shipman said. "Furthermore, large dogs like those identified by Germonpré either can help carry the prey home or, by guarding the carcass from other carnivores, can make it possible for the hunters to camp at the kill sites." Shipman said that these predictions already have been confirmed by other analyses. In addition, she said, "if hunters working with dogs catch more prey, have a higher intake of protein and fat, and have a lower expenditure of energy, their reproductive rate is likely to rise."

Another unusual feature of these large mammoth kill sites is the presence of extraordinary numbers of other predators, particularly wolves and foxes. "Both dogs and wolves are very alert to the presence of other related carnivores -- the canids -- and they defend their territories and food fiercely," Shipman explained. "If humans were working and living with domesticated dogs or even semi-domesticated wolves at these archaeological sites, we would expect to find the new focus on killing the wild wolves that we see there."

Two other types of studies have yielded data that support Shipman's hypothesis. Hervé Bocherens and Dorothee Drucker of the University of Tübingen in Germany, carried out an isotopic analysis of the ones of wolves and purported dogs from the Czech site of Predmostí. They found that the individuals identified as dogs had different diets from those identified as wolves, possibly indicating feeding by humans. Also, analysis of mitochondrial DNA by Olaf Thalmann of the University of Turku in Finland, and others, showed that the individuals identified as dogs have a distinctive genetic signature that is not known from any other canid. "Since

mitochondrial DNA is carried only by females, this finding may indicate that these odd canids did not give rise to modern domesticated dogs and were simply a peculiar, extinct group of wolves," Shipman said. "Alternatively, it may indicate that early humans did domesticate wolves into dogs or a doglike group, but the female canids interbred with wild wolf males and so the distinctive female mitochondrial DNA lineage was lost."

As more information is gathered on fossil canids dated to between 45,000 and 15,000 years ago, Shipman's hunting-dog hypothesis will be supported "if more of these distinctive doglike canids are found at large, long-term sites with unusually high numbers of dead mammoths and wolves; if the canids are consistently large, strong individuals; and if their diets differ from those of wolves," Shipman said. "Dogs may indeed be man's best friend."

<http://bit.ly/1kIKGZN>

Learn New Skills With Superhuman Speed

Wearable computers could provide the muscle memory to learn guitar chords or dance steps

By Ariel Bleicher

The glove looks humdrum, like a garment you might pick up at a sporting-goods store. It's made of soft black leather and fingerless, like a cyclist's or weightlifter's glove. The similarity is, however, deceiving.

future report icon "I have a glove that can teach you how to play a piano melody," Thad Starner declares when I call to chat about the future of wearable computing. Now a professor at the Georgia Institute of Technology and the technical lead of Google Glass, he helped pioneer the field in the 1990s as a student at MIT. "During this conversation, you could have learned 'Amazing Grace.'" "Really?" I say. "While we're talking?" "Sure," he says and invites me to Atlanta to see for myself.



By activating tiny vibration motors in its fingertips, the Mobile Music Touch glove speeds up the process of learning to play a piano melody. Photo: Georgia Tech
Caitlyn Seim, a Ph.D student, slips the glove onto my hand. Inside each of the five finger holes she has sewn a flat vibration motor. The five tiny vibrators, which perch atop my digits like gemstones on rings, are wired to a microcontroller on the back of my hand. Seim has programmed it to fire the motors in the same sequence that my fingers would strike keys on a piano.

But she doesn't tell me which tune I'll be learning. "You'll just feel a little buzzing," she says, flipping on the electronics. Then Starner whisks me away to show off his lab's myriad other projects: a language-translation app for Google Glass, a magnetic tongue implant for voicing silent commands to a computer, a smart vest to help divers communicate with dolphins, smart chew toys to help police dogs communicate with handlers, and all manner of other wonderfully wacky wearables. Once every minute for the next 2 hours, the motors in the glove vibrate across my fingers. I try to figure out the pattern: buzz...middle finger...buzz...ring fin...buzz...buzz...ger...buzz...uh...buzz...buzz...crap. "IMPOSSIBLE," I write in my notebook.

At last, Starner escorts me to a keyboard. He plays the first passage of a song - 15 notes that the glove has supposedly taught me. I recognize the tune. It's Beethoven's "Ode to Joy." I take off the glove.

"Start here," Starner says, hitting the first note. I lay my fingers on the keys. Middle finger...middle finger...ring finger... "I don't know," I say, embarrassed.

"Don't think about it," Starner says.

I start again. Middle...middle...ring...pinky...pinky...ring...middle...pointer... "This is crazy!" I say, still playing. And I don't stop. I finish the first passage, then play the second, and start into the third.

"Now, hold on!" Starner interjects. "Have you played this before?"

"Never," I say. It's true - I never took piano lessons. Befuddled, he inspects the glove and discovers it's been programmed to vibrate all four phrases of the song - 61 notes, not 15. Typically, he explains, he and his students teach only one phrase at a time. I approach the keyboard again. I fumble a few tries - I'm learning, after all - but within minutes, I can play the melody perfectly. I feel giddy, like I've just discovered an innate talent I never knew I had.

"You just know what to do - it's insane," Seim notes. She recently taught herself to play "Ode to Joy" by wearing the glove while writing an application for a research grant. "It's almost like watching a phantom hand."

Starner and his colleagues believe that the repeated buzzing from the glove creates a muscle memory that enables a wearer to learn to play a song with far less practice than it would take without haptic stimulation. They have also studied the glove's effect on people with spinal cord injuries and found that it can help them regain some sensation and dexterity in their hands. The researchers are now beginning experiments to test whether haptic gloves can teach braille typing and stenography - evidence that the technology could impart not just patterns but also language.

"We don't know the limits," Starner says. "Can we put these sorts of vibration motors on people's legs and teach them how to dance? Can we teach people how to throw a better baseball?" He mentions a scene from the sci-fi thriller *The Matrix* in

which the film's heroes, Neo and Trinity, hijack a helicopter: "Can you fly that thing?" Neo asks his right-hand woman. "Not yet," she says. The film cuts to Trinity's eyelids flickering as the knowledge pours through a data port at the back of her skull. Seconds later they're in the air.

"Of course you can't do that," I say.

Starnes grins. "Not yet."

<http://www.bbc.com/news/health-27625640>

Measles cases in the US reach 20-year high

Public health experts in the US are urging people to get vaccinated after a spike in measles cases in the country this year.

The Centres for Disease Control and Prevention reported 288 cases of measles in the first five months of 2014 - the largest number for 20 years.

The outbreak is thought to be linked to US citizens travelling to the Philippines.

The CDC says timely vaccination is the best way to prevent measles.

Dr. Anne Schuchat, director of CDC's National Centre for Immunizations and Respiratory Diseases, said many US healthcare providers had never seen or treated a patient with measles because of the country's robust vaccination efforts and rapid response to outbreaks.

Measles was eliminated from the United States in 2000, meaning that for more than 12 months there was no longer any continuous measles transmission.

She said: "The current increase in measles cases is being driven by unvaccinated people, primarily US residents, who got measles in other countries, brought the virus back to the United States and spread to others in communities where many people are not vaccinated." "Many of the clusters in the US began following travel to the Philippines where a large outbreak has been occurring since October 2013."

Two doses

Of the 288 cases, 280 were thought to have been imported from at least 18 countries. Ninety per cent of all measles cases in the US occurred in people who were not vaccinated or whose vaccination status was unknown. More than one in seven cases has led to stays in hospital.

In the US, the CDC recommends two doses of measles, mumps, and rubella (MMR) vaccine for everyone starting at age 12 months. For those travelling abroad, the CDC recommends that babies older than six months receive the MMR vaccine.

Measles is a serious viral illness that is highly contagious.

The initial symptoms of measles develop around 10 days after infection. These can include cold-like symptoms, red eyes and sensitivity to light, a high temperature or fever and greyish white spots in the mouth and throat.

After a few days, a red-brown spotty rash will appear. This usually starts behind the ears and then spreads around the head and neck before spreading to the rest of the body.

Measles is still common in many parts of the world, including countries in Europe, Asia, the Pacific, and Africa.

<http://bit.ly/1klR8zM>

Forget the dentist's drill, use lasers to heal teeth

Open wide, this won't hurt a bit. That might actually be true if the dentist's drill is replaced by a promising low-powered laser that can prompt stem cells to make damaged hard tissue in teeth grow back.

18:26 29 May 2014 by Lauren Hitchings

Such minimally invasive treatment could one day offer an easy way to repair or regrow our pearly whites.

When a tooth is chipped or damaged, dentists replace it with ceramic or some other inert material, but these deteriorate over time.

To find something better, researchers have begun to look to regenerative medicine and in particular to stem cells to promote tissue repair. Most potential stem cell therapies require the addition of growth factors or chemicals to coax dormant stem cells to differentiate into the required cell type. These chemicals would be applied either directly to the recipient's body, or to stem cells that have been removed from the body and cultured in a dish for implantation.

But such treatments have yet to make it into the doctor's clinic because the approach needs to be precisely controlled so that the stem cells don't differentiate uncontrollably.

Let there be light

Praveen Arany at the National Institute of Dental and Craniofacial Research in Bethesda, Maryland, and his colleagues wondered whether they could use stem cells to heal teeth, but bypass the addition of chemicals by harnessing the body's existing mechanisms. "Everything we need is in the existing tooth structure – the adult stem cells, the growth factors, and exactly the right conditions," says Arany. So they tried laser light, because it can promote regeneration in heart, skin, lung, and nerve tissues.

To mimic an injury, Arany's team used a drill to remove a piece of dentin – the hard, calcified tissue beneath a tooth's enamel that doesn't normally regrow – from the tooth of a rat. They then shone a non-ionising, low-power laser on the exposed tooth structure and the soft tissue underneath it. This allowed the light to reach the dental stem cells deep inside the pulp of the tooth.

Twelve weeks after a single 5-minute treatment, new dentin had formed in the cavity. Similar dentin production was seen in mice and in cultured human dental stem cells.

It not quite the end of the dentist's intervention though, they would still need to cap the tooth to protect it, because the stem cells that produce enamel are not present in adults.

Sweet spot

The team found that the laser light indirectly activates growth factors called TGF-betas, which stimulate stem cells in teeth to regenerate dentin. These growth factors are present in many tissue types, and have key roles in many other biological processes including development, immune responses, inflammation and wound healing.

The laser essentially creates "micro-injuries" that free growth factor molecules, activate stem cells and promote regeneration, says stem cell biologist James Monaghan of Northeastern University in Boston. "As long as the stem cells are accessible, this may be a promising approach."

"There is a therapeutic sweet spot in this mechanism, between the low-powered laser applications, and the wide range of biological possibilities that TGF-beta offers," says Arany.

The simplicity and likely low cost of the procedure are also advantages, he says. "Patients may experience some discomfort following the procedure, as would be expected in all healing processes, but at the low power setting for stimulating dentin, the laser treatment itself is barely discernible," says Arany.

Journal reference: Science Translational Medicine, DOI: 10.1126/scitranslmed.3008234

http://www.eurekalert.org/pub_releases/2014-05/uomh-rfp053014.php

Radiation for prostate cancer linked to secondary cancers, study finds

Survivors should be aware of symptoms of rectal, bladder cancer

ANN ARBOR, Mich. - Among men treated for prostate cancer, those who received radiation therapy were more likely to develop bladder or rectal cancer, according to a new study from the University of Michigan Comprehensive Cancer Center.

"Overall the incidence of these cancers is low. But when men have received radiation treatments, it's important to evaluate carefully any symptoms that could be a sign of bladder or rectal cancer," says senior study author Kathleen A. Cooney, M.D., professor of hematology/oncology and urology at the U-M Medical School. The study, which will be presented at the American Society of Clinical Oncology annual meeting, looked at 441,504 men diagnosed with prostate cancer between 1992 and 2010. Men were identified from the Surveillance, Epidemiology and End Results (SEER) program, a network of National Cancer Institute-sponsored,

population-based cancer registries that collect information on cancer diagnoses and treatment. SEER performs regular follow-up for survival and to capture new invasive cancer diagnoses.

The researchers looked at the number of secondary cancers that developed 10 or more years after men were diagnosed with prostate cancer. As a whole, men diagnosed with prostate cancer were at a lower risk of developing a second cancer. But when researchers looked at patients who received external beam radiation therapy, they found these patients were estimated to be 70 percent more likely to be diagnosed with a rectal cancer and 40 percent more likely for bladder cancer than the general public.

Radiation therapy is a standard treatment for prostate cancer and the researchers stress that their findings should not prohibit anyone from choosing this treatment, in particular men who are not good candidates for surgery.

"Prostate cancer has an excellent prognosis. But because patients typically survive a long time, it raises concerns about the risk of second cancers," says study author Elizabeth J. Davis, M.D., a fellow at the U-M Medical School. "Long-term survivors who have undergone treatment with radiation and their physicians should be careful to monitor for symptoms of bladder and rectal cancer."

Full results of the study were published online in Cancer.

Additional authors: Cecilia Yee M.S., Jennifer Beebe-Dimmer M.P.H, Ph.D., both of Karmanos Cancer Institute and Wayne State University School of Medicine

Funding: National Institutes of Health grants P50 CA69568, HHSN261201300011I and P30 CA022453 Disclosure: None

Reference: American Society of Clinical Oncology annual meeting, May 30-June 3, 2014, abstract No. 5034; Cancer, DOI: 10.1002/cncr.28769

http://www.eurekalert.org/pub_releases/2014-05/cu-ade053014.php

Australia's deadly eruptions the reason for the first mass extinction

A Curtin University researcher has shown that ancient volcanic eruptions in Australia 510 million years ago significantly affected the climate, causing the first known mass extinction in the history of complex life.

Published in prestigious journal *Geology*, Curtin's Associate Professor Fred Jourdan, along with colleagues from several Australian and international institutions, used radioactive dating techniques to precisely measure the age of the eruptions of the Kalkarindji volcanic province.

Dr Jourdan and his team were able to prove the volcanic province occurred at the same time as the Early-Middle Cambrian extinction from 510-511 million years ago – the first extinction to wipe out complex multicellular life.

"It has been well-documented that this extinction, which eradicated 50 per cent of species, was related to climatic changes and depletion of oxygen in the oceans, but

the exact mechanism causing these changes was not known, until now," Dr Jourdan said.

"Not only were we able to demonstrate that the Kalkarindji volcanic province was emplaced at the exact same time as the Cambrian extinction, but were also able to measure a depletion of sulphur dioxide from the province's volcanic rocks – which indicates sulphur was released into the atmosphere during the eruptions.

"As a modern comparison, when the small volcano Pinatubo erupted in 1991, the resulting discharge of sulphur dioxide decreased the average global temperatures by a few tenths of a degree for a few years following the eruption.

"If relatively small eruptions like Pinatubo can affect the climate just imagine what a volcanic province with an area equivalent to the size of the state of Western Australia can do."

The team then compared the Kalkarindji volcanic province with other volcanic provinces and showed the most likely process for all the mass extinctions was a rapid oscillation of the climate triggered by volcanic eruptions emitting sulphur dioxide, along with greenhouse gases methane and carbon dioxide.

"We calculated a near perfect chronological correlation between large volcanic province eruptions, climate shifts and mass extinctions over the history of life during the last 550 million years, with only one chance over 20 billion that this correlation is just a coincidence," Dr Jourdan said.

Dr Jourdan said the rapid oscillations of the climate produced by volcanic eruptions made it difficult for various species to adapt, ultimately resulting in their demise. He also stressed the importance of this research to better understand our current environment.

"To comprehend the long-term climatic and biological effects of the massive injections of gas in the atmosphere by modern society, we need to recognise how climate, oceans and ecosystems were affected in the past," he said.

The paper's abstract, High-precision dating of the Kalkarindji large igneous province, Australia, and synchrony with the Early–Middle Cambrian (Stage 4) extinction, is available at: <http://geology.gsapubs.org/content/early/2014/04/22/G35434.1.abstract>. A full version is available on request.

http://www.eurekalert.org/pub_releases/2014-05/dumc-ssm053014.php

Stopping statins may benefit terminally ill patients

People in the late stages of cancer and other terminal illnesses are not only unharmed by discontinuing statins for cholesterol management, they may benefit
CHICAGO – People in the late stages of cancer and other terminal illnesses are not only unharmed by discontinuing statins for cholesterol management, they may benefit, according to a study presented Friday by researchers at Duke Medicine representing a national research network.

The finding addresses a thorny question in treating people with life-limiting illnesses: When, if ever, is it appropriate to discontinue medications prescribed for other conditions that will likely not lead to their death?

In an analysis presented at the American Society of Clinical Oncology annual meeting in Chicago, the researchers reported that discontinuing statins in patients with advanced illnesses resulted in improved overall quality of life, lower costs and no increased deaths. In fact, the patients who stopped taking statins appeared to live slightly longer.

"When you look at the number of medications people take when they are dying, it doubles in the last year of life," said lead author Amy Abernethy, M.D., Ph.D., director of the Center for Learning Health Care at the Duke Clinical Research Institute and a member of the Duke Cancer Institute. Abernethy represented the Palliative Care Research Cooperative Group, a national research network focused on improving care for people with serious illnesses.

"Cancer patients, for example, take medications for pain, nausea and other problems associated with advanced disease," Abernethy said. "Many don't have an appetite, and simply swallowing medications can be a problem. So the issue is whether some longstanding medications such as cholesterol-lowering drugs might be safely discontinued, but there has been little research to help guide clinicians in making that recommendation."

Abernethy said the researchers identified statins as a good candidate to explore the issue, because the drug is widely prescribed and benefits can take years to accrue. Other drugs the researchers could eventually study include medications for blood pressure and blood clots.

In their study of statins, Abernethy and colleagues enrolled 381 patients who faced the likelihood of dying within a year. All patients had been taking statins for at least three months; roughly half were randomized to continue taking the drug, the other half to discontinuing it.

The researchers followed the patients for up to a year to monitor survival, cardiovascular events and changes in quality of life.

Among the 192 study patients who continued statins, the median survival was 190 days; the 192 participants who stopped taking the drugs had a median survival of 229 days.

Those who discontinued the drugs reported a better overall quality of life, particularly in their psychological wellbeing, and saved money: \$716 per person over the course of the trial for name-brand drugs, and \$629 for generics.

Using U.S. population estimates, the researchers reported that as much as \$603 million a year could be saved if patients in the late stages of fatal illnesses were to cut out statins.

"This is a decision that needs to be discussed between patients and their doctors; it's not something that should be done independently or in a one-size-fits-all manner," Abernethy said. "But our study found that patients who discontinued statins reported improvements in quality of life. This runs counter to the idea that discontinuing a treatment would cause people to somehow feel as if they were getting less care or inadequate care."

Abernethy is a leading advocate for extending palliative care -- extra support from care teams to relieve both pain and improve quality of life -- to patients facing life-limiting illnesses. She said findings from this study should force new discussions. "These are conversations that need to be had," she said. "This brings us to a new era of asking how to right-size care, and how to bring evidence to that issue. There is an important message here that taking things away isn't always bad."

In addition to Abernethy, study authors include Don Taylor at Duke, along with Jean Kutner, Diane Fairclough and Patrick J. Blatchford at the University of Colorado; Laura Hanson at the University of North Carolina; Christine Ritchie at the University of California, San Francisco; and Janet Bull, Four Seasons.

The National Institute of Nursing Research provided funding for the study (UC4-NR012584, U24-NR014637).

http://www.eurekalert.org/pub_releases/2014-05/eso-rod052914.php

Risk of death highest following surgery in afternoons, at weekends, and in February

New research presented at this year's Euroanaesthesia show that on weekends, in the afternoons and in February are the times when the risk of death following surgery is the highest.

The research is by Dr Felix Kork and Professor Claudia Spies, Charité - University Medicine Berlin, Germany and colleagues.

Hospital mortality is subject to day-night, weekly and seasonal variability. This has been shown for various populations, settings, and in different regions of the world. However, a cyclic influence on hospital mortality has not been shown in patients after surgery. In this study, the researchers investigated the daily, weekly, and seasonal variability of hospital mortality in patients after surgery.

A retrospective analysis was carried out patients who underwent surgery between 2006 and 2011 at the two University Hospital Campuses of Charité Tertiary Care University Center, Berlin. Data was then modelled to work out cyclical patterns. In this first analysis of the data, a total of 218,758 patients were included. Hospital mortality showed variability over the course of the day, during different weekdays, and different months. Surgery conducted in the afternoon was associated with 21% increased risk of death compared with surgery conducted at other times of day. Surgery at the weekend was associated with a 22% increased risk of death

compared with surgery on weekdays. February was the highest risk month for surgery, with surgery in February associated with a 16% increased risk of death compared with surgery in all other months. Further work on the data will be carried out in the coming months, including looking at the possible reasons behind the variations.

The authors say: "Several factors may have influenced this outcome. For example, it may be that standard of care differs throughout the day and between weekdays and weekends. Although we controlled for risk factors including emergency surgery in our study, it may very well be that the patients treated in the afternoon and on the weekends were more severely ill. We need more data to draw conclusions regarding seasonal variation in postoperative outcome."

They add: "Despite having an accredited quality management system in place in our hospitals, as well as having the European Society of Anaesthesiology's Helsinki Declaration of Patient Safety in Anaesthesiology implemented, this study shows that we should seek to further improve patient safety."

<http://bit.ly/1hr1jnJ>

Tech Can't Save Us From Global Warming Catastrophe

Big ideas like space mirrors and creating more clouds won't help with global warming, but cutting emissions will, argues a new study.

Jun 1, 2014 03:00 AM ET // by Paul Heltzel

"Climate engineering doesn't offer a perfect option," said Daniela Cusack, an assistant professor of geography at UCLA and the study's lead author, in a release. "The perfect option is reducing emissions." We have the technology we need right now, say the authors, to reduce the amount of CO2 being added to the atmosphere each year by 7 gigatons. Human activity creates about 9 gigatons each year. A gigaton is 1 billion tons. (A gigaton here, a gigaton there, pretty soon you're talking about real carbon.) Curbing forest destruction could contain up to 1.3 gigatons of carbon in plant material annually, the study reports.

"We have the technology, and we know how to do it," Cusack said. "It's just that there doesn't seem to be political support for reducing emissions."

The group looked at five strategies for slowing climate change: cutting emissions, storing carbon through plants, weather modification (cloud seeding), storing carbon dioxide as a liquid underground and solar reflection.

The authors seemed slightly freaked about creating more clouds, actually. "Cloud seeding sounds simple," Cusack said. "But we really don't understand what would happen to the climate if we started making more clouds."

The most promising technology studied was carbon sequestering, the authors found, but none appeared to be as effective as just cutting emissions.

The study appears in latest issue of the journal *Frontiers in Ecology and the Environment*.

<http://nyti.ms/1hr1U98>

Study May Alter Approach to Prostate Cancer

New study finds men given chemotherapy early in their treatment for advanced disease lived a median of nearly 14 months longer than those who did not

By ANDREW POLLACK JUNE 1, 2014

CHICAGO - Many men with prostate cancer put off using chemotherapy as long as possible, fearing its side effects.

But a new study has found that men given chemotherapy early in their treatment for advanced disease lived a median of nearly 14 months longer than those who did not get early chemotherapy. The result could upend the established treatment practice, researchers said here on Sunday.

“We haven’t seen survival benefits like that for any therapy in prostate cancer,” said Dr. Michael J. Morris, an associate professor at the Memorial Sloan-Kettering Cancer Center, who was not involved in the study but was selected to publicly comment on it at the annual meeting of the American Society of Clinical Oncology. Another study being presented on Sunday found that drugs called aromatase inhibitors might be better than the standard drug tamoxifen in preventing a recurrence of disease in premenopausal women with early breast cancer. Both studies are being featured in the plenary session on Sunday, meaning they were deemed among the most noteworthy of the more than 5,000 studies being presented at the meeting. In a conference that typically celebrates the latest and greatest drug, all four studies chosen for the plenary session this year are about better ways of using older drugs, showing that there can be a lot to learn even after drugs get to market.

Dr. Nicholas J. Vogelzang, an author of the study on prostate cancer, said that the findings would change practice and that he had already started discussing this option with patients. The challenge, he said, is getting men to agree. “Not many of them want to do chemotherapy, even though the numbers are convincing,” said Dr. Vogelzang, who works at the Comprehensive Cancer Centers of Nevada.

The study’s findings apply to a fairly narrow group of patients - men whose cancer has already spread beyond the prostate gland at the time of diagnosis, or whose cancer has come back after surgery or radiation treatment and still remains susceptible to hormone therapy.

Only a small fraction of men have metastatic prostate cancer at the time of the initial diagnosis because prostate cancer screening using a blood test typically detects the disease before it has spread.

But screening is expected to become less common because a government advisory committee, the United States Preventive Services Task Force, has recommended against routine screening, saying that more men are harmed by unnecessary treatments for prostate cancer than are saved from death by screening. That could lead to an increase in men whose initial diagnosis is metastatic cancer, Dr. Vogelzang said.

The study, sponsored by the National Cancer Institute, involved 790 men who received either only hormone therapy or hormone therapy in addition to at most six infusions of docetaxel spaced three weeks apart.

Those who received the chemotherapy lived a median of 57.6 months, compared with 44.0 months in the control group, a difference of 13.6 months. The difference in survival was even greater - 17 months - for the patients whose cancer had spread more extensively. Dr. Morris of Sloan-Kettering said those men were the best candidates for early chemotherapy.

Docetaxel is sold under the brand name Taxotere by Sanofi, but generic versions are also available. It was approved for metastatic prostate cancer in 2004. In the last few years, several other drugs have been approved, like Zytiga from Johnson & Johnson and Xtandi from Medivation and Astellas Pharma.

But docetaxel and the newer drugs are typically used after hormone therapy has stopped working. In that setting, each of them has extended median survival by about two to five months in clinical trials.

Dr. Matthew R. Cooperberg, associate professor of urology at the University of California, San Francisco, said doctors were starting to use the newer agents before docetaxel, pushing chemotherapy further back in the sequence.

So the new study “is, to an extent, bucking the tide,” he said. “This trial may be evidence that the role for chemo is earlier, when patients are healthier and the disease burden is relatively low.”

The results also raise the question of whether the other prostate cancer drugs would also provide a much greater survival advantage if used earlier. Some trials are underway to determine that.

One issue is that early treatment is often handled by urologists, not oncologists. And many urologists do not administer chemotherapy.

Dr. Morris said he did not think earlier use of docetaxel would diminish sales of the newer agents. Men will eventually become resistant to hormone therapy, he said, and will need the newer agents.

In breast cancer, women with estrogen-responsive disease typically take drugs for at least five years after their tumor has been removed surgically, to prevent cancer from recurring.

Aromatase inhibitors are generally considered a better choice than tamoxifen for postmenopausal women. But aromatase inhibitors work only when women have low estrogen levels, which usually rules them out for premenopausal women. The new study - actually two studies being analyzed together to accumulate nearly 4,700 patients - involved suppressing the functioning of the ovaries so that the younger women could take an aromatase inhibitor.

Five years of an aromatase inhibitor in addition to ovarian suppression proved superior to five years of tamoxifen in addition to ovarian suppression. After five years, 91.1 percent of those who received the aromatase inhibitor, exemestane, were free of cancer, compared with 87.3 percent of those who received tamoxifen with ovarian suppression. (In the United States, tamoxifen is typically used without ovarian suppression.)

Some experts said they were a bit skeptical that the results would change practice, noting that so far there was no difference between the groups in how long the women lived. And side effects must be evaluated, they said. Those include both the joint pain caused by aromatase inhibitors as well as the hot flashes and bone loss that could come from putting women into early menopause so they could use the aromatase inhibitor.

Ovarian suppression is typically accomplished using drugs like goserelin. Another study presented here on Friday showed that goserelin could help preserve fertility in young breast cancer patients.

Exemestane is sold under the brand name Aromasin by Pfizer, though generic versions are commonly used.

<http://bit.ly/1n3d5DX>

'Quadrapeutics' works in preclinical study of hard-to-treat tumors

Animal tests show Rice-developed technology effective against aggressive cancer

HOUSTON - The first preclinical study of a new Rice University-developed anti-cancer technology found that a novel combination of existing clinical treatments can instantaneously detect and kill only cancer cells -- often by blowing them apart -- without harming surrounding normal organs. The research, which is available online this week Nature Medicine, reports that Rice's "quadrapeutics" technology was 17 times more efficient than conventional chemoradiation therapy against aggressive, drug-resistant head and neck tumors.

The work was conducted by researchers from Rice, the University of Texas MD Anderson Cancer Center and Northeastern University.

"We address aggressive cancers that cannot be efficiently and safely treated today," said Rice scientist Dmitri Lapotko, the study's lead investigator. "Surgeons often cannot fully remove tumors that are intertwined with important organs.

Chemotherapy and radiation are commonly used to treat the residual portions of

these tumors, but some tumors become resistant to chemoradiation. Quadrapeutics steps up when standard treatments fail. At the same time, quadrapeutics complements current approaches instead of replacing them."

Lapotko said quadrapeutics differs from other developmental cancer treatments in that it radically amplifies the intracellular effect of drugs and radiation only in cancer cells. The quadrapeutic effects are achieved by mechanical events -- tiny, remotely triggered nano-explosions called "plasmonic nanobubbles." Plasmonic nanobubbles are non-stationary vapors that expand and burst inside cancer cells in nanoseconds in response to a short, low-energy laser pulse. Plasmonic nanobubbles act as a "mechanical drug" against cancer cells that cannot be surgically removed and are otherwise resistant to radiation and chemotherapy.

In prior studies, Lapotko showed he could use plasmonic nanobubbles alone to literally blow cells apart. In quadrapeutics, his team is using them to detect and kill cancer cells in three ways. In cancer cells that survive the initial explosions, the bursting nanobubbles greatly magnify the local doses of both chemotherapy drugs and radiation. All three effects -- mechanical cell destruction, intracellular drug ejection and radiation amplification -- occur only in cancer cells and do not harm vital healthy cells nearby.

To administer quadrapeutics, the team uses four clinically approved components: chemotherapy drugs, radiation, near-infrared laser pulses of low energy and colloidal gold.

"Quadrapeutics shifts the therapeutic paradigm for cancer from materials -- drugs or nanoparticles -- to mechanical events that are triggered on demand only inside cancer cells," Lapotko said. "Another strategic innovation is in complementing current macrotherapies with microtreatment. We literally bring surgery, chemotherapies and radiation therapies inside cancer cells."

The first component of quadrapeutics is a low dose of a clinically validated chemotherapy drug. The team tested two: doxorubicin and paclitaxel. In each case, the scientists used encapsulated versions of the drug that were tagged with antibodies designed to target cancer cells. Thanks to the magnifying effect of the plasmonic nanobubbles, the intracellular dose -- the amount of the drug that is active inside cancer cells -- is very high even when the patient receives only a few percent of the typical clinical dose.

The second component is an injectable solution of nontoxic gold colloids, tiny spheres of gold that are thousands of times smaller than a living cell. Quadrapeutics represents a new use of colloidal gold, which has been used for decades in the clinical treatment of arthritis. In quadrapeutics, the gold colloids are tagged with cancer-specific clinically approved antibodies that cause them to accumulate and

cluster together inside cancer cells. These gold "nanoclusters" do nothing until activated by a laser pulse or radiation.

The third quadrapeutic component is a short near-infrared laser pulse that uses 1 million times less energy than a typical surgical laser. A standard endoscope delivers the laser pulse to the tumor, where the gold nanoclusters convert the laser energy into plasmonic nanobubbles.

The fourth component is a single, low dose of radiation. The gold nanoclusters amplify the deadly effects of radiation only inside cancer cells, even when the overall dose to the patient is just a few percent of the typical clinical dose.

"What kills the most-resistant cancer cells is the intracellular synergy of these components and the events we trigger in cells," Lapotko said. "This synergy showed a 100-fold amplification of the therapeutic strength of standard chemoradiation in experiments on cancer cell cultures."

In the Nature Medicine study, the team tested quadrapeutics against head and neck squamous cell carcinoma (HNSCC), an aggressive and lethal form of cancer that had grown resistant to both chemotherapy drugs and radiation. Quadrapeutics proved so deadly against HNSCC tumors that a single treatment using just 3 percent of the typical drug dose and 6 percent of the typical radiation dose effectively eliminated tumors in mice within one week of the administration of quadrapeutics.

Lapotko, a faculty fellow in biochemistry and cell biology and in physics and astronomy, said he is working with colleagues at MD Anderson and Northeastern to move as rapidly as possible toward prototyping and a human clinical trial. In clinical applications, quadrapeutics will be applied as either a stand-alone or intra-operative procedure using standard endoscopes and other clinical equipment and encapsulated drugs such as Doxil or Lipoplatin. Though the current study focused on head and neck tumors, Lapotko said quadrapeutics is a universal technology that can be applied for local treatment of various solid tumors, including other hard-to-treat types of brain, lung and prostate cancer. He said it might also prove especially useful for treating children due to its safety.

"The combination of aggressiveness and drug and radiation resistance is particularly problematic in tumors that cannot be fully resected, and new efficient solutions are needed," said Dr. Ehab Hanna, a surgeon and vice chair of the Department of Head and Neck Surgery at MD Anderson, who was not involved with the testing or development of quadrapeutics. "Technologies that can merge and amplify the effects of surgery, drugs and radiation at the cellular level are ideal, and the preclinical results for quadrapeutics make it a promising candidate for clinical translation."

Study co-authors included Rice research scientist Ekaterina Lukianova-Hleb, MD Anderson researchers Xiangwei Wu and Xiaoyang Ren and Northeastern researchers Vladimir Torchilin and Rupa Sawant.

The research was supported by the National Institutes of Health, the National Science Foundation and the Virginia and L.E. Simmons Family Foundation.

VIDEO is available at: http://youtu.be/_pgH6YMby3M

A copy of the Nature Medicine paper is available at: <http://dx.doi.org/10.1038/nm.3484>

<http://bit.ly/1m53eu1>

Trial results promising for curing puppies' parvo

A North Dakota company that discovered an antibody technology while trying to cure flocks of dying geese is using its research for a more warm and fuzzy purpose: saving puppies.

Early tests performed on about 50 puppies in seven U.S. states for Grand Forks-based Avianax have resulted in a 90 percent cure rate for canine parvovirus, which spreads through animal waste and direct contact between dogs, usually at kennels, shelters and shows. Some puppies die from the virus and others are euthanized because the antibiotics and other medicine needed to treat it can be too expensive - sometimes up to \$2,000 - and take too long.



This May 30, 2014 photo provided by KC Pet Project, shows two puppies that were treated for canine parvovirus at the Kansas City Pet Project, one of the largest shelters in the country. A Grand Forks, N.D., company is testing a cure for the disease that would make it cheaper and easier to treat the dogs. (AP Photo/KC Pet Project)

It isn't clear how many dogs contract parvo annually, since the disease isn't required to be reported. At the Kansas City Pet Project, one of eight test sites and among the largest shelters in the United States, about five cases a month wind up on the "parvo ward." Officials with the Missouri shelter believe the treatment will lead to a dramatic increase in their "parvo graduates."

"When the box arrived we were yelling, 'Woo, the geese antibodies are here!'" shelter spokeswoman Tori Fugate said. "Just the fact that someone is caring out there is pretty remarkable. A lot of open admission shelters choose to not treat parvo because it's considered too much of a resource."

Avianax chief operating officer Richard Glynn hopes to start selling the parvoONE antibody-based treatment - that is, harvested from the yokes of goose eggs - for \$75 a dose by next spring.

"I think there will be a lot of puppy owners who will be very happy," Glynn said.

The U.S. Department of Agriculture issued a conditional permit for the field trials that are taking place. Such permits are normally reserved for outbreaks or other dire situations, but this one passed muster because there's no product specifically targeted for parvovirus, said Jeremy Vrchota, Avianax's sales director and regulatory liaison.

Officials with the USDA's Animal and Plant Inspection Service did not respond to phone messages left by The Associated Press.

The company's path to puppy love began a decade ago after a mysterious disease - later found to be West Nile virus - spread among flocks at the South Dakota-based Schiltz Goose Farm, the largest goose producer in North America. Farm owners James and Richard Schiltz and Glynn, who was working for them, found researchers at the University of North Dakota who were interested in the project. The group, led by Dr. David Bradley, the UND medical school's chair of microbiology and immunization, discovered antibodies in the geese that they could purify and put back into other birds. The treatment worked.

"We went to the Mayo Clinic and they looked at all our work," Glynn said. "They called it a game-changing technology."

Avianax quickly found promising links between goose antibodies and treatments for other diseases, including rabies, dengue fever, avian flu and some cancers.

Because they didn't have the money or time to explore testing for human diseases, the group set their sights on the veterinary market and eventually settled on saving puppies.

Treating parvovirus currently can cost, at a minimum, \$500 for antibiotics, intravenous fluids, painkillers and stomach medicine and generally takes six days, said Dr. Darin Meulebroeck, chief medical officer for Avianax.

The trials have shown the new drug can work as quickly as two days, he said.

"We've lost a couple that have been so severe ... there's no drug that is going to treat 100 percent of everything," Meulebroeck said.

The tests run through November.

Glynn said Avianax has "stuck in there" with the help of key researchers and believes it is on the verge of saving human lives with a similar antibody - although it could take more than five years to reach the market.

The U.S. Army is interested in using the technology for Andres virus, which has been found to lead to a fatal respiratory disease. Safety trials are scheduled in the next two years.

"We went from being goose herders from South Dakota to an antibody company," Glynn said. "And we're not done yet."

<http://bit.ly/1gXoCFk>

Speaking 2 languages benefits the aging brain

New research reveals that bilingualism has a positive effect on cognition later in life.

Findings published in *Annals of Neurology*, a journal of the American Neurological Association and Child Neurology Society, show that individuals who speak two or more languages, even those who acquired the second language in adulthood, may slow down cognitive decline from aging.

Bilingualism is thought to improve cognition and delay dementia in older adults. While prior research has investigated the impact of learning more than one language, ruling out "reverse causality" has proven difficult. The crucial question is whether people improve their cognitive functions through learning new languages or whether those with better baseline cognitive functions are more likely to become bilingual.

"Our study is the first to examine whether learning a second language impacts cognitive performance later in life while controlling for childhood intelligence," says lead author Dr. Thomas Bak from the Centre for Cognitive Aging and Cognitive Epidemiology at the University of Edinburgh.

For the current study, researchers relied on data from the Lothian Birth Cohort 1936, comprised of 835 native speakers of English who were born and living in the area of Edinburgh, Scotland. The participants were given an intelligence test in 1947 at age 11 years and retested in their early 70s, between 2008 and 2010. Two hundred and sixty two participants reported to be able to communicate in at least one language other than English. Of those, 195 learned the second language before age 18, 65 thereafter.

Findings indicate that those who spoke two or more languages had significantly better cognitive abilities compared to what would be expected from their baseline. The strongest effects were seen in general intelligence and reading. The effects were present in those who acquired their second language early as well as late. The Lothian Birth Cohort 1936 forms the Disconnected Mind project at the University of Edinburgh, funded by Age UK. The work was undertaken by The University of Edinburgh Centre for Cognitive Ageing and Cognitive Epidemiology, part of the cross council Lifelong Health and Wellbeing Initiative (MR/K026992/1) and has been made possible thanks to funding from the Biotechnology and Biological Sciences Research Council (BBSRC) and Medical Research Council (MRC).

"The Lothian Birth Cohort offers a unique opportunity to study the interaction between bilingualism and cognitive aging, taking into account the cognitive abilities predating the acquisition of a second language" concludes Dr. Bak. "These

findings are of considerable practical relevance. Millions of people around the world acquire their second language later in life. Our study shows that bilingualism, even when acquired in adulthood, may benefit the aging brain."

After reviewing the study, Dr. Alvaro Pascual-Leone, an Associate Editor for *Annals of Neurology* and Professor of Medicine at Harvard Medical School in Boston, Mass. said, "The epidemiological study by Dr. Bak and colleagues provides an important first step in understanding the impact of learning a second language and the aging brain. This research paves the way for future causal studies of bilingualism and cognitive decline prevention."

This study is published in Annals of Neurology. Media wishing to receive a PDF of this article may contact sciencenewsroom@wiley.com

Full citation: "Does Bilingualism Influence Cognitive Aging?" Thomas H Bak, Jack J Nissan, Michael M Allerhand and Ian J Deary. Annals of Neurology; Published Online: June 2, 2014 (DOI:10.1002/ana.24158).

<http://cnet.co/1hr6vbn>

NSA said to collect millions of images for facial recognition
Surveillance agency collecting millions of images daily for identifying and tracking intelligence targets, documents obtained by The New York Times reveal.

by [Steven Musil](#)

The National Security Agency is collecting millions of images intercepted from global communications for a facial-recognition program to identify and track intelligence targets, according to classified documents described by [The New York Times](#).

The agency is using sophisticated software to harvest "millions of images per day" from emails, text messages, social media, videoconferences, and other communications, according to the documents. Once focused primarily on collecting telephone and email communications data, NSA officials believe the programs hold "tremendous untapped potential" that could revolutionize how the agency tracks surveillance targets, according to the documents, which were obtained by former NSA contractor Edward Snowden.

"It's not just the traditional communications we're after: It's taking a full-arsenal approach that digitally exploits the clues a target leaves behind in their regular activities on the net to compile biographic and biometric information" that can help "implement precision targeting," noted a 2010 document.

One NSA presentation described by the newspaper included several images of the same man in different settings and appearances, along with data points such as travel status and known associates. It wasn't clear how many images had been collected.

An NSA representative told CNET that the agency's foreign surveillance programs are designed to comply with US laws and policy direction.

"We would not be doing our job if we didn't seek ways to continuously improve the precision of signals intelligence activities -- aiming to counteract the efforts of valid foreign intelligence targets to disguise themselves or conceal plans to harm the United States and its allies," NSA spokesperson Vanee Vines said in a statement. "The lawful collection of foreign identity intelligence allows NSA to better identify and track such targets."

Although facial recognition technology has attracted growing attention in recent years from law enforcement and commercial interests, its reception has been rocky. Privacy advocates [raised concerns in April over a facial-recognition database](#) being developed by the FBI that could hold 52 million images by next year. While the FBI said the database could be a useful crime-fighting tool, the Electronic Frontier Foundation said its biggest concern with the database was the inclusion of face images for non-criminal purposes.

[Facebook faced legal opposition](#) from the German government over a controversial photo-tagging feature it rolled out in 2011. The social network is currently working on artificial intelligence software it says is capable of [matching faces in images with nearly the same accuracy as humans](#). The [DeepFace](#) facial verification system uses a 3D modeling technique to detect faces, matching faces in large data sets with an accuracy rate of more than 97 percent.

The technology's application to commerce is also being explored. A Finnish company said last year it was developing a mobile payment system that would allow customers to complete transactions by having a [point-of-sale camera snap a mug shot](#) that could be compared to a database.