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Lashing out at your spouse? Check your blood sugar

Study finds that 'hangry' husbands and wives get more aggressive

COLUMBUS, Ohio – Lower levels of blood sugar may make married people angrier at their spouses and even more likely to lash out aggressively, new research reveals.

In a 21-day study, researchers found that levels of blood glucose in married people, measured each night, predicted how angry they would be with their spouse that evening.

At the end of the 21 days, people who had generally lower levels of glucose were willing to blast their spouses with unpleasant noises at a higher volume and for a longer time than those who had higher glucose levels.

The study shows how one simple, often overlooked factor – hunger caused by low levels of blood glucose - may play a role in marital arguments, confrontations and possibly even some domestic violence, said Brad Bushman, lead author of the study and professor of communication and psychology at The Ohio State University.

Blood glucose levels can be brought up most quickly by eating carbohydrates or sugary foods. "People can relate to this idea that when they get hungry, they get cranky," Bushman said. It even has a slang term: "hangry" (hungry + angry). "We found that being hangry can affect our behavior in a bad way, even in our most intimate relationships," he said.

The study, which took three years to complete, appears online in the Proceedings of the National Academy of Sciences. Bushman conducted the research with C. Nathan DeWall of the University of Kentucky; Richard S. Pond of the University of North Carolina at Wilmington; and Michael D. Hanus of Ohio State.

The research involved 107 married couples. The study started with the couples completing a relationship satisfaction measure, which asked each spouse how much they agreed with statements like "I feel satisfied with our relationship."

The researchers measured anger in a unique way, developed and validated by DeWall in previous studies.

All participants were given a voodoo doll that they were told represented their spouse, along with 51 pins. At the end of each day, for 21 consecutive days, the participants inserted 0 to 51 pins in the doll, depending on how angry they were with their spouse. They did this alone, without their spouses being present, and recorded the number of pins they stuck in the doll. Each person also used a blood glucose meter to measure glucose levels before breakfast and every evening before bed for the 21 days. The result: The lower the participants' evening blood glucose levels, the more pins they stuck in the doll representing their spouse. This association was present even after the researchers took into account the couples' relationship satisfaction.

"When they had lower blood glucose, they felt angrier and took it out on the dolls representing their spouse," Bushman said. "Even those who reported they had good relationships with their spouses were more likely to express anger if their blood glucose levels were lower."

But it wasn't just the dolls who took the brunt of the anger. After the 21 days, the couples came into the laboratory to take part in an experimental task. They were told they would compete with their spouse to see who could press a button faster when a target square turned red on the computer – and the winner on each trial could blast his or her spouse with loud noise through headphones.

In reality, though, they weren't playing against their spouse – they were playing against a computer that let them win about half the time. Each time they "won," the participants decided how loud of a noise they would deliver to their spouse and how long it would last. Their spouses were in separate rooms during the experiment, so participants didn't know they weren't really delivering the noise blast.

"Within the ethical limits of the lab, we gave these participants a weapon that they could use to blast their spouse with unpleasant noise," Bushman said.

Results showed that people with lower average levels of evening glucose sent louder and longer noise to their spouse – even after controlling for relationship satisfaction and differences between men and women.

Further analysis showed that those who stuck more pins in the voodoo doll representing their spouse were more likely to deliver louder and longer noise blasts, as well. "We found a clear link between aggressive impulses as seen with the dolls and actual aggressive behavior," he said.

Why does low blood sugar make people more prone to anger and aggression?

Bushman said that glucose is fuel for the brain. The self-control needed to deal with anger and aggressive impulses takes energy, and that energy is provided in part by glucose.

"Even though the brain is only 2 percent of our body weight, it consumes about 20 percent of our calories. It is a very demanding organ when it comes to energy," he said. "It's simple advice but it works: Before you have a difficult conversation with your spouse, make sure you're not hungry."

The research was funded by a grant from the National Science Foundation.

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Chinese herbal remedy as good as methotrexate for treating rheumatoid arthritis

And combination of Tripterygium wilfordii Hook F plus methotrexate even better

Triptergium wilfordii クロヅル

A traditional Chinese herbal remedy used to relieve joint pain and inflammation works as well as methotrexate, a standard drug treatment that is frequently prescribed to control the symptoms of active rheumatoid arthritis, reveals research published online in the *Annals of the Rheumatic Diseases*.

Furthermore, combining the herbal remedy with methotrexate - the disease modifying drug (DMARD) most commonly used to treat rheumatoid arthritis - was more effective than treatment with methotrexate alone, the findings showed.

Triptergium wilfordii Hook F, or TwHF for short, is used in traditional Chinese medicine to treat joint pain, swelling, and inflammation, and is already approved for the treatment of rheumatoid arthritis in China.

The research team randomly assigned 207 patients with active rheumatoid arthritis to one of three treatment groups: methotrexate 12.5 mg once a week; or TwHF 20 mg three times a day; or a combination of the two over a period of 24 weeks.

The researchers wanted to find out which of these approaches would sufficiently alleviate symptoms to reach an ACR 50 response. This indicates a 50% improvement in the number of tender or swollen joints and other criteria including pain, disability, and the doctor's assessment of disease severity. It's a measure defined by the American College of Rheumatology.

Most (174; 84%) of the participants completed the full 24 weeks of the trial. The proportion of patients achieving ACR 50 was almost 46.5% in those treated with methotrexate alone; 55% in those treated with TwHF alone; and just under 77% in those treated with both. Similar clinically significant patterns of improvement in disease activity and remission rates also occurred among the three treatment groups. There was little difference between the frequency or type of side effects experienced in the different treatment groups, although the number of women who developed irregular periods was slightly higher in those treated with TwHF.

More than 300 compounds have been identified in TwHF, including diterpenoids, which experimental research suggests can suppress genes controlling inflammation and dampen down the immune response, the authors point out. And an extract of the root has recently been investigated for its potential to treat autoimmune diseases and some cancers, say the researchers.

They caution that 24 weeks is too short a time to evaluate disease progression, and that the dose of methotrexate used in the trial is lower than that typically given to patients in the West.

But they suggest that TwHF could be a promising approach to the treatment of active rheumatoid arthritis, particularly as not all patients respond to DMARDs, and because these drugs are expensive.

[Comparison of Tripterygium wilfordii Hook F with methotrexate in the treatment of active rheumatoid arthritis (TRIFRA): a randomised, controlled clinical trial Online First doi 10.1136/annrheumdis-2013-204807]

http://www.eurekalert.org/pub_releases/2014-04/bmj-lsi041014.php#rssowlmlink

Lower salt intake likely to have had key role in plummeting cardiovascular disease deaths in past decade

Average salt intake fell by 15 percent in 2003-11 in England; heart disease and stroke deaths fell by around 40 percent

The 15% fall in dietary salt intake over the past decade in England is likely to have had a key role in the 40% drop in deaths from heart disease and stroke over the same period, concludes research published in the online journal BMJ Open. But average intake across the nation is still far too high, warn the authors. And much greater effort is needed to curb the salt content of the foods we eat, they insist.

Dietary salt is known to increase blood pressure, which is itself a major risk factor for heart disease and stroke.

The authors base their findings on an analysis of data from more than 31,500 people taking part in the Health Survey for England for the years 2003 - when initiatives to curb population salt intake began across the UK - 2006, 2008, and 2011. This survey involves a random representative sample of the adult population of England living in private households, and includes information on diet and blood pressure measurements.

The average population salt intake was calculated from urine collected over a 24 hour period in almost 3000 people who were part of the National Diet and Nutrition Survey between 2003 and 2011. This survey involves random samples of the population. During this period, nationally collated figures show that stroke deaths fell by 42% while deaths from coronary heart disease dropped by 40% in England.

Similarly, the prevalence of several risk factors for cardiovascular disease also fell, including average cholesterol, blood pressure (3/1.4 mm Hg), and smoking, although average weight (Body Mass Index) rose. And fruit and vegetable consumption rose slightly. With the exception of increasing weight gain, all these trends, along with better treatment of cardiovascular disease and its risk factors would have probably contributed to the dramatic falls in stroke and heart disease deaths, explain the authors.

But daily salt intake fell by an average of 1.4 g during this period, amounting to a drop of 15%. And among those not taking blood pressure lowering drugs, average blood pressure still fell by 2.7/1.1 mm Hg, even after taking into account other influential factors.

Salt intake was not measured in this particular group, but the substantial fall in salt consumption in the population samples suggests that the decrease in blood pressure would largely have been attributable to less dietary salt rather than to medication, say the authors. And previously published research suggests that the contribution of blood pressure lowering drugs to population falls in blood pressure is relatively small, they say.

The authors caution that they used several sets of data, involving different people, so were not able to track changes at the individual level, nor were they able to account for physical activity levels.

Nevertheless, they conclude: "The reduction in salt intake is likely to be an important contributor to the falls in blood pressure in England from 2003 to 2011. As a result, the decrease in salt intake would have played an important role in the reduction in stroke and ischaemic heart disease mortality during this period."

And they go on to say that despite considerable progress, 70% of the adult population is still eating more than the recommended 6g/day, with 80% of intake coming from processed foods.

"Therefore, continuing and much greater efforts are needed to achieve further reductions in salt intake to prevent the maximum number of stroke and heart disease deaths," they urge.

[Salt reduction in England from 2003 to 2011: its relationship to blood pressure, stroke and ischaemic heart disease mortality doi 10.1136/bmjopen-2013-004549]

http://www.eurekalert.org/pub_releases/2014-04/mcog-oda041414.php#rssowlmlink

Osteoporosis drugs appear to impede cell membrane repair

A class of drugs widely used to treat osteoporosis appears to impede a cell's ability to repair a protective outer membrane that helps determine what enters and exits, researchers report.

AUGUSTA, Ga. –The inability to quickly repair a membrane is lethal to a cell and may help explain the rare and serious side effect of jawbone destruction that can occur following dental work in patients taking these drugs, said Caroline Lewis, a sophomore at the Medical College of Georgia at Georgia Regents University.

"The bottom line is it inhibits cell membrane repair in two distinct cell types," Lewis said. She is among five winners of the 2014 National Medical Students Competition of the American College of Physicians. Lewis presented her work April 12 during the college's Internal Medicine 2014 meeting in Orlando.

Working in the lab of Dr. Paul McNeil, an MCG cell biologist specializing in cell membrane repair, Lewis found that kidney epithelial cells from monkeys and muscle cells from mice both lost their ability to quickly repair their outer membrane after exposure to zoledronate, a commonly used bisphosphonate, Lewis said. Without drug exposure, cells quickly recovered from a microscope laser injury.

"That is healthy, normal repair," she said, citing a video showing the normal cell experiencing only a brief flicker of fluorescence where hit by a laser. On the other hand, zoledronate-exposed cells quickly filled with a fluorescent dye the researchers placed in the petry dish.

"All this dye coming into the cell means there is still a disruption and no repair occurred to sort of mend the fence," Lewis said. "We know these cells are dying, Basically these videos speak for themselves."

"It's a paradox," added McNeil. "On the one hand, (the drug) is given to people mainly to promote bone health, increase bone density. But in the case of a jaw that has suffered, for example, a tooth extraction, the exact opposite occurs."

He theorized cell membrane repair was contributing to destruction of the jawbone and the lining of the mouth after a 2012 report in the Journal of Proteome Research that bisphosphonates bind to cell membrane proteins vital to membrane repair. Since the severe side effect seems to occur only following dental work, McNeil made the connection.

While it's not clear whether this failure to repair is happening in other parts of the body, McNeil and Lewis note that cell membrane repair is typically a constant throughout the body.

"Pretty much every day of our life, even exercising, you are contracting your muscles, the muscle cells rub past each other and that friction causes microscopic tears in the membrane," Lewis said. "If those cells can't repair an injury, they die because they can' t maintain internal homeostasis."

Next steps include more cell studies, including those on jawbone cells, McNeil said. Kidney epithelial cells and muscle cells used in this study are routinely used in cell membrane repair research, and cell repair mechanisms tend to be consistent across cell types, even across different species, McNeil noted.
He also is pursuing the potential protective properties of vitamin E for these patients. McNeil reported in December 2011 in the journal Nature Communications that vitamin E, a powerful antioxidant found in most foods, helps repair tears in the plasma membrane. In the meantime, Lewis suggests that patients taking the drugs talk with their physicians if they have concerns. Some physicians and dentists recommend a drug holiday for these patients before having dental work.
Bisphosphonates are thought to work primarily by inhibiting bone-consuming cells called osteoclasts, which balance the activty of bone-producing osteoblasts, a balance that's lost in osteoporosis. Bisphosophonate-related osteonecrosis of the jaw, or BRON, is among a fairly long list of side effects for these drugs, including rashes swelling, upper chest pain, irregular heartbeat, and painful or swollen gums and loosening of the teeth, according to MedlinePlus Drug Information.
Bisphosphonates also are used to treat hypercalcemia, high blood levels of calcium that can result from cancer, an overactive parathyroid, and calcium supplements; as well as multiple myeloma, cancer of the plasma cells; and cancer that has spread to the bone. Lewis, who is from Savannah, Ga., worked with McNeil last summer as a participant in the MCG Dean's Student Summer Research Program.

http://www.eurekalert.org/pub_releases/2014-04/sfu-ssw041414.php#rssowlmlink

Study says we're over the hill at 24

It's a hard pill to swallow, but if you're over 24 years of age you've already reached your peak in terms of your cognitive motor performance, according to a new Simon Fraser University study.

SFU's Joe Thompson, a psychology doctoral student, associate professor Mark Blair, Thompson's thesis supervisor, and Andrew Henrey, a statistics and actuarial science doctoral student, deliver the news in a just-published PLOS ONE Journal paper.
In one of the first social science experiments to rest on big data, the trio investigates when we start to experience an age-related decline in our cognitive motor skills and how we compensate for that.
The researchers analysed the digital performance records of 3,305 StarCraft 2 players, aged 16 to 44. StarCraft 2 is a ruthless competitive intergalactic computer war game that players often undertake to win serious money. Their performance records, which can be readily replayed, constitute big data because they represent thousands of hours worth of strategic real-time cognitive-based moves performed at varied skill levels.
Using complex statistical modeling, the researchers distilled meaning from this colossal compilation of information about how players responded to their opponents and more importantly, how long they took to react.
"After around 24 years of age, players show slowing in a measure of cognitive speed that is known to be important for performance," explains Thompson, the lead author of the study, which is his thesis. "This cognitive performance decline is present even at higher levels of skill."
But there's a silver lining in this earlier-than-expected slippery slope into old age. "Our research tells a new story about human development," says Thompson.
"Older players, though slower, seem to compensate by employing simpler strategies and using the game's interface more efficiently than younger players, enabling them to retain their skill, despite cognitive motor-speed loss."
For example, older players more readily use short cut and sophisticated command keys to compensate for declining speed in executing real time decisions.
The findings, says Thompson, suggest "that our cognitive-motor capacities are not stable across our adulthood, but are constantly in flux, and that our day-to-day performance is a result of the constant interplay between change and adaptation."
Thompson says this study doesn't inform us about how our increasingly distracting computerized world may ultimately affect our use of adaptive behaviours to compensate for declining cognitive motor skills.
But he does say our increasingly digitized world is providing a growing wealth of big data that will be a goldmine for future social science studies such as this one.
Simon Fraser University is consistently ranked among Canada's top comprehensive universities and is one of the top 50 universities in the world under 50 years old. With campuses in Vancouver, Burnaby and Surrey, B.C., SFU engages actively with the community in its research and teaching, delivers almost 150 programs to more than 30,000 students, and has more than 125,000 alumni in 130 countries.

http://www.eurekalert.org/pub_releases/2014-04/uos-sti041014.php#rssowlmlink

Simple test in the ambulance saves lives after heart attack, new study finds

A new study from the University of Surrey, published today in the journal Heart, has identified a positive link between the survival of heart attack patients and the use of an electrocardiogram, by ambulance crews

A new study from the University of Surrey, published today in the journal Heart, has identified a positive link between the survival of heart attack patients and the use of an electrocardiogram (ECG), by ambulance crews. Researchers, funded by the British Heart Foundation (BHF), analysed data from almost half a million adults admitted with a heart attack to hospitals in England and Wales, noting whether patients who came to hospital by ambulance had had an ECG test or not.

The results showed that the number of patients who died within 30 days of hospital admission was significantly lower when an ECG test had been carried out by ambulance crews. The study also revealed that a third of patients admitted to hospital with a heart attack are not having the test in the ambulance, with certain groups of patients, including women, the elderly and people from black and minority ethnic groups, less likely to have an ECG. A further important finding from this study was that having an ECG in the ambulance was also the strongest predictor of a patient receiving treatment to reopen a blocked coronary artery. The use of this treatment is proven to reduce heart damage and improve the survival of patients.

Lead author, Professor Tom Quinn from the University of Surrey, said: "Every NHS ambulance is equipped with an ECG machine. While there is evidence from other countries that having an ECG test in the ambulance leads to faster treatment, our study is the first to determine that the test is actually associated with improved survival after a heart attack.

"Ambulance services in the NHS compare favourably to countries such as the USA, where only a quarter of such patients get an ECG, but we need to do more to ensure that the groups we identified as not getting the test have improved care.

"Hopefully our results will reinforce to paramedics the importance of carrying out an ECG when they suspect a heart attack, as well as flag up the types of patients who are currently less likely to receive this test, leaving them more vulnerable to poor outcomes."

Dr Mike Knapton, Associate Medical Director at the BHF, said: "This research suggests that if someone suffering a suspected heart attack has a simple ECG test before they reach hospital, it can help save their life. The test helps paramedics provide the most appropriate treatment outside hospital and means that hospital staff are more prepared when the patient arrives.

"The results, made possible by studying huge numbers of medical records, clearly support existing guidelines on using an ECG test before patients reach hospital. So it's vital that all patients who show signs of a heart attack have this simple test."

http://www.wired.com/2014/04/el-nino-effects/#rssowlmlink

If El Niño Comes This Year, It Could Be a Monster

Attention, weather superfans: El Niño might be coming back. And this time, we could be in for a big one.

By Adam Mann

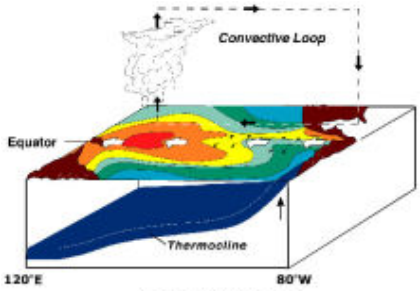
Official NOAA Climate Prediction Center estimates peg the odds of El Niño's return at 50 percent, but many climate scientists think that is a lowball estimate. And there are several indications that if it materializes, this year's El Niño could be massive, a lot like the 1997-98 event that was the strongest on record.

"I think there's no doubt that there's an El Niño underway," said climate scientist Kevin Trenberth of the U.S. National Center for Atmospheric Research. "The question is whether it'll be a small or big one."

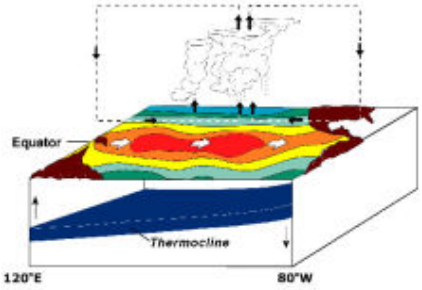
On top of some late-'90s nostalgia, a strong El Niño would bring pronounced changes to weather patterns around the globe, and possibly relief from some of the less-pleasant weather trends that have dominated headlines this year. After a Polar Vortex-fueled, unbearably cold winter in the U.S. Midwest and East Coast, a strong El Niño could bring warmer, drier weather in late 2014. And to parched California and its prolonged drought, El Niño might provide drenching rainstorms to fill up reservoirs. But the news won't all be good. Rainstorms in California could mean floods and mudslides and, coupled with climate change, El Niño could bring harsher droughts to parts of Australia and Africa. Beyond general outlines, it can be tough to say exactly what will happen with El Niño, so we're going to break down some potential scenarios.

El Niño (which is Spanish for "the Niño") is a recurring weather pattern affecting the world every two to seven years. In the tropical Pacific Ocean, the trade winds typically blow east to west, gathering warm water as they go and pooling it in the west. This creates a temperature gradient with cold water in the east, near the coast of South America, and warmer water southwest of Hawaii. "But at some point the system says, 'There's too much warm water piling up here, I'm going to have an El Niño,'" said Trenberth.

The trade winds at this point usually weaken or even reverse entirely, moving warm water eastward. As it travels, this warm water starts emerging from deep in the ocean and heating up the atmosphere. These are the conditions that scientists are seeing right now. Moreover, the blob of warm water in the east is unusually large this year, leading many researchers to predict a monstrous El Niño is on its way.



Normal Conditions



El Niño Conditions

"The main question right now is if this entire warm-pool region will accelerate to the eastern basin or stick in the middle of the Pacific," said meteorologist Michael Ventrice of Weather Services International.

If the warm water decides to stick around at the International Date Line or so, we will get what is called an El Niño "Modoki" (which is Japanese for "similar, but different," a word that every language should really have). Cold water would remain in the eastern Pacific during El Niño Modoki, leading to less rainfall in California than during a strong El Niño. But scientists have only noticed El Niño Modokis events in a few recent years and they are not yet exactly sure what brings it about.

Should the warm pool make it all the way to the South American coast, a much stronger "full-basin" El Niño will appear. And then we could be in for some big weather changes.

A strong El Niño could start affecting the world as early as the fall. The Pacific hurricane season, which gets active around September, is greatly enhanced during El Niño. This likely means more tropical thunderstorms that could affect eastern Pacific areas such as Mexico. In contrast, Atlantic hurricanes are suppressed, meaning fewer and less severe storms with a lower chance of making landfall and doing damage.

The winter is when El Niño really gets going, though. Moisture flows from Hawaii to southern California in an atmospheric river colloquially known as the "Pineapple Express." This creates heavy rainfall that dumps on the region. Though this could bring some relief from California's drought, it also comes with the risk of flash floods and mudslides because the ground has been so hard and dry.

El Niño has other effects further into North America. It tends to enhance the jet stream, creating a wall that prevents Arctic air (and the Polar Vortex) from dipping down to mid-latitudes. East Coast winters are generally drier and warmer during El Niño years, which is probably good news to those still smarting from this recent frigid season. The mild winter has interesting downstream effects, like a boost for the U.S. economy during the Christmas season.

"We saw a lot of retail sales go up in 1997," said Ventrice. "People were going outside spending more money."

Other economic consequences aren't as sanguine. A full-basin El Niño disrupts cycles of fish in the eastern Pacific Ocean. Many of these species are usually caught and ground up into fishmeal, which is fed to farm animals in the U.S. The increased price of fishmeal drives meat prices up as well.

There is some indication that El Niño years coincide with stronger than average tornado seasons. Some of the worst years for tornadoes have occurred during what could be called "Hall of Fame" El Niño years such as 1982 and 1998. But the bottom line, said climate scientist Klaus Wolter of the University of Colorado, Boulder, is that it's complicated. Tornadoes are caused by many different factors, and predicting what this year's season will look like is difficult.

There is another large-scale effect in the atmosphere that this year's El Niño is likely to interact with, and that is climate change. The last large El Niño in 1997-98 occurred with lower levels of CO2 and things have changed in the intervening decade and a half. The Indian Ocean, for instance, has seen increased storm activity, which tends to detract from activity in the Pacific. "How this all evolves is certainly worth watching," said Trenberth.

El Niño dries out places like India and Indonesia, causing a less severe monsoon. And it increases the risk of drought in places like Australia and Africa. With climate change, droughts have been growing more severe so this upcoming season could be a bad one. The end of El Niño also tends to heat up surface temperatures slightly, as the warm equatorial waters dump their energy into the atmosphere, the effects of which are usually felt approximately half a year later. The end of the last big El Niño was in 1998, the warmest year on record. Another temperature record holder is 2005, which followed an El Niño year.

"There's a big chance that in 2015 there is going to be a bump in the global temperature," said Klaus Wolter.

Finally, though a strong El Niño is looking ever more likely, it is far from a done deal. In 2012, a big El Niño appeared to be building up and ended up crashing before it got too far along. But if conditions remain as they are right now, by June researchers will know that El Niño is on its way.

http://bit.ly/1gPy3Em

Scientists Create a Copper-Based Catalyst that Produces Large Quantities of Ethanol

A team of scientists from Stanford University has created a copper-based catalyst that produces large quantities of ethanol from carbon monoxide gas at room temperature.

Stanford University scientists have found a new, highly efficient way to produce liquid ethanol from carbon monoxide gas. This promising discovery could provide an eco-friendly alternative to conventional ethanol production from corn and other crops, say the scientists. Their results are published in the April 9 advanced online edition of the journal Nature.

"We have discovered the first metal catalyst that can produce appreciable amounts of ethanol from carbon monoxide at room temperature and pressure – a notoriously difficult electrochemical reaction," said Matthew Kanan, an assistant professor of chemistry at Stanford and coauthor of the Nature study.

Most ethanol today is produced at high-temperature fermentation facilities that chemically convert corn, sugarcane and other plants into liquid fuel. But growing crops for biofuel requires thousands of acres of land and vast quantities of fertilizer and water. In some parts of the United States, it takes more than 800 gallons of water to grow a bushel of corn, which, in turn, yields about 3 gallons of ethanol.

The new technique developed by Kanan and Stanford graduate student Christina Li requires no fermentation and, if scaled up, could help address many of the land- and water-use issues surrounding ethanol production today. "Our study demonstrates the feasibility of making ethanol by electrocatalysis," Kanan said. "But we have a lot more work to do to make a device that is practical."

Novel electrodes

Two years ago, Kanan and Li created a novel electrode made of a material they called oxide-derived copper. They used the term "oxide-derived" because the metallic electrode was produced from copper oxide.

"Conventional copper electrodes consist of individual nanoparticles that just sit on top of each other," Kanan said. "Oxide-derived copper, on the other hand, is made of copper nanocrystals that are all linked together in a continuous network with well-defined grain boundaries. The process of transforming copper oxide into metallic copper creates the network of nanocrystals."

For the Nature study, Kanan and Li built an electrochemical cell – a device consisting of two electrodes placed in water saturated with carbon monoxide gas. When a voltage is applied across the electrodes of a conventional cell, a current flows and water is converted to oxygen gas at one electrode (the anode) and hydrogen gas at the other electrode (the cathode). The challenge was to find a cathode that would reduce carbon monoxide to ethanol instead of reducing water to hydrogen. "Most materials are incapable of reducing carbon monoxide and exclusively react with water," Kanan said. "Copper is the only exception, but conventional copper is very inefficient."

In the Nature experiment, Kanan and Li used a cathode made of oxide-derived copper. When a small voltage was applied, the results were dramatic. "The oxide-derived copper produced ethanol and acetate with 57 percent faradaic efficiency," Kanan said. "That means 57 percent of the electric current went into producing these two compounds from carbon monoxide. We're excited because this represents a more than 10-fold increase in efficiency over conventional copper catalysts. Our models suggest that the nanocrystalline network in the oxide-derived copper was critical for achieving these results."

Carbon neutral

The Stanford team has begun looking for ways to create other fuels and improve the overall efficiency of the process. "In this experiment, ethanol was the major product," Kanan said. "Propanol would actually be a higher energy-density fuel than ethanol, but right now there is no efficient way to produce it."

In the experiment, Kanan and Li found that a slightly altered oxide-derived copper catalyst produced propanol with 10 percent efficiency. The team is working to improve the yield for propanol by further tuning the catalyst's structure. Ultimately, Kanan would like to see a scaled-up version of the catalytic cell powered by electricity from the sun, wind or other renewable resource.

For the process to be carbon neutral, scientists will have to find a new way to make carbon monoxide from renewable energy instead of fossil fuel, the primary source today. Kanan envisions taking carbon dioxide (CO_2) from the atmosphere to produce carbon monoxide, which, in turn, would be fed to a copper catalyst to make liquid fuel. The CO_2 that is released into the atmosphere during fuel combustion would be re-used to make more carbon monoxide and more fuel – a closed-loop, emissions-free process.

"Technology already exists for converting CO_2 to carbon monoxide, but the missing piece was the efficient conversion of carbon monoxide to a useful fuel that's liquid, easy to store and nontoxic," Kanan said. "Prior to our study, there was a sense that no catalyst could efficiently reduce carbon monoxide to a liquid. We have a

solution to this problem that's made of copper, which is cheap and abundant. We hope our results inspire other people to work on our system or develop a new catalyst that converts carbon monoxide to fuel."
The Nature study was coauthored by Jim Ciston, a senior staff scientist with the National Center for Electron Microscopy at Lawrence Berkeley National Laboratory.
The research was supported by Stanford University, the National Science Foundation and the U.S. Department of Energy. Publication: Christina W. Li, et al., "Electroreduction of carbon monoxide to liquid fuel on oxide-derived nanocrystalline copper," Nature, 2014; doi:10.1038/nature13249 Source: Mark Shwartz, Stanford University

http://phys.org/news/2014-04-asian-air-pollution-affect-pacific.html#rssowlmlink

Asian air pollution affect Pacific Ocean storms

In the first study of its kind, scientists have compared air pollution rates from 1850 to 2000 and found that anthropogenic (man-made) particles from Asia impact the Pacific storm track that can influence weather over much of the world.

The team, which includes several researchers from Texas A&M University, has had its work published in the current issue of Proceedings of the National Academy of Sciences (PNAS).
Yuan Wang, Yun Lin, Jiaxi Hu, Bowen Pan, Misti Levy and Renyi Zhang of Texas A&M's Department of Atmospheric Sciences, along with colleagues from Pacific Northwest National Laboratory, the University of California at San Diego and NASA's Jet Propulsion Laboratory, contributed to the work.
The team used detailed pollution emission data compiled by the Intergovernmental Panel on Climate Change and looked at two scenarios: one for a rate in 1850 – the pre-Industrial era – and from 2000, termed present-day.
By comparing the results from an advanced global climate model, the team found that anthropogenic aerosols conclusively impact cloud formations and mid-latitude cyclones associated with the Pacific storm track.
"There appears to be little doubt that these particles from Asia affect storms sweeping across the Pacific and subsequently the weather patterns in North America and the rest of the world," Zhang says of the findings.
Hurricane
"The climate model is quite clear on this point. The aerosols formed by human activities from fast-growing Asian economies do impact storm formation and global air circulation downstream. They tend to make storms deeper and stronger and more intense, and these storms also have more precipitation in them. We believe this is the first time that a study has provided such a global perspective."
In recent years, researchers have learned that atmospheric aerosols affect the climate, either directly by scattering or absorbing solar radiation, and indirectly by altering cloud formations. Increasing levels of such particles have raised concerns because of their potential impacts on regional and global atmospheric circulation.
In addition, Zhang says large amounts of aerosols and their long-term transport from Asia across the Pacific can clearly be seen by satellite images.
The Pacific storm track represents a critical driver in the general global circulation by transporting heat and moisture, the team notes. The transfer of heat and moisture appears to be increased over the storm track downstream, meaning that the Pacific storm track is intensified because of the Asian air pollution outflow.
"Our results support previous findings that show that particles in the air over Asia tend to affect global weather patterns," Zhang adds. "It shows they can affect the Earth's weather significantly."
Yuan Wang, who conducted the research with Zhang while at Texas A&M, currently works at NASA's Jet Propulsion Laboratory as a Caltech Postdoctoral Scholar.
More information: "Assessing the effects of anthropogenic aerosols on Pacific storm track using a multiscale global climate model," by Yuan Wang et al. PNAS, 2014. www.pnas.org/cgi/doi/10.1073/pnas.1403364111

http://www.eurekalert.org/pub_releases/2014-04/p-mmw040814.php#rssowlmlink

Mouse model would have predicted toxicity of drug that killed 5 in 1993 clinical trial

Over 20 years after the fatal fialuridine trial, a study published this week in PLOS Medicine demonstrates that mice with humanized livers recapitulate the drug's toxicity.

The work suggests that this mouse model should be added to the repertoire of tools used in preclinical screening of drugs for liver toxicity before they are given to human participants in clinical trials.
A retrospective analysis by the US National Academy of Sciences of all preclinical fialuridine toxicity tests, which included studies in mice, rats, dogs, and monkeys, concluded that the available animal data provided no indication that the drug would cause liver failure in humans. Working on a mouse model in which approximately 90% of the animal's liver cells are replaced by human liver cells, Jeffrey Glenn and Gary Peltz, from Stanford University, USA, and colleagues now show that it is possible to detect the toxicity of fialuridine, and possibly other drugs that poison human liver cells.
When the researchers treated mice with humanized livers with fialuridine, they found that the drug caused liver failure. The clinical symptoms (jaundice and lethargy), laboratory abnormalities (elevated transaminase and

lactate levels), and anatomical changes to the liver in the drug-treated mice mirrored those observed in human participants in the fialuridine trial.
To test whether the mouse model could specifically identify the toxicity of fialuridine but would not raise "false alarm" on other drugs, the researchers treated the humanized liver mice with a second drug called sofosbuvir. Sofosbuvir belongs to the same class of drugs as fialuridine, but it has been tested in humans and was found not to have liver toxicity at doses within a few orders of magnitude of the effective dose. Sofosbuvir-treated mice did not show symptoms of liver failure.
Because the humanized mice used in these studies have an impaired immune system, they cannot be used to warn of toxicity that is mediated by the immune system. Nevertheless, since the liver is the "detox" organ, toxicity caused by drugs that act directly on the liver is a common problem in drug development. And because of important differences between human and animal livers, the researchers say "toxicology studies using mice with humanized livers could have a large impact on drug development and could improve the safety of drugs that will subsequently be tested in humans". They express hope that, as suggested by their findings, "the use of 21st century methodologies could improve the safety of 21st century drug development".
Funding: D.X., T.N., M.Z., J.G., and G.P. were partially supported by funding from a transformative RO1 award (1R01DK0909921) from the NIDDK. This work was also partially supported by Eli Lilly and Company through the Lilly Research Award Program (LRAP). No funding bodies had any 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.
Citation: Xu D, Nishimura T, Nishimura S, Zhang H, Zheng M, et al. (2014) Fialuridine Induces Acute Liver Failure in Chimeric TK-NOG Mice: A Model for Detecting Hepatic Drug Toxicity Prior to Human Testing. PLoS Med 11(4): e1001628. doi:10.1371/journal.pmed.1001628

http://www.eurekalert.org/pub_releases/2014-04/wac-rdf041514.php#rssowlmlink

Rising demand for herbal medicine can increase cultivation of medicinal trees

Formalizing trade in herbal medicinal products has the potential to increase the demand for on-farm grown raw material and raise the level of cultivation of medicinal tree species in smallholder farms.

NAIROBI, Kenya - A study carried out by the World Agroforestry Centre (ICRAF) in Kenya shows that trade in herbal medicinal products is rising in the urban areas and formalization in terms of better hygienic packaging and labeling of the products is likely to increase cultivation of these tree species.
Traditional medicine is practiced in in many rural areas in the developing world. The World Health Organization estimates that about 80% of Africans rely on traditional medicine, a great proportion of which is herbal, to meet their health needs and this could increase because of the rising acceptability of natural therapies.
The study published in the scientific journal, Forests Trees and Livelihoods, says that In Kenya, the majority of traditional medicines are sold as wild plant parts, but in urban areas, demand for traditional medicines is rising and this is leading to increased formalization of the market, with traditional medicines now found in powders, liquids and creams.
Jonathan Muriuki, lead author of the study and research scientist at ICRAF, believes that as lifestyles improve, consumers demand better quality. "This opens up greater opportunities for trade in medicinal tree products among actors in the value chain, such as collectors, producers, healers, processors, manufacturers and even exporters," outlines Muriuki.
Muriuki and co-authors set out to learn where medicinal plant traders in Kenya sourced their raw materials and to determine if formalization of the market could provide more opportunities for cultivation.
"Cultivation would not only provide a sustainable supply of medicinal products but also increase the incomes of poor smallholder farmers while addressing current problems of over-harvesting and resource degradation which have reduced the abundance of wild materials."
Their research revealed that 49 per cent of traders in herbal medicine sourced materials from farms and the demand was rising. However, 69 per cent of traders expressed a preference for materials sourced from the wild mainly because they perceived these plants would have higher potency than farm-grown material. Such perception is based on the expectation that wild plants will have grown to full maturity and in rich soils with less interference from human activities such as chemical application.
Those who preferred farm-sourced material said this was because of expected higher quality from good crop husbandry, increasing scarcity in the wild, and for some, a deliberate choice to conserve wild resources.
"While these types of formal enterprise are fairly recent in Kenya, we found that they are all experiencing annual growth and demanding more uniform raw materials which cultivation can provide," says Muriuki.
The study reveals that most farmers sell timber and fruits from their trees but are not selling medicinal tree products because they do not have access to markets "Farmers stated they would sell medicinal products if they

had access to market opportunities," says Muriuki. "Access to markets for other tree products has led to increased cultivation of tree species providing these, so it would be fair to assume the same could be applied for medicinal trees".
To improve the market in traditional medicines, the study recommends linking traders to farmers in the form of grower groups, especially women, which could initially focus on the most traded species as alternative crops are recommended.

http://www.scientificamerican.com/article/the-crisis-in-scientific-results-is-a-matter-of-biology/

The "Crisis" in Scientific Results Is a Matter of Biology

Biology is making it harder for scientists to reproduce one another's experiments

May 1, 2014 |By Veronique Kiermer

Science works by iteration.' Scientists repeat their peers' work and build on their findings. The literature of peer-reviewed scientific papers is the record of this step-by-step process. In recent years, however, prominent reports have suggested that many scientists are not able to replicate others' published results. Is scientific progress going wrong on an unprecedented scale? Before we jump to that conclusion, it would help to consider the changing nature of science itself - particularly biology.
Basic biomedical research and its translation into therapeutic interventions to cure diseases are at the center of this issue. In an ideal world, academic scientists identify targets for drugs - typically proteins involved in disease - and industry scientists look for agents that interfere with those targets' function.
In reality, more often than not, industry scientists find that they cannot replicate the effects seen by academics in a sufficiently robust way to justify drug development. Worse, many promising drug candidates fail in phase II clinical trials when their efficacy is put to the test.
The world seemed simpler in the 1970s, when molecular biology brought us concepts such as "gene A leads to protein B, which leads to function C." Thinking this way, scientists uncovered amazing mechanistic insights and, sometimes, designed effective drugs - the cancer drug Gleevec is the poster child of that reductionist approach. Wouldn't it be nice if drug discovery always went this way?
Those first drugs, however, were low-hanging fruit. Biology is much more complicated than simple schematics. Biological processes do not work in linear ways independently of one another but in tightly interconnected networks. In each branch of these networks, layers of regulatory controls constantly change the nature and abundance of the molecular players. We know little about the inner workings of human cells.
To illustrate how little, consider how genes are controlled. The modern study of gene regulation started in the 1950s, but researchers only started to unravel the complex array of histone modifications that fine-tune chromatin control of gene expression 20 years ago. The fact that RNA interference, another mode of gene regulation, is pervasive has only been realized in the past 10 years. What else don't we know yet?
Laboratory biologists deal with complexity on a daily basis. Mice bred with identical DNA behave differently. Two cells growing side by side in a petri dish cannot be considered identical. In the variable environment of the cell, it is difficult to distinguish a change that is meaningful to a process from one that is unrelated.
Working in a modern lab also entails using sensitive apparatuses, rare technical skills and biological reagents - antibodies and enzymes, for example - which are themselves variable.
In such noisy systems, it is easy to mistake a chance observation for a robust, biologically meaningful effect. Biologists have to undertake large studies that can guarantee the statistical significance of observations, and they need self-critical analysis to avoid inadvertent biases. Scientists cannot be too careful to avoid falling prey to their own enthusiasm.
In that regard, they need the support of their institutions and the journals that publish their results. Some journals, such as Nature, have introduced checklists to ensure that scientists consider and report key information about experiments. (Scientific American is part of Nature Publishing Group.) Still, research institutions should provide more training and supervision of younger scientists. Institutions and funders should manage their incentive systems to limit undue pressures on researchers and promote best practices.
The need for replicating results is as important as ever. But it is inevitable that results obtained in one cell line might not exactly match those in another. They in turn might not be completely predictive of the observations in animal models, let alone human beings.
The literature of published results is still strong. To keep it that way, the scientific community cannot afford to be complacent. It must pay attention to the professionalism of researchers and take into account the complexity of biology.

http://scitechdaily.com/newly-designed-nanoparticles-can-deliver-three-cancer-drugs-time/#rssowlmlink

Newly Designed Nanoparticles Can Deliver Three Cancer Drugs at a Time

In a newly published study, MIT chemists detail how they designed nanoparticles that can deliver three cancer drugs at a time.

Delivering chemotherapy drugs in nanoparticle form could help reduce side effects by targeting the drugs directly to the tumors. In recent years, scientists have developed nanoparticles that deliver one or two chemotherapy drugs, but it has been difficult to design particles that can carry any more than that in a precise ratio.

Now MIT chemists have devised a new way to build such nanoparticles, making it much easier to include three or more different drugs. In a paper published in the Journal of the American Chemical Society, the researchers showed that they could load their particles with three drugs commonly used to treat ovarian cancer.

"We think it's the first example of a nanoparticle that carries a precise ratio of three drugs and can release those drugs in response to three distinct triggering mechanisms," says Jeremiah Johnson, an assistant professor of chemistry at MIT and the senior author of the new paper.

Such particles could be designed to carry even more drugs, allowing researchers to develop new treatment regimens that could better kill cancer cells while avoiding the side effects of traditional chemotherapy. In the JACS paper, Johnson and colleagues demonstrated that the triple-threat nanoparticles could kill ovarian cancer cells more effectively than particles carrying only one or two drugs, and they have begun testing the particles against tumors in animals. Longyan Liao, a postdoc in Johnson's lab, is the paper's lead author.

Putting the pieces together

Johnson's new approach overcomes the inherent limitations of the two methods most often used to produce drug-delivering nanoparticles: encapsulating small drug molecules inside the particles or chemically attaching them to the particle. With both of these techniques, the reactions required to assemble the particles become increasingly difficult with each new drug that is added.

Combining these two approaches - encapsulating one drug inside a particle and attaching a different one to the surface - has had some success, but is still limited to two drugs.

Johnson set out to create a new type of particle that would overcome those constraints, enabling the loading of any number of different drugs. Instead of building the particle and then attaching drug molecules, he created building blocks that already include the drug. These building blocks can be joined together in a very specific structure, and the researchers can precisely control how much of each drug is included.

Each building block consists of three components: the drug molecule, a linking unit that can connect to other blocks, and a chain of polyethylene glycol (PEG), which helps protect the particle from being broken down in the body. Hundreds of these blocks can be linked using an approach Johnson developed, called "brush first polymerization."

"This is a new way to build the particles from the beginning," Johnson says. "If I want a particle with five drugs, I just take the five building blocks I want and have those assemble into a particle. In principle, there's no limitation on how many drugs you can add, and the ratio of drugs carried by the particles just depends on how they are mixed together in the beginning."

Varying combinations

For this paper, the researchers created particles that carry the drugs cisplatin, doxorubicin, and camptothecin, which are often used alone or in combination to treat ovarian cancer.

Each particle carries the three drugs in a specific ratio that matches the maximum tolerated dose of each drug, and each drug has its own release mechanism. Cisplatin is freed as soon as the particle enters a cell, as the bonds holding it to the particle break down on exposure to glutathione, an antioxidant present in cells. Camptothecin is also released quickly when it encounters cellular enzymes called esterases.

The third drug, doxorubicin, was designed so that it would be released only when ultraviolet light shines on the particle. Once all three drugs are released, all that is left behind is PEG, which is easily biodegradable.

This approach "represents a clever new breakthrough in multidrug release through the simultaneous inclusion of different drugs, through distinct chemistries, within the same … platform," says Todd Emrick, a professor of polymer science and engineering at the University of Massachusetts at Amherst who was not involved in the study.

Working with researchers in the lab of Paula Hammond, the David H. Koch Professor of Engineering and a member of MIT's Koch Institute for Integrative Cancer Research, the team tested the particles against ovarian cancer cells grown in the lab. Particles carrying all three drugs killed the cancer cells at a higher rate than those that delivered only one or two drugs.

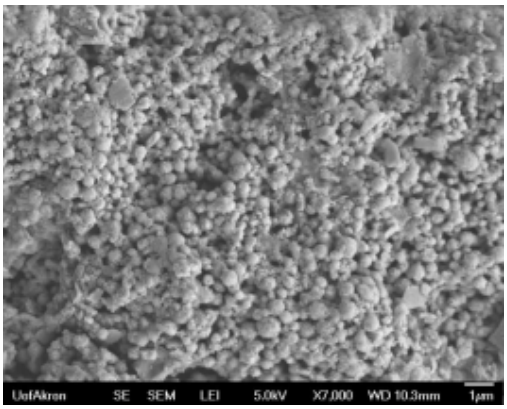
Johnson's lab is now working on particles that carry four drugs, and the researchers are also planning to tag the particles with molecules that will allow them to home to tumor cells by interacting with proteins found on the cell surfaces.
Johnson also envisions that the ability to reliably produce large quantities of multidrug-carrying nanoparticles will enable large-scale testing of possible new cancer treatments. "It's important to be able to rapidly and efficiently make particles with different ratios of multiple drugs, so that you can test them for their activity," he says. "We can't just make one particle, we need to be able to make different ratios, which our method can easily do."
Other authors of the paper are graduate students Jenny Liu and Stephen Morton, and postdocs Erik Dreaden and Kevin Shopsowitz.
The research was funded by the MIT Research Support Committee, the Department of Defense Ovarian Cancer Research Program Teal Innovator Award, the National Institutes of Health, the National Sciences and Engineering Research Council, and the Koch Institute Support Grant from the National Cancer Institute.
Publication: Longyan Liao, et al., "A Convergent Synthetic Platform for Single-Nanoparticle Combination Cancer Therapy: Ratiometric Loading and Controlled Release of Cisplatin, Doxorubicin, and Camptothecin," J. Am. Chem. Soc., 2014; DOI: 10.1021/ja502011g

http://phys.org/news/2014-04-australian-brush-turkey-eggs-ideas-germ-resistant.html#rssowlmlink

Australian brush-turkey eggs inspire ideas for germ-resistant coatings

Brush-turkey's eggshell surface - dotted with nanospheres - blocks bacteria

Phys.org -Rather than sit on its eggs to incubate them, the Australian brush-turkey buries them in rotting vegetation. While bacterial decomposition heats the eggs, it doesn't infect them. University of Akron scientists probed the phenomenon and discovered that the brush-turkey's eggshell surface - dotted with nanospheres - blocks bacteria. The finding, featured as the cover article in the April 2014 Journal of Experimental Biology, inspires possibilities for synthetic coatings that mimic the eggshell's germ-resistant properties.



"The eggshell is not like any other we have seen before. It looks like a tiny asteroid field," says UA visiting assistant professor Liliana D'Alba, describing what she and her research colleagues discovered when they examined the eggshell surface with a scanning electron microscope.

Nanoparticles that cover the surface of the Australian brush-turkey's eggshells make them superhydrophobic and decrease bacterial attachment.

After testing the brush-turkey egg white, an important line of defense against infections, the scientists found its antimicrobial function to be no more exceptional than that of other bird eggs. They then examined the brush-turkey eggshell to find out if the nanoparticles shielded bacteria. Since water provides a breeding ground for bacteria, the researchers applied water to the eggshell to determine its hydrophobicity, or water repellency. Like water on a freshly polished car, water on the brush-turkey egg beaded up.
"Most bacteria grow best when water is available, and these eggs appear to reduce water on their surface," D'Alba says, noting that conversely, water spreads across the shell surface of eggs without nanospheres, such as chicken eggs.
The compelling finding provided indirect evidence of the eggshell's suspected antimicrobial properties and impelled the scientists to further examine the brush-turkey eggs and compare them to chicken eggs.
"The true test came when we directly measured how well bacteria stuck to the surface of the egg and, critically, penetrated through it to the egg contents," says Matthew Shawkey, associate professor of biology and integrated bioscience. "In both cases, brush-turkey eggs well outperformed chicken eggs.
The eggs' rough surface could serve double-duty, preventing bacteria from infecting the eggs by both limiting water and averting bacteria, according to the researchers. The eggshells' robust surface provokes ideas for developing a mimic synthetic coating to benefit medical, food processing, and manufacturing industries, to name just a few, the scientists say.
"Microorganisms grow anywhere. The potential application of a coating inspired by the surface structure of the brush-turkey egg is very wide," D'Alba says. "It could be of great benefit and applicable to any instrument or working area in contact with water."
More information: jeb.biologists.org/content/217/7/1116.full

http://www.eurekalert.org/pub_releases/2014-04/uos-spc041414.php#rssowlmlink

Study provides crucial new information about how the ice ages came about

An international team of scientists has discovered new relationships between deep-sea temperature and ice-volume changes to provide crucial new information about how the ice ages came about.

Researchers from the University of Southampton, the National Oceanography Centre and the Australian National University developed a new method for determining sea-level and deep-sea temperature variability over the past 5.3 million years. It provides new insight into the climatic relationships that caused the development of major ice-age cycles during the past two million years.

The researchers found, for the first time, that the long-term trends in cooling and continental ice-volume cycles over the past 5.3 million years were not the same. In fact, for temperature the major step toward the ice ages that have characterised the past two to three million years was a cooling event at 2.7 million years ago, but for ice-volume the crucial step was the development of the first intense ice age at around 2.15 million years ago. Before these results, these were thought to have occurred together at about 2.5 million years ago.

The results are published in the scientific journal Nature.

Co-author Dr Gavin Foster, from Ocean and Earth Science at the University of Southampton, says: "Our work focused on the discovery of new relationships within the natural Earth system. In that sense, the observed decoupling of temperature and ice-volume changes provides crucial new information for our understanding of how the ice ages developed.

"However, there are wider implications too. For example, a more refined sea-level record over millions of years is commercially interesting because it allows a better understanding of coastal sediment sequences that are relevant to the petroleum industry. Our record is also of interest to climate policy developments, because it opens the door to detailed comparisons between past atmospheric CO2 concentrations, global temperatures, and sea levels, which has enormous value to long-term future climate projections."

The team used records of oxygen isotope ratios (which provide a record of ancient water temperature) from microscopic plankton fossils recovered from the Mediterranean Sea, spanning the last 5.3 million years. This is a particularly useful region because the oxygen isotopic composition of the seawater is largely determined by the flow of water through the Strait of Gibraltar, which in turn is sensitive to changes in global sea level – in a way like the pinching of a hosepipe.

As continental ice sheets grew during the ice ages, flow through the Strait of Gibraltar was reduced, causing measurable increases in the oxygen isotope O-18 (8 protons and 10 neutrons) relative to O-16 (8 protons and 8 neutrons) in Mediterranean waters, which became preserved in the shells of the ancient plankton. Using long drill cores and uplifted sections of sea-floor sediments, previous work had analysed such microfossil-based oxygen isotope records from carefully dated sequences.

The current study added a numerical model for calculating water exchange through the Strait of Gibraltar as a function of sea-level change, which allowed the microfossil records to be used as a sensitive recorder of global sea-level changes. The new sea-level record was then used in combination with existing deep-sea oxygen isotope records from the open ocean, to work out deep-sea temperature changes.

Lead author, Professor Eelco Rohling of Australian National University, says: "This is the first step for reconstructions from the Mediterranean records. Our previous work has developed and refined this technique for Red Sea records, but in that location it is restricted to the last half a million years because there are no longer drill cores. In the Mediterranean, we could take it down all the way to 5.3 million years ago. There are uncertainties involved, so we included wide-ranging assessments of these, as well as pointers to the most promising avenues for improvement. This work lays the foundation for a concentrated effort toward refining and improving the new sea-level record."

Noting the importance of the Strait of Gibraltar to the analysis, co-author Dr Mark Tamisiea from the National Oceanography Centre, Southampton adds: "Flow through the Strait will depend not only on the ocean's volume, but also on how the land in the region moves up and down in response to the changing water levels. We use a global model of changes in the ocean and the ice sheets to estimate the deformation and gravity changes in the region, and how that will affect our estimate of global sea-level change."

http://www.eurekalert.org/pub_releases/2014-04/cfb-tsc041514.php

The surprising consequences of banning chocolate milk

What would happen if chocolate milk were banned from school cafeterias?

For many children eating school lunch, chocolate milk is a favorite choice. What would happen if chocolate milk were banned from school cafeterias? "Students take 10% less milk, waste 29% more and may even stop eating school meals," says Andrew Hanks, PhD.

In a recent article published in PLOS ONE, researchers for the Cornell Center for Behavioral Economics in Child Nutrition Programs (B.E.N. Center), reported results from data collected at 11 Oregon elementary schools where chocolate milk had been banned from the cafeterias and replaced with skim milk. While this policy eliminated the added sugar in chocolate milk, there were unexpected nutritional and economic backlashes.
The new Cornell Food and Brand Lab study by Andrew Hanks, David Just, and Brian Wansink, found that eliminating chocolate milk from the elementary schools decreased total milk sales by 10%, indicating that many students substituted white for chocolate milk. Even though more students were taking white milk, they wasted 29% more than before. Nutritionally, after the milk substitution, students on average consumed less sugar and fewer calories, but also consumed less protein and calcium. Additionally, the ban may have been a factor in a 7% decrease in District's Lunch Program participation.
Removing flavored milk from cafeterias decreases added sugar, yet the economic and nutritional costs warrant reconsidering a less restrictive policy. Nicole Zammit, former Assistance Director of Nutrition Services at Eugene School District, was not surprised that banning chocolate milk had negative consequences. She had this to say, "Given that the role of the federal school meal program is to provide nutritious meals to students who may otherwise have no access to healthy foods– I wouldn't recommend banning flavored milk unless you have a comprehensive plan in place to compensate for the lost nutrients when kids stop drinking milk altogether."
In conclusion, co-author and Director of the Cornell Food and Brand Lab, Brian Wansink recommends, "There are other ways to encourage kids to select white milk without banning the chocolate. Make white milk appear more convenient and more normal to select. Two quick and easy solutions are: Put the white milk in the front of the cooler and make sure that at least 1/3 to 1/2 of all the milk is white."

http://www.eurekalert.org/pub_releases/2014-04/m-hdl041614.php#rssowlmlink

High disease load reduces mortality of children

Trans-generational defense mechanism in humans proved

Children who have been conceived during a severe epidemic are more resistant against other pathogens later in life. For the first time this has been proved by researchers at the Max Planck Institute for Demographic Research (MPIDR) in Rostock, Germany, for the 18th century epidemics of measles and smallpox in the Canadian province of Québec. Children who were conceived during the wave of measles in 1714 and 1715 died significantly less often from smallpox 15 years later than children who had been conceived before the measles epidemic. This is the result of a study published in the scientific journal PLOS ONE by Max Planck researcher Kai Willführ and Mikko Myrskylä from the London School of Economics and Political Science.
"We have proved that parents can essentially prepare their children for future diseases," says bio-demographer Willführ. "The underlying mechanism is not purely genetic, nor is the children's resistance restricted to single pathogens." Scientists call such a transfer a "functional trans-generational effect." Parents who faced an increased disease load during conception not only gave their children protection against this one infection, but the defence against pathogens apparently also worked better in the next generation against different illnesses like smallpox.
The moment of conception was critical for life or death for many children during the 1730 smallpox epidemic. The probability of dying from smallpox had dropped to less than 15 percent for children conceived during the measles epidemic in 1714 and 1715 compared to their brothers or sisters who had been conceived and born before the measles epidemic. But there was a high price to pay. Those children who were so resistant to smallpox survived the later epidemic with greater probability. But during the time between the two waves of epidemics, their mortality was three times that of their siblings who had been conceived before the earlier measles epidemic and thus were less resistant to smallpox.
"The way children's bodies fight diseases seems to be optimized for a world with high pathogen load if it was also high at conception," says MPIDR researcher Kai Willführ. But the children's resistance does not fit into a world with fewer pathogens and works less well under normal circumstances.
"It was only during conception and pregnancy that measles could have given an advantage that parents passed on to the next generation," says Kai Willführ. When the children conceived at the peak of the measles epidemic were born, the measles epidemic had already passed; the pathogens were no longer in the environment. It can be ruled out that children simply became immune. In principle it is possible for a mother to pass her antibodies, and thus immunity, to her baby. This happens through the placenta during pregnancy and through breast milk after birth. But this protection is limited to the same illness the mother had immunity against. In Québec this would have been measles. However, in this study the researchers found that the children were also resistant against another disease, namely smallpox. For the first time, the scientists could separate the mortality effects of the different diseases, because they traced the life course of each child individually and of their siblings. For

their study they investigated birth cohorts from 1705 to 1724 and their mortality until the year 1740. They achieved data about births and deaths from transcriptions of old church registers of the historical population of the St. Lawrence River valley in the Canadian province of Québec.
Kai Willführ, Mikko Myrskylä: Disease Load at Conception Predicts Survival in Later Epidemics in a Historical French-Canadian Cohort, Suggesting Functional Trans-Generational Effects in Humans in: PLOS ONE, online advance publication April 16

http://bit.ly/1jcUyQX

Slow-motion tremors make Tokyo megaquake more likely

The people of Tokyo have long lived in fear of another great earthquake, and those fears are increasingly justified.

14:00 16 April 2014 by Jeff Hecht

Slow-motion earthquakes have become more common beneath the city in the last few years, causing tectonic stresses to build up. The after-effects of the 2011 Tōhoku megaquake are also prodding the area in the direction of a big quake, but seismologists cannot predict when it might occur, nor which part of the region's complex fault system will break.
Shinzaburo Ozawa of the Geospatial Information Authority of Japan in Tsukuba used GPS sensors to track the surface motion of the Bōsō peninsula, the eastern side of Tokyo Bay. Between 28 December 2013 and 10 January 2014, he detected centimetre-scale shifts. These were caused by two tectonic plates, kilometres below the surface, slipping by about 10 centimetres. The motion released as much energy as a magnitude-6.5 earthquake, but it caused no damage because it was spread over two weeks.
Seismographs do not record such slow slips, so they went unnoticed until GPS came along, says Heidi Houston of the University of Washington in Seattle, who was not involved in the research.
The concern is that the slow-slip quakes seem to be coming more frequently, a sign of increasing tectonic stress in the region. The latest slip came only 2.2 years after the previous one, a month-long slip in October and November 2011. The first slips detected, beginning in 1996, were 6.4 years apart.
The earlier-than-expected Bōsō slip is a reminder that "it is essential to keep a close eye on the deformation and seismicity in this region," says Roland Burgmann of the University of California, Berkeley, who was not involved in the study.

Shifting plates

Ozawa's research adds to the evidence that a big Tokyo quake is on the way. After the 2011 Tōhoku quake, seismicity in the Tokyo area initially jumped tenfold, then levelled off at three times the earlier rate.
Based on that increase, a study last year estimated a 17 per cent probability of a large shock under Tokyo between March 2013 and March 2018. That is two-and-a-half-times higher than if the Tōhoku quake had not happened (Geophysical Research Letters, doi.org/scz). The events after the Tōhoku quake have "completely rearranged the whole system in north-east Japan", says Burgmann. "They definitely point to the very complicated area around Tokyo becoming a zone of greater hazard."
Four tectonic plates meet in the Tokyo area, and as a result it has suffered several quakes above magnitude 7 in the past four centuries. The largest in the past 1000 years was the Genroku quake, estimated to have been magnitude 8.2, that killed 2300 people on 31 December 1703 and produced a tsunami that killed several thousand more. However, the deadliest was the magnitude-7.9 Great Kantō earthquake of 1 September 1923 (pictured, above right), which killed 100,000 people – with some help from a typhoon. Since 1960, 1 September has been Disaster Prevention Day across Japan.
Journal reference: Geophysical Research Letters, DOI: 10.1002/2014GL060072

http://www.medscape.com/viewarticle/823690?src=rss

Green Tea's Impact on Cognitive Function Now Visible

Green tea appears to boost memory by enhancing functional brain connectivity, a new imaging study suggests.

Megan Brooks

A study led by Stefan Borgwardt, MD, PhD, from the Department of Psychiatry, University of Basel, Switzerland, shows that drinking a green tea extract enhances memory performance, a finding that researchers suggest may have important clinical implications for the treatment of neuropsychiatric disorders, including cognitive impairment.
This is "the first evidence for the putative beneficial effect of green tea on cognitive functioning, in particular, on working memory processing at the neural system level by suggesting changes in short-term plasticity of parieto-frontal brain connections," the investigators write.
The study was published online March 19 in *Psychopharmacology*.

Boosts Brain Plasticity

Several studies have suggested that green tea enhances cognitive functioning. However, until now, the neural mechanisms underlying these putative benefits have been unclear.

To determine whether green tea extract modulates effective brain connectivity during a working memory task and whether connectivity parameters are related to task performance, the investigators recruited 12 healthy male volunteers who consumed either a milk whey–based soft drink containing 27.5 grams of green tea extract or a similar drink without green tea. Participants were given working memory tasks while undergoing functional magnetic resonance imaging (fMRI).

fMRI results showed increased connectivity between the parietal and the frontal cortex of the brain with the green tea extract, and these neuronal findings correlated positively with improvement in task performance.

"Our findings suggest that green tea might increase the short-term synaptic plasticity of the brain," Dr. Borgwardt said in a statement.

"Modeling effective connectivity among frontal and parietal brain regions during working memory processing might help to assess the efficacy of green tea for the treatment of cognitive impairments in neuropsychiatric disorders such as dementia," the researchers conclude.

The study was supported by grants from Rivella, which manufacturers the soft drink used in the study. The company had no role in study design, collection, analysis, interpretation of the data, writing of the report, or decision to submit for publication. The authors have disclosed no relevant financial relationships.

Psychopharmacology. Published online March 19, 2014. Full article

http://nyti.ms/1ti3tbW

An Easier Way to Delay Cutting the Cord

Doctors in the delivery room are increasingly urged to hold off cutting the umbilical cord of a newborn.

By CATHERINE SAINT LOUIS

Delayed clamping, as it's called, allows blood to continue flowing from the placenta, improving iron stores in the baby. But the practice has been slow to catch on in part because doctors have also been advised that for it to be most effective, they also must hold the wet, screaming infant at the level of the mother's vagina for a crucial minute or longer so that gravity will help blood flow.

Doctors have long considered the maneuver awkward, and now a new study, published on Wednesday in The Lancet, has found that it is probably unnecessary. Babies who were placed on their mothers' stomachs before clamping fared just as well as those who were held lower, the researchers found.

"They found no difference whether the baby was at abdomen level or on the chest, or the baby was held at the vagina," said Dr. Tonse Raju, the chief of the pregnancy and perinatology branch at the National Institute of Child Health and Human Development, who wrote a comment accompanying the study. "It made no difference in terms of extra blood the baby got."

The authors hope their finding will convince doctors reluctant to delay cord clamping to start the practice.

"A mother would prefer to have the baby on top of her," Dr. Néstor Vain, the lead author and a professor of pediatrics at the University of Buenos Aires in Argentina. "And that doesn't change the amount of placental transfusion, and facilitates the procedure for the obstetrician."

The study assigned 194 healthy full-term babies to be placed on their mother's abdomen or chest for two minutes and 197 babies to be held at the level of the vagina for two minutes. All of the newborns were still attached to umbilical cords, and weighed before and after the allotted time. The group placed on their mothers' abdomens gained 53 grams of blood, while the babies held lower gained 56 grams.

Delayed clamping of the cord remains underused despite mounting evidence that it helps reduce iron deficiency in babies and poses no added risk of maternal blood loss. (A recent analysis did find roughly 2 percent more babies whose cord clamping was delayed had to be treated for jaundice.)

One reason the practice hasn't been more widely adopted could be simply that holding a bloody, squirming newborn is cumbersome, said Dr. Raju. A minute or two in this position, he said, can feel like "an eternity" with an exhausted mother looking on.

Obstetricians also increasingly recognize the benefits of early skin-to-skin contact, said Dr. Jeffrey Ecker, the chairman of the committee on obstetric practice of the American College of Obstetricians and Gynecologists. Immediate contact helps the baby stay warm, promotes maternal-infant bonding and may even improve breast-feeding. The new study suggests no trade-off is necessary.

"You can delay cord clamping and do skin-to-skin contact, and it's not going to affect the volume of blood that is added to a baby's circulation," said Dr. Ecker, who was not involved in the study.

Premature babies and newborns who needed resuscitation or were delivered via cesarean section were excluded from the study. Research still is needed into blood flow in the umbilical cord in these infants.

Diane Farrar, an author of a review of alternative positions before cord clamping, said some cesarean births may be different for two reasons. "You cut through the uterus, and the uterus doesn't contract as well, so the effect on placental transfusion may be different, may be less," said Dr. Farrar, a senior research fellow at the Bradford Institute for Health Research in England.
Also, after a C-section the surgeon will sometimes hold the baby up. "If the cord is still intact," she said, "that's a long way up for baby to go, and there's a potential for blood to drain from the baby to the placenta if you do that."

http://bit.ly/1f2z2gl

Non-vaccine Drug Ready to Fight Measles

A drug that could contain measles outbreaks works on animals, researchers reported today.

Apr 16, 2014 02:07 PM ET // by Sheila M. Eldred

In animals infected with a virus closely related to the one that causes the measles, the drug reduced the virus, prevented death and promoted immunity.
The drug is cheap to produce and shelf-stable, and it could be stockpiled if approved for humans in order to suppress local outbreaks, researchers said. Such a drug could help permanently eradicate the disease.
Despite a global initiative to eradicate measles begun over a decade ago, measles deaths have hovered around 150,000 since 2007 due to insufficient vaccine in developing countries combined with parental concerns about vaccines in first world countries, Dr. Richard Plemper of the Institute for Biomedical Sciences at Georgia State University said in a press conference. "People have collectively forgotten the dangers of this disease," he said. "It's the most contagious virus that we have today."
That led Plemper to collaborate with the Emory Center for Drug Development and the Paul-Ehrlich Institute in Germany on an oral drug that could treat people who have had contact with someone infected with the measles virus but who have not developed symptoms.
It's not, he emphasized, an alternative to vaccination. "We decided we may need to combine efforts to eradicate it," he said, since "at the end of the day, it's an individual decision [to vaccinate]." "The emergence of strong antiviral immunity in treated animals is particularly encouraging, since it suggests that the drug may not only save an infected individual from disease but contribute to closing measles immunity gaps in a population," Plemper said in a press release.
Research is in early stages; it could be years before the drug would be available to humans. Researchers plan to study potential toxicity in monkeys next.

http://www.medscape.com/viewarticle/823716?src=rss

Herbal Supplements Are Top Complementary Medicine in the US

Nonvitamin, nonmineral dietary supplements, chiropractic manipulation, yoga, and massage therapy are the most common complementary health approaches among US adults, but rates of use vary by area of the country, according to the Centers for Disease Control and Prevention (CDC).

Megan Brooks

The National Center for Complementary and Alternative Medicine, part of the National Institutes of Health, defines complementary health approaches as "a group of diverse medical and health care interventions, practices, products or disciplines that are not generally considered part of conventional medicine."
Jennifer A. Peregoy, MPH, from the CDC's National Center for Health Statistics, Hyattsville, Maryland, and colleagues analyzed data for 34,525 US adults aged 18 years and older who provided information on complementary health approaches as part of the 2012 National Health Interview Survey.
Nonvitamin, nonmineral dietary supplements were the most popular complementary health approach in 2012, reported by 17.9% of adults, more than twice that of all other approaches, the researchers report in a National Center for Health Statistics Data Brief published online April 16.
Chiropractic and osteopathic manipulation was used by 8.5% of adults, yoga by 8.4%, massage therapy by 6.8%, meditation by 4.1%, and special diets by 3.0%.

Regional Variation

The use of nonvitamin, nonmineral dietary supplements was highest in the Mountain (28.7%), Pacific (23.3%), and West North Central US (23.1%); the Mid Atlantic, West South Central, and South Atlantic regions had the lowest use rates (all around 13%).
Use of practitioner-based chiropractic or osteopathic manipulation was nearly twice as high in the West North Central region (16.4%) as in the US overall (8.5% national average). The East South Central US (6.5%), South Atlantic (6.2%), and West South Central regions (5.9%) have lower rates compared with the national average. Rates in the Pacific (9.3%) and East North Central (9.5%) were on par with the national average.

"The use of yoga with deep breathing or meditation was roughly 40% higher in the Pacific [12.1%] and Mountain [11.5%] regions than the national average [8.4%]," the report states. The East South Central (5.1%), West South Central (6.0%), South Atlantic (6.8%), and Mid Atlantic (7.1%) regions had lower yoga use rates than the nation as a whole.

The use of massage therapy was higher in the Pacific (9.4%), Mountain (9.4%), and West North Central (8.4%) regions than the national average of 6.8%. The East South Central had the lowest use of massage therapy in the United States, at 2.5%.

Previous research has demonstrated regional differences in use of complementary health approaches, Dr. Peregoy and colleagues note in their report, "and this report reveals that those regional differences persist across a wide range of complementary health approaches."

They note that environmental and cultural factors unique to towns, regions, and economic factors have long been linked to differences in health behaviors and general health measures in the US population. They say similar environmental and cultural factors may also be at play in the regional differences seen with complementary health approaches.

"Regional Variation in Use of Complementary Health Approaches by US Adults." National Center for Health Statistics Data Brief 146. Published online April 16, 2014. Full text

http://www.eurekalert.org/pub_releases/2014-04/wuis-tso041414.php#rssowlmlink

The story of animal domestication retold

Scientists now think wild animals interbred with domesticated ones until quite recently

Many of our ideas about domestication derive from Charles Darwin, whose ideas in turn were strongly influenced by British animal-breeding practices during the 19th century, a period when landowners vigorously pursued systematic livestock improvement. It is from Darwin that we inherit the ideas that domestication involved isolation of captive animals from wild species and total human control over breeding and animal care. But animal management in this industrial setting has been applied too broadly in time and space, said Fiona Marshall, PhD, professor of anthropology at Washington University in St. Louis. It is not representative of the practices of the Neolithic herders who first domesticated animals nor — for that matter — of contemporary herders in nonindustrial societies.

Together with Keith Dobney, PhD, of the University of Aberdeen in Scotland; Tim Denham, PhD, of the Australian National University; and José Capriles, PhD, of the Universidad de Tarapacá in Chile, Marshall wrote a review article that summarizes recent research on the domestication of large herbivores for "The Modern View of Domestication," a special feature of *The Proceedings of the National Academy of Sciences* published April 29.

Recent research on the domestication of donkeys, camelids (which includes dromedaries, Bactrian camels, llamas and alpacas) pigs, cattle, sheep and goats suggests that neither intentional breeding nor genetic isolation were as significant as traditionally thought, the scientists said.

"Our findings show little control of breeding, particularly of domestic females, and indicate long-term gene flow, or interbreeding, between managed and wild animal populations," Marshall said.

Why is it important to get domestication right? "Our livestock is losing genetic diversity even faster than some wild animals, because of management practices like artificial insemination," Marshall said. "We took only a bit of the diversity from the wild for domestication, and what we're looking at now is lopping it off really fast so we'll be left with little diversity to survive all the climate and disease issues we're facing. It really is a crisis situation. "If we don't understand what it is we might be about to lose, then we don't count the cost of loss accurately or know how to plan for the future," she said.

A walk on the wild side

For most of history, artificial selection on large herbivores was probably weak, Marshall said. "Herders could not afford to kill many animals, particularly large-bodied animals with long gestation periods. To keep herd size stable, herders probably culled or castrated males surplus to the growth needs of the herd, allowing all females to breed," she said. These management practices placed only light selection pressure on the herd's gene pool.

Paradoxically, environmental selection may, in many instances, have been stronger than artificial selection. Early herds were vulnerable to disease, droughts and storms, disasters that would have forced pastoralists to replenish herds from wild populations better adapted to harsh local conditions.

Sometimes domesticated animals were intentionally bred with wild ones, Marshall said. "Wild animals are generally faster, stronger and better adapted to the local conditions than domesticated ones. So, for example, Beja herders in Northeastern Africa intentionally bred their donkeys with African wild asses in order to produce stronger transport animals."

"And sometimes interbreeding was accidental," she said. "Even today in the Gobi, researchers report that domestic camels sometimes join wild herds after becoming separated from their own. Wild and domestic camels meet at shared oases, and wild males also can become extremely aggressive and may collect domestic females to the dismay of pastoralists."
In the Andes, Capriles said, wild and domestic camelids have interbred in such complex ways that alpacas are maternally related to both wild vicunas and guanacos, and the same is true for llamas.
Artificial selection was probably weakest and gene flow highest in the case of pack animals such as donkeys or camelids. But even in the case of pigs or cattle, interbreeding between domestic and wild animals has created long and complex evolutionary and domestication histories that challenge assumptions regarding genetic isolation and long-held definitions of domestication.

The curl in the pigs' tails

The domestication of pigs is one of these stories. Dobney, Greger Larson, PhD, and their team have shown that pigs were domesticated at least twice, in eastern Anatolia and in central China. Analysis of mitochondrial DNA (DNA in a cell organelle that is inherited from the mother) shows that early herders took pigs with them from Anatolia to western Europe. And analysis of ancient DNA shows that, once in Europe, the domesticated pigs interbred with the wild boars. These hybridized populations then rapidly replaced the original domesticates, first in Europe and then, later, across Anatolia itself.
In China, the story is somewhat different. There is little evidence that the domestic herds in central China interbred with wild boars. But early agriculturists took their pigs to southeastern Asia and there, deliberately or accidentally, recruited local wild boar lineages into their domestic stock.
All of the New Guinea domestic pigs and those of the islands in the tropical Pacific Ocean carry DNA from those southeast Asian wild boar populations.
The interesting question is why the pigs in central China didn't interbreed with wild boar populations in central China. Dobney suggests that management practices may have made a difference. It is possible that in China where settlements were dense, people started keeping pigs in pens, whereas in Europe, even in medieval times, people took their pigs to forage in the forests, where they might encounter wild boars.
The pig story illustrates how much our understanding of domestication events has changed. The anomaly is the isolated domestic population, not the prolonged interbreeding among domestic and wild animals, which in most domesticated species seems to have continued to recent times.

What would Darwin say?

"The research is really exciting because it is making us completely rethink what it means to be domesticated," Marshall said. "The boundaries between wild and domesticated animals were much more blurred for much longer than we had realized."
"To untangle the history of domestication," Denham said, "scientists will need to bring to bear all of the evidence at their disposal, including archeological and ethnographic evidence, and the analysis of both modern and ancient DNA."
"We must also investigate sources of selection more critically," Marshall said, "bearing in mind the complex interplay of human and environmental selection and the likelihood of long-term gene flow from the wild."
It's probably fortunate the Darwin had clear examples of animal breeding to consider as he thought about evolution. The first chapter of "On the Origin of Species" discusses the domestication of animals such as as pigeons, cattle and dogs, and Darwin then uses artificial selection as a springboard to introduce the theory of natural selection. It turns out that animal domestication is more complex, and the role of natural selection more important than Darwin thought. It is also the case that the people who first domesticated animals valued wild ones more than did Darwin's Victorian neighbors.

"The Modern View of Domestication," a special issue of PNAS edited by Greger Larson and Dolores R. Piperno, resulted from a meeting entitled "Domestication as an Evolutionary Phenomenon: Expanding the Synthesis," held April 7, 2011, that was funded and hosted by the National Evolutionary Synthesis Centre (National Science Foundation EF-0905606) in 2011.

http://www.eurekalert.org/pub_releases/2014-04/smh-adl041714.php#rssowlmlink

Adrenaline does little to increase patient's survival after cardiac arrest

Giving patients adrenaline after they suffer a cardiac arrest outside of a hospital does not increase their prospects of surviving long-term, according to new research conducted at St. Michael's Hospital.

TORONTO - "The vast number of patients who have a cardiac arrest get adrenaline, which has been the drug recommended in treating cardiac arrest for decades," said Dr. Steve Lin, an emergency physician and trauma team leader at St. Michael's. "Yet, despite advances in medical treatment, long-term survival rates of patients who suffer a cardiac outside a hospital and receive adrenaline remains low."
The findings were published in the journal Resuscitation.

When a person has a cardiac arrest, his or her heart stops beating. Unless the heart is restarted within minutes, the person usually dies. More than 90 per cent of people who experience a cardiac arrest outside of a hospital will die before reaching a hospital or soon after.
Dr. Lin and his colleagues looked at clinical trials and data involving out-of-hospital cardiac arrests that were published in medical journals up to July 2013 and found that adrenaline showed no benefit in survival to discharge from hospital or neurological outcomes.
"It is thought that the short-term benefit of adrenaline in improving coronary blood flow may occur at the expense of other organs," said Dr. Lin. "The drug can cause small blood vessels in other organs to contract, such as in the gut, liver, and kidneys, thus limiting the blood flow to these organs."
While adrenaline is also given to patients who suffer cardiac arrest in hospitals, Dr. Lin looked only at studies of those outside of a hospital because the cause of cardiac arrest tends to be different between the two settings. Those outside a hospital tend to be related to heart disease and heart attacks. Cardiac arrests in the hospital are usually related to the reasons why a patient would be in the hospital, such as infections or respiratory diseases.
Dr. Lin is a research fellow at Rescu—a program based at St. Michael's that focuses on developing processes and interventions to improve outcomes for patients who suffer life- threatening trauma and cardiac emergencies outside of hospitals.
Dr. Lin said that because a standard dose of one milligram of adrenaline showed to be effective in regaining a person's pulse after a cardiac arrest, physicians also questioned what sort of impact a high dose of adrenaline might have. "When compared to patients who received a standard dose of adrenaline, those who received a high dose had an even greater chance of regaining their pulse after a cardiac arrest," he said. "The long-term survival rate, however, did not increase."
Dr. Lin said that those in the medical community need to discuss and study whether adrenaline should still be administered during cardiac arrests. He recommends that paramedics focus on early use of defibrillators and effective CPR instead.
"The use of adrenaline has been the standard of care for so long that it's been hard to change the culture," said Dr. Lin. "We have reached a point in time where physicians and paramedics have to change the way we think."
Dr. Lin said about 40,000 Canadians suffer cardiac arrest outside of a hospital every year and that in Toronto, less than 10 per cent survive long enough to be discharged from hospital.

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Is Parkinson's an autoimmune disease?

Attack by own immune system may kill neurons in Parkinson's disease

NEW YORK, NY - The cause of neuronal death in Parkinson's disease is still unknown, but a new study proposes that neurons may be mistaken for foreign invaders and killed by the person's own immune system, similar to the way autoimmune diseases like type I diabetes, celiac disease, and multiple sclerosis attack the body's cells. The study was published April 16, 2014, in Nature Communications.
"This is a new, and likely controversial, idea in Parkinson's disease; but if true, it could lead to new ways to prevent neuronal death in Parkinson's that resemble treatments for autoimmune diseases," said the study's senior author, David Sulzer, PhD, professor of neurobiology in the departments of psychiatry, neurology, and pharmacology at Columbia University College of Physicians & Surgeons.
The new hypothesis about Parkinson's emerges from other findings in the study that overturn a deep-seated assumption about neurons and the immune system.
For decades, neurobiologists have thought that neurons are protected from attacks from the immune system, in part, because they do not display antigens on their cell surfaces. Most cells, if infected by virus or bacteria, will display bits of the microbe (antigens) on their outer surface. When the immune system recognizes the foreign antigens, T cells attack and kill the cells. Because scientists thought that neurons did not display antigens, they also thought that the neurons were exempt from T-cell attacks.
"That idea made sense because, except in rare circumstances, our brains cannot make new neurons to replenish ones killed by the immune system," Dr. Sulzer says. "But, unexpectedly, we found that some types of neurons can display antigens."
Cells display antigens with special proteins called MHCs. Using postmortem brain tissue donated to the Columbia Brain Bank by healthy donors, Dr. Sulzer and his postdoc Carolina Cebrián, PhD, first noticed—to their surprise—that MHC-1 proteins were present in two types of neurons. These two types of neurons—one of which is dopamine neurons in a brain region called the substantia nigra—degenerate during Parkinson's disease.
To see if living neurons use MHC-1 to display antigens (and not for some other purpose), Drs. Sulzer and Cebrián conducted in vitro experiments with mouse neurons and human neurons created from embryonic stem

cells. The studies showed that under certain circumstances—including conditions known to occur in Parkinson's—the neurons use MHC-1 to display antigens. Among the different types of neurons tested, the two types affected in Parkinson's were far more responsive than other neurons to signals that triggered antigen display.
The researchers then confirmed that T cells recognized and attacked neurons displaying specific antigens.
The results raise the possibility that Parkinson's is partly an autoimmune disease, Dr. Sulzer says, but more research is needed to confirm the idea.
"Right now, we've showed that certain neurons display antigens and that T cells can recognize these antigens and kill neurons," Dr. Sulzer says, "but we still need to determine whether this is actually happening in people. We need to show that there are certain T cells in Parkinson's patients that can attack their neurons."
If the immune system does kill neurons in Parkinson's disease, Dr. Sulzer cautions that it is not the only thing going awry in the disease. "This idea may explain the final step," he says. "We don't know if preventing the death of neurons at this point will leave people with sick cells and no change in their symptoms, or not."
The paper is titled: "MHC-1 expression renders catecholaminergic neurons susceptible to T-cell-mediated degeneration."
Other contributors are: from CUMC, Ellen Kanter, Jonathan Mandelbaum, Jean P. Vonsattel, and John D. Loike; from Sloan-Kettering Institute, Julius Steinbeck, Lorenz Studer, Sadna Budhu, and Luigi Zecca; from the National Research Council of Italy, Fabio Zucca and Pierluigi Mauri.
The authors declare no financial or other conflicts of interest. Columbia University and the La Jolla Institute for Allergy & Immunology have filed a patent application relating to T cell responses and Parkinson's disease.
The research was supported by the NIH (R01NS064155 and U01NS082157), Caja Madrid Foundation; the JPB Foundation; the Parkinson's Disease Foundation; the Udall Center of Excellence at Columbia; the University of Milan the Italian Ministry of Education, University and Research; the Department of Defense; the Michael J. Fox Foundation; the M.E.M.O. Hoffman Foundation; the German Research Council; and NYSTEM.

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Multitarget TB drug could treat other diseases, evade resistance

A drug under clinical trials to treat tuberculosis could be the basis for a class of broad-spectrum drugs that act against various bacteria, fungal infections and parasites, yet evade resistance, according to a study by University of Illinois chemists and collaborators.

CHAMPAIGN, Ill. - Led by U. of I. chemistry professor Eric Oldfield, the team determined the different ways the drug SQ109 attacks the tuberculosis bacterium, how the drug can be tweaked to target other pathogens from yeast to malaria – and how targeting multiple pathways reduces the probability of pathogens becoming resistant. SQ109 is made by Sequella Inc., a pharmaceutical company.
"Drug resistance is a major public health threat," Oldfield said. "We have to make new antibiotics, and we have to find ways to get around the resistance problem. And one way to do that is with multitarget drugs. Resistance in many cases arises because there's a specific mutation in the target protein so the drug will no longer bind. Thus, one possible route to attacking the drug resistance problem will be to devise drugs that don't have just one target, but two or three targets."
Oldfield read published reports about SQ109 and realized that the drug would likely be multifunctional because it had chemical features similar to those found in other systems he had investigated. The original developers had identified one key action against tuberculosis – blocking a protein involved in building the cell wall of the bacterium – but conceded that the drug could have other actions within the cell as well since it was found to kill other bacteria and fungi that lacked the target protein. Oldfield believed he could identify those actions – and perhaps improve upon SQ109.
"I was reading Science magazine one day and saw this molecule, SQ109, and I thought, that looks a bit like molecules we've been studying that have multiple targets," Oldfield said. "Given its chemical structure, we thought that some of the enzymes that we study as cancer and antiparasitic drug targets also could be SQ109 targets. We hoped that we could make some analogs that would be more potent against tuberculosis, and maybe even against parasites."
By studying SQ109 for themselves, Oldfield's team determined that SQ109 does indeed block other proteins involved in critical functions in bacteria, fungi and parasites – but not humans. They found it inhibits two enzymes that make the molecule menaquinone, which is involved in generating the cell's energy. Then they found that SQ109 had a third action, called uncoupling, which makes the cell membrane permeable – essentially transforming the membrane from a wall to a screen door.
Then, the team created a dozen chemical analogs – molecules that are structurally and functionally similar, but tweaked to be more effective or less toxic – and tested them against cultures of bacteria, fungi, parasites and human cells. They found that they could make analogs with maximum effectiveness against certain classes of pathogens; for example, one analog turned out to be five times more potent against the tuberculosis bacterium

than the original SQ109. They also found analogs that kill the parasites that cause the most serious and common form of malaria.
Now, the researchers are working with international collaborators to apply SQ109 analogs against other infectious diseases rampant in the tropical world, such as Chagas' disease, leishmaniasis and sleeping sickness. Oldfield believes that multiple-target drugs, like SQ109 and its analogs, hold the key to antibiotic development in the age of drug resistance and the rise of so-called "superbugs." Evidence supports that assessment: So far, in experiments with tuberculosis, no instances of SQ109 resistance have been reported.
The National Institutes of Health supported this work.

http://www.eurekalert.org/pub_releases/2014-04/nsfc-vbm041714.php#rssowlmlink

Vitamin B3 might have been made in space, delivered to Earth by meteorites

Ancient Earth might have had an extraterrestrial supply of vitamin B3 delivered by carbon-rich meteorites, according to a new analysis by NASA-funded researchers.

The result supports a theory that the origin of life may have been assisted by a supply of key molecules created in space and brought to Earth by comet and meteor impacts.
"It is always difficult to put a value on the connection between meteorites and the origin of life; for example, earlier work has shown that vitamin B3 could have been produced non-biologically on ancient Earth, but it's possible that an added source of vitamin B3 could have been helpful," said Karen Smith of Pennsylvania State University in University Park, Pa. "Vitamin B3, also called nicotinic acid or niacin, is a precursor to NAD (nicotinamide adenine dinucleotide), which is essential to metabolism and likely very ancient in origin." Smith is lead author of a paper on this research, along with co-authors from NASA's Goddard Space Flight Center in Greenbelt, Md., now available online in the journal Geochimica et Cosmochimica Acta.
This is not the first time vitamin B3 has been found in meteorites. In 2001 a team led by Sandra Pizzarello of Arizona State University, in Tempe discovered it along with related molecules called pyridine carboxylic acids in the Tagish Lake meteorite.
In the new work at Goddard's Astrobiology Analytical Laboratory, Smith and her team analyzed samples from eight different carbon-rich meteorites, called "CM-2 type carbonaceous chondrites" and found vitamin B3 at levels ranging from about 30 to 600 parts-per-billion. They also found other pyridine carboxylic acids at similar concentrations and, for the first time, found pyridine dicarboxylic acids.
"We discovered a pattern – less vitamin B3 (and other pyridine carboxylic acids) was found in meteorites that came from asteroids that were more altered by liquid water. One possibility may be that these molecules were destroyed during the prolonged contact with liquid water," said Smith. "We also performed preliminary laboratory experiments simulating conditions in interstellar space and showed that the synthesis of vitamin B3 and other pyridine carboxylic acids might be possible on ice grains."
Scientists think the solar system formed when a dense cloud of gas, dust, and ice grains collapsed under its own gravity. Clumps of dust and ice aggregated into comets and asteroids, some of which collided together to form moon-sized objects or planetesimals, and some of those eventually merged to become planets.
Space is filled with radiation from nearby stars as well as from violent events in deep space like exploding stars and black holes devouring matter. This radiation could have powered chemical reactions in the cloud (nebula) that formed the solar system, and some of those reactions may have produced biologically important molecules like vitamin B3.
Asteroids and comets are considered more or less pristine remnants from our solar system's formation, and many meteorites are prized samples from asteroids that happen to be conveniently delivered to Earth. However, some asteroids are less pristine than others. Asteroids can be altered shortly after they form by chemical reactions in liquid water. As they grow, asteroids incorporate radioactive material present in the solar system nebula. If enough radioactive material accumulates in an asteroid, the heat produced as it decays will be sufficient to melt ice inside the asteroid. Researchers can determine how much an asteroid was altered by water by examining chemical and mineralogical signatures of water alteration in meteorites from those asteroids.
When asteroids collide with meteoroids or other asteroids, pieces break off and some of them eventually make their way to Earth as meteorites. Although meteorites are valued samples from asteroids, they are rarely recovered immediately after they fall to Earth. This leaves them vulnerable to contamination from terrestrial chemistry and life.
The team doubts the vitamin B3 and other molecules found in their meteorites came from terrestrial life for two reasons. First, the vitamin B3 was found along with its structural isomers – related molecules that have the same chemical formula but whose atoms are attached in a different order. These other molecules aren't used by life. Non-biological chemistry tends to produce a wide variety of molecules -- basically everything permitted by the materials and conditions present -- but life makes only the molecules it needs. If contamination from

terrestrial life was the source of the vitamin B3 in the meteorites, then only the vitamin should have been found, not the other, related molecules. Second, the amount of vitamin B3 found was related to how much the parent asteroids had been altered by water. This correlation with conditions on the asteroids would be unlikely if the vitamin came from contamination on Earth.

The team plans to conduct additional interstellar chemistry experiments under more realistic conditions to better understand how vitamin B3 can form on ice grains in space. "We used pyridine-carbon dioxide ice in the initial experiment," said Smith. "We want to add water ice (the dominant component of interstellar ices) and start from simpler organic precursors (building-block molecules) of vitamin B3 to help verify our result."

Smith performed the research at Goddard as a graduate student at Pennsylvania State University, University Park, Pa. Funding came from the Penn State Astrobiology Research Center and the Goddard Center for Astrobiology via the NASA Astrobiology Institute. The research was also funded by the NASA Pennsylvania Space Grant Consortium and the NASA Cosmochemistry Program. For more information about the Tagish Lake meteorite, visit:
http://www.nasa.gov/centers/goddard/news/features/2011/tagish-lake.html

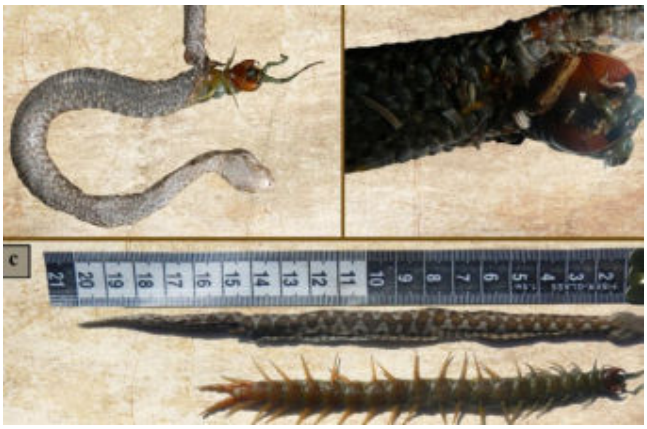
http://news.discovery.com/animals/centipede-eats-snake-from-inside-out-140417.htm#mkcpgn=rssnws1

Centipede Eats Snake from Inside Out

A group of researchers stumbled upon a grisly scene during a field study in Macedonia last year: a dead nose-horned viper with a centipede's head sticking out of its ruptured abdomen.

Apr 17, 2014 03:00 AM ET // by Megan Gannon, Live Science News Editor

After a post-mortem, the scientists think it's possible that the centipede quite literally eviscerated the snake from the inside out.



The remnants of the death match were discovered on May 14, 2013, on Golem Grad, an island in Lake Prespa, and described last month in a brief report published in the journal Ecologica Montenegrina.

The unfortunate nose-horned viper (Vipera ammodytes) was a young female that stretched about 2 inches longer than the centipede (7.9 vs. 6 inches, or 20.3 vs. 15.4 centimeters). But the centipede (Scolopendra cingulate) was actually heavier than the snake, tipping the scales at 114 percent of the snake's body weight (4.8 vs. 4.2 grams, or 0.17 vs. 0.14 ounces).

This unlucky viper messed with the wrong centipede. Scientists think it's possible the centipede tried gnawing its way out of the snake after it was swallowed. **Arsovski et al Ecologica Montenegrina**

Nose-horned vipers regularly take on small mammals, lizards and birds, and they've been known to eat centipedes successfully, too. But in this particular case, the snake "gravely underestimated" the size and strength of its prey, the scientist wrote.

A dissection revealed that the snake's visceral organs were missing, or in other words, "the entire volume of its body was occupied by the centipede," the scientists wrote. For this reason, the researchers think it's possible the snake's dinner tried to claw its way out, destroying the viper's internal organs along the way, before eventually dying.

"In general, this invertebrate is extremely tough: It is very hard to kill a full-grown Scolopendra (personal observation)," the authors of the study wrote of the centipede. "Therefore, we cannot dismiss the possibility that the snake had swallowed the centipede alive, and that, paradoxically, the prey has eaten its way through the snake, almost reaching its freedom."

http://www.newscientist.com/article/dn25437-threatwatch-is-the-mers-virus-spreading-its-wings

Threatwatch: Is the MERS virus spreading its wings?

The Philippines and Malaysia have identified their first-ever MERS cases.

17:23 17 April 2014 by Debora MacKenzie

Meanwhile, cases of the respiratory virus have surged sharply in Saudi Arabia and neighbouring countries since February; Saudi doctors have resigned as healthcare workers are hit with the virus; and the price of surgical masks and garlic, reputedly an anti-viral, have reportedly risen in Jeddah, Saudi Arabia, where 43 people have been struck by the virus since March. MERS (Middle East respiratory syndrome) surfaced in Saudi Arabia in 2012, and it has certainly been hitting the headlines lately. Is it about to hit the fan, too, and go global?

Not just yet – but it is doing worrying things: striking healthcare workers and pilgrims, hitching rides on commercial flights, and perhaps travelling incognito.

The cases in Malaysia and the Philippines are unconnected but both, coincidentally, were reported yesterday. The virus is not at large in those countries. Both people were infected in the Arabian peninsula.
A Filipino hospital worker in Abu Dhabi, in the United Arab Emirates, fell ill with MERS and died there on 10 April. Health authorities tested the people the victim had been in contact with and found 10 more infected healthcare workers.
One of them, a Filipino male nurse, had flown back to the Philippines on 15 April. He and nine local contacts in the Philippines are in quarantine, and so far none has shown any symptoms. But that's another worrying thing: of the 10 who tested positive for the MERS virus in Abu Dhabi, three had only mild disease, and five had no symptoms at all. Two are in hospital.

Silent spread

The virus is turning up in many of the people being tested because they are contacts of known cases, but many of these people do not themselves develop the severe pneumonia that has killed 93 of the 243 known cases of MERS. That means it is probably infecting a lot more people than we know about.
That may be of little importance from an epidemiological perspective if people with mild or asymptomatic infections cannot spread the disease any further. There's no evidence that they can – but many MERS cases had no contact with known cases before they fell ill, suggesting there may be such silent spread.
Much will be resolved when epidemiologists work out whether the virus really does come from camels. Many – though not all – cases not clearly linked to other sick humans had contact with camels before falling ill. Recent research suggests camels may be the normal home of the virus, rather than merely passing it on from another animal.
The case of the Filipino healthcare worker is just one of the large proportion of MERS cases among healthcare professionals. In Jeddah, 38 cases have been diagnosed in a clustered outbreak that began in late March, many of them healthcare workers. Four doctors at the King Fahad Hospital have tendered their resignations in protest, and authorities are offering danger pay to medical staff who treat people with MERS.
This is uneasily reminiscent of the virus's Chinese cousin, SARS, which spread worldwide in 2003, and struck healthcare workers in particular. This threat is amplified in the Arabian peninsula, where many healthcare workers are foreign guest-workers – who, like the Filipino nurse, return to their home countries carrying the virus with them. This week, Saudi health authorities stated that 36 of the country's first 194 cases were foreigners.

Pilgrim risk

The Malaysian case raises another risk. The 54-year-old man had just performed umrah, the minor Muslim pilgrimage to Mecca outside the holy month of Ramadan: he flew from Jeddah, the site of the current outbreak, and died 13 April in Johor state, near Singapore. Malaysian authorities are trying to trace other passengers on Turkish Airlines TK93 from Jeddah to Istanbul and TK60, from Istanbul to Kuala Lumpur on March 29. Some of the 64 people reportedly quarantined in the man's home town are said to have symptoms.
Occasional sick travellers – also confirmed in the UK, France, Germany, Italy and Tunisia – have not so far spawned secondary outbreaks. What is worrying about the Malaysian case is that he was a pilgrim. From the beginning, public health officials have worried that most MERS has been in Saudi Arabia, which welcomes 3 million pilgrims annually for the hajj, and comparable numbers for umrah during the rest of the year.
The Saudis have been very careful: for the last hajj they recommended that elderly or unwell would-be pilgrims stay home instead, and announced afterwards that no cases of MERS were found in any pilgrims. Now, that is no longer true – and in fact it may not have been true before, either, as many pilgrims return to countries considerably less medically advanced than Malaysia. Pilgrims who return with the virus might fall ill or spread it silently without being tested. As with many things about MERS, whether that is happening remains a mystery for now – an increasingly worrying one.

http://scitechdaily.com/kepler-discovers-earth-size-planet-orbiting-star-habitable-zone/#rssowlmlink

Kepler Discovers Earth-Size Planet Orbiting a Star in the 'Habitable Zone'

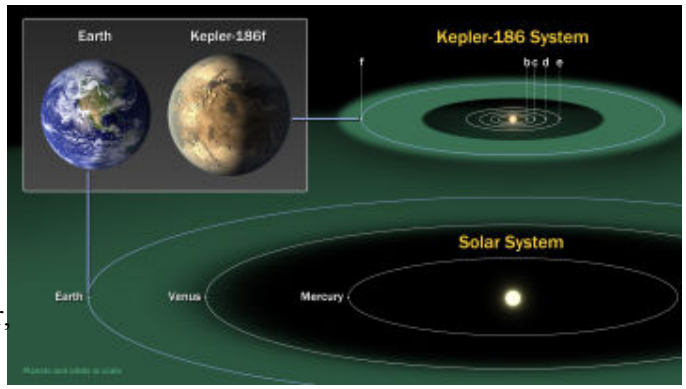
Astronomers have discovered the first Earth-size planet orbiting a star in the "habitable zone," confirming that Earth-size planets exist in the habitable zones of other stars and signaling a significant step closer to finding a world similar to Earth.

Source: Michele Johnson, Ames Research Center; NASA

Using NASA's Kepler Space Telescope, astronomers have discovered the first Earth-size planet orbiting a star in the "habitable zone" — the range of distance from a star where liquid water might pool on the surface of an orbiting planet. The discovery of Kepler-186f confirms that planets the size of Earth exist in the habitable zone of stars other than our sun.

While planets have previously been found in the habitable zone, they are all at least 40 percent larger in size than Earth and understanding their makeup is challenging. Kepler-186f is more reminiscent of Earth.

"The discovery of Kepler-186f is a significant step toward finding worlds like our planet Earth," said Paul Hertz, NASA's Astrophysics Division director at the agency's headquarters in Washington. "Future NASA missions, like the Transiting Exoplanet Survey Satellite and the James Webb Space Telescope, will discover the nearest rocky exoplanets and determine their composition and atmospheric conditions, continuing humankind's quest to find truly Earth-like worlds."



The diagram compares the planets of our inner solar system to Kepler-186, a five-planet star system about 500 light-years from Earth in the constellation Cygnus. The five planets of Kepler-186 orbit an M dwarf, a star that is is half the size and mass of the sun. **NASA Ames/SETI Institute/JPL-Caltech**

Although the size of Kepler-186f is known, its mass and composition are not. Previous research, however, suggests that a planet the size of Kepler-186f is likely to be rocky.

"We know of just one planet where life exists — Earth. When we search for life outside our solar system we focus on finding planets with characteristics that mimic that of Earth," said Elisa Quintana, research scientist at the SETI Institute at NASA's Ames Research Center in Moffett Field, California, and lead author of the paper published today in the journal Science. "Finding a habitable zone planet comparable to Earth in size is a major step forward."

Kepler-186f resides in the Kepler-186 system, about 500 light-years from Earth in the constellation Cygnus. The system is also home to four companion planets, which orbit a star half the size and mass of our sun. The star is classified as an M dwarf, or red dwarf, a class of stars that makes up 70 percent of the stars in the Milky Way galaxy. "M dwarfs are the most numerous stars," said Quintana. "The first signs of other life in the galaxy may well come from planets orbiting an M dwarf."

Kepler-186f orbits its star once every 130-days and receives one-third the energy from its star that Earth gets from the sun, placing it nearer the outer edge of the habitable zone. On the surface of Kepler-186f, the brightness of its star at high noon is only as bright as our sun appears to us about an hour before sunset.

"Being in the habitable zone does not mean we know this planet is habitable. The temperature on the planet is strongly dependent on what kind of atmosphere the planet has," said Thomas Barclay, research scientist at the Bay Area Environmental Research Institute at Ames, and co-author of the paper. "Kepler-186f can be thought of as an Earth-cousin rather than an Earth-twin. It has many properties that resemble Earth."

The four companion planets, Kepler-186b, Kepler-186c, Kepler-186d, and Kepler-186e, whiz around their sun every four, seven, 13, and 22 days, respectively, making them too hot for life as we know it. These four inner planets all measure less than 1.5 times the size of Earth.

The next steps in the search for distant life include looking for true Earth-twins — Earth-size planets orbiting within the habitable zone of a sun-like star — and measuring the their chemical compositions. The Kepler Space Telescope, which simultaneously and continuously measured the brightness of more than 150,000 stars, is NASA's first mission capable of detecting Earth-size planets around stars like our sun.

Ames is responsible for Kepler's ground system development, mission operations, and science data analysis. NASA's Jet Propulsion Laboratory in Pasadena, California, managed Kepler mission development. Ball Aerospace & Technologies Corp. in Boulder, Colorado, developed the Kepler flight system and supports mission operations with the Laboratory for Atmospheric and Space Physics at the University of Colorado in Boulder.

The Space Telescope Science Institute in Baltimore archives, hosts and distributes Kepler science data. Kepler is NASA's 10th Discovery Mission and was funded by the agency's Science Mission Directorate.

The SETI Institute is a private, nonprofit organization dedicated to scientific research, education and public outreach. The mission of the SETI Institute is to explore, understand and explain the origin, nature and prevalence of life in the universe.

Publication: Elisa V. Quintana, et al., "An Earth-Sized Planet in the Habitable Zone of a Cool Star," Science 18 April 2014: Vol. 344 no. 6181 pp. 277-280; DOI: 10.1126/science.1249403

PDF Copy of Related Study: Formation, tidal evolution and habitability of the Kepler-186 system

http://www.eurekalert.org/pub_releases/2014-04/aafc-cim041514.php#rssowlmlink

Chronic inflammation may be linked to aggressive prostate cancer

Chronic inflammation in benign prostate tissue was associated with high-grade, or aggressive, prostate cancer

PHILADELPHIA — The presence of chronic inflammation in benign prostate tissue was associated with high-grade, or aggressive, prostate cancer, and this association was found even in those with low prostate-specific antigen (PSA) levels, according to a study published in Cancer Epidemiology, Biomarkers & Prevention, a journal of the American Association for Cancer Research.

An analysis of prostate tissue biopsies collected from some participants of the placebo arm of the Prostate Cancer Prevention Trial (PCPT) found that those whose benign prostate tissue had chronic inflammation had 1.78 times higher odds of having prostate cancer, and 2.24 times higher odds of having an aggressive disease (characterized by Gleason sum of seven to 10), compared with those whose benign prostate tissue had no inflammation.

"We had the unique opportunity to investigate biopsy tissue from patients who had no indication to prompt a biopsy," said Elizabeth A. Platz, Sc.D., MPH, professor in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Md. "Participants in the PCPT who were not diagnosed with prostate cancer during the trial were recommended to undergo prostate biopsy at the end of that trial, which meant that prostate tissue was available not just for men who had the diagnosis of prostate cancer, but also for those who did not have the diagnosis.

"We found that men who had at least one biopsy core with inflammation had a higher likelihood of having high-grade prostate cancer compared with those who did not have any inflammation in their biopsy tissue," said Platz. "While we know that inflammation is common in prostate tissue from men who have some indication to prompt a biopsy, such as high PSA or an abnormal digital rectal examination [DRE], we were surprised to find that the prevalence of chronic inflammation in the men who didn't have any such indication was really high, about 78 percent."

Between 1993 and 1997, 18,882 men who were at least 55 years old and had a normal DRE with a serum PSA of 3 ng/ml or less, were recruited to the PCPT. All participants completed questionnaires that included demographics, lifestyle, and medical factors, and were followed for seven years after they were randomly assigned to receive either finasteride or placebo.

The investigators screened all participants for prostate cancer by PSA and DRE during annual visits. Those who had an indication underwent a "for-cause" biopsy if they had cancer, and those who did not have prostate cancer diagnosed during the trial were recommended to undergo an "end-of-study" biopsy at the end of the trial even if they did not have an indication.

From the placebo arm of this study, Platz and colleagues sampled 191 prostate cancer cases and 209 frequency-matched controls for whom biopsy tissue was available. They performed histopathological evaluation of the biopsy samples to identify the prevalence and extent of inflammation, and types of inflammation, i.e., acute or chronic inflammation.

They found that 86.2 percent of cases and 78.2 percent of controls had at least one biopsy core with inflammation, most of which was chronic, and this difference was statistically significant. They also found that the association between chronic inflammation and aggressive prostate cancer did not change after adjusting for known risk factors including body-mass index, pack-years of cigarettes smoked, and history of diabetes.

In addition, this association held true even among men whose PSA levels were less than 2 ng/mL. "We detected chronic inflammation in prostate tissue of men who had prostate cancer but had PSA levels lower than 2 ng/ml, and thus our work supports an association between inflammation and prostate cancer that is not explained by PSA-associated detection bias," said Platz.

Among men whose PSA levels were less than 2 ng/ml at the time of biopsy, those whose prostate tissue had inflammation had 4.11 times higher odds of having aggressive prostate cancer, compared with those whose prostate tissue did not have any inflammation.

"Our team is next studying the type of inflammatory cells that may be influencing the risk of aggressive prostate cancer," said Platz. "This study is a stellar example of multidisciplinary research involving epidemiologists, pathologists, immunologists, urologists, and biostatisticians," Platz added.

Angelo De Marzo, M.D., Ph.D., professor in the Department of Pathology at the Johns Hopkins Hospital, is a co-leader of this study.

This study and the PCPT, which was conducted by Southwest Oncology Group, were funded by the National Cancer Institute. Platz and De Marzo declare no conflicts of interest.

http://phys.org/news/2014-04-strategy.html#rssowlmlink

Innovative strategy to facilitate organ repair

A significant breakthrough could revolutionize surgical practice and regenerative medicine.

A team led by Ludwik Leibler from the Laboratoire Matière Molle et Chimie (CNRS/ESPCI Paris Tech) and Didier Letourneur from the Laboratoire Recherche Vasculaire Translationnelle (INSERM/Universités Paris Diderot and Paris 13), has just demonstrated that the principle of adhesion by aqueous solutions of nanoparticles can be used in vivo to repair soft-tissue organs and tissues. This easy-to-use gluing method has been tested on rats. When applied to skin, it closes deep wounds in a few seconds and provides aesthetic, high quality healing.

It has also been shown to successfully repair organs that are difficult to suture, such as the liver. Finally, this solution has made it possible to attach a medical device to a beating heart, demonstrating the method's potential for delivering drugs and strengthening tissues. This work has just been published on the website of the journal Angewandte Chemie.

In an issue of Nature published in December last year, a team led by Ludwik Leibler presented a novel concept for gluing gels and biological tissues using nanoparticles. The principle is simple: nanoparticles contained in a solution spread out on surfaces to be glued bind to the gel's (or tissue's) molecular network. This phenomenon is called adsorption. At the same time the gel (or tissue) binds the particles together. Accordingly, myriad connections form between the two surfaces. This adhesion process, which involves no chemical reaction, only takes a few seconds. In their latest, newly published study, the researchers used experiments performed on rats to show that this method, applied in vivo, has the potential to revolutionize clinical practice.

In a first experiment, the researchers compared two methods for skin closure in a deep wound: traditional sutures, and the application of the aqueous nanoparticle solution with a brush. The latter is easy to use and closes skin rapidly until it heals completely, without inflammation or necrosis. The resulting scar is almost invisible.

In a second experiment, still on rats, the researchers applied this solution to soft-tissue organs such as the liver, lungs or spleen that are difficult to suture because they tear when the needle passes through them. At present, no glue is sufficiently strong as well as harmless for the organism. Confronted with a deep gash in the liver with severe bleeding, the researchers closed the wound by spreading the aqueous nanoparticle solution and pressing the two edges of the wound together. The bleeding stopped. To repair a sectioned liver lobe, the researchers also used nanoparticles: they glued a film coated with nanoparticles onto the wound, and stopped the bleeding. In both situations, organ function was unaffected and the animals survived.

"Gluing a film to stop leakage" is only one example of the possibilities opened up by adhesion brought by nanoparticles. In an entirely different field, the researchers have succeeded in using nanoparticles to attach a biodegradable membrane used for cardiac cell therapy, and to achieve this despite the substantial mechanical constraints due to its beating. They thus showed that it would be possible to attach various medical devices to organs and tissues for therapeutic, repair or mechanical strengthening purposes.

This adhesion method is exceptional because of its potential spectrum of clinical applications. It is simple, easy to use and the nanoparticles employed (silica, iron oxides) can be metabolized by the organism. It can easily be integrated into ongoing research on healing and tissue regeneration and contribute to the development of regenerative medicine.

More information: "Organ Repair, Hemostasis, and In Vivo Bonding of Medical Devices by Aqueous Solutions of Nanoparticles."Anne Meddahi-Pellé, Aurélie Legrand, Alba Marcellan, Liliane Louedec, Didier Letourneur, Ludwik Leibler. Angewandte Chemie. Published online April 16, 2014. DOI: 10.1002/anie.201401043

http://phys.org/news/2014-04-methylation-neanderthals-denisovans-modern-humans.html#rssowlmlink

Researchers create methylation maps of Neanderthals and Denisovans, compare them to modern humans

A team of Israeli, Spanish and German researchers has for the first time created a map of gene expression in Neanderthals and Denisovans and has compared them with modern humans.

Phys.org - In their paper published in the journal Science, the team describes how they applied epigentics to the study of our two closest known ancestors and discovered variations that might account for their differences in body shape and susceptibility to some modern neurological diseases.

Scientists know that it's not just our DNA structure that determines how we look and what we're capable of doing, there's another factor involved—the expression of our genes—they can be turned on or off at some point, allowing or preventing certain traits from developing. This process is known as DNA methylation—where methyl group chemicals attach to DNA and prevent them from behaving as they would otherwise. In this new

effort, the researchers looked at methylation in Neanderthals and Denisovans to learn more about how they might have been different from us.
Studying methylation in preserved fossils involves noting the way the methyl chemical cytosine decays over long periods of time. Unmethylated cytosines decay to one type of chemical while unmethylated cyctones decay to another. By measuring the amounts of the two resultant chemicals found in fossilized bone fragments, the researchers were able to create methylation maps of Neanderthals and Denisovans, which they then compared with similar maps for modern humans.
The comparisons revealed differences in approximately 2000 different regions, though one in particular stood out—an HoxD cluster that prior research has shown plays an important role in the development of body structure—a finding that could help explain the shorter, stouter limbs (and other features) of our extinct cousins. Interestingly, the team also found that some of the highly methylated regional areas that appear in modern humans do not appear in either Neanderthals or Denisovans, regions that have been associated with neurological disorders such as schizophrenia and autism—a finding that may help shed some light on their source.
Unfortunately, the maps created by the research team are still incomplete, they only had a few bone fragments to work with—they're hoping future studies (and fossil finds) will reveal more. In the meantime, they plan to conduct similar work on other species, such as horses, to help reveal the types of methylation that occurred as they were domesticated.
More information: Reconstructing the DNA Methylation Maps of the Neandertal and the Denisovan, Science, DOI: 10.1126/science.1250368

ABSTRACT
Ancient DNA sequencing has recently provided high-coverage archaic human genomes. However, the evolution of epigenetic regulation along the human lineage remains largely unexplored. We reconstructed the full DNA methylation maps of the Neandertal and the Denisovan by harnessing the natural degradation processes of methylated and unmethylated cytosines. Comparing these ancient methylation maps to those of present-day humans, we identified ~2000 differentially methylated regions (DMRs). Particularly, we found substantial methylation changes in the HOXD cluster that may explain anatomical differences between archaic and present-day humans. Additionally, we found that DMRs are significantly more likely to be associated with diseases. This study provides insight into the epigenetic landscape of our closest evolutionary relatives and opens a window to explore the epigenomes of extinct species.

http://www.eurekalert.org/pub_releases/2014-04/hu-ftn041814.php#rssowlmlink

Finding turns neuroanatomy on its head

Harvard researchers present new view of myelin

Harvard neuroscientists have made a discovery that turns 160 years of neuroanatomy on its head.
Myelin, the electrical insulating material long known to be essential for the fast transmission of impulses along the axons of nerve cells, is not as ubiquitous as thought, according to a new work lead by Professor Paola Arlotta of the Harvard Stem Cell Institute (HSCI) and the University's Department of Stem Cell and Regenerative Biology, in collaboration with Professor Jeff Lichtman, of Harvard's Department of Molecular and Cellular Biology.
"Myelin is a relatively recent invention during evolution," says Arlotta. "It's thought that myelin allowed the brain to communicate really fast to the far reaches of the body, and that it has endowed the brain with the capacity to compute higher level functions." In fact, loss of myelin is a feature of a number of devastating diseases, including multiple sclerosis and schizophrenia. But the new research shows that despite myelin essential roles in the brain, "some of the most evolved, most complex neurons of the nervous system have less myelin than older, more ancestral ones" Arlotta, co-director of the HSCI neuroscience program, says.
What this means, Arlotta says, is that the higher in the cerebral cortex one looks – the closer to the top of the brain, which is its most evolved region - the less myelin one finds. Not only that, but "neurons in this part of the brain display a brand new way of positioning myelin along their axons that has not been previously seen. They have 'intermittent myelin' with long axon tracts that lack myelin interspersed among myelin-rich segments.
Arlotta continues: "contrary to the common assumptions that neurons use a universal profile of myelin distribution on their axons, the work indicate that different neurons choose to myelinate their axons differently. In classic neurobiology textbooks myelin is represented on axons as a sequence of myelinated segments separated by very short nodes that lack myelin. This distribution of myelin was tacitly assumed to be always the same, on every neuron, from the beginning to the end of the axon. This new work finds this not to be the case."
The results of the research by Arlotta and post doctoral fellow Giulio Srubek Tomassy, the first author on the report, are published in the latest edition of Science, the journal of the American Association for the Advancement of Science.

The paper is accompanied by a "Perspective" by R. Douglas Fields, of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, at the National Institutes of Health, who says that Arlotta and Tomassy's findings raise important questions about the purpose of myelin, "are likely to spark new concepts about how information is transmitted and integrated in the brain."
Arlotta and Tomassy collaborated closely on the new work with postdoctoral fellow Daniel Berger of the Lichtman group, which generated one of the two massive electron microscopy data bases that made the work possible.
"The fact that it is the most evolved neurons, the ones that have expanded dramatically in humans, suggests that what we're seeing might be the "future". As neuronal diversity increases and the brain needs to process more and more complex information, neurons change the way they use myelin to "achieve" more", says Arlotta.
It is possible, said Tomassy, that these profiles of myelination "may be giving neurons an opportunity to branch out and 'talk' to neighboring neurons". For example, because axons cannot make synaptic contacts when they are myelinated, a possibility is that these long myelin gaps may be needed to increase neuronal communication and synchronize responses across different neurons. Perhaps, he and Arlotta postulate, the intermittent myelin is intended to fine-tune the electrical impulses traveling along the axons, in order to allow the emergence of highly complex neuronal behaviors.

http://www.medscape.com/viewarticle/823878?src=rss

Effective Treatment for Fibromyalgia May Now Be Possible

Fibromyalgia much better understood now and effective treatment is now possible

Laurie Barclay, MD

Fibromyalgia and other "centralized" pain states are much better understood now than previously, and effective treatment is now possible, according to a clinical review published in the April 16 issue of *JAMA*. A conference on October 4, 2012, at the Medicine Grand Rounds, Beth Israel Deaconess Medical Center, Boston, Massachusetts, aimed to review fibromyalgia epidemiology, pathophysiology, diagnosis, and treatment.
"Fibromyalgia is present in as much as 2% to 8% of the population, is characterized by widespread pain, and is often accompanied by fatigue, memory problems, and sleep disturbances," writes Daniel J. Clauw, MD, from the University of Michigan, Ann Arbor.
The evidence base for this review was meta-analyses, contemporary evidence-based treatment guidelines, and other pertinent medical literature on fibromyalgia from 1955 to March 2014, retrieved via MEDLINE and the Cochrane Central Registry of Controlled Trials. Dr. Clauw based his treatment recommendations on the most recent guidelines from the Canadian Pain Society and graded them from 1 to 5 on the basis of the quality of underlying evidence.
Original diagnostic criteria for fibromyalgia published in 1990 required chronic widespread pain with a number of tender points, whereas newer criteria are entirely symptom-based and do not require counts of the number of tender points. A patient-completed symptom survey addresses pain locations and the presence and severity of fatigue, sleep disturbances, memory difficulties, headaches, irritable bowel, and mood problems.
Fibromyalgia can be diagnosed and treated in the primary care setting, with specialty referral needed only if the diagnosis is uncertain, if patients do not respond to treatment, or if there are significant comorbid psychiatric issues.

Pharmacological and Other Treatments Now Available

Among the many therapies currently available for managing fibromyalgia and supported by high levels of evidence are nonpharmacological modalities including education, exercise, and cognitive behavioral therapy, and pharmacologic agents such as tricyclics, serotonin norepinephrine reuptake inhibitors, and gabapentinoids.
The optimal approach to treatment is to integrate pharmacologic and nonpharmacologic therapy while involving patients as active participants. All patients should be educated about the nonprogressive nature of their condition and about the importance of playing an active role in their own care through stress reduction, sleep, and exercise.
Pharmacotherapy should be guided by symptoms accompanying pain. All patients should receive a sufficient therapeutic trial of a low-dose tricyclic drug such as cyclobenzaprine, amitriptyline, or nortriptyline. A serotonin norepinephrine reuptake inhibitor may be needed in patients with comorbid depression or fatigue, whereas comorbid anxiety or sleep issues may respond to a gabapentinoid.
Successful treatment may require concomitant use of several drug classes. Nonsteroidal anti-inflammatory drugs and acetaminophen may be useful to treat comorbid "peripheral pain generators," but opioids should be avoided.
"Fibromyalgia and other 'centralized' pain states are much better understood now than ever before," Dr. Clauw writes. "Fibromyalgia may be considered as a discrete diagnosis or as a constellation of symptoms

characterized by central nervous system pain amplification with concomitant fatigue, memory problems, and sleep and mood disturbances. Effective treatment for fibromyalgia is now possible."

Dr. Clauw has performed consulting and/or served on scientific advisory boards for Pfizer, Lilly, Forest Laboratories, Johnson & Johnson, Purdue Pharma, Nuvo, Cerephex, Tonix, Iroko, and Takeda. He has received grant support from Pfizer, Forest, Merck, Nuvo, and Cerephex.

JAMA. 2014;311:1547-1555. Full text

http://nyti.ms/QzcgHd

House Calls Are Making a Comeback

A relic from the medical past - the house call - is returning to favor as part of some hospitals' palliative care programs, which are sending teams of physicians, nurses, social workers, chaplains and other workers to patients' homes after they are discharged.

By MILT FREUDENHEIM APRIL 19, 2014

The goal is twofold: to provide better treatment and to cut costs.

Walter Park, 68, of San Francisco says house calls prevented an expensive return visit to the hospital, where he initially stayed for seven weeks after a heart attack in 2012.

After his discharge, palliative care specialists from the University of California, San Francisco, were among those who visited his home to monitor his physical and emotional health. He got help with tasks as varied as household chores and organizing the 20 pills he takes daily for his heart and other conditions.

Confusion continues to exist over what palliative care is and whom it is for. Broadly, it is meant to ease symptoms and pain, and focus on quality of life for severely ill patients, who can choose between continuing or halting traditional medical treatment.

Palliative care also occurs in hospitals, but an added emphasis on home care has been a selling point. A vast majority of patients would rather be at home than in a hospital anyway, said Dr. R. Sean Morrison, co-director of the new Patty and Jay Baker National Palliative Care Center at Mount Sinai Hospital in New York and director of the National Palliative Care Research Center.

Home care is generally cheaper than hospital care, and for more than a decade, government programs such as Medicare and Medicaid have worked to create incentives for hospitals to switch to less-expensive treatment. Recently, under the Affordable Care Act, Medicare has begun to penalize hospitals when, under certain conditions, patients are readmitted within 30 days after discharge.

Some insurers, including Medicare, pay for house calls by doctors and nurses specializing in advanced care. In cases where insurance does not cover this type of palliative care, hospitals are financing it themselves, sometimes with grants.

Dr. Steven Pantilat, an internal medicine physician who leads the palliative care program at the University of California, San Francisco, says his hospital subsidizes some home care because "there is sufficient improvement in quality and costs to make the investment a good idea all around."

A 2007 study by Dr. Richard Brumley and colleagues, found that palliative care patients who received in-home, interdisciplinary care were less likely to visit the emergency room or be admitted to the hospital than those receiving more-standard home care, resulting in lower costs. The study, financed by the Kaiser Permanente Garfield Memorial Fund, covered terminally ill patents.

In Boston, palliative care doctors at Massachusetts General Hospital and at Brigham and Women's Hospital make house calls. Nurse care managers, social workers and others also visit discharged patients in their homes or keep in touch by telephone as needed, said Dr. Timothy Ferris, who runs the Partners HealthCare accountable care organization.

Nurses from Partners HealthCare at Home, an affiliate with 900 employees, may also visit discharged patients. "The home care nurse is the eyes and ears and stethoscope in the patient's house," Dr. Ferris said.

Accountable care organizations, created under the Affordable Care Act, have the flexibility to pay for in-home palliative care services, he added, and his organization has done so.

Palliative care teams work with a patient's regular doctors and specialists "to provide an added layer of support for people living with serious illness," said Dr. Diane E. Meier, professor of geriatrics and palliative medicine at the Icahn School of Medicine at Mount Sinai Hospital and co-director of the Patty and Jay Baker National Palliative Care Center.

They can address issues that someone who focuses intensively on a particular disease or organ system often cannot, she said — things like expert help with pain management, depression, fatigue and support for "exhausted and overwhelmed family caregivers." They also offer practical help so patients can remain in their homes, she said.

While patients nearing the end of life can choose palliative care in a hospice setting rather than undergo expensive and risky treatment — many doctors say it is valuable for that very reason — it can also exist alongside efforts to treat and cure patients.

"There are a lot of people, including my mother, who don't fit the criteria for hospice," said Cameron Egan. In 2012, doctors told Ms. Egan's mother, Jacqueline Andersen of San Francisco, that clearing her four clogged heart arteries would be unacceptably risky. Her health seemed fragile but fairly stable, and doctors could not estimate how long she would live.

Ms. Andersen, a retired high school English teacher, was clear that she did not want to spend more time in the hospital, said another daughter, Adrian King, who said, "She wanted to go home." Ms. Egan moved in with her mother to care for her.

Dr. Pantilat helped oversee Ms. Andersen's case, conferring with Ms. Egan, Ms. King and two other daughters on her care. He visited Ms. Andersen at home, and she received home visits from a spiritual counselor, who discussed her life, her fears and her attitudes about the end of her life, Ms. Egan said.

Ms. Andersen had an array of medical problems but "she was really with it," Ms. King said. "There was no time that any of us thought she was diminished mentally." Ms. Andersen died in February 2013, at 82, seven months after leaving the hospital. The day before, Ms. King said, she and her mother had "one of our classic Scrabble games."

"She was in fine spirits when I left her, making sure I put the San Francisco 49ers flag in a vase in her window," Ms. King said.

Dr. Pantilat said: "Without palliative care, it is likely Jackie would have been readmitted to the hospital, and the chances are 50-50 or more that she would have ended up having an operation. I also think her pain would not have been as well controlled.

"You can imagine what the cost of open-heart surgery would have been," he said. "Tremendous. Avoiding even one hospitalization would have paid for all the palliative care she received."

Proponents of palliative care say it can prompt people with terminal illnesses to face the future realistically. The focus is on making them comfortable, rather than exposing them to painful and expensive treatments.

But palliative care also seeks to extend life, Dr. Meier of Mount Sinai says. Several studies have shown that it "may be associated with a significant prolongation of life for some patient populations," she noted in a 2011 article, adding that more research was needed to confirm whether these findings were applicable more generally.

Mr. Park, the heart attack survivor in San Francisco, said his plans had changed. In 2012, his palliative care team urged him to identify his short- and long-term goals. He said he wanted to attend the second Obama inauguration and return to his volunteer work at a nonprofit agency that helps older Americans. He was present at the January 2013 swearing-in, and later he resumed his volunteer work.

He is now looking forward to spending time with his two grandchildren, ages 8 and 11. "I used to plan only three years ahead," Mr. Park said. "Now I really want to see my grandkids grow up and graduate."