http://www.eurekalert.org/pub_releases/2014-06/wsu-wrc062514.php

WSU researchers chart an ancient baby boom

Southwest US experience holds a lesson in over-population

PULLMAN, Wash. - Washington State University researchers have sketched out one of the greatest baby booms in North American history, a centuries-long "growth blip" among southwestern Native Americans between 500 to 1300 A.D.

It was a time when the early features of civilization - including farming and food storage - had matured to where birth rates likely "exceeded the highest in the world today," the researchers write in the Proceedings of the National Academy of Sciences.

A crash followed, said Tim Kohler, WSU Regents professor of anthropology, offering a warning sign to the modern world about the dangers of overpopulation. "We can learn lessons from these people," said Kohler, who coauthored the paper with graduate student Kelsey Reese.

Funded by the National Science Foundation, the study looks at a century's worth of data on thousands of human remains found at hundreds of sites across the Four Corners region of the Southwest. While many of the remains have been repatriated, the data let Kohler assemble a detailed chronology of the region's Neolithic Demographic Transition, in which stone tools reflect an agricultural transition from cutting meat to pounding grain.

"It's the first step towards all the trappings of civilization that we currently see," said Kohler. Jean-Pierre Bocquet-Appel, a French expert on prehistoric populations and guest editor of the PNAS article, has called the transition "one of the fundamental processes of human history."

Maize, which we know as corn, was grown in the region as early as 2000 B.C. At first, populations were slow to respond, probably because of low productivity, said Kohler. But by 400 B.C., he said, the crop provided 80 percent of the region's calories. Crude birth rates - the number of newborns per 1,000 people per year - were by then on the rise, mounting steadily until about 500 A.D.

The growth varied across the region. People in the Sonoran Desert and Tonto Basin, in what is today Arizona, were more culturally advanced, with irrigation, ball courts, and eventually elevated platform mounds and compounds housing elite families.

Yet birth rates were higher among people to the north and east, in the San Juan basin and northern San Juan regions of northwest New Mexico and southwest Colorado.

Kohler said the Sonoran and Tonto people would have difficulty finding new farming opportunities for many children, since corn farming required irrigation. Water from canals may have also carried harmful protozoa, bacteria and viruses.

But groups to the northeast would have been able to expand maize production into new areas as their populations grew, he said.

Around 900 A.D., populations remained high but birth rates began to fluctuate. The mid-1100s saw one of the largest known droughts in the Southwest. The region likely hit its carrying capacity, with continued population growth and limited resources similar to what Thomas Malthus predicted for the industrial world in 1798.

From the mid-1000s to 1280 - by which time all the farmers had left - conflicts raged across the northern Southwest but birth rates remained high.

"They didn't slow down - birth rates were expanding right up to the depopulation," said Kohler. "Why not limit growth? Maybe groups needed to be big to protect their villages and fields."

"It was a trap," said Kohler. "A Malthusian trap but also a violence trap."

The northern Southwest had as many as 40,000 people in the mid-1200s, but within 30 years it was empty, leaving a mystery that has consumed several archaeological careers, including Kohler's. Perhaps the population got too large to feed itself as climates deteriorated, but as people began to leave, it would have been hard to maintain the social unity needed for defense and new infrastructure, said Kohler.

Whatever the reason, he said, the ancient Puebloans point up that, "population growth has its consequences."

http://www.eurekalert.org/pub_releases/2014-06/uoc--ihe063014.php

In human evolution, changes in skin's barrier set Northern Europeans apart

UCSF study questions role of skin pigment in enabling survival at higher latitudes

The popular idea that Northern Europeans developed light skin to absorb more UV light so they could make more vitamin D – vital for healthy bones and immune function – is questioned by UC San Francisco researchers in a new study published online in the journal Evolutionary Biology.

Ramping up the skin's capacity to capture UV light to make vitamin D is indeed important, according to a team led by Peter Elias, MD, a UCSF professor of dermatology. However, Elias and colleagues concluded in their study that changes in the skin's function as a barrier to the elements made a greater contribution than alterations in skin pigment in the ability of Northern Europeans to make vitamin D.

Elias' team concluded that genetic mutations compromising the skin's ability to serve as a barrier allowed fair-skinned Northern Europeans to populate latitudes

where too little ultraviolet B (UVB) light for vitamin D production penetrates the atmosphere.

Among scientists studying human evolution, it has been almost universally assumed that the need to make more vitamin D at Northern latitudes drove genetic mutations that reduce production of the pigment melanin, the main determinant of skin tone, according to Elias.

"At the higher latitudes of Great Britain, Scandinavia and the Baltic States, as well as Northern Germany and France, very little UVB light reaches the Earth, and it's the key wavelength required by the skin for vitamin D generation," Elias said.

"While is seems logical that the loss of the pigment melanin would serve as a compensatory mechanism, allowing for more irradiation of the skin surface and therefore more vitamin D production, this hypothesis is flawed for many reasons," he continued. "For example, recent studies show that dark-skinned humans make vitamin D after sun exposure as efficiently as lightly-pigmented humans, and osteoporosis – which can be a sign of vitamin D deficiency – is less common, rather than more common, in darkly-pigmented humans."

Furthermore, evidence for a south to north gradient in the prevalence of melanin mutations is weaker than for this alternative explanation explored by Elias and colleagues.

In earlier research, Elias began studying the role of skin as a barrier to water loss. He recently has focused on a specific skin-barrier protein called filaggrin, which is broken down into a molecule called urocanic acid – the most potent absorber of UVB light in the skin, according to Elias. "It's certainly more important than melanin in lightly-pigmented skin," he said.

In their new study, the researchers identified a strikingly higher prevalence of inborn mutations in the filaggrin gene among Northern European populations. Up to 10 percent of normal individuals carried mutations in the filaggrin gene in these northern nations, in contrast to much lower mutation rates in southern European, Asian and African populations.

Moreover, higher filaggrin mutation rates, which result in a loss of urocanic acid, correlated with higher vitamin D levels in the blood. Latitude-dependent variations in melanin genes are not similarly associated with vitamin D levels, according to Elias. This evidence suggests that changes in the skin barrier played a role in Northern European's evolutionary adaptation to Northern latitudes, the study concluded.

Yet, there was an evolutionary tradeoff for these barrier-weakening filaggrin mutations, Elias said. Mutation bearers have a tendency for very dry skin, and are vulnerable to atopic dermatitis, asthma and food allergies. But these diseases have appeared only recently, and did not become a problem until humans began to live in densely populated urban environments, Elias said.

The Elias lab has shown that pigmented skin provides a better skin barrier, which he says was critically important for protection against dehydration and infections among ancestral humans living in sub-Saharan Africa. But the need for pigment to provide this extra protection waned as modern human populations migrated northward over the past 60,000 years or so, Elias said, while the need to absorb UVB light became greater, particularly for those humans who migrated to the far North behind retreating glaciers less than 10,000 years ago.

The data from the new study do not explain why Northern Europeans lost melanin. If the need to make more vitamin D did not drive pigment loss, what did? Elias speculates that, "Once human populations migrated northward, away from the tropical onslaught of UVB, pigment was gradually lost in service of metabolic conservation. The body will not waste precious energy and proteins to make proteins that it no longer needs."

For the Evolutionary Biology study, labeled a "synthesis paper" by the journal, Elias and co-author Jacob P. Thyssen, MD, a professor at the University of Copenhagen, mapped the mutation data and measured the correlations with blood levels of vitamin D. Labs throughout the world identified the mutations. Daniel Bikle, MD, PhD, a UCSF professor of medicine, provided expertise on vitamin D metabolism.

The research was funded by the San Francisco Veterans Affairs Medical Center, the Department of Defense, the National Institutes of Health, and by a Lundbeck Foundation grant.

http://www.eurekalert.org/pub_releases/2014-06/afot-nta063014.php

New Tel Aviv University research links Alzheimer's to brain hyperactivity

Study identifies molecular mechanism that triggers hyperactivity of brain circuits in early stages of the disease

Patients with Alzheimer's disease run a high risk of seizures. While the amyloid-beta protein involved in the development and progression of Alzheimer's seems the most likely cause for this neuronal hyperactivity, how and why this elevated activity takes place hasn't yet been explained – until now.

A new study by Tel Aviv University researchers, published in Cell Reports, pinpoints the precise molecular mechanism that may trigger an enhancement of neuronal activity in Alzheimer's patients, which subsequently damages memory and learning functions. The research team, led by Dr. Inna Slutsky of TAU's Sackler Faculty of Medicine and Sagol School of Neuroscience, discovered that the amyloid precursor protein (APP), in addition to its well-known role in producing

amyloid-beta, also constitutes the receptor for amyloid-beta. According to the study, the binding of amyloid-beta to pairs of APP molecules triggers a signalling cascade, which causes elevated neuronal activity.

Elevated activity in the hippocampus - the area of the brain that controls learning and memory - has been observed in patients with mild cognitive impairment and early stages of Alzheimer's disease. Hyperactive hippocampal neurons, which precede amyloid plaque formation, have also been observed in mouse models with early onset Alzheimer's disease."These are truly exciting results," said Dr. Slutsky. "Our work suggests that APP molecules, like many other known cell surface receptors, may modulate the transfer of information between neurons."

With the understanding of this mechanism, the potential for restoring memory and protecting the brain is greatly increased.

Building on earlier research

The research project was launched five years ago, following the researchers' discovery of the physiological role played by amyloid-beta, previously known as an exclusively toxic molecule. The team found that amyloid-beta is essential for the normal day-to-day transfer of information through the nerve cell networks. If the level of amyloid-beta is even slightly increased, it causes neuronal hyperactivity and greatly impairs the effective transfer of information between neurons.

In the search for the underlying cause of neuronal hyperactivity, TAU doctoral student Hilla Fogel and postdoctoral fellow Samuel Frere found that while unaffected "normal" neurons became hyperactive following a rise in amyloid-beta concentration, neurons lacking APP did not respond to amyloid-beta. "This finding was the starting point of a long journey toward decoding the mechanism of APP-mediated hyperactivity," said Dr. Slutsky.

The researchers, collaborating with Prof. Joel Hirsch of TAU's Faculty of Life Sciences, Prof. Dominic Walsh of Harvard University, and Prof. Ehud Isacoff of University of California Berkeley, harnessed a combination of cutting-edge high-resolution optical imaging, biophysical methods and molecular biology to examine APP-dependent signalling in neural cultures, brain slices, and mouse models. Using highly sensitive biophysical techniques based on fluorescence resonance energy transfer (FRET) between fluorescent proteins in close proximity, they discovered that APP exists as a dimer at presynaptic contacts, and that the binding of amyloid-beta triggers a change in the APP-APP interactions, leading to an increase in calcium flux and higher glutamate release – in other words, brain hyperactivity.

A new approach to protecting the brain

"We have now identified the molecular players in hyperactivity," said Dr. Slutsky. "TAU postdoctoral fellow Oshik Segev is now working to identify the exact spot where the amyloid-beta binds to APP and how it modifies the structure of the APP molecule. If we can change the APP structure and engineer molecules that interfere with the binding of amyloid-beta to APP, then we can break up the process leading to hippocampal hyperactivity. This may help to restore memory and protect the brain."

Previous studies by Prof. Lennart Mucke's laboratory strongly suggest that a reduction in the expression level of "tau" (microtubule-associated protein), another key player in Alzheimer's pathogenesis, rescues synaptic deficits and decreases abnormal brain activity in animal models. "It will be crucial to understand the missing link between APP and 'tau'-mediated signalling pathways leading to hyperactivity of hippocampal circuits. If we can find a way to disrupt the positive signalling loop between amyloid-beta and neuronal activity, it may rescue cognitive decline and the conversion to Alzheimer's disease," said Dr. Slutsky.

The study was supported by European Research Council, Israel Science Foundation and Alzheimer's Association grants.

http://www.eurekalert.org/pub_releases/2014-06/uos-asc062914.php

A step closer to bio-printing transplantable tissues and organs: Study

Researchers have made a giant leap towards the goal of 'bio-printing' transplantable tissues and organs for people affected by major diseases and trauma injuries, a new study reports.

Scientists from the Universities of Sydney, Harvard, Stanford and MIT have bio-printed artificial vascular networks mimicking the body's circulatory system that are necessary for growing large complex tissues.

"Thousands of people die each year due to a lack of organs for transplantation," says study lead author and University of Sydney researcher, Dr Luiz Bertassoni. "Many more are subjected to the surgical removal of tissues and organs due to cancer, or they're involved in accidents with large fractures and injuries.

"Imagine being able to walk into a hospital and have a full organ printed – or bio-printed, as we call it – with all the cells, proteins and blood vessels in the right place, simply by pushing the 'print' button in your computer screen.

"We are still far away from that, but our research is addressing exactly that. Our finding is an important new step towards achieving these goals.

"At the moment, we are pretty much printing 'prototypes' that, as we improve, will eventually be used to change the way we treat patients worldwide."

The research challenge – networking cells with a blood supply.

Cells need ready access to nutrients, oxygen and an effective 'waste disposal' system to sustain life. This is why 'vascularisation' – a functional transportation system – is central to the engineering of biological tissues and organs.

"One of the greatest challenges to the engineering of large tissues and organs is growing a network of blood vessels and capillaries," says Dr Bertassoni.
"Cells die without an adequate blood supply because blood supplies oxygen that's necessary for cells to grow and perform a range of functions in the body."
"To illustrate the scale and complexity of the bio-engineering challenge we face, consider that every cell in the body is just a hair's width from a supply of oxygenated blood. "Replicating the complexity of these networks has been a stumbling block preventing tissue engineering from becoming a real world clinical application." But this is what researchers have now achieved.

What the researchers achieved

Using a high-tech 'bio-printer', the researchers fabricated a multitude of interconnected tiny fibres to serve as the mold for the artificial blood vessels. They then covered the 3D printed structure with a cell-rich protein-based material, which was solidified by applying light to it. Lastly they removed the bio-printed fibres to leave behind a network of tiny channels coated with human endothelial cells, which self organised to form stable blood capillaries in less than aweek.
The study reveals that the bioprinted vascular networks promoted significantly better cell survival, differentiation and proliferation compared to cells that received no nutrient supply.

Significance of the breakthrough

According to Dr Bertassoni, a major benefit of the new bio-printing technique is the ability to fabricate large three-dimensional micro-vascular channels capable of supporting life on the fly, with enough precision to match individual patients' needs.
"While recreating little parts of tissues in the lab is something that we have already been able to do, the possibility of printing three-dimensional tissues with functional blood capillaries in the blink of an eye is a game changer," he says.
"Of course, simplified regenerative materials have long been available, but true regeneration of complex and functional organs is what doctors really want and patients really need, and this is the objective of our work.

http://www.eurekalert.org/pub_releases/2014-06/wfbm-chs063014.php

Common herbal supplement can cause dangerous interactions

St. John's wort can be dangerous when taken with many commonly prescribed drugs

Winston-Salem, N.C. - St. John's wort, the leading complementary and alternative treatment for depression in the United States, can be dangerous when taken with many commonly prescribed drugs, according to a study by researchers at Wake Forest Baptist Medical Center.
The researchers reported that the herbal supplement can reduce the concentration of numerous drugs in the body, including oral contraceptive, blood thinners, cancer chemotherapy and blood pressure medications, resulting in impaired effectiveness and treatment failure.
"Patients may have a false sense of safety with so-called 'natural' treatments like St. John's wort," said Sarah Taylor, M.D., assistant professor of dermatology at Wake Forest Baptist and lead author of the study. "And it is crucial for physicians to know the dangers of 'natural' treatments and to communicate the risks to patients effectively."
The study is published in the current online issue of The Journal of Alternative and Complementary Medicine.
To determine how often S. John's wort (SJW) was being prescribed or taken with other medications, the team conducted a retrospective analysis of nationally representative data collected by the National Ambulatory Medical Care Survey from 1993 to 2010. The research team found the use of SJW in potentially harmful combinations in 28 percent of the cases reviewed.
Possible drug interactions can include serotonin syndrome, a potentially fatal condition that causes high levels of the chemical serotonin to accumulate in your body, heart disease due to impaired efficacy of blood pressure medications or unplanned pregnancy due to contraceptive failure, Taylor said.
Limitations of the study are that only medications recorded by the physician were analyzed. However, she said the rate of SJW interactions may actually be underestimated because the database did not include patients who were using SJW but did not tell their doctor.
"Labeling requirements for helpful supplements such as St. John's wort need to provide appropriate cautions and risk information," Taylor said, adding that France has banned the use of St. John's wort products and several other countries, including Japan, the United Kingdom, and Canada, are in the process of including drug-herb interaction warnings on St. John's wort products.
"Doctors also need to be trained to always ask if the patient is taking any supplements, vitamins, minerals or herbs, especially before prescribing any of the common drugs that might interact with St. John's wort."
Co-authors are Steven Feldman, M.D., and Scott Davis, M.A., of Wake Forest Baptist.
Funding was provided by the Center for Dermatology Research at Wake Forest Baptist.

http://www.eurekalert.org/pub_releases/2014-06/foas-itn063014.php

Is the next 'new' cancer drug already in your medicine cabinet?

Antihistamines may play a role in reducing the growth of tumors

New research published in the Journal of Leukocyte Biology suggests that antihistamines may play a role in reducing the growth of tumors by interfering with the activity of myeloid derived suppressor cells

It turns out that the same types of drugs that help reduce watery eyes and runny noses during allergy season might also help ward off tumors too. A new research report appearing in the July 2014 issue of The Journal of Leukocyte Biology suggests that antihistamines may have significant anti-cancer properties as they interfere with the function of a type of cell that is known to reduce the body's ability to fight tumors (called "myeloid derived suppressor cells").

"This research is very exciting as it draws a connection between two diseases that aren't commonly linked: allergy and cancer," said Daniel H. Conrad, Ph.D., a researcher involved in the work from the Department of Microbiology and Immunology at Virginia Commonwealth University in Richmond, Virginia. "It's important to realize, however, that this connection is very novel and more research is needed before we know if antihistamines can be used effectively in cancer therapies."

To make this discovery, Conrad and colleagues examined two groups of mice that involve myeloid derived suppressor cells. The first group of mice was infected with a rodent intestinal helminth to simulate a strong allergic response. Then they were injected with myeloid derived suppressor cells and treated with anti-histamines, cetirizine or cimetidine. Treatment with these anti-histamines reversed the effects of myeloid derived suppressor cells. The second group of mice had tumors and were injected with myeloid derived suppressor cells and treated with the antihistamine, cimetidine. In this group, the antihistamine also reversed the enhanced tumor growth normally seen with myeloid derived suppressor cell injection. Finally, the scientists examined blood from patients with allergy symptoms (typically associated with increased histamine release). The scientists found that these patients had increased circulating myeloid derived suppressor cells over non-allergic controls.

"Antihistamines may be one of the most commonly used over-the-counter drugs, but this report shows that we still have much to learn about their potential benefits," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology. "It is certainly not yet time to prophylactically administer antihistamines for cancer prevention, but the more we learn about myeloid derived suppressor cells, the more interesting these cells and their products become as immunotherapy targets in cancer. These new results suggest that we must be open-minded about seemingly distantly related immune mechanisms to examine."

Details: Rebecca K. Martin, Sheinei J. Saleem, Lauren Folgosa, Hannah B. Zellner, Sheela R. Damle, Giang-Kim T. Nguyen, John J. Ryan, Harry D. Bear, Anne-Marie Irani, and Daniel H. Conrad. Mast cell histamine promotes the immunoregulatory activity of myeloid-derived suppressor cells. J. Leukoc. Biol. July 2014 96:151-159; doi:10.1189/jlb.5A1213-644R ; http://www.jleukbio.org/content/96/1/151.abstract

http://phys.org/news/2014-06-urban-legends-viral.html

This is why some urban legends go viral

Urban legends get around, but we don't really understand why.

We conducted a study to explain how misinformation spreads surprisingly fast and why people feel compelled to share it.

There are many urban legends and often they can fill us with horror. You may well have heard the story about the two people who have cybersex only to realise months later, when they meet, that they are father and daughter.

Or what about the girl who keeps her heavily hair-sprayed beehive so high, never washing or taking it down, until one day she suddenly drops dead only for doctors to find that a poisonous spider had nested in her hair before biting and killing her?

Then there's the story about the woman who hears a baby crying outside her house in the middle of the night. She calls the police, only to be warned not to open her door because a serial killer is luring women this way.

These examples are a form of contemporary folklore, which are told as true and set in post-industrial settings. They are passed on by word of mouth, through text messages, chain emails and Facebook posts, and in that process they evolve and thrive.

Some of them have even inspired horror films. Take the classic slasher Candyman, based on the widespread urban legend "Bloody Mary", which says that calling out their name five times in the mirror makes the ghost-like figure appear.

There have been others, such as the less successful Urban Legends film series. A number of websites, most notably snopes.com, are dedicated to their collection and analysis.

While many of us regard urban legends as just a bit of harmless fun, they can sometimes have negative consequences on individuals and communities, spreading fear and mistrust. For instance, a Chinese restaurant in Doncaster, recently faced bankruptcy after a local urban legend spread that a customer had choked on a microchip from a retired racing greyhound cooked up in a dish.

But what is it about urban legends that make them so culturally successful? In a paper recently published in the British Journal of Psychology, based on work I conducted at Durham University with Jamie Tehrani and Emma Flynn, we examined the idea that the success of urban legends can be explained by the way our brains evolved to learn, remember and transmit certain types of (mis)information more readily than others. Their success could be explained by two key biases in our cognition.

Our minds fall for simple biases

The first suggests that we evolved to notice and remember information about our environment that is important for our survival. The second suggests that we evolved

greater intelligence in order to keep track of social interactions and relationships. These hypotheses suggest that we are evolved to be disposed to social and survival information, leaving us susceptible to notice, remember and pass on stories that contain this information, even if it does not reflect reality.

To examine how these cognitive biases might influence how urban legends are passed on from one person to another, our study used a design in the vein of "Chinese Whispers", the children's game in which information is passed from one child to another by whispering in their ears only once. By the time the information has reached the end child, it has invariably changed.

We gave participants urban legends that contained social information, survival information or a combination of both, who read and then wrote down these stories from memory. The product of their recall was given to the next participant and this process was repeated down the chain.

Another set of participants were presented with a number of "headlines" based on urban legends and asked which stories they would prefer to read. After reading each story they were asked which stories they would be more likely to pass on to another person.

People matter more than the environment

The study showed two things. First, people were attracted to stories that contained survival threats and social relationships. They were also likely to pass them both on to another person. Second, and this is more important, urban legends which contained social information, such as that in the cybersex legend, or combined survival information with social information, such as that in the baby-crying legend, were more successfully remembered than those that only involved survival information, such as that in the spider-in-the-hair legend.

This supports the theory that human intelligence and memory primarily evolved to deal with the challenges of living in large social groups with complex relationships, rather than dealing with the challenges posed by our environment, which is a commonly held view. They also help explain why urban legends can be found that involve both social interaction and survival threats.

We are attracted to both types of information and willing to pass both types of story on, but stories which contain social information live longer in our memory. It also helps to explain why so many stories – not just urban legends but also traditional folklore, novels, soap operas and internet memes – are about families, factions, friendships and fallings-out as well as death and disease.

http://nyti.ms/1oupqlb

After the Trees Disappear

Ash Forests After Emerald Ash Borers Destroy Them

By Maggie Koerth-Baker

This past winter was the coldest Detroit had experienced in 36 years. Across the upper Midwest, cities shivered, and more than 90 percent of the surface area of the Great Lakes froze solid. It seemed like ideal weather to kill an unwanted insect. But it did little to stop the emerald ash borer, an invasive Asian beetle that is devastating ash trees from Minnesota to New York.

“We didn’t find a single dead larva,” said Deborah G. McCullough, a professor of entomology and forestry at Michigan State, who led a study of ash trees in Lower Michigan over the winter.

Even before the severe winter, Dr. McCullough and other scientists had come to the glum conclusion that they were going to lose the decade-long battle against the ash borer. Now they are assessing the cascade of consequences for Midwestern and Northeastern forests, both urban and wild.

The effects will go far beyond what you see on a hike or how you feel about the loss of a tree on your property. They will ripple through forest ecosystems, affecting other plants, animals and water supplies.

An adult emerald ash borer. The larvae burrow into trees during the winter, cutting off access to nutrients and water. **Credit Minnesota Department of Natural Resources, via Associated Press**

Emerald ash borers do their damage as larvae, eating into the bark and burrowing deep into the trunk to insulate themselves against the cold. In the process, they cut off access to the nutrients and water that the tree needs to survive; it is like severing a human’s network of veins and arteries.

After surviving the unusually cold winter, the beetles emerged in spring as adults. Now they are mating and laying eggs, leaving the next generation of larvae to tunnel through the trees’ internal organs. They can kill an ash tree in as little as two years.

Back in 2002, when the borers were first discovered in North America - in Windsor, Ontario - experts thought it might be possible to eradicate them. But after about six months, researchers realized that the insects had been here for years, probably decades, and had already started spreading across the upper Midwest.

Despite a few moments of optimism since, hope has faded quickly.

"Ninety-nine percent of the ashes in North America are probably going to die," said Andrew M. Liebhold, a research entomologist with the United States Forest Service.

Nobody was really studying the ecology of ash forests until the borers began destroying them. But now scientists are beginning to see what that change might look like.

A 2009 study in the journal Biological Invasions listed 43 native insect species that rely on ash trees for food or breeding. Those insects are the food supply for birds, including woodpeckers.

"You end up with a different ecosystem that different species prefer and where the old ones can't do as well," said Kathleen Knight, a research ecologist with the Forest Service.

Invasive insects have been eradicated in the past, but the invasion must be detected early, while it is still localized.

In the summer of 1998, when the Asian long-horned beetle was found in Chicago, people were already on the lookout for the bug, which had previously turned up in New York. Easier to spot than the smaller and less flamboyant emerald ash borer, the long-horned beetle quickly became the focus of an eradication effort that combined insecticides, public awareness and the felling of hundreds of trees in infected neighborhoods.

In 2007, the beetle was officially declared eradicated in Chicago, but it has since been found attacking trees in Massachusetts.

To tackle the emerald ash borers, scientists have experimented with chemical traps that attract the insects and can help spot the leading edge of an invasion into new forests when they can still be stopped.

But the traps are not very sensitive, Dr. Liebhold said, and often reveal an invasion only years after the beetles have been established.

The emerald ash borers' effect may not be as dire as Dr. Liebhold predicts. Dr. McCullough, the entomologist at Michigan State, noted that the bugs' conquest varied by tree species and location. Of the four major species, black ash and green ash are probably lost, but the beetles kill only 60 percent to 70 percent of blue ash. White ash falls somewhere in between.

And while the eight billion ash trees in wild forests cannot really be protected, ash trees in the city may stand a chance because of the development of new insecticides.

Still, the losses are bound to have severe consequences. When ash trees die, they leave gaps in the leaf canopy that allow sunlight to reach parts of the forest floor that were previously shaded. Dr. Knight, of the Forest Service, has found that those gaps provide an opportunity for invasive honeysuckle bushes to grow unchecked.

"In the worst-case scenario, it becomes a dense, impenetrable thicket of shrubs in the understory," she said.

The thicket prevents native plants from growing and is likely to affect which kinds of animals can thrive there.

While the emerald ash borer is a particularly destructive bug, it's not the only invasive insect on the march.

Another is the hemlock woolly adelgid, also from Asia. Each the size of a poppy seed, adelgids make fluffy, white egg sacs in which they wrap themselves and which attach to the undersides of hemlock branches. Safely stuck to the tree, the adelgid inserts a feeding tube and proceeds to suck the sap out of the tree like a vampire.

As with the emerald ash borers, the adelgids' size and life cycle made them hard to notice until it was too late. While not as deadly or as fast as the ash borers, adelgids have worked their way north from Virginia over the last 50 years, and are capable of killing off more than 50 percent of the hemlocks in infected forests.

Though the percentage of dead trees is lower, the devastation can be just as wide, said David Orwig, a senior ecologist in the adelgid-infected Harvard Forest. That's because, unlike ash, hemlocks often grow in groves of nothing but hemlock. Even if not all are wiped out, the die-off changes the character of the forest - from dark, cool and moist to sunnier, warmer and drier.

These shifts are like a domino that leads to a series of ecological effects. A 2008 study published by Dr. Orwig in The Canadian Journal of Forestry Research showed that the change in the type and quantity of leaves building up on the forest floor as more hemlocks die caused soils to accumulate higher levels of nitrogen. That excess nitrogen can leach into nearby streams, Dr. Orwig said, where it can change what plants and animals grow there.

It's important to note that a different ecosystem is not the same as no ecosystem. When ash trees and hemlocks die, they are replaced by other kinds of trees. Over time, a new environmental system takes root. Few people living today remember when the Northeast was covered in forests of American chestnut. That species all but died out more than half a century ago from a series of fungal infections. Today, the forests and the life they harbor are very different; in many cases, hemlocks replaced the chestnuts. And now something else will replace the hemlocks.

But we will still have lost something valuable, Dr. Liebhold said.

"The forests and the species that exist there, they're part of America and what defines America," he said. "Without being too corny, they're a symbol of what this country is."

Correction: July 3, 2014

An article on Tuesday about the destruction of ash forests by emerald ash borers misstated the number of ash trees in wild forests in North America. It is eight billion, not million.

http://www.bbc.com/news/health-28087258

Miniature 'super-clotting balls help stop bleeding'

Scientists have developed miniature super-clotting balls which could help stop catastrophic bleeding after injury.

By Smitha Mundasad Health reporter, BBC News

In research published in the journal PNAS, the extremely small particles were injected into mice.

The "super-clotters" clumped cells together quickly, plugging up blood vessels and improving chances of survival after severe trauma.

Further research will determine whether they could one day help treat humans.

Uncontrolled bleeding after explosions is a leading cause of death on the battlefield. And major haemorrhage after road traffic accidents and other serious injuries contribute to more than two million deaths worldwide each year.

But few options exist to stop internal bleeding quickly in the field.

'Thinner than human hair'

The human body has natural clotting cells such as platelets which clog together to form plugs in injured vessels, stemming blood flow.

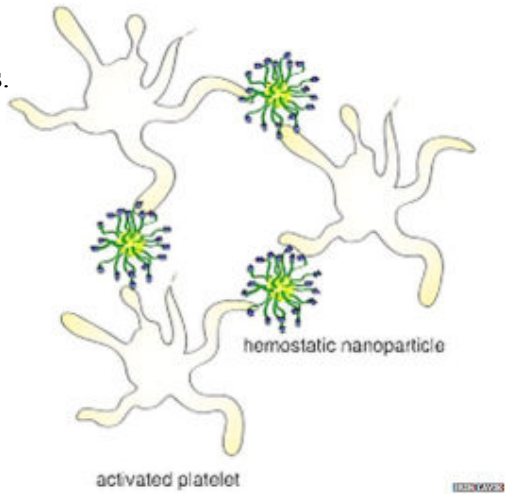
This system works well for cuts and scrapes but can be overwhelmed during massive trauma.

Researchers at Case Western Reserve University, Wayne State University and Virginia Tech in the US have synthesised the super-clotting balls - known as haemostatic nanoparticles.

The tiny spherical particles - some 200 times thinner than a human hair - have tentacle-like arms made of protein chains. These arms form links with natural clotting cells present in blood, clumping them together.

The body then continues with a cascade of processes, leading to a web-like mesh which stops blood flow.

In research published in the Proceedings of the National Academy of Sciences, the scientists found injecting these particles into the bloodstream of injured mice helped improve survival rates from 60% to 90%.



The extremely small particles have several protein arms which form bonds with blood cells

'Just add water'

Prof Erin Lavik of Case Western Reserve University and senior author of the study, told the BBC: "In the blast trauma model there is bleeding from many different organs so being able to administer something simply that can stop bleeding at many sites and improve survival is very exciting."

The super-clotting balls can last up to two weeks as a dry powder and can be made into a solution rapidly by just adding a salt or sugar water mixture. Currently most blood products used to treat major bleeding need to be refrigerated and have a shelf-life of a few days.

Mark Morrison of the Institute of Nanotechnology, who was not involved in the research, says: "The materials used to synthesise these particles are well-known and have been used for sometime so this should help avoid interactions with the human immune system. "However, there needs to be further work on how the particles affect the natural clotting cascade and other body processes. We need to know how long they last in the body too." The researchers plan to do further studies in larger animal models before considering human trials.

http://www.eurekalert.org/pub_releases/2014-07/aps-che070114.php

Chinese herbal extract may help kill off pancreatic cancer cells

University of Minnesota researchers find an extract of the thunder god vine effective in blocking a protein that helps pancreatic cancer cells survive

Bethesda, Md. - A diagnosis of pancreatic cancer - the fourth most common cause of cancer death in the U.S. - can be devastating. Due in part to aggressive cell replication and tumor growth, pancreatic cancer progresses quickly and has a low five-year survival rate (less than 5 percent).

GRP78, a protein that protects cells from dying, is more abundant in cancer cells and tissue than in normal organs and is thought to play a role in helping pancreatic cancer cells survive and thrive. Researchers at the University of Minnesota have found triptolide, an extract of the Chinese herb thunder god vine (Tirpterygium wilforii), suppresses GRP78, eventually leading to pancreatic cancer cell death.

For mammals to use the proteins in our bodies, a process called protein folding must occur in the endoplasmic reticulum (ER) of cells. If proteins are not folded fast enough, unfolded proteins begin to build up and the cell becomes stressed. Prolonged ER stress activates a cellular process called the "unfolded protein response (UPR)". Initially, the UPR helps kick-start the cell's protein-folding ability, allowing it to function properly again. But if the problem doesn't resolve, the UPR triggers cell death.

GRP78 helps cells survive long enough for the UPR to kick in and correct protein-folding problems. However, GRP78 is available in higher quantities in pancreatic

cancer cells, which assists the cancer cells in evading cell death, allowing them to live and multiply.

Triptolide has previously been shown to have a negative effect on pancreatic cancer cell viability and to block growth and spread of these cells. In this study led by Ashok Saluja, Ph.D., researchers observed the effects of triptolide on human pancreatic cancer cells and tissue. They found that the UPR worked properly in triptolide-treated cells to allow cell death in malfunctioning cells.

"Our study shows that although increased expression of GRP78 confers a survival advantage to the tumor cells, prolonged exposure to triptolide induces chronic ER stress, which eventually leads to cell death," the authors stated. "In this context, inhibition of GRP78 by activation of the ER stress pathway by triptolide offers a novel mechanism for inhibiting the growth and survival of pancreatic cancer cells."

The article "Triptolide activates unfolded protein response leading to chronic ER stress in pancreatic cancer cells" is published in the American Journal of Physiology - Gastrointestinal and Liver Physiology. It is highlighted as one of this month's "best of the best" as part of the American Physiological Society's APSselect program. View the full study here: ow.ly/yxpMq. Read all of this month's selected research articles at apsselect.physiology.org/.

http://www.eurekalert.org/pub_releases/2014-07/tl-tln063014.php

The Lancet: Nearly 80 percent of US deaths in the first 3 decades of life are due to unintentional injury or violence

Expansion of clinical and community injury prevention strategies shows promise

A new report on unintentional injury and violence in the United States, published in The Lancet as part of a new Series, The health of Americans [1], has found that prevention strategies across society show a great deal of promise in preventing unintended deaths and injuries.

According to the report, by CDC researchers from Atlanta, USA, more Americans between the ages of one and 30 die from injury than from any other cause. Every year, nearly 180 000 people in the USA die from preventable causes such as automobile crashes, drowning, firearm-related injuries, falls, assault, and drug overdoses; equivalent to one injury death every 3 minutes.

In 2010 alone, the top three causes of death for those aged between one and 30 were unintentional injury, suicide, and homicide. Almost four fifths of deaths among people in this age group were due to injuries, with only one fifth due to chronic diseases and only 1% due to infectious diseases. In 2010, among people of all ages, 121 000 died due to unintentional injuries, including automobile crashes, poisoning, and suffocation.

Rates of suicide and homicide are unequally distributed across groups, the report found. Suicides were twice as common as homicides (38 364 deaths in 2010 alone, versus 16 259). The highest rates of suicide are found in Native American and Alaskan Natives (16.9 per 100 000) and non-Hispanic whites (14.9). Homicide rates for African Americans (18.6) were double those of the nearest group (Native Americans and Alaskan Natives) and several times higher than other groups. Large disparities between men and women were also observed in the rates of suicide (19.8 vs 5.0) and homicide (8.3 vs 2.2).

Opioid painkillers such as oxycodone and hydrocodone are also a large source of injury deaths. The number of deaths from these painkillers has nearly quadrupled since 1990, with 38 329 people dying from drug overdoses in 2010 alone.

In 2010, the 31.2 million unintentional and violence-related nonfatal injuries had an estimated cost of over US$500 billion dollars in medical care and lost productivity. According to the report, that figure "does not include the costs associated with non-medically treated injuries, legal costs or indirect costs from other health problems associated with or exacerbated by violence and injuries."

According to lead author Dr. Tamara M. Haegerich, PhD, at the Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, there is a lot that can be done to prevent injuries and death. "Injuries and violence are not accidents and are not inevitable. They can be prevented. Yet, although figures in public health maintain a common understanding of the definition, causes, and solutions to injuries and violence, this recognition might not be widely accepted by other audiences, including policy makers, clinical health professionals, and the public."*

"The scientific evidence to support prevention of injury and violence is strong. We know the factors that place people at risk and it is possible to intervene with cost effective interventions. Child safety seats, seatbelt laws, and drink driving laws are good examples of interventions that have been proven effective at reducing the number of deaths due to injury, as well as reducing costs. Other interventions, such as in-home visitation by nurses and therapeutic foster care as an alternative to juvenile incarceration, and universal school-based violence prevention programs have proven effective, and expanding these programmes could reduce the numbers of injuries even further."*

http://www.scientificamerican.com/article/blind-mice-cured-by-running/

Blind Mice Cured by Running

Exercise combined with visual stimulation helps to quickly restore vision in unused eyes

By Simon Makin and Nature magazine

Running helps mice to recover from a type of blindness caused by sensory deprivation early in life, researchers report. The study, published on 26 June in eLife, also illuminates processes underlying the brain's ability to rewire itself in

response to experience - a phenomenon known as plasticity, which neuroscientists believe is the basis of learning.

More than 50 years ago, neurophysiologists David Hubel and Torsten Wiesel cracked the 'code' used to send information from the eyes to the brain. They also showed that the visual cortex develops properly only if it receives input from both eyes early in life. If one eye is deprived of sight during this 'critical period', the result is amblyopia, or 'lazy eye', a state of near blindness. This can happen to someone born with a droopy eyelid, cataract or other defect not corrected in time. If the eye is opened in adulthood, recovery can be slow and incomplete.

In 2010, neuroscientists Christopher Niell and Michael Stryker, both at the University of California, San Francisco (UCSF), showed that running more than doubled the response of mice's visual cortex neurons to visual stimulation (see 'Neuroscience: Through the eyes of a mouse'). Stryker says that it is probably more important, and taxing, to keep track of the environment when navigating it at speed, and that lower responsiveness at rest may have evolved to conserve energy in less-demanding situations. "It makes sense to put the visual system in a high-gain state when you're moving through the environment, because vision tells you about far away things, whereas touch only tells you about things that are close," he says.

Visual recovery

It is generally assumed that activity stimulates plasticity (see 'Neurodevelopment: Unlocking the brain'), so Stryker and his colleague Megumi Kaneko, also a neuroscientist at UCSF, wondered whether running might influence the plasticity of the visual cortex. They induced amblyopia in mice by suturing one eye shut for several months, during and after the critical period of visual development. They then re-opened the mice's eyes and divided them into two groups. Mice in one group were shown a 'noisy' visual pattern while running on a treadmill for four hours a day for three weeks. The pattern was chosen to activate nearly all the cells in the mice's primary visual cortex. The researchers recorded the mice's brain activity using intrinsic signal imaging, a method similar to functional magnetic resonance.

After a week these mice showed more responsiveness in the part of the cortex corresponding to the eye that had been closed. After two weeks, responses were comparable to those of normal mice that had never been visually deprived. The other group, housed in cages and without extra visual stimulation, had a much slower response to their newly reopened eye and never reached normal response levels.

Further experiments revealed that neither running nor visual stimulation alone had this effect. Recovery was also specific to the stimulus. Mice viewing the noise pattern did not show improved responses to a pattern of drifting bars, and vice versa, suggesting that only the visual circuits activated during running recover.

"What is amazing is the robustness of this phenomenon," says Massimo Scanziani, a neurobiologist at the University of California, San Diego. "It's powerful and highly reproducible, which is ideal for studying the mechanism."

Stryker and his colleagues do not yet know whether their findings apply to humans, but they plan further work to find out.

http://www.bbc.com/news/health-28090420

Frozen testicle 'live birth first'

A sample of frozen testicle has been used to produce live offspring in experiments on mice, Japanese researchers report.

By James Gallagher Health editor, BBC News website

The breakthrough could have important implications for boys with cancer who become infertile due to chemotherapy treatments.

Fertility experts said the data was "very encouraging" and they hoped human trials would not be too far away.

The findings have been published in the journal Nature Communications.

Sperm samples can be frozen before cancer treatment starts in order to allow men to have children at a later date should the drugs damage the testes.

But this is not an option for boys who have yet to go through puberty.

"With the increasing cure rate of paediatric cancers, infertility has become an important concern for patients and their families," the report's authors said.

Frozen

In the study, scientists froze a sample of testicle from mice five days after birth.

A range of assisted reproduction techniques - including artificial insemination and injecting partly developed sperm into an egg - were used. Baby mice were produced, which were able to mate and produce a further generation of healthy mice.

Prof Takehiko Ogawa, from Yokohama City University, told the BBC: "This is the first time in animals. "I predict it will take at least a couple of years before it is done in humans, it's not so easy. "We are now working on human samples, which are very different from mice tissue, I have to find some trick to make it work, so it's very difficult to predict how long that will take."

He said succeeding would be "really encouraging" for a child being treated and their family. He said he had seen the huge difference it made to the lives of older men who were able to freeze their sperm.

'Encouraging'

Dr Allan Pacey, a fertility researcher at the University of Sheffield, told the BBC: "Growing sperm in the laboratory for men who were sterilised as boys during

cancer treatment is arguably preferable to trying to work out a way to transplant their tissue back into their testicle when they are ready to become dads.

"This is because we want to avoid inadvertently giving them the cancer back if there are cancer cells lurking in the stored testicular tissue.

"However, we would need to check that lab-made sperm were genetically normal and that any babies born are going to be healthy and fertile themselves. "But based on this research in mice, the data looks encouraging and I hope that proper trials in humans will soon begin."

Another challenge that will need to be overcome is getting the frozen testicular tissue to produce sperm. Mice begin producing sperm very early on, while the delay is more than a decade in human males.

A way of cajoling the underdeveloped tissue to produce sperm will need to be developed, although it is thought exposure to testosterone should work.

http://nyti.ms/1qXMLg4

Noisy Predators Put Plants on Alert, Study Finds

Research suggests that some plants are sensitive to caterpillar sounds

By Douglas Quenqua

It has long been known that some plants can respond to sound. But why would a plant evolve the ability to hear? Now researchers are reporting that one reason may be to defend itself against predators.

To see whether predator noises would affect plants, two University of Missouri researchers exposed one set of plants to a recording of caterpillars eating leaves, and kept another set of plants in silence. Later, when caterpillars fed on the plants, the set that had been exposed to the eating noises produced more of a caterpillar-repelling chemical.

Evidently, the chomping noises primed the plant to produce the deterrent. “So when the attack finally happens, it’s kaboom,” said Heidi Appel, a chemical ecologist and an author of the study. The chemical comes “faster and often in greater amounts.”

Plants exposed to other vibrations, like the sound of wind or different insects, did not produce more of the chemical, suggesting they could tell the difference between predator noises and atmospheric ones. The researchers published their work in the journal Oecologia.

Previous research on plants and sounds have found that two genes in rice switch on in response to music and clear tones, and that corn roots will lean toward vibrations of a specific frequency. (Research from the 1970s suggesting that plants prefer classical to rock music has largely been dismissed.)

But plants “don’t normally experience music or pure tones in their environment,” said Reginald B. Cocroft, a behavioral ecologist and another author of the new study. “We wanted to ask, ‘Why would plants evolve this ability to hear sounds or vibrations?’”

Dr. Cocroft was surprised just how sensitive the plants were to the caterpillar sounds. “There were feeding vibrations that got a strong response from plants that vibrated the leaf up and down by less than one ten-thousandth of an inch,” he said.

Precisely how the plants detected the vibrations is not clear, but the researchers suspect it involves mechanoreceptors, proteins in animal and plant cells that respond to pressure or distortion. “Finding that out is our next step,” Dr. Appel said.

http://www.eurekalert.org/pub_releases/2014-07/du-am070114.php

A 'magic moment' for unwed parents

Marriage between unwed parents more likely when child is young, but bonds are fragile

DURHAM, N.C. -- If unwed parents are going to get married, the best window of opportunity for that union seems to be before their child turns 3, says a new study from Duke University. But patterns vary greatly by race, with more African-American mothers marrying much later than mothers of other races or ethnicities.

Federal policies have often presumed that unmarried parents will be most receptive to marriage right after a baby's birth, a period that has been dubbed the "magic moment." The new study is the first to test that assumption, said author Christina Gibson-Davis.

"It turns out the 'magic moment' lasts longer than conventional wisdom has held," said Gibson-Davis, who teaches sociology at Duke's Sanford School of Public Policy and is a faculty fellow of the Duke Center for Child and Family Policy. "And for some subgroups, that moment lasts even longer."

Among African-American mothers, most marriages occurred after the child turned 3, says the study, which appears online July 2 in Demography.

The study also found that most children born out of wedlock don't remain so: 64 percent of children born out of wedlock see their moms get married, Gibson-Davis said. Many of those marriages don't last, however. Nearly half of post-conception marriages end in divorce, and those numbers are higher still for African-American women.

"These marriages are fragile," Gibson-Davis said. "If you think that stable marriage is beneficial for kids, very few kids born out of wedlock are experiencing that."

The odds improve somewhat when mothers marry their child's biological father, Gibson-Davis said. After 10 years, 38 percent of post-conception marriages involving biological parents had dissolved. In the same period of time, 54 percent of marriages to a stepfather had ended. Those findings held true across racial lines.

The study draws upon a nationally representative survey that looks at 5,255 U.S. children born out of wedlock.

Despite years of public attention to children born out of wedlock, big gaps remain in our picture of how these children actually live, Gibson-Davis said.

"Those who would promote marriage have more work to do," Gibson-Davis said.

CITATION: "Magic Moment? Maternal Marriage in Children Born out of Wedlock," Christina Gibson-Davis. Demography, July 2, 2014. DOI: 10.1007/s13524-014-0308-7

http://news.discovery.com/human/health/how-can-ebola-be-stopped-140701.htm

How Can Ebola Be Stopped?

It sounds like the perfect script for a horror movie: A virus with no vaccine and no cure kills hundreds of people; despite containment efforts, it keeps spreading.

Jul 2, 2014 06:00 AM ET // by Sheila M. Eldred

But it's actually all too real in West Africa, where doctors have said Ebola is now "out of control."

While scientists dig for clues that could help develop medicine or better vaccine, the only prevention technique remains isolation. And despite health care workers who wear hazmat-like suits, use bleach as soap, and burn bedding instead of washing and re-using, the World Health Organization announced today that the virus has killed at least 467 people and spread throughout Guinea, Sierra Leone and Liberia, making this the most deadly and farthest-reaching outbreak of the disease since it first appeared in 1976.

While containment is possible in theory, breaks in protocol compromise the effort -- and are common in countries where both the disease and foreign medical workers are feared. In one Sierra Leone village, residents burned down the treatment center, convinced that the patients were being given medicine that caused the disease. And some patients escape hospitals to hide.

"Rumors are rife that if you eat three large onions, for example, you won't get Ebola -- but if you go to the hospital, you will get it," said Dan Epstein, a WHO spokesman in Switzerland.

One of the most revered local customs could account for much of the disease's spread, Ebola experts say: Local tradition calls for washing a corpse before it is buried, putting everyone who participates in the ritual in touch with bodily fluids that contain the virus.

What Is Ebola?

"The cultural practices are so deeply imbedded that local people have told health care workers that if they did not adhere to the ablutions (ritual washing of the corpse), they would be shunned by everyone in their family and village," said Dr. William Schaffner, an infectious disease specialist at Vanderbilt University Medical Center.

Government task forces have run radio and television ads to try to counter the myths, but mistrust of the government can render them ineffective, said Epstein.

In a perfect world, the virus could be contained through isolation and tracking, he said.

"You would have all the people who were infected immediately go to a health clinic and be put in an isolation ward, cared for by nurses and doctors in full personal protective equipment," Epstein said. "Also in a perfect world, you'd be able to go into the villages where there have been outbreaks without opposition and be able to tell people that their burial practices are dangerous to their community."

You'd also be able to trace every person that every infected person had recent contact with and monitor them for symptoms, important for a disease that can have a 21-day incubation period, he said -- much as the U.S. Centers for Disease Control and Prevention did last spring with a MERS case in Indiana. That's one reason experts don't think the disease will impact countries with certain health care protocols already in place, like the U.S.

The reality in West Africa, however, is nowhere near that best-case scenario. In fact, the area may be especially conducive to the disease's spread -- perhaps even more so than in Central Africa, where the disease had been found previously. West Africa's road system and higher population density make travel easier -- and containment harder, said Robert Garry, a microbiology professor at Tulane University School of Medicine who recently returned from West Africa, where he has been working on Lassa fever efforts for years. Garry believes that because not every case has been reported or tracked, we may be seeing just the tip of the iceberg.

"I don't think it's going to be over anytime soon. Each one of those infected [and not reported] people could infect 10 more -- or hundreds," he said.

International health organizations, including the WHO and Doctors Without Borders, have said they have reached their limits, and that more government intervention - "drastic action" - is needed. A meeting of health ministers from 11 countries to explore ways to prevent the virus from spreading will be held Wednesday and Thursday. "We need to look for nontraditional ways to get help," Garry said.

http://phys.org/news/2014-07-world-cocoa-crop-big-boost.html

World's cocoa crop could get a big boost from a simple, non-toxic spray

World's cocoa crop could get a big boost from a simple, non-toxic spray

Cocoa farmers this year will lose an estimated 30 to 40 percent of their crop to pests and disease, and with chocolate prices having risen globally by roughly two-thirds in the past decade, concern is growing about sustainability in cocoa production. Of particular concern are the environmental impact and human health

risks of toxic agrichemicals – organochloride insecticides and heavy-metal-based fungicides – used in cocoa production to fight pests and disease.

But scientists at Penn State's Huck Institutes of the Life Sciences have found – in a safe, biodegradable compound – a potential alternative to the hazardous antifungal agents currently being used to combat one of the most damaging cacao diseases, Phytophthora pod rot (also known as Black Pod), responsible for an estimated 20 to 30 percent loss in yield annually.

Mark Guiltinan and Yufan Zhang, with Siela Maximova and in collaboration with Phil Smith of the Metabolomics Core Facility, have discovered that spraying the leaves of the Theobroma cacao tree with a low-concentration glycerol solution triggers the plant's defense response and enhances its natural disease resistance.

"Right now," says Guiltinan, "cocoa farmers are using fungicides and other chemicals that are very effective but are also highly toxic compounds, very persistent in the soil, and relatively expensive. Glycerol, on the other hand, is extremely non-toxic; it's super safe, super cheap, biodegradable, and it triggers the plants' defenses very efficiently – it only takes small amounts to trigger the whole plant defense system.

"The plant immune system," he continues, "is made up of many different components that – imagine, if you can – are like little micromachines. It has five or ten major components that all have little safeties on them, and safeties on the safeties, and things that turn them on and off and regulate them. Some of these components are always running at some level and the system is a complicated thing on a hair trigger, always ready to go. You just give it a little trip and off it goes – all the little micromachines will be activated in a certain sequence and the whole thing takes off, so glycerol is one of the ways we've found to come in and trigger this to happen."

Glycerol, a simple sugar-alcohol compound called a polyol, is a colorless, odorless, viscous liquid commonly used in soaps and other cosmetic products and is produced in different ways, including as a byproduct of biofuel production where it is removed from plant or animal fats in a process known as transesterification.

"When you make biodiesel," Guiltinan says, "you end up with a massive amount of glycerol that nobody really has a good use for, and it's super cheap because of that."

Zhang adds that the production of glycerol from biofuels "is projected to increase ten-fold in the next ten years, as high as six times the projected demand, and people are already generating excessive amounts of glycerol that they don't know what to do with. There are journals focusing specifically on the use of glycerol and other biodiesel products, and research is being done on all different kinds of byproducts from the biodiesel industry to find out what how these compounds could be used."

Testing a hypothesis

"At the very beginning," says Zhang, "we weren't focusing on glycerol's effects on the cacao plant's defenses. We were more focused on its effects related to fatty acid biosynthesis – but digging deeper, we found that glycerol also has an effect triggering the plant's defense response."

The Guiltinan Lab studies two main aspects of the cacao tree: one has to do with the quality of the cocoa solids and fats being produced in the cacao seed, and the other is focused on disease resistance in the plant.

Zhang was working on a project to better understand what genes are implicated in the quality of fats in the cocoa bean, so it was "somewhat serendipitous," says Guiltinan, that he discovered a paper describing a potential intersection with disease resistance: in some model plant species, certain types of glycerol-related fatty acids triggered the plants' key defense mechanisms. Zhang decided to test this on the cacao tree.

"What we found," says Zhang, "is that a low (100 mM) concentration of glycerol sprayed on the cacao tree's leaves is sufficient to trigger its defense response. The concentration you use to spray the plants is really important because higher concentrations have a really bad effect, causing cell death and lesions on the leaf tips."

Normally plants wouldn't encounter glycerol being sprayed on them "It's an exogenous chemical that we're adding," Guiltinan explains, "but it's a pretty small molecule that can go through the cell wall and membranes and get into the cell body."

Zhang notes that all the leaf surfaces will absorb things – pesticides, micronutrients, other chemicals – and the plant's tissues will assimilate them. "We just dissolve the glycerol in water and add a little surfactant to break the cell extension on the leaf surface and make it easier to move the glycerol molecule into the cell," he says.

Collaboration

Because Zhang and the other researchers in the Guiltinan Lab work mainly with molecular biology techniques, they needed additional expertise in analytical chemistry in order to be able to assess glycerol's action in the cacao plant, and so they reached out to their long-time collaborator Phil Smith, co-director of the Metabolomics Core Facility.

"We've been doing things with Phil for many years on different projects," says Guiltinan. "For this study, we needed to be able to detect and quantify specific individual molecules of interest in a big mixture of all kinds of molecules, which is pretty hard to do."

When leaves are sprayed or soaked with the glycerol solution, "you want to see whether the glycerol really gets into the cells and what kind of effect it has in the cellular environment," Zhang says. "We know that when the glycerol does

penetrate into the leaf cells, it converts to a bioactive form known as glycerol 3-phosphate (G3P) which then reacts with a fatty acid species called oleic acid and changes the fatty acid profile of the cells. So we worked with Phil, using mass spectrometry to detect the concentration of G3P in the cells as well as the changes in the fatty acid profile." Analyzing these data, Zhang was able to determine a concentration of glycerol solution sufficient to trigger the plant's defense response without causing adverse effects such as leaf burn.

"Basically," adds Guiltinan, "Phil and his machines allowed us to detect and separate and measure the amount of these molecules, which is the most important thing – to be able to quantify them; it's not easy to do, and frankly, we couldn't do it without the facility and the equipment and – most importantly – Phil's know-how."

Potential impact

As the Lab prepares to take its discovery to the field for trials, Guiltinan is hopeful that cocoa farmers will adopt the use of glycerol in their operations.

"Glycerol is really cheap," he says, "and it's going to get even cheaper the more biofuels are made. It's safe, biodegradable, and if it can yield good results in the field, then we'll have something really useful.

Many cocoa farmers don't have access to agrichemicals or can't afford them. The only other alternative these farmers have is genetics – breeding for resistant strains – which is ongoing but slow. "There are tropical biofuel crops that can be grown with cocoa," Guiltinan says, "so theoretically a farmer could cultivate a small plot and make his own glycerol. With the price of cocoa going up, maybe some of these farmers will eventually be able to invest more in other chemicals, but I think it's a great idea to start promoting safer ones like glycerol as a better, more affordable alternative so maybe farmers will begin to move in that direction. That's our hope."

More information: "Applying Glycerol as a Foliar Spray Activates the Defense Response and Enhances Disease Resistance of Theobroma cacao." Zhang Y, Smith P, Maximova SN, Guiltinan MJ. Mol Plant Pathol. 2014 May 27. DOI: 10.1111/mpp.12158 . [Epub ahead of print] PMID: 24863347 [PubMed - as supplied by publisher]

http://phys.org/news/2014-07-low-cost-world-amputees.html

Low-cost 'helping hand' for Third World amputees created by designer

A hi-tech artificial hand costing just £200 has been designed by a University of Derby student hoping to help lower arm amputees in the Third Word.

The 'Myo' low-cost prosthesis is one of a range of new products created by the University's final year students, which will be on display at the New Designers 2014 exhibition, at London's Business Design Centre, from tomorrow (Thursday July 3) until Saturday (July 5).

The annual graduate design show features more than 3,000 talented, newly-graduated designers from the UK's leading universities.

Matt Thompson, 24, who has just completed a BSc (Hons) Product Design Engineering degree course at Derby, designed his Myo hand with developing and Third World countries in mind. He said: "Disease and war unfortunately means there's a lot of demand for prosthetic limbs in poorer countries. Researching the subject, I found out that upper limb prostheses are more complicated and expensive than lower limb ones, and also that good ones are beyond the financial reach of most people living in those countries.

Product Design student Matt Thompson with the Myo prosthetic hand.

"It cost me about £200 in materials to build the Myo hand. It's made of a tough nylon resin called Zytel with non-slip grips for the fingers. The fingers are fully articulated and what will really bring the cost of the hand's electronics down is that I replaced the many individual motors for different actions, with just two, which will work off a rotating disc in the Myo's wrist."

Low-cost 'helping hand' for Third World amputees created by designer

The arm would be controlled through the use of electromyography, a system used for many artificial limbs. Three electrodes will run from the Myo hand to the real upper arm of the amputee, who would be taught to control the prosthetic hand using the upper arm's individual muscle movements.

Matt will be showing models of the Myo at the New Designers Exhibition and will shortly be producing a fully-functioning prototype. "I don't think anyone else has managed to create a low-cost artificial hand where, effectively, one control disc could make all of the hand's fingers move independently. I'm hoping the Myo can be refined and mass marketed, to bring its costs down even further.

"I believe it could make life a lot easier for many upper limb amputees in poorer parts of the world," added Matt, who is originally from Ipswich.

Having just completed his degree course, Matt has already secured a designer role with the 3form Design company, based in Andover, Hampshire.

Dan Garner, Programme Leader for BSc (Hons) Product Design Engineering at the University of Derby, said: "The Myo is an amazing and innovative piece of work by Matt, with a real chance of making a big social impact. It is the kind of ingenuity and enterprise we encourage on the University's Product Design courses."

http://bit.ly/VqV9df

One Lichen Species Is Actually 126, And Probably More

D.glabratum *is actually 126 different species of lichen, and possibly hundreds more*

by Ed Yong

One of the best ways of finding new species is to sequence the genes of existing ones. Often, scientists discover genetically distinct populations that count as species in their own right, hiding in plain sight. So, the African elephant turns out to be two genetically distinct groups of African elephants. A skipper butterfly is actually ten skipper butterflies. There are two Nile crocodiles, and possibly four killer whales. Time and again, scientists have peered at a creature's DNA and discovered that one species is actually two, or three, or a dozen.

Or perhaps hundreds.

Until ten years ago, scientists talked about the lichen *Dictyonema glabratum* as if it were a single species. Its large, conspicuous, and elegant fronds are found throughout the Americas, and many teams have studied its chemistry and ecology. But until Robert Lücking from the Field Museum started looking at its genes, no one realised the most startling truth about *D.glabratum*: it's actually 126 different species of lichen, and possibly hundreds more.

It's "the most spectacular case of unrecognized species richness" in any group of large organisms, says Lücking.

Lichens are fungi that form alliances with either an alga or a bacterium. The fungus captures water and minerals, while its partner makes food by harvesting the sun's energy. This partnership is clearly a successful one: the beautiful bushes, fronds and pixie cups of lichens are found on every continent, including Antarctica, and there are some 18,000 known species.

D.glabratum was apparently one of them. The late Estonian fungus specialist Erast Parmasto described it in 1978 but Lücking's team have been slowly chipping away at this single identity since 2004. When they discovered a second distinct lichen in Costa Rica, one species became two. When they compared the genes of a small number of specimens in 2013, two species became 16.

Now, the team, including graduate student Manuela Dal-Forno, has finished analysing 356 samples collected throughout Central and South America - more than ten times the number from their earlier study. And with that, 16 species became 126, which the team are classifying under two new groups: *Cora* and *Corella*.

The weird thing is that many of these species aren't hidden ones. Unlike the African elephants or Nile crocodiles, where genetically distinct populations look very similar, these lichens have striking differences. Some are a soothing turquoise blue, others a ghostly white. Some grow on rocks, others on trees and shrubs. Some have distinctive features, like fine hairs or crinkled margins. They're so different that it really shouldn't have taken a genetic analysis to tell them apart.

The problem is that you can only see this glorious diversity by studying the lichens in the wild - and most scientists had worked with specimens that were dried and stored in herbariums. Take them out of their natural setting, and important ecological cues vanish. Dry them out, and their stunning palette collapses into a few boring hues. Lücking's team escaped this trap by snapping a high-resolution photo of every lichen that they took a sample from. "We were absolutely stunned by the result," he says.

Lücking also suspects that many lichenologists were also hamstrung by a weird circular logic. Lichens can look very different depending on where and how they grow, so a single species can take on many guises. That made it easier to believe that very different specimens were actually the same lichen, or that very big specimens were simply older versions of smaller ones. Only DNA could shatter that unity, and it's not finished yet.

The team divided North and South America into a grid, and showed that 101 of their 126 species were found in just one square. This suggests that *D.glabratum* isn't a continent-spanning lichen, but hundreds of incredibly localised ones. And all of these came from just 20 of the 209 squares, implying that there are probably many more *Cora* and *Corella* lichens left to discover in other parts of the Americas.

How many more? The team tried to predict a number by accounting for how many species they know about in different habitats, how widespread each species is, and how thoroughly they sampled each part of the Americas. They ended up with an estimate of 452 of these lichens in total - "an unthinkably dramatic increase from a single species".

"This work beautifully illustrates how little we know about the numbers of fungi on Earth," says Anne Pringle from Harvard University, who studies lichens. "I'm struck by the beauty of the lichens illustrated in the paper, and wonder if local peoples knew these species already, even though they aren't described within the formal scientific literature."

"We have already identified other groups of macrolichens that likely will show similar patterns of unrecognized species - at least double the number of species, if not more," says Lücking. "For taxonomy it means there is a huge amount of work left and nothing can be taken for granted."

Most of these species live in paramos - small habitats in the Andes Mountains, above the forests but below the snow. In these cool worlds, the lichens control the amount of water and nutrients in the soil, setting stable foundations for food webs that include Andean condors, spectacled bears, and a unique range of fast-evolving plants.

"These ecosystems are highly threatened and have disappeared to a large extent," says Lücking. "Each paramo that disappears takes unique species down with it. Previously, it was believed that all paramos were similar, so their genetic diversity could be conserved by conserving just a few fragments. But now we know that this is not the case."

"Lichens are ecosystems, housing myriad other organisms within a thallus (or body), including other fungi and bacteria." adds Pringle. "If we lose one of these lichens, I wonder what else we might lose?"

Reference: *Lücking, Dal-Forno, Sikaroodi, Gillevet, Bungartz, Moncada, Yanez-Ayabaca, Chaves, Coca, Lawrey. 2014. A single macrolichen constitutes hundreds of unrecognized species. PNAS* http://dx.doi.org/10.1073/pnas.1403517111

http://phys.org/news/2014-07-words-sentences.html

Which happened first: Did sounds form words, or words form sentences?

The origins of language is, in some ways, more complicated to study than the origins of other biological traits because language does not fossilize or leave behind physical traces the way that bones and tissues do. However, there are other ways to study the origins of language, such as watching children learn to speak, analyzing genetics, and exploring how animals communicate.

A recent review of animal communication in particular has yielded an intriguing discovery: while structured animal call sequences (for example, birdsong) are widespread, it is very rare that meaningless sounds produced by animals form meaningful sequences, as they do in human languages. This observation, combined with supporting evidence from human languages, has led linguists to suggest that syntax (the structure and rules of language, such as sentence structure) may have evolved before phonemes (the meaning-differentiating sounds that do not themselves have meaning).

The researchers, Katie Collier, et al., at the University of Zurich in Switzerland, have published a review paper on this idea that syntax evolved before phonology in a recent issue of the *Proceedings of The Royal Society B*. In their study, the researchers also hypothesize that syntax is a cognitively simpler process than phonology.

Building blocks of language

Collier, a PhD student at the University of Zurich, explains exactly what phonology and syntax are.

"A simple example for phonology would but the way the phonemes /k/, /a/ and /t/ that have no meaning in themselves and are used in many different words come together to form the word 'cat,'" Collier told *Phys.org*. "Syntax is the next layer where meaningful words come together into larger meaningful structures, such as 'the cat ate the mouse.' Phonology and syntax describe the way sounds form words and then words form sentences, rather than referring to the sounds and sentences themselves."

animal communication	human language	definitions	visual representation
lexical syntax lexicoding compositional	grammar (syntax and morphology)	**the way meaningful parts (morphemes, words) go together to form sentences** a sequence of meaningful elements whose meaning is a function of the meaning of the individual elements that compose it and the way they are structured together	A → A B → B C → C A + B C + B
phonological syntax phonocoding combinatorial	idioms (lexicon)	**an expression whose meaning is not predictable from the parts that compose it**	
	phonetics	**the physical properties of sounds (phones)** meaningless sounds are combined into sequences, the sequences obtained having no conventional meaning	no meaning no meaning
	phonology phonemics	**minimal meaning-differentiating units (phonemes) that do not themselves bear meaning recombine to create meaningful expressions** meaningful elements combine into a meaningful sequence whose meaning is not a function of the meaning of the parts.	no meaning X Y Z Z = single-segment morpheme

Terms and definitions of different types of sound combinations used in animal communication research (non-bold type) and in linguistics (bold). In the visual representation, the circles of different colors on the left represent the different sounds to be combined. They can either have a meaning (represented by a letter as in the case of lexical syntax) or they can have no meaning. On the right, the series of circles represent call combinations that can have a meaning that is a function of the meaning of its parts (e.g., A + B), no meaning, or a new meaning (e.g., X). **Credit: Collier, et al. ©2014 The Royal Society**

At first, the idea that syntax evolved before phonology seems counterintuitive, and it's true that it goes against the traditional linguistic view that phonology is simpler than syntax.

"It may seem counterintuitive, but it is not quite as simple as saying sentences evolved before grunts," Collier explained. "Animal calls or grunts most probably existed before 'sentences.' Most of these calls do not have meaning in the way that human words have meaning. A few have what we call functional reference, where they seem to denote an external object or event, such as a leopard for example. However, these calls cannot be decomposed into smaller sounds. They come as a single unit, unlike our words that are made up of several sounds that are reused in many different words.

This is why we argue that there are no known examples of phonology in animal communication. On the other hand, as discussed in our paper, several species seem to combine these referential calls together to obtain new meanings in a similar way to very simple sentences in human language, which is why we argue that they may have a form of rudimentary syntax.

"I suppose a very simple way of looking at it would be to say that some animal species have 'words' that they can combine into 'sentences,' but their 'words' are simpler, less flexible than ours, made out of one block, rather than several reusable ones."

Monkey syntax

In their paper, the researchers reviewed a wide range of evidence that seems to support the origins of syntax before phonology. In the primate world, two species of monkeys - Campbell monkeys and putty-nosed monkeys - demonstrate this idea in slightly different ways. Both species have two main predators, leopards and crowned eagles, and both species give specific calls when they detect these predators. Campbell monkeys call "krak" at a leopard sighting and "hok" for an eagle sighting. For putty-nosed monkeys, the calls are "pyow" for leopard and "hack" for eagle.

While it's interesting that these monkeys seem to have specific "words" for different things, what's more interesting to linguists is that the monkeys modify these words to mean something different yet related. For example, the Campbell monkeys add the suffix "-oo" to both "words." The "krak-oo" call is given to any general disturbance, while the "hok-oo" call is given to any disturbance in the canopy. The researchers explain that the "-oo" suffix is analogous to the suffix "-like," changing the meaning of the call from "leopard" to "leopard-like (disturbance)." Due to how it combines two meaningful sounds to create a new meaning, this structure is an example of a rudimentary syntax. The way that putty-nosed monkeys alter their calls is more complicated. Whereas "pyow" means "leopard" and "hack" means "eagle," a sequence of two or three "pyows" followed by up to four "hacks" means "let's go," causing the group to move.

There are a few different explanations for how this sequence may have originated. One possibility is that the sequence may be an idiom, where the original sequence may have meant "leopard and eagle," later becoming "danger all over," followed by "danger all over, therefore let's go," and finally just "let's go."

A second possibility is that "pyow" and "hack" may have more abstract meanings, such as "move-on-ground" and "move-in-air," and their meanings change depending on the context of the situation. Although neither explanation demonstrates with certainty that the putty-nosed monkeys structure their calls with a syntax, the sequences leave that possibility open.

Emerging human language

Further evidence in support of the idea that syntax evolved before phonology in human language comes from analyzing a variety of human languages themselves, including sign languages. As far as linguists know, all human languages have syntax, but not all have phonology. The Al-Sayyid Bedouin Sign Language (ABSL) used by a small society in the Negev region of Israel is an emerging language that has been around for less than 75 years. Interestingly, it does not have phonology. For the ABSL, this means that a single object can be represented by a variety of hand shapes. However, the ABSL still has syntax and grammatical regularity, as demonstrated by the existence of rules for combining signs. Perhaps the presence of syntax but not phonology suggests that syntax originates first in the evolution of a young language, and perhaps also that it is simpler than phonology.

When looking at this hypothesis more closely, many aspects of it make sense. From a cognitive perspective, syntax may be simpler to process than phonology because it is easier to remember a few general rules than many phonemes. Having syntax allows speakers to express many concepts with only a few words. As language develops further, and still more concepts need to be communicated, phonology emerges to provide a larger vocabulary. The evolution of phonology may also be strongly influenced by cultural, rather than biological, evolutionary processes. The researchers hope to further develop these ideas in the future.

"To support our hypothesis that syntax evolved before phonology, a lot of work can still be done," Collier said. "Many animal communication systems are still very little understood or described and the more we learn about them, the more we can adjust and refine our hypothesis. From the linguistic side of things, studying more emerging languages (mainly sign languages) would show if there is a pattern for syntax to develop before phonology in human languages."

More information: Katie Collier, et al. "Language evolution: syntax before phonology?" *Proceedings of The Royal Society B*. DOI: 10.1098/rspb.2014.0263

http://www.eurekalert.org/pub_releases/2014-07/uoc--uac070214.php

Upending a cancer dogma

In a bizarre twist, Cyclin D, long believed to promote cancer, actually activates tumor suppressor

Researchers at the University of California, San Diego School of Medicine say a protein essential to regulating cell cycle progression – the process of cell division and replication – activates a key tumor suppressor, rather than inactivating it as previously thought.

"The finding is the result of literally 20 years of work in my lab," said Steven F. Dowdy, PhD, professor in the Department of Cellular and Molecular Medicine at UC San Diego. "It completely turns upside-down what was thought to be a

fundamental aspect of cell cycle progression in all cancer cells driven by one of the most common genetic pathways mutated in cancer, namely the p16-cyclin D pathway." The findings are published in the journal eLife.

Cyclin D is synthesized during the first stage of cell replication and is believed to help drive the complex, multi-stage process, including interaction with the retinoblastoma (Rb) protein, whose function is to prevent excessive cell growth by inhibiting cell cycle progression until a cell is ready to divide. Rb acts as a tumor suppressor.

But mutated or dysfunctional Rb is associated with several major cancers and Cyclin D has long been described as an oncogene that promotes cancer because it was believed to inactivate the Rb tumor suppressor function through a process called phosphorylation, which involves phosphate molecules being added to proteins, essentially turning them on or off.

Dowdy and colleagues painstakingly counted the number of phosphates added to Rb during cell cycle progression. There are as many as 14, but the scientists found that cyclin D adds just a single phosphate at one, and only one, of the 14 locations during the early G1 phase of cell cycle progression, essentially make 14 different versions of the Rb tumor suppressor. The single phosphate serves to activate Rb, not inactivate it as had been thought for over 20 years.

The researchers said the findings fundamentally change the understanding of G1 cell cycle regulation and the molecular origins of many associated cancers. It is critically important to understand how a genetic pathway actually functions and the consequences of interrupting it, especially in this case where there are multiple drug inhibitors of cyclin D being tested in clinical trials for breast cancer.

Moreover, how the next cyclin, cyclin E, that actually does inactivate Rb becomes activated has not been heavily investigated because it was thought to be the less important second domino, whereas we now know it is the first domino, added Dowdy.

Co-authors include Anil M. Narasimha, Manuel Kaulich and Gary S. Shapiro, UCSD Department of Cellular and Molecular Medicine; and Yoon J. Choi and Piotr Sicinski, Harvard Medical School and Dana-Farber Cancer Institute.

http://www.eurekalert.org/pub_releases/2014-07/meae-rrc063014.php

Researchers regrow corneas -- first known tissue grown from an adult human stem cell

Limbal stem cells, identified with new marker, could reverse a leading cause of blindness

Boston - Boston researchers have identified a way to enhance regrowth of human corneal tissue to restore vision, using a molecule known as ABCB5 that acts as a marker for hard-to-find limbal stem cells. This work, a collaboration between the Massachusetts Eye and Ear/Schepens Eye Research Institute (Mass. Eye and Ear), Boston Children's Hospital, Brigham and Women's Hospital and the VA Boston Healthcare System, provides promise to burn victims, victims of chemical injury and others with damaging eye diseases. The research, published this week in Nature, is also one of the first known examples of constructing a tissue from an adult-derived human stem cell.

Limbal stem cells reside in the eye's basal limbal epithelium, or limbus, and help maintain and regenerate corneal tissue. Their loss due to injury or disease is one of the leading causes of blindness. In the past, tissue or cell transplants have been used to help the cornea regenerate, but it was unknown whether there were actual limbal stem cells in the grafts, or how many, and the outcomes were not consistent.

In this study, researchers were able to use antibodies detecting ABCB5 to zero in on the stem cells in tissue from deceased human donors and use them to regrow anatomically correct, fully functional human corneas in mice.

"Limbal stem cells are very rare, and successful transplants are dependent on these rare cells," says Bruce Ksander, Ph.D., of Mass. Eye and Ear, co-lead author on the study with post-doctoral fellow Paraskevi Kolovou, M.D. "This finding will now make it much easier to restore the corneal surface. It's a very good example of basic research moving quickly to a translational application."

ABCB5 was originally discovered in the lab of Markus Frank, M.D., of Boston Children's Hospital, and Natasha Frank, M.D., of the VA Boston Healthcare System and Brigham and Women's Hospital, co-senior investigators on the study, as being produced in tissue precursor cells in human skin and intestine. In the new work, using a mouse model developed by the Frank lab, they found that ABCB5 also occurs in limbal stem cells and is required for their maintenance and survival, and for corneal development and repair. Mice lacking a functional ABCB5 gene lost their populations of limbal stem cells, and their corneas healed poorly after injury.

"ABCB5 allows limbal stem cells to survive, protecting them from apoptosis [programmed cell death]," says Markus Frank. "The mouse model allowed us for the first time to understand the role of ABCB5 in normal development, and should be very important to the stem cell field in general." according to Natasha Frank.

Markus Frank is working with biopharmaceutical industry to develop a clinical-grade ABCB5 antibody that would meet U.S. regulatory approvals. "A single lab cannot do a study like this," says Natasha Frank, also affiliated with the Harvard Stem Cell Institute. "It integrates genetics, knockout mice, antibodies, transplantation - a lot of technical expertise that we were lucky came together in a very nice way."

Researchers include Bruce R. Ksander, Paraskevi E. Kolovou, Sean P. McGuire, Meredith S. Gregory, William J. B. Vincent and James D. Zieske (Schepens Eye Research Institute/Massachusetts Eye and Ear and Harvard Medical School); Brian J. Wilson, Karim R. Saab, and Jie Ma (Boston Children's Hospital), Qin Guo (Boston Chidren's Hospital, VA Boston Healthcare System), Victor L. Perez and Fernando Cruz-Guilloty (Bascom Palmer Eye Institute, University of Miami Miller School of Medicine), Winston W.Y. Kao and Mindy K. Call (University of Cincinnati Medical Center), Budd A. Tucker (Stephen A Wynn Institute for Vision Research, Carver College of Medicine, University of Iowa), Qian Zhan and George Murphy (Brigham and Women's Hospital), Kira L. Lathrop (University of Pittsburgh), Clemens Alt, Luke J. Mortensen and Charles P. Lin (Massachusetts General Hospital and Harvard Medical School), Markus H. Frank (Boston Children's Hospital, Brigham and Women's Hospital, Harvard Medical School) and Natasha Y. Frank (VA Boston Healthcare System, Boston Children's Hospital, Brigham and Women's Hospital, Harvard Medical School).

The research was supported by the National Institute of Neurological Disorders and Stroke (grant K08NS051349), the Veterans Administration (BLR&D 1I01BX000516 and VA RR&D 1I01RX000989), the Harvard Stem Cell Institute, the National Cancer Institute (R01CA113796, R01CA158467, R01CA138231), the Department of Defense (PR0332453), the National Institutes of Health (R01EY018624, P30EY014801, R01EY021768, R01CA138231, R01EB017274, U01HL100402, P41EB015903 and NIH New Innovator Award DP2OD007483), the Corley Research Foundation, the Western Pennsylvania Medical Eye Bank Core Grant for Vision Research (EY08098), the Howard Hughes Medical Institute and the Life Sciences Research Foundation.

http://bit.ly/1lHqghn

Tibetans' altitude tolerance may have come from our extinct relatives

A combination of mutations is found in Tibetans and Denisovans.

by John Timmer - July 3 2014, 2:00am TST

The Denisovans, relatives of the Neanderthals who inhabited Asia before modern humans arrived, are known only from a scattering of small bones and a wealth of DNA data. So far, all of that originates from a single Siberian cave (called Denisova, naturally). Like the Neanderthals, the Denisovans interbred with those modern humans once they arrived. But the modern populations who have the most Denisovan DNA are far from Siberia, occupying southern Asia and some Pacific islands.

Now, a tiny fragment of Denisovan DNA has also been found in a group that's much closer to Siberia: the Tibetans. And all indications are that it helps them adapt to the extreme elevations of the Tibetan plateau.

Large parts of that plateau are 4,000 meters (2.5 miles) above sea level. The populations native to the area have lower infant mortality and higher birth weights than people who have relocated to the area. In addition, the Tibetans have acclimated to the altitude without relying on increased red blood cell counts, which is how most other people respond after spending time at altitude. Higher red blood cell counts mean a more viscous blood, which creates its own health hazard, so this difference is also likely to be very advantageous.

With the advent of molecular genetics, it became possible to determine what is different in the TIbetans' DNA that accounts for their comfort at altitude. Several recent studies have done just that and come up with a variety of genes that appear to be behind it. Many of these studies have identified a gene called EPAS1 as a likely candidate for helping the locals handle the altitude.

Now, a large international team of researchers has gone back and taken a closer look at EPAS1, sequencing the version of the gene in 40 Tibetans and 40 of their close relatives, the Han Chinese. Looking at the 130,000 bases surrounding the gene, they find that there are many differences in this region between the two populations - many more than you'd expect to have occurred in the short time these two populations have been separated. In fact, in a small core area, there are five closely linked changes that are distinct to Tibetans, far more than are likely to accumulate even under the strongest evolutionary selection.

(Nearly distinct to Tibetans, at least. There are two Han individuals, one from Beijing and one from southern China, that also appear to carry a copy of the Tibetan version of this gene.)

To get a better perspective of how this DNA showed up in Tibetans, the researchers started looking at other human genomes from around the world. None of the people from the 1,000 Genomes project had anything that looked like the Tibetan sequence. But a search of the databases turned up one human population who did: the Denisovans. In fact, in the core sequence near EPAS1, the Denisovans shared all five of the changes found in the Tibetans. The similarity extended outside this core region, as well.

In general, the Denisovan contribution to the DNA of Han Chinese is so low that it's been difficult to identify with any certainty. And the population that has the most Denisovan DNA, the Melanesians, doesn't have the Denisovan version of the EPAS1 gene. But the new results clearly indicate that even a small, difficult-to-detect contribution can have dramatic effects on the populations who receive it.

This isn't the first case where versions of genes that were picked up from archaic humans appear to be helpful; other examples involve immune function and skin coloration. This makes a lot of sense, given that the Neanderthals and Denisovans had been living in some environments for tens of thousands of years before modern humans showed up. The authors of the new paper conclude, "we are now also starting to understand that adaptation to local environments may have been facilitated by gene flow from other hominins that may already have been adapted to those environments."

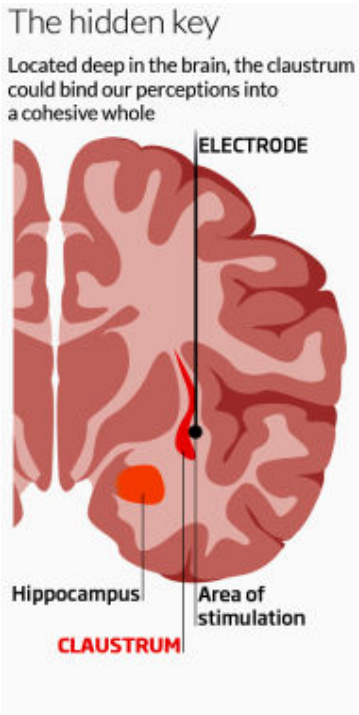
Nature, 2014. DOI: 10.1038/nature13408 (About DOIs).

http://www.eurekalert.org/pub_releases/2014-07/uoc--ua070214.php

UCLA addresses 'lost in translation' issues in Chinese medicine

A need for accurate, high-quality Chinese-English translations

Millions of people in the West today utilize traditional Chinese medicine, including acupuncture, herbs, massage and nutritional therapies. Yet only a few U.S. schools that teach Chinese medicine require Chinese-language training and only a handful of Chinese medical texts have so far been translated into English.



Given the complexity of the language and concepts in these texts, there is a need for accurate, high-quality translations, say researchers at UCLA's Center for East–West Medicine. To that end, the center has published a document that includes a detailed discussion of the issues involved in Chinese medical translation, which is designed to help students, educators, practitioners, researchers, publishers and translators evaluate and digest Chinese medical texts with greater sensitivity and comprehension.

"This publication aims to raise awareness among the many stakeholders involved with the translation of Chinese medicine," said principal investigator and study author Dr. Ka-Kit Hui, founder and director of the UCLA center.

The 15-page document, "Considerations in the Translation of Chinese Medicine" was developed and written by a UCLA team that included a doctor, an anthropologist, a China scholar and a translator. It appears in the current online edition of the Journal of Integrative Medicine.

Authors Sonya Pritzker, a licensed Chinese medicine practitioner and anthropologist, and Hanmo Zhang, a China scholar, hope the publication will promote communication in the field and play a role in the development of thorough, accurate translations.

The document highlights several important topics in the translation of Chinese medical texts, including the history of Chinese medical translations, which individuals make ideal translators, and other translation-specific issues, such as the delicate balance of focusing translations on the source-document language while considering the language it will be translated into.

It also addresses issues of technical terminology, period-specific language and style, and historical and cultural perspective. For example, depending on historical circumstances and language use, some translations may be geared toward a Western scientific audience or, alternately, it may take a more natural and spiritual tone. The authors note that it is sometimes helpful to include dual translations, such as "windfire eye/acute conjunctivitis," in order to facilitate a link between traditional Chinese medical terms and biomedical diagnoses.

The final section of the document calls for further discussion and action, specifically in the development of international collaborative efforts geared toward the creation of more rigorous guidelines for the translation of Chinese medicine texts.

"Considerations in the Translation of Chinese Medicine," was inspired by the late renowned translator and scholar Michael Heim, a professor in the UCLA departments of comparative literature and Slavic studies. A master of 12 languages, he is best known for his translation into English of Czech author Milan Kundera's "The Unbearable Lightness of Being." The new UCLA document is dedicated to him.

The document, the authors say, was influenced in large part by the American Council of Learned Societies' "Guidelines for the Translation of Social Science Texts," which are intended to promote communications in the social sciences across language boundaries. It was also influenced by Pritzker's longstanding anthropological study of translation in Chinese medicine, which is detailed in her new book, "Living Translation: Language and the Search for Resonance in U.S. Chinese Medicine," recently published by Berghahn Books.

Funded by a UCLA Transdisciplinary Seed Grant, the document is available for free in both English and Chinese (PDF format) on the UCLA Center for East–West Medicine website.

http://bit.ly/1mUbFYJ

Consciousness on-off switch discovered deep in brain

ONE moment you're conscious, the next you're not. For the first time, researchers have switched off consciousness by electrically stimulating a single brain area.

by Helen Thomson

Scientists have been probing individual regions of the brain for over a century, exploring their function by zapping them with electricity and temporarily putting them out of action. Despite this, they have never been able to turn off consciousness – until now.

Although only tested in one person, the discovery suggests that a single area – the claustrum – might be integral to combining disparate brain activity into a seamless package of thoughts, sensations and emotions. It takes us a step closer to answering

a problem that has confounded scientists and philosophers for millennia – namely how our conscious awareness arises.

Many theories abound but most agree that consciousness has to involve the integration of activity from several brain networks, allowing us to perceive our surroundings as one single unifying experience rather than isolated sensory perceptions.

One proponent of this idea was Francis Crick, a pioneering neuroscientist who earlier in his career had identified the structure of DNA. Just days before he died in July 2004, Crick was working on a paper that suggested our consciousness needs something akin to an orchestra conductor to bind all of our different external and internal perceptions together.

With his colleague Christof Koch, at the Allen Institute for Brain Science in Seattle, he hypothesised that this conductor would need to rapidly integrate information across distinct regions of the brain and bind together information arriving at different times. For example, information about the smell and colour of a rose, its name, and a memory of its relevance, can be bound into one conscious experience of being handed a rose on Valentine's day.

The pair suggested that the claustrum – a thin, sheet-like structure that lies hidden deep inside the brain – is perfectly suited to this job (*Philosophical Transactions of The Royal Society B*, doi.org/djjw5m).

It now looks as if Crick and Koch were on to something. In a study published last week, Mohamad Koubeissi at the George Washington University in Washington DC and his colleagues describe how they managed to switch a woman's consciousness off and on by stimulating her claustrum. The woman has epilepsy so the team were using deep brain electrodes to record signals from different brain regions to work out where her seizures originate. One electrode was positioned next to the claustrum, an area that had never been stimulated before.

When the team zapped the area with high frequency electrical impulses, the woman lost consciousness. She stopped reading and stared blankly into space, she didn't respond to auditory or visual commands and her breathing slowed. As soon as the stimulation stopped, she immediately regained consciousness with no memory of the event. The same thing happened every time the area was stimulated during two days of experiments (*Epilepsy and Behavior*, doi.org/tgn).

To confirm that they were affecting the woman's consciousness rather than just her ability to speak or move, the team asked her to repeat the word "house" or snap her fingers before the stimulation began. If the stimulation was disrupting a brain region responsible for movement or language she would have stopped moving or talking almost immediately. Instead, she gradually spoke more quietly or moved less and less until she drifted into unconsciousness. Since there was no sign of epileptic brain activity during or after the stimulation, the team is sure that it wasn't a side effect of a seizure.

Koubeissi thinks that the results do indeed suggest that the claustrum plays a vital role in triggering conscious experience. "I would liken it to a car," he says. "A car on the road has many parts that facilitate its movement – the gas, the transmission, the engine – but there's only one spot where you turn the key and it all switches on and works together. So while consciousness is a complicated process created via many structures and networks – we may have found the key."

Awake but unconscious

Counter-intuitively, Koubeissi's team found that the woman's loss of consciousness was associated with increased synchrony of electrical activity, or brainwaves, in the frontal and parietal regions of the brain that participate in conscious awareness.

Although different areas of the brain are thought to synchronise activity to bind different aspects of an experience together, too much synchronisation seems to be bad. The brain can't distinguish one aspect from another, stopping a cohesive experience emerging.

Since similar brainwaves occur during an epileptic seizure, Koubeissi's team now plans to investigate whether lower frequency stimulation of the claustrum could jolt them back to normal. It may even be worth trying for people in a minimally conscious state, he says. "Perhaps we could try to stimulate this region in an attempt to push them out of this state."

Anil Seth, who studies consciousness at the University of Sussex, UK, warns that we have to be cautious when interpreting behaviour from a single case study. The woman was missing part of her hippocampus, which was removed to treat her epilepsy, so she doesn't represent a "normal" brain, he says.

However, he points out that the interesting thing about this study is that the person was still awake. "Normally when we look at conscious states we are looking at awake versus sleep, or coma versus vegetative state, or anaesthesia." Most of these involve changes of wakefulness as well as consciousness but not this time, says Seth. "So even though it's a single case study, it's potentially quite informative about what's happening when you selectively modulate consciousness alone."

"Francis would have been pleased as punch," says Koch, who was told by Crick's wife that on his deathbed, Crick was hallucinating an argument with Koch about the claustrum and its connection to consciousness.

"Ultimately, if we know how consciousness is created and which parts of the brain are involved then we can understand who has it and who doesn't," says Koch. "Do robots have it? Do fetuses? Does a cat or dog or worm? This study is incredibly intriguing but it is one brick in a large edifice of consciousness that we're trying to build."

http://bit.ly/1mUgjpK

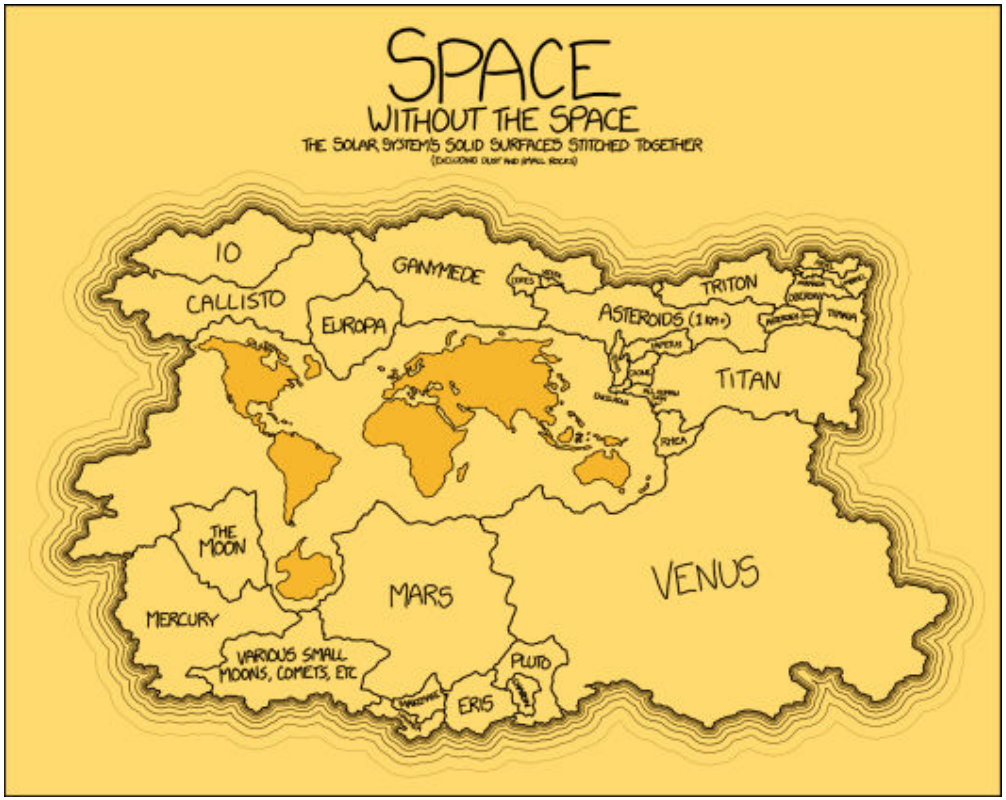
Flatten Out the Moons and Planets, And You Can See Just How Big Earth Actually Is

Comparing their surface areas side-by-side gives a sense of scale to some of the solar system's inhabitants

By Colin Schultz

Infographics and interactives abound to show you just show BIG space really is - and how small the things that inhabit it are. Relatively speaking, of course. But almost none of us have any real frame of reference to help us understand objects at this scale. Often, the planets and moons of the solar system are put into scale with sports equipment analogies: If the Earth were the size of a basketball, the Moon would be the size of a tennis ball!

Over at xkcd, cartoonist Randall Munroe came up with an eye-opening way to represent many of the medium-sized objects in our solar system. Reproduced above, Munroe's map flattens out the Earth and the Moon, along with a host of other planets and moons, easily showing how they really compare. It's surprising to see



that Ganymede, the largest moon in the solar system (one of Jupiter's), is about the same size as Europe and Africa. Mars and Mercury, meanwhile, are surprisingly close in size.

Even here, though, the complexities of representing the vast range of sizes of things in the solar system is apparent. While all of these planets and moons are nicely stitched side-by-side, they'd be little more than a speck on Jupiter's flattened face.

http://bit.ly/1kpC1C2

First Birds Valued Fashion Over Flight

Archaeopteryx sported feathered "trousers" on its hind limbs

by Jennifer Viegas

Archaeopteryx, the iconic early bird that lived around 150 million years ago, sported feathered "trousers" on its hind limbs as well as other decorative feathers, and researchers now believe at least some non-avian dinosaur and bird feathers evolved for flashy display before they were later recruited for flight.

That's the conclusion of a new study, published in the journal Nature, which describes a remarkable new specimen of Archaeopteryx that includes extensive feather preservation.

"The excellent preservation of the feathers in the new specimen helps to clarify many contentious issues," senior author Oliver Rauhut of Ludwig-Maximilians University Munich told Discovery News. "The specimen not only shows the wing and tail feathers in great detail, but also body plumage and feathers along the hind limbs…(which are) similar to the feather 'trousers' found in many modern birds of prey."

The researchers determined that quill-like feathers covered Archaeopteryx's entire body up to its head. Its hind limb feathers were symmetrical, indicating they didn't help with flight.

Its tail feathers were extremely long -- more than 60 percent of the length of its bony tail -- with some being asymmetrical and therefore useful in flight. Its wing feathers were also suitable for flight, and appear to have been just as strong as those seen in modern flying birds.

Recreation of Archaeopteryx **Bayerische Staatssammlung für Paläontologie und Geologie**

"There are a number of indications that Archaeopteryx was capable of aerial locomotion, but just how well it could fly remains debated," Rauhut said, adding

that the jury is still out as to whether Archaeopteryx was a non-avian dinosaur or a bird. That's because the transition from one to the other happened gradually.
Current evidence does, however, suggest that Archaeopteryx was a representative of the main evolutionary lineage going toward birds. The evidence also suggests that Archaeopteryx and its dinosaur predecessors were colorful and flashy.
Rauhut shared that "it is very likely that dinosaurs could see colors, and many animals that have this capability tend to be colorful." Prior studies support this theory. He and his team suspect that, like modern birds, the colorful feathers likely were used in displays, such as for mating.
It appears that proto-feathers originally evolved for regulating body temperature. The quill-like contour feathers, on the other hand, could have first evolved for show.
"Once present, these feathers could then be adapted for many other functions, such as balance during fast running, protecting and shading the eggs during breeding, and flight," Rauhut said.
"This is a fine and important piece of work on a great new specimen," said Mark Norell, division chair and curator-in-charge of the American Museum of Natural History's Division of Paleontology. "It clearly shows that the evolution of hind limb feathers is very complex and the evolution of feathers as a whole is de-coupled from flight."
Lawrence Witmer, a professor of anatomy and paleontology at Ohio University, also believes that the new specimen "is a really important find."
Witmer added, "When you combine the new information from Archaeopteryx with what we see in other bird-like dinosaurs and dinosaur-like birds, the picture that emerges is that maybe (quilled) feathers evolved more as ornaments for display and were later co-opted by evolution for flight … maybe multiple times. I think the authors make a good case. The display argument is very compelling."

http://www.medscape.com/viewarticle/827719

Dark Chocolate May Relieve Walking Pain in PAD

After eating a small bar of dark chocolate, patients with moderate to severe peripheral arterial disease (PAD) could walk slightly farther and longer on a treadmill

ROME, ITALY - Shortly after eating the equivalent of a small bar of dark, but not milk, chocolate, patients with moderate to severe peripheral arterial disease (PAD) could walk slightly farther and longer on a treadmill before having to stop due to pain, in a proof-of-concept study[1].
The research suggests that polyphenols in the dark chocolate may improve circulation in PAD patients, but further study is needed to confirm this, according to lead author **Dr Lorenzo Loffredo** (Sapienza University of Rome, Italy), senior author **Dr Francesco Violi** (Sapienza University of Rome), and colleagues. Two hours "after eating the dark [but not the milk] chocolate, PAD patients walked an average of 11% farther and 15% longer" than when they did not eat chocolate, Drs. Loffredo and Violi noted in an email to ***heartwire*** .
"PAD is characterized by reduced flow to the limbs, [and so far] there are no drugs that improve this blood flow, but dark chocolate could [potentially do this]."
However, "this is only a pilot study," they stressed. On the other hand, "if the results of our study are confirmed by future studies with chronic ingestion of polyphenols, it would open up novel therapeutic strategies in this setting using a natural substance," they said. The study is published July 2, 2014, in the *Journal of the American Heart Association.*

Polyphenols, Oxidative Stress, and PAD

PAD typically manifests in patients as intermittent claudication, where blood flow to the limbs is impaired during exercise, likely partly due to impaired nitric-oxide generation and oxidative stress. Patients experience weakness, numbness, or cramping in their muscles due to decreased blood flow.
However, cocoa and dark chocolate, which are rich in polyphenols, dilate arteries by reducing oxidative stress and increasing nitric-oxide generation. The researchers hypothesized that patients with PAD could walk farther and longer before experiencing leg cramps if they first ingested cocoa.
They recruited 20 patients - 14 men and 6 women - who had Fontaine stage IIb PAD, meaning they had leg pain when they walked less than 200 m, about half the length of an American football field. The patients were 60 to 78 years old.
In this crossover study, the patients were randomized to receive 40 g (about 200 calories) of dark chocolate (≥85% cocoa) or milk chocolate (≤35% cocoa).
For each type of chocolate, the patients had blood drawn early in the morning to analyze oxidative stress and other variables. An hour later, they did a treadmill walking test, and then half an hour later they were given the 40 g of chocolate. Two hours after eating the chocolate, they had more blood tests and a second treadmill test.
After eating dark chocolate, the patients walked, on average, almost 12 m (39 ft) farther and about 17 seconds longer than their distance and times obtained without eating chocolate. Eating milk chocolate did not improve walking times or distances.
"The different effect of dark and milk chocolate on walking autonomy supports the hypothesis that polyphenol content may be responsible for this effect, because dark chocolate is richer in polyphenol compared with milk chocolate," the researchers write.
After the participants ate dark chocolate, their serum nitric-oxide levels increased, arterial endothelial function improved, and biochemical measures of oxidative stress decreased.

The findings are not transferable to clinical practice just yet, since it was a small study that lacked a placebo group, and the long-term effect on PAD from regularly indulging in a small piece of dark chocolate is unknown.

"Extremely Preliminary," Beware of Extra Calories

"Other investigations have shown that polyphenols, including those in dark chocolate, may improve blood-vessel function; but this study is extremely preliminary, and I think everyone needs to be cautious when interpreting the findings," **American Heart Association** (AHA) spokesperson **Dr Mark Creager** (Brigham and Women's Hospital and Harvard Medical School, Boston, MA) said in a statement. For example, after early promise, the antioxidants vitamin C and vitamin E did not turn out to improve cardiovascular health.

Moreover, chocolate is high in calories, sugar, and fat. A typical American chocolate bar provides 94 calories from sugar (24 g) and 8 g of saturated fat, according to statement from the AHA. The AHA recommends that daily sugar consumption should not be more than 150 calories (9 tsp) for men or 100 calories (6 tsp) for women, and saturated fat should not be more than 5% to 6% of daily calories. Cloves, dried peppermint, celery seed, capers, and hazelnuts are low in calories and fat and high in polyphenols.

The authors had no disclosures.

References

1. Loffredo L, Perri L, Catasca E, et al. Dark chocolate acutely improves walking autonomy in patients with peripheral artery disease. J Am Heart Assoc *2014; DOI:10.1161/JAHA.114.001072. Available at: http://jaha.ahajournals.org.*

http://www.eurekalert.org/pub_releases/2014-07/elf-wte070214.php

WHO targets elimination of TB in over 30 countries

New framework to eliminate tuberculosis (TB) in countries with low levels of the disease

ROME, ITALY - The World Health Organization (WHO) today, together with the European Respiratory Society (ERS), presented a new framework to eliminate tuberculosis (TB) in countries with low levels of the disease. Today there are 33* countries and territories where there are fewer than 100 TB cases per million population.

The framework outlines an initial "pre-elimination" phase, aiming to have fewer than 10 new TB cases per million people per year by 2035 in these countries. The goal is to then achieve full elimination of TB by 2050, defined as less than 1 case per million people per year.

Although TB is preventable and curable, in these 33 settings 155 000 people still fall ill each year and 10 000 die. Millions are infected and at risk of falling ill.

The proposed framework builds on approaches that are already proving successful. It was developed with experts from low-burden countries and adapted from the new WHO global TB strategy, 2016-35, approved by the World Health Assembly in May 2014. Country representatives gathered to discuss the framework and its implementation at a meeting co-hosted by WHO and the European Respiratory Society (ERS) in Rome in collaboration with the Italian Ministry of Health.

Italy is one of the 21 European countries addressed by the framework. The 33 countries, territories and areas also include seven from the Americas, three from WHO's Eastern Mediterranean Region, and two from WHO's Western Pacific Region.

The countries recognize the common need to reenergize the efforts to eliminate TB as a public health problem and prevent its resurgence. As TB rates have fallen in many of these countries, attention to this public health threat has waned and capacity to respond could be weakened.

"Low TB-burden countries already have the means to drive down TB cases dramatically by 2035," says Dr Hiroki Nakatani, WHO Assistant Director-General. "Universal health coverage, which ensures everyone has access to the health services they need without suffering financial hardship as a result, is the bedrock. The key is to target smart TB interventions towards the people who need them most."

The new WHO framework highlights the effectiveness of eight key interventions, in a coherent package for impact in the target countries:

1. Ensure funding and stewardship for planning and services of high quality;
2. Address most vulnerable and hard-to-reach groups;
3. Address special needs of migrants; cross-border issues;
4. Undertake screening for active TB and latent TB infection in high-risk groups and provide appropriate treatment; manage outbreaks;
5. Optimize MDR-TB prevention and care;
6. Ensure continued surveillance and programme monitoring and evaluation
7. Invest in research and new tools;
8. Support global TB control.

Among the most vulnerable groups are people who are poor or homeless, migrants, and members of ethnic minorities. In addition, people who use drugs or are incarcerated, and people with compromised immune systems (e.g. people living with HIV, malnutrition, diabetes, smokers and heavy drinkers) all have a much greater risk of falling ill with TB. Many of these vulnerable groups face barriers in accessing health services.

Addressing tuberculosis in the context of cross-border migration can also pose a significant challenge to health service providers. Many undergoing a course of TB

treatment may have no option but to relocate for work, even if they have not completed their TB treatment. "Countries with a low incidence of TB are uniquely positioned to reach historically low levels of TB," adds Dr Mario Raviglione, Director of WHO's Global TB Programme. "They can serve as global trailblazers." Globalization and increased population movements enable TB - an airborne infectious disease - to continue to spread across communities and countries. To eliminate the disease in low-burden countries it will be vital to dramatically scale up TB prevention and care in high-incidence countries. This interdependency calls for concerted action and tight collaboration between countries with high and low burden of TB.

"Powerful antibiotics and better living standards have almost pushed the disease out of many high-income countries. But we still have not succeeded. And if we do the wrong things now, TB could rebound, including with more drug-resistant forms," says Professor G.B. Migliori from ERS. "But if we get it right, and recommit to fighting the disease, both at home and abroad, TB will eventually no longer be a public health threat."

Note to editors:

In May, the World Health Assembly adopted the WHO's new global TB strategy for the period 2016-2035, which aims to reduce global TB incidence by 90% and end the global TB epidemic. The strategy emphasizes global collaboration and national adaptation. It stresses that the national TB-control response needs to be tailored to local epidemiological and health system context.

**Australia, Austria, Bahamas, Belgium, Canada, Costa Rica, Cuba, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Jamaica, Jordan, Luxembourg, Malta, Netherlands, New Zealand, Norway, Puerto Rico, Slovakia, Slovenia, Sweden, Switzerland, United Arab Emirates, United States of America, West Bank and Gaza Strip*

http://www.eurekalert.org/pub_releases/2014-07/icl-nsd070114.php

New study discovers biological basis for magic mushroom 'mind expansion'

New research shows that our brain displays a similar pattern of activity during dreams as it does during a mind-expanding drug trip.

Psychedelic drugs such as LSD and magic mushrooms can profoundly alter the way we experience the world but little is known about what physically happens in the brain. New research, published in Human Brain Mapping, has examined the brain effects of the psychedelic chemical in magic mushrooms, called 'psilocybin,' using data from brain scans of volunteers who had been injected with the drug.

The study found that under psilocybin, activity in the more primitive brain network linked to emotional thinking became more pronounced, with several different areas in this network - such as the hippocampus and anterior cingulate cortex - active at the same time. This pattern of activity is similar to the pattern observed in people who are dreaming. Conversely, volunteers who had taken psilocybin had more disjointed and uncoordinated activity in the brain network that is linked to high-level thinking, including self-consciousness.

Psychedelic drugs are unique among other psychoactive chemicals in that users often describe 'expanded consciousness,' including enhanced associations, vivid imagination and dream-like states. To explore the biological basis for this experience, researchers analysed brain imaging data from 15 volunteers who were given psilocybin intravenously while they lay in a functional magnetic resonance imaging (fMRI) scanner. Volunteers were scanned under the influence of psilocybin and when they had been injected with a placebo

"What we have done in this research is begin to identify the biological basis of the reported mind expansion associated with psychedelic drugs," said Dr. Robin Carhart-Harris from the Department of Medicine, Imperial College London. "I was fascinated to see similarities between the pattern of brain activity in a psychedelic state and the pattern of brain activity during dream sleep, especially as both involve the primitive areas of the brain linked to emotions and memory. People often describe taking psilocybin as producing a dreamlike state and our findings have, for the first time, provided a physical representation for the experience in the brain."

The new study examined variation in the amplitude of fluctuations in what is called the blood-oxygen level dependent (BOLD) signal, which tracks activity levels in the brain. This revealed that activity in important brain networks linked to high-level thinking in humans becomes unsynchronised and disorganised under psilocybin. One particular network that was especially affected plays a central role in the brain, essentially 'holding it all together', and is linked to our sense of self. In comparison, activity in the different areas of a more primitive brain network became more synchronised under the drug, indicating they were working in a more co-ordinated, 'louder' fashion. The network involves areas of the hippocampus, associated with memory and emotion, and the anterior cingulate cortex which is related to states of arousal.

Lead author Dr Enzo Tagliazucchi from Goethe University, Germany said: "A good way to understand how the brain works is to perturb the system in a marked and novel way. Psychedelic drugs do precisely this and so are powerful tools for exploring what happens in the brain when consciousness is profoundly altered. It is the first time we have used these methods to look at brain imaging data and it has given some fascinating insight into how psychedelic drugs expand the mind. It really provides a window through which to study the doors of perception."

Dr. Carhart-Harris added: "Learning about the mechanisms that underlie what happens under the influence of psychedelic drugs can also help to understand their

possible uses. We are currently studying the effect of LSD on creative thinking and we will also be looking at the possibility that psilocybin may help alleviate symptoms of depression by allowing patients to change their rigidly pessimistic patterns of thinking. Psychedelics were used for therapeutic purposes in the 1950's and 1960's but now we are finally beginning to understand their action in the brain and how this can inform how to put them to good use."

The data was originally collected at Imperial College London in 2012 by a research group led by Dr. Carhart-Harris and Professor David Nutt from the Department of Medicine, Imperial College London. Initial results revealed a variety of changes in the brain associated with drug intake. To explore the data further Dr. Carhart-Harris recruited specialists in the mathematical modelling of brain networks, Professor Dante Chialvo and Dr Enzo Tagliazucchi to investigate how psilocybin alters brain activity to produce its unusual psychological effects.

As part of the new study, the researchers applied a measure called entropy. This was originally developed by physicists to quantify lost energy in mechanical systems, such as a steam engine, but entropy can also be used to measure the range or randomness of a system. For the first time, researchers computed the level of entropy for different networks in the brain during the psychedelic state. This revealed a remarkable increase in entropy in the more primitive network, indicating there was an increased number of patterns of activity that were possible under the influence of psilocybin. It seemed the volunteers had a much larger range of potential brain states that were available to them, which may be the biophysical counterpart of 'mind expansion' reported by users of psychedelic drugs.

Previous research has suggested that there may be an optimal number of dynamic networks active in the brain, neither too many nor too few. This may provide evolutionary advantages in terms of optimizing the balance between the stability and flexibility of consciousness. The mind works best at a critical point when there is a balance between order and disorder and the brain maintains this optimal number of networks. However, when the number goes above this point, the mind tips into a more chaotic regime where there are more networks available than normal. Collectively, the present results suggest that psilocybin can manipulate this critical operating point.

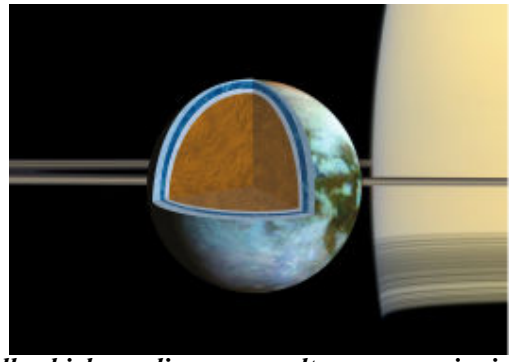
The research was funded and intellectually supported by the Beckley Foundation. Professor Chialvo is from the Consejo Nacional de Investigaciones Cientificas y Tecnologicas (CONICET), Argentina and Dr Tagliazucchi is based at Goethe University, Germany.

1. Reference: Tagliazucchi, E. et al. 'Enhanced repertoire of brain dynamical states during the psychedelic experience' Human Brain Mapping, 2014.
http://onlinelibrary.wiley.com/doi/10.1002/hbm.22562/abstract.

http://phys.org/news/2014-07-ocean-saturn-moon-salty-dead.html

Ocean on Saturn moon could be as salty as the Dead Sea

Scientists analyzing data from NASA's Cassini mission have firm evidence the ocean inside Saturn's largest moon, Titan, might be as salty as the Earth's Dead Sea.



Researchers found that Titan's ice shell, which overlies a very salty ocean, varies in thickness around the moon, suggesting the crust is in the process of becoming rigid.
Credit: NASA/JPL/SSI/Univ. of Arizona/G. Mitri/University of Nantes

Phys.org - The new results come from a study of gravity and topography data collected during Cassini's repeated flybys of Titan during the past 10 years. Using the Cassini data, researchers presented a model structure for Titan, resulting in an improved understanding of the structure of the moon's outer ice shell. The findings are published in this week's edition of the journal Icarus.

"Titan continues to prove itself as an endlessly fascinating world, and with our long-lived Cassini spacecraft, we're unlocking new mysteries as fast as we solve old ones," said Linda Spilker, Cassini project scientist at NASA's Jet Propulsion Laboratory (JPL) in Pasadena, California, who was not involved in the study.

Additional findings support previous indications the moon's icy shell is rigid and in the process of freezing solid. Researchers found that a relatively high density was required for Titan's ocean in order to explain the gravity data. This indicates the ocean is probably an extremely salty brine of water mixed with dissolved salts likely composed of sulfur, sodium and potassium. The density indicated for this brine would give the ocean a salt content roughly equal to the saltiest bodies of water on Earth.

"This is an extremely salty ocean by Earth standards," said the paper's lead author, Giuseppe Mitri of the University of Nantes in France. "Knowing this may change the way we view this ocean as a possible abode for present-day life, but conditions might have been very different there in the past."

Cassini data also indicate the thickness of Titan's ice crust varies slightly from place to place. The researchers said this can best be explained if the moon's outer shell is stiff, as would be the case if the ocean were slowly crystalizing, and turning to ice. Otherwise, the moon's shape would tend to even itself out over time, like warm candle wax. This freezing process would have important implications for the

habitability of Titan's ocean, as it would limit the ability of materials to exchange between the surface and the ocean.

A further consequence of a rigid ice shell, according to the study, is any outgassing of methane into Titan's atmosphere must happen at scattered "hot spots" - like the hot spot on Earth that gave rise to the Hawaiian Island chain. Titan's methane does not appear to result from convection or plate tectonics recycling its ice shell.

How methane gets into the moon's atmosphere has long been of great interest to researchers, as molecules of this gas are broken apart by sunlight on short geological timescales. Titan's present atmosphere contains about five percent methane. This means some process, thought to be geological in nature, must be replenishing the gas. The study indicates that whatever process is responsible, the restoration of Titan's methane is localized and intermittent.

"Our work suggests looking for signs of methane outgassing will be difficult with Cassini, and may require a future mission that can find localized methane sources," said Jonathan Lunine, a scientist on the Cassini mission at Cornell University, Ithaca, New York, and one of the paper's co-authors. "As on Mars, this is a challenging task."

More information: Icarus, www.sciencedirect.com/science/... ii/S0019103514001444

http://www.eurekalert.org/pub_releases/2014-07/uoc--rsi062614.php

Rapid surgical innovation puts patients at risk for medical errors

Surgeons call for national safety measures to protect patients

Researchers at the University of California, San Diego School of Medicine have found that the risk of patient harm increased two-fold in 2006 – the peak year that teaching hospitals nationwide embraced the pursuit of minimally invasive robotic surgery for prostate cancer. Results of the study are published in the July 2 online issue of JAMA Surgery.

"This study looked at the stages of innovation and how the rapid adoption of a new surgical technology - in this case, a surgical robotic system - can lead to adverse events for patients," said Kellogg Parsons, MD, MHS, surgical oncologist, UC San Diego Health System and first author of the paper. "There is a real need for standardized training programs, rules governing surgeon competence and credentialing, and guidelines for hospital privileging when novel technologies reach the operating rooms of teaching and community hospitals."

In 2003, there were an estimated 617 minimally invasive robotic prostatectomies (MIRPs) performed in the United States. By 2009, this number increased to 37,753 procedures. In 2005, patients were twice as likely to experience an adverse event if they were undergoing MIRPs compared to a traditional open surgical procedure. The following year –2006 – was considered the tipping point for the adoption of MIRP when it equaled or exceeded 10 percent of all cases.

"The trend observed here is not new to robotic surgery. The same phenomena occurred with the move to minimally invasive approaches to gallbladder and kidney surgeries, both surgeries that are now well documented to improve safety and outcomes," said Christopher Kane, MD, professor of surgery and interim chair of the Department of Surgery, UC San Diego School of Medicine, who was not involved with the study. "Whenever a new technology is adopted there is a temporary period where there may be an increased risk to the patient. This can be reduced by extensive surgical training, vigorous credentialing standards and extended mentorship by experienced surgeons. This report should encourage the adoption of more rigorous credentialing standards proposed by professional organizations rather than by individual hospitals."

Kane added that robotic prostatectomy by experienced surgeons has proven to be beneficial to the patient with less blood loss, reduced infections and shorter hospital stays.

"A responsibility of deploying a surgical technology should include the responsibility to monitor it as it diffuses throughout the real world to ensure safety," said David C. Chang, PhD, MPH, MBA, director of Outcomes Research at UC San Diego School of Medicine and the paper's senior author. "Surveillance of surgical safety should be ongoing, much like the Centers for Disease Control monitor changes in trends of infectious diseases across the country."

The UC San Diego team used Patient Safety Indicators, developed by the Agency for Healthcare Research and Quality (AHRQ), to develop a nationwide data sample to analyze surgical provider performance and potential in-hospital adverse events from 2003-2009. Data for the prevalence of robotic prostatectomy was pulled from AHRQ and compared to published data from Intuitive Surgical Inc., the manufacturer of the da Vinci robotic system.

"One potential intervention would be the development of standardized training and credentialing programs, much like the aviation industry requires of flight crews inexperienced with new types of aircraft," said Parsons, who is also an associate professor of surgery at UC San Diego School of Medicine. "An independent, continuously updated tracking system for the adoption of new surgical technology is also essential. Prior estimates of robotic prostatectomy uptake, provided exclusively by the robot manufacturer, substantially overestimated the speed with which it was adopted by the surgical community."

Contributors to this paper included Karen Messner, PhD, Lerrin Palazzi, MPH, and Sean Stroup, MD, all at UC San Diego School of Medicine.

http://www.eurekalert.org/pub_releases/2014-07/cp-ws062614.php

With 'biological sunscreen,' mantis shrimp see the reef in a whole different light

In an unexpected discovery, researchers have found that the complex eyes of mantis shrimp are equipped with optics that generate ultraviolet (UV) color vision.

Mantis shrimp's six UV photoreceptors pick up on different colors within the UV spectrum based on filters made from an ingredient other animals depend on as built-in biological sunscreen, according to research reported in the Cell Press journal Current Biology on July 3.

"The mantis shrimp visual system contains six types of photoreceptors functioning completely outside the visual range of humans," says Michael Bok of the University of Maryland Baltimore County. "Surprisingly, they produce their six UV photoreceptors using only two types of visual pigments by pairing one visual pigment with one of four UV filters. The UV filters block certain wavelengths of light from reaching the photoreceptors, chromatically shifting their sensitivity."

The filters are composed of so-called mycosporine-like amino acids (or MAAs), which are commonly found in the skin or exoskeleton of marine organisms, where they absorb damaging UV rays. They do the same thing in mantis shrimp eyes, but for an entirely novel purpose. "The effect is akin to putting red-tinted glasses over your eyes that block other wavelengths of light, except this is being done at the photoreceptor cellular level in shrimp," Bok explains.

This is an image of mantis shrimp eyes. **Michael Bok**

Exactly why mantis shrimp need such a sophisticated visual system remains mysterious, Bok says. Mantis shrimp use their eyes to navigate and spot predators and prey on the vibrant reef that is their home. Mantis shrimp also have complex social interactions that are likely mediated by distinct visual signals on their bodies. Their complex eyes, which include 16 or more types of photoreceptors in all, may provide them with a complex color and polarization visual system without a big brain to post-process lots of information. In other words, their eyes may sense and respond to complex visual inputs without the need to think very hard about it, Bok explains.

Despite the new discovery, the researchers say, it's still tough to imagine the reef as mantis shrimp see it. "The way their eyes are built and how visual information is processed in their brains is so fundamentally different [from] humans that is very difficult to conceptualize what the world actually looks like to them," Bok says.

Current Biology, Dellinger et al.: "A specialized bird pollination system involving a bellows mechanism for pollen transfer and staminal food body rewards."

http://www.eurekalert.org/pub_releases/2014-07/uosc-iod070314.php

Ironing out details of the carbon cycle

Dissolved iron in North Atlantic traced to sources

Iron is present in tiny concentrations in seawater. On the order of a few billionths of a gram in a liter. "I did a calculation once on a ton of ocean water," says Seth John, an assistant professor in the department of marine science at the University of South Carolina. "The amount of iron in that ton of water would weigh about as much as a single eyelash." Given that there is so little iron in seawater, one might conclude that its presence there is inconsequential.

Hardly. Iron is one of the essential elements of life. Found in enzymes like myoglobin and hemoglobin and cytochrome P450, iron is an essential cog in the biomachinery of every living cell. And its scarcity in the ocean, the earth's wellspring of life, only magnifies its importance.

"The key reason that everybody cares about iron is because it limits the growth of phytoplankton, such as algae, in maybe a fifth of the ocean," says John, a researcher in the School of Earth, Ocean and Environment in South Carolina's College of Arts and Sciences.

In those iron-poor places, there's plenty of everything else that phytoplankton, the base of the food web, need to grow - sunlight, carbon, fixed nitrogen, water. Just a small change in the amount of iron that finds its way there can have a dramatic impact on the growth of photosynthetic organisms and their concomitant uptake of carbon dioxide.

When algae and other phytoplankton grow, they take carbon dioxide out of the atmosphere, converting it into proteins and other carbon-based molecules that constitute living cells. And it takes very little iron to keep this process going - in a typical cell, for every atom of iron, there are about a million atoms of carbon, says John. A little iron goes a long way in allowing phytoplankton to grow and pull carbon dioxide out of the air. Knowing how iron moves into the oceans is thus crucial for scientists to fully understand the details of the carbon cycle on earth.

John and his colleagues have spent the past several years working to fill in those details. They've been collecting ocean samples and developing their analytical techniques for quantifying different natural isotopes of iron in seawater, which is one means of tracking the origins of the dissolved metal.

Iron finds its way into seawater from a variety of sources. The ratio of the stable natural isotopes iron-56 and iron-54 from these sources can differ from the ratio in the earth's crust because a number of chemical processes change the ratio by favoring the release of one of the two isotopes. The processes controlling release of iron from distinct sources vary, and so different sources can have characteristic iron-56/iron-54 ratios. Tiny variations in this ratio in seawater samples thus provide insight into the origin of the iron found there.

For example, one source is sediments from the ocean's floor, from which iron is typically released into the ocean under very low-oxygen (anoxic) conditions, and release of 'light' iron-54 is favored. Another source is dust from the atmosphere, from which Fe is typically released into the ocean with processes favoring 'heavy' iron-56. Using this information, the researchers were able to establish, for the first time, where dissolved iron in seawater had originated.

John and postdoctoral associate Tim Conway have developed a high-throughput means of purifying seawater samples and determining the iron-56/iron-54 ratio, a method capable of handling the nearly 600 samples they collected in a high-resolution transect of the north Atlantic Ocean on a GEOTRACES cruise.

From those samples, they were able to show in a paper published in the journal Nature that the largest source of iron in the north Atlantic, somewhere between 70 and 90 percent, comes from dust that blows in from the Sahara desert.

The results are helping define a very poorly understood but essential component of the carbon cycle.

"It could help us understand past climate change, like glacial-interglacial cycles," says John. "There would have been huge changes in dust fluxes to the ocean in glacial times, and so understanding how much iron comes from dust in the modern day helps us figure out whether that was an important driver of glacial-interglacial cycles."

The breakdown of the sources might surprise many, according to John and Conway.

"I think that a lot of people thought that there would be a lot of dust in the north Atlantic, and so while it's very satisfying to have proved that, it's perhaps more surprising that there's 20 percent that comes from other sources," says John. "I think before we published this paper, you would have found many, many people who would have guessed that that was zero percent or very close to zero percent."

"That's one interesting thing that the iron isotopes really show on the east margin," says Conway. "Off the coast of Africa you have really high iron, and in the past most people attributed that just to dust. We can show from the iron isotopes that there's actually iron coming from sediments.

"People have always argued whether it was dust or sediments. This is one of the first studies to really show clearly that sediments are important as well."

http://www.eurekalert.org/pub_releases/2014-07/uomh-cbb070314.php

Could boosting brain cells' appetites fight disease? New research shows promise

Univeristy of Michigan researcher & California colleagues show importance of autophagy in neurological disease -- and opportunity for new drugs

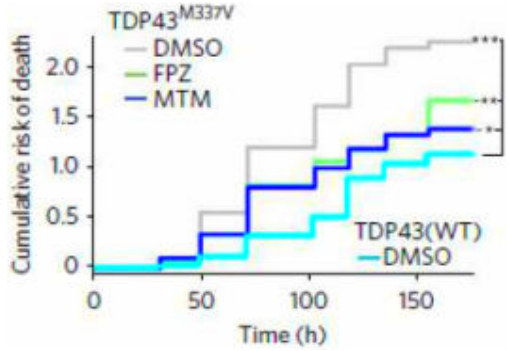
ANN ARBOR, Mich. - Deep inside the brains of people with dementia and Lou Gehrig's disease, globs of abnormal protein gum up the inner workings of brain cells – dooming them to an early death.

But boosting those cells' natural ability to clean up those clogs might hold the key to better treatment for such conditions.

That's the key finding of new research from a University of Michigan Medical School physician scientist and his colleagues in California and the United Kingdom. They reported their latest findings this week in the journal Nature Chemical Biology.

Though the team showed the effect worked in animals and human neurons from stem cells, not patients, their discoveries point the way to find new medicines that boost the protein-clearing cleanup process.

The work also shows how an innovative microscope technique can help researchers see what's going on inside brain cells, as they labor to clear out the protein buildup.



Two drugs that boost autophagy led to longer survival of neurons grown from stem cells derived from the cells of patients with ALS (middle two lines). **University of Michigan/Nature Chemical Biology**

The researchers focused on a crucial cell-cleaning process called autophagy – a hot topic in basic medical research these days, as scientists discover its important role in many conditions. In autophagy, cells bundle unwanted materials up, break them down and push the waste products out.

In the newly published research, the team showed how the self-cleaning capacity of some brain cells gets overwhelmed if the cells make too much of an abnormal protein called TDP43. The found that cells vary greatly in how quickly their autophagy capacity gets swamped.

But they also showed how three drugs that boost autophagy – speeding up the clean-out process – could keep the brain cells alive longer.

Longer-living, TDP43-clearing brain cells are theoretically what people with Lou Gehrig's disease (amyotrophic lateral sclerosis or ALS) and certain forms of dementia (called frontotemporal) need. But only further research will show for sure.

Sami Barmada, M.D., Ph.D., the U-M neurologist and scientist who is first author of the new study, says the new findings are encouraging – and so is the success of a microscope technique used in the research. His new lab, in the U-M Department of Neurology, is continuing to refine ways to view the inner workings of nerve cells.

"Using this new visualization technique, we could truly see how the protein was being cleared, and therefore which compounds could enhance the pace of clearance and shorten the half-life of TDP43 inside cells," he says. "This allowed us to see that increased autophagy was directly related to improved cell survival."

Barmada worked on the team at the Gladstone Institutes and the University of California San Francisco headed by Steven Finkbeiner, M.D., Ph.D., that published the new findings. The team used stem cells derived from the cells of people who have ALS to grow neurons and astrocytes – the two types of brain cell most crucial to normal brain function.

Because he both sees patients in clinic and studies neurological disease in the laboratory, Barmada brings a special perspective to the research.

At U-M, he specializes in treating patients who have neurological diseases that affect both thinking and muscle control. About a third of ALS patients develop signs of frontotemporal dementia, also called FTD – and about 10 percent of people with FTD also have a motor neuron disease that affects their brain's ability to control muscle movement.

One of the drugs tested in the study, an antipsychotic drug developed in the 1960s to treat people with schizophrenia, had actually shown some anti-dementia promise in human ALS patients, but comes with many side effects. Barmada notes that Finkbeiner's team at the Gladstone Institute is already working to identify other compounds that could produce the effect with fewer side effects.

Interestingly, small studies have suggested that people with schizophrenia who take antipsychotic drugs are much less likely to develop ALS.

Barmada's work at U-M now focuses on the connection between brain cells' ability to clear abnormal proteins. He also studies the cells' regulation of RNA molecules created as part of expressing protein-encoding genes. Looking further upstream in the protein-producing process could yield further clues to why disease develops and what can be done about it, he says.

The research was sponsored by Barmada's National Institutes of Neurological Disorders and Stroke grant NS072233, as well as Finkbeiner's grants (NS039074, NS083390, NS081844 and NS07837), by the ALS Association, the Robert Packard Center for ALS Research, the William H. Adams Foundation, and Target ALS. In addition to Barmada and Finkbeiner, the research team included Andrey Tsvetkov, Arpana Arjun, Andreas Serio, and Siddharthan Chandran, as well as others.

Barmada also receives funding from the U-M Medical School's Protein Folding Disorders Initiative, part of the school's Fast Forward Strategic Research Initiative.

Reference: Nature Chemical Biology (2014) doi:10.1038/nchembio.1563

http://bit.ly/1q7mSt1

Ability to Adapt Gave Early Humans the Edge Over Other Hominins

Features thought to be characteristic of early* Homo *lineages actually evolved before* Homo *arose. Rather, our flexible nature defines us

By Mohi Kumar

From the cold Arctic to the sweltering Sahara, from the high Himalayas to the deep reaches of the Amazon, humans are everywhere. Our ability to adapt and even thrive in a variety of environments is one of the hallmarks of our species.

Skulls of the genus* Homo*, including two from* Homo erectus *on the right **(Chip Clark, Smithsonian Human Origins Program/Guram Bumbiashvili, Georgian National Museum)**

In fact, adaptability might be THE defining characteristic of our broader genus, *Homo*. According to new research published in *Science*, the ability of early humans to adjust to wild climate fluctuations likely enabled them to diversify, differentiate, and spread out of Africa 1.85 million years ago.

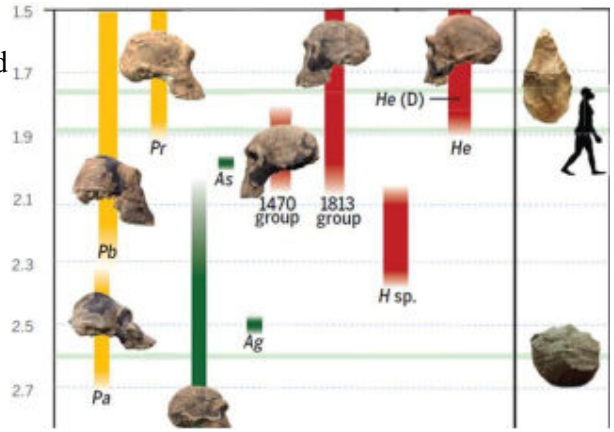
Before this study, prevailing scientific thought generally held that several traits - large brains, long legs, the ability to make tools, a prolonged time before juveniles mature into adults - all evolved together as a package between 2.4 and 1.8 million years ago. This collection of traits, scientists thought, separated the *Homo* genus from other hominins, such as *Australopithecus* or *Ardipithecus*, and arose when the Earth's climate became cooler and drier and the African grasslands expanded in range.

However, a close examination of how early hominin fossils correlate with the emergence of certain behaviors seems to show otherwise. Many of the traits thought to make up this *Homo* package evolved independently, and some not even

in *Homo* species at all. For example, "the origin of stone tool making doesn't correlate to anything regarding the origins of the genus *Homo*," says coauthor Richard Potts, a paleoanthropologist and director of Smithsonian's Human Origins Program.

Further, some features once considered characteristic to members of early *Homo* lineages, such as long hind limbs, can be found in *Australopithecus* species - hominins that existed before the earliest *Homo* walked the earth. *Australopithecus* died out around 2 million years ago.

Tracking the origins of *Homo's* supposedly defining traits involved a thorough review of fossils from three hominin groups - *Paranthropus, Australopithecus,* and *Homo*. Researchers paid careful attention to when these groups and the species within them emerged and died out.



Hominin evolution from 3.0 million to 1.5 million years ago. Green: *Australopithecus*, Yellow: *Paranthropus*, Red: *Homo*. The icons indicate from the bottom the first appearance of stone tools at ~2.6 million years ago, the dispersal of *Homo* to Eurasia at ~1.85 million years ago, and the appearance of stone axes at ~1.76 million years ago. The cultural milestones do not correlate with the known first appearances of any of the currently recognized *Homo* specimens. (Courtesy of Antón, Potts and Aiello/*Science*)

Scientists can tell different species apart "based on differences in the shape of their skulls, especially their face and jaws," explains Susan Antón, a professor of anthropology at New York University and the paper's lead author. These differences persist over hundreds of thousands of years in the fossil record, defining distinct species.

With the fossil record for hominins divvied up into genera and species, the next step was to date when the species had lived. In the East African Rift Valley, determining the age of a fossil can be done rather reliably. Sediments surrounding fossil finds contain ash and pumice from volcanic eruptions - minerals in this ash and pumice can be dated using radioisotopes.

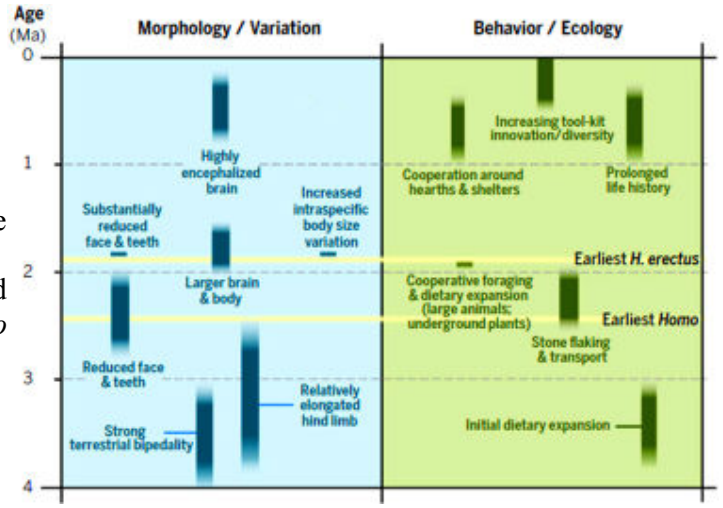
With the dates of the fossils established, what's left was to pinpoint the age of the emergence of different behaviors. Figuring out when *Homo* migrated out of Africa is easy enough and can be done by dating fossils found in Eurasia. Early stone tools and hand axes found in East Africa can also be dated according to the minerals in the sediments that surround them.

Some traits, however, are more difficult to date. The ability to walk upright over long distances required the scientists to look at the fossils themselves. "We know where the muscles attached based on fossil bones; we can measure the cross-sectional area of the thigh bones and look at the mechanical properties of the pelvises that occur in the fossil records," Potts explains.

Matching those findings to the fact that, as Potts notes, "animals that have elongated legs have greater strides and greater efficiency in locomotion," allowed the scientists to estimate when long-distance walking emerged.

What results from these analyses is the realization that there is no simple, clear picture; no obvious mechanism as to why the genus we know as *Homo* came to arise and dominate. What we've long thought of as a coherent picture - the package of traits that make *Homo* species special - actually formed slowly over time. Stone tools first started appearing around 2.6 million years ago. *Homo* species left Africa 1.85 million years ago. Stone axes started to be used around 1.76 million years ago.

And by at least 3 million years ago, *Australopithecus* developed elongated limbs and the ability to traverse long distances. In fact, a similarly close look at other traits thought to be associated with the origin of *Homo* shows that they are similarly scattered through time, and not necessarily unique to early humans.



***Evolutionary timeline of important anatomical, behavioral and life history characteristics that were once thought to be associated with the origin of the genus Homo or earliest H. erectus.* (Antón et al., Science/AAAS 2014)**

So what could have propelled our earliest ancestors to change? According to a detailed climate model of the past that was refined by the authors, the *Homo* lineage did not originate during a calm, cool, stable climate period as previously thought. Rather, East Africa at the time was dynamic, with "fluctuating moisture and aridity, [and] shifting resource regimes," the authors write.

That early *Homo* species would have had to cope with this constantly-changing climate fits with the idea that it was not our hands, nor our gait, nor our tools that made us special. Rather, it was our adaptability.

Unstable climate conditions not only "favored the evolution of the roots of human flexibility in our ancestors," explains Potts. "The origin of our human genus is characterized by early forms of adaptability. There's a phasing of evolutionary innovations over time, and many evolved traits are not unique to the genus *Homo* even if the entire package is unique to *Homo sapiens."*

http://bit.ly/1obsIa0

Magnetic bubble may give space probes a soft landing

PARACHUTES made of plasma trapped in a magnetic field could soon be helping space probes glide safely back to Earth.

03 July 2014 by Robin Hague

Two private aerospace companies have won NASA contracts to demonstrate magnetoshell aerocapture, a way of shrouding a falling spacecraft in a magnetic bubble akin to the plasma shield around Earth. But whereas Earth's magnetosphere protects it from solar radiation, a similar bubble around a spacecraft creates drag, slowing it down. If a test next year proves successful, the technique could help future probes land heavy loads on Mars or bring back human missions to deep space.

"I'm really excited about these awards that have been made," says Michelle Munk at NASA's Space Technology Mission Directorate in Hampton, Virginia. "It's a low-cost way to investigate these kinds of things and see if they will bear fruit."

When a spacecraft enters a planet's atmosphere, it ploughs into air molecules at high speed, creating intense heat. Structures designed to create drag can slow the descent, but probes must also rely on heat shieldsMovie Camera that either burn away or insulate to protect the cargo inside. The heavier the payload, the more challenging the task of getting the craft down in one piece.

For larger landers, NASA has been looking at lightweight technologies such as an inflatable "flying saucer" for Mars missions, tested last week over Hawaii (see 'Flying saucer' makes a splash). Magnetoshell aerocapture is one of the most revolutionary ideas, says Munk. It not only slows a craft's descent but can also greatly reduce heating.

Last month, aerospace firm MSNW of Redmond, Washington, won a NASA grant to demonstrate the technique on a CubeSat. The small, boxy satellite should be delivered to the International Space Station in 2015. It will then be deployed and attempt to enter Earth's atmosphere without burning up.

The satellite will carry a copper coil, powered by a lithium-ion battery, that generates a magnetic field around the probe. As it descends, the spacecraft will eject a small amount of plasma. This gets trapped in the magnetic field, creating a protective bubble that stops air molecules colliding with the craft and producing heat.

The air molecules flow into the plasma bubble and absorb electrons from it, becoming ionised. The newly ionised air becomes trapped in the magnetic field, and the craft ends up dragging a patch of atmosphere with it, effectively creating a parachute of gas.

The CubeSat's magnetoshell aerocapture system will be built by Altius Space Machines of Louisville, Colorado. NASA awarded it a contract to develop such systems, which will feature an external magnetic coil up to 5 metres across. These could be used on larger landers, including human missions to deep space that need to return to Earth, says Altius's Jonathan Goff.

The system has hefty power requirements that will strain the limits of any battery the CubeSat could carry, says Goff. But if the test succeeds, it could also boost efforts to make rockets reusable, allowing parts discarded in orbit to return to Earth intact, he says. "Basically it's a way of moving beyond the Apollo throwaway philosophy."

http://www.wired.com/2014/07/chimpanzee-bonobo-gestures/

Scientists Translate Chimpanzee and Bonobo Gestures That Resemble Human Language

Scientists have described the communications of chimpanzees and bonobos in new and unsurpassed detail, offering a lexicon for our closest living relatives and even a glimpse into the origins of human language.

By Brandon Keim

The research, contained in two new studies published July 3 in Current Biology, focuses on physical gestures. These are the primary form of communication in bonobos and chimps, used more readily than vocalizations.

One study describes how a certain bonobo gesture conveys an informational complexity not previously observed in non-human great apes. The other study identifies the meanings of no fewer than 36 chimpanzee gestures.

"What we've shown is a very rich system of many different meanings," said primatologist Richard Byrne of Scotland's University of St. Andrews, co-author of the chimpanzee study. "We have the closest thing to human language that you can see in nature."

Byrne's co-author, fellow University of St. Andrews primatologist Catherine Hobaiter, spent 18 months observing a group of chimpanzees in the Budongo Forest Reserve in western Kenya. Hobaiter painstakingly documented more than 4,500 gestures in 3,400 incidents of chimp-to-chimp gesturing, noting both the motions used and the responses of nearby chimps.

Subsequent statistical analysis boiled those observations down to 36 established gestures and 15 clear-cut meanings. (Multiple gestures are sometimes used for the same purpose, perhaps conveying some not-yet-understood nuance.) Stomping two feet, for example, is used to initiate play. Reaching means, "I want that," and an air-hug embrace is a request for contact.

The latter two gestures can be seen in the video below, in which a young female chimp named Rafia asks for a leaf sponge, which chimps use to drink. Rebuffed by her older sister and another adult female, she throws a tantrum, then ignores her mother's request for a hug.

The gestures aren't quite so flexible as human language, which can be repurposed to describe a vast range of situations and intentions. Neither do they possess syntactical rules of word order or sentence structure.

Nevertheless, it's a marvelously rich system of communication. It also lends support to the notion that human language didn't evolve from scratch over the last few million years, but is rooted in cognitive capacities and gestural proclivities that run deep in our primate family.

The other new study, co-authored by primatologists Emilie Genty and Klaus Zuberbühler of Switzerland's University of Neuchâtel, follows on that theme, though with a focus on a single bonobo gesture: stretching an arm towards another bonobo, sweeping it inwards, then finishing with a wrist-twirl that turns a downward-facing palm upwards.

Bonobos are famous for their pleasure-seeking proclivities - they have lots of sex - and, perhaps not surprisingly, the gesture is used in that context, as an invitation to sex in a more secluded place. But what makes the gesture special, report Genty and Zuberbühler, is its so-called semantic content, the compound meanings conveyed by the gesture's constituent actions.

The inwards sweep indicates the gesture's object, and the hand-turn symbolizes the path to a private spot. The gesture is typically followed by a body-turn towards towards the intended path; the signaler then look backs, checking whether the message was received.

That degree of informational richness is very much a part of human language, but hadn't before been observed in other great apes, said Genty. "There has so far been a lack of good evidence for semantic content in ape gestures and vocalizations," she said. "But that doesn't mean it is absent."

Genty hopes to find more such examples in bonobos, as do Hobaiter and Byrne in chimpanzees. Hobaiter is also curious whether, just as different chimpanzees groups frequently use tools in different ways, there might also be gestural dialects. Ultimately, said Hobaiter, it may be possible to combine information about gestures, facial expressions and vocal calls into an even more comprehensive chimp lexicon.

One limitation of the researchers' approach is that it can only identify gestures that provoke an action. Those that convey something more subtle - two chimps talking about the weather, for example, or reminiscing about the good old days - can't now be interpreted. Whether such conversations occur is an open question.

"I have the impression that there were some meanings we couldn't capture," Hobaiter said. Sometimes, she recalled, a chimpanzee would gesture to another, then appear satisfied, though nothing else seemed to happen. Said Hobaiter, "I'd love to know what was going on!"

http://bit.ly/1rBNmGS

Study links disposing of wastewater to Oklahoma earthquakes

The dramatic increase in earthquakes in central Oklahoma since 2009 is likely attributable to subsurface wastewater injection at just a handful of disposal wells, finds a new study to be published in the journal Science on July 3, 2014.

The research team was led by Katie Keranen, professor of geophysics at Cornell University, who says Oklahoma earthquakes constitute nearly half of all central and eastern U.S. seismicity from 2008 to 2013, many occurring in areas of high-rate water disposal.

"Induced seismicity is one of the primary challenges for expanded shale gas and unconventional hydrocarbon development. Our results provide insight into the process by which the earthquakes are induced and suggest that adherence to standard best practices may substantially reduce the risk of inducing seismicity," said Keranen. "The best practices include avoiding wastewater disposal near major faults and the use of appropriate monitoring and mitigation strategies."

The study also concluded:

Four of the highest-volume disposal wells in Oklahoma (~0.05% of wells) are capable of triggering ~20% of recent central U.S. earthquakes in a swarm covering nearly 2,000 square kilometers, as shown by analysis of modeled pore pressure increase at relocated earthquake hypocenters.

Earthquakes are induced at distances over 30 km from the disposal wells. These distances are far beyond existing criteria of 5 km from the well for diagnosis of induced earthquakes.

The area of increased pressure related to these wells continually expands, increasing the probability of encountering a larger fault and thus increasing the risk of triggering a higher-magnitude earthquake.

"Earthquake and subsurface pressure monitoring should be routinely conducted in regions of wastewater disposal and all data from those should be publicly accessible. This should also include detailed monitoring and reporting of pumping volumes and pressures," said Keranen. 'In many states the data are more difficult to

obtain than for Oklahoma; databases should be standardized nationally. Independent quality assurance checks would increase confidence. "

More information: *Sharp increase in central Oklahoma seismicity since 2008 induced by massive wastewater injection," by K.M. Keranen, Science, 2014.*
www.sciencemag.org/lookup/doi/... 1126/science.1255802

http://phys.org/news/2014-07-cancer-immunotherapy-dogs.html

First cancer immunotherapy for dogs developed

Nearly every second dog develops cancer from the age of ten years onward. A few therapies derived from human medicine are available for dogs.

A very successful form of therapy by which antibodies inhibit tumor growth has not been available for animals so far. Scientists at the inter-university Messerli Research Institute of the Vetmeduni Vienna, the Medical University of Vienna, and the University of Vienna have developed, for the first time, antibodies to treat cancer in dogs. The scientists published their research data in the journal *Molecular Cancer Therapeutics*.

As in humans, cancers in dogs have complex causes. The interaction of the environment, food, and genetic disposition are the most well known factors. Today nearly all methods of human medicine are basically available for dogs with cancer, but this was not true of cancer immunotherapy so far.

So-called cancer immunotherapy - which is the treatment of tumors by the use of antibodies - has been established and used very successfully in human medicine for about 20 years.

Since cancer cells bear very specific antigens on the surface, the corresponding antibodies bind to these molecules and thus inhibit tumor growth. The mechanism that becomes effective is a destructive signal sent by the antibody to the inside of the cancer cell and initiates its death.

In a second mechanism, the immune system of the patient also destroys the "marked" tumor in a more efficient way.

The target is nearly identical in humans and dogs

Josef Singer and Judith Fazekas, both lead authors of the study, discovered that a receptor frequently found on human tumor cells (epidermal growth factor receptor or EGFR) is nearly 100 percent identical with the EGF receptor in dogs. In human medicine EGFR is frequently used as the target of cancer immunotherapy because many cancer cells bear this receptor on their surface.

The so-called anti-EGFR antibody binds to cancer cells and thus triggers the destruction of the cells. "Due to the high similarity of the receptor in humans and dogs, this type of therapy should work well in dogs too," the scientists say. The binding site of the antibody to EGFR in man and dogs differs only in respect of four amino acids.

Antibody trimmed to "dog"

To ensure best possible binding of the antibody to cancer cells in dogs, the human antibody had to be trimmed to "dog" in the laboratory. In human medicine this process is known as the "humanization" of an antibody.

The antibody originally produced in the mouse has to be adjusted to the species for which it is used. Singer and Fazekas replaced the corresponding elements in the "humanized" antibody with elements from the dog. In experiments on dog cancer cells in the laboratory it was found that the newly developed antibodies did, in fact, bind to canine cancer cells with greater specificity.

The head of the study, Professor Erika Jensen-Jarolim, explains as follows: "We expect dogs to tolerate these anti-cancer antibodies well. This will be investigated in clinical studies in the future and is expected to greatly improve the treatment as well as the diagnosis of cancer in dogs."

Improvement of diagnosis

The newly developed antibody provides an additional benefit for dogs. As in human medicine, antibodies can be coupled with signal molecules. When the antibody binds to a cancer cell in the organism, the coupled antibody - in this case a radioactive isotope - can be rendered visible and is thus able to show where tumors and even metastases are located. When the selected isotope also contributes to the decay of cancer cells, the approach is known as "theranostics" (therapy and diagnostics).

"The Veterinary Medical University, Vienna will be the first center in the world to offer the most modern immunological cancer diagnosis procedure for dogs. Of special interest to me as a doctor of human medicine is the fact that, by using this approach, we will be able to initiate improvements that will benefit humans as well," says Jensen-Jarolim.

The first anti-EGFR antibody (cetuximab) for cancer treatment in human medicine was developed by the company Merck. In humans it is primarily used for the treatment of bowel cancer.

Cancer immunotherapy is mainly applied in combination with chemotherapy and radiotherapy. In veterinary medicine, immunotherapy will be employed for the treatment of mammary ridge cancer (milk line cancer) in dogs. It may also be used as part of a combination therapy.

More information: *The article "Generation of a Canine Anti-EGFR (ErbB-1) Antibody for Passive Immunotherapy in Dog Cancer Patients", by Josef Singer, Judit Fazekas, Wei Wang, Marlene Weichselbaumer, Miroslawa Matz, Alexander Mader, Willibald Steinfellner, Sarah Meitz, Diana Mechtcheriakova, Yuri Sobanov, Michael Willmann, Thomas Stockner, Edzard Spillner, Renate Kunert and Erika Jensen-Jarolim was published in the Journal Molecular Cancer Therapeutics. DOI: 10.1158/1535-7163.MCT-13-0288*

http://bit.ly/1m5tsB3

Stopping harmful climate change is surprisingly cheap

by Fred Pearce

Saving our skins might be surprisingly cheap. To avoid dangerous climate change, the world needs to boost spending on green energy by $1 trillion a year.

That sounds scarily large, but we could cover a lot of it using the subsidies currently handed to fossil fuels.

Governments have agreed to limit global warming to 2°C, because more than that may be impossible to adapt to. "We need to drastically transform our energy system," says David McCollum of the International Institute for Applied Systems Analysis in Laxenburg, Austria. "It is high time we thought about how much capital is needed."

McCollum's team plugged that gap by analysing six different models that combine data on greenhouse gas emissions, energy scenarios and investment costs.

The numbers work like this. Investment in low-carbon energy is currently $200 billion a year. But that isn't enough. For a 70 per cent chance of keeping below 2°C, the investment will have to rise to $1.2 trillion a year.

Move the subsidies

Spending is set to rise as energy demand increases and governments meet their existing climate commitments. The world is probably already committed to doubling green energy investment to $400 billion a year by 2050, says McCollum. But even with that, we still need to find another $800 billion a year.

That sounds like a lot to make up. But global investment in energy is already $1 trillion a year and rising, says McCollum. The problem is that much of that investment goes to fossil fuels. According to the International Energy Agency, government subsidies for fossil fuels are around $500 billion a year – six times more than subsidies for renewables.

"The magnitude of the clean-energy investment challenge is roughly similar to today's fossil-fuel subsidies," says McCollum. So if we used the subsidies for coal, oil and natural gas to invest in solar, wind and nuclear energy, global warming would be close to being solved.

It is "a very good analysis", says Niklas Höhne of Ecofys, a think tank in Utrecht, the Netherlands. He says the $1.2 trillion bill looks like good value for money. Besides, "investments have a return, so they may not represent a burden at all. They can be quite profitable. The burden is really an opportunity."

What is inescapable is that time is short, because most energy infrastructure has a lifetime of 30 to 60 years. "Unless the [clean energy investment] gap is filled rather quickly, the 2°C target could potentially become out of reach," says McCollum.

Journal reference: *Climate Change Economics, DOI: 10.1142/S2010007813400101*

http://www.eurekalert.org/pub_releases/2014-07/tl-tln070314.php

The Lancet: New trial suggests cheaper drugs for common heart attack procedure could improve outcomes and save health budgets millions

A new study published in The Lancet compares outcomes for two drugs used to prevent blood clot formation during emergency heart attack treatment.

The study suggests that use of one of the drugs, heparin, could result in improved outcomes (such as a reduced rate of repeat heart attacks), compared to the other drug tested, bivalirudin, which is in widespread use in high-income countries, and is around 400 times more expensive than heparin.

The results of the HEAT-PPCI trial suggest that systematic use of heparin rather than bivalirudin after primary percutaneous coronary intervention (PPCI) – the most commonly used treatment for heart attack, which unblocks the arteries carrying blood to the heart – could save health services substantial sums of money, at the same time as potentially improving patient outcomes.

Patients who undergo PPCI usually receive a combination of antithrombotic drugs to prevent any further blood clots forming during the procedure and after it has been completed. The most commonly used antithrombotic drugs are unfractionated heparin and bivalirudin, and although several previous trials have compared the two drugs, the evidence is unclear as to which drug results in better outcomes.

The trial took place at the Liverpool Heart and Chest Hospital in the UK, where 1829 patients undergoing emergency angiography (an x-ray examination of the heart's arteries after a suspected heart attack) were recruited to the trial. More than four fifths of these patients then went on to receive PPCI; approximately half received heparin, and half received bivalirudin. Researchers then recorded how many patients in both groups experienced a major adverse cardiac event, such as death or another heart attack, within 28 days after surgery.

The results show that overall rates of major adverse cardiac events were significantly lower in the group who received heparin, although the rates of adverse events were low, as expected, in both groups. Within 28 days after surgery, 46 patients (5•1%) in the bivalirudin group died, compared to 39 (4•3%) of patients in the heparin group; 24 patients (2•7%) in the bivalirudin group had another heart attack in the same period, compared to 7 patients (0•8%) in the heparin group. Although bleeding complications are an acknowledged risk of antithrombotic drugs, there was no significant difference between the groups in the rate of complications.

According to lead author Dr Rod Stables, of the Liverpool Heart and Chest Hospital NHS Foundation Trust, UK, "As far as we are aware, our study is one of the first trials to recruit 100% of eligible patients presenting with the medical

condition being examined, which means that it more closely resembles real life practice than many previous trials. The results suggest that the use of heparin has some advantage over bivalirudin in avoiding major adverse events, mainly in terms of reduced recurrent, additional heart attacks in patients recovering from PPCI. This finding might provide an opportunity, rare in modern health care, to provide improved outcomes at much reduced cost."*

In a linked Comment, Peter Berger and James Blankenship of Geisinger Health System, in Pennsylvania, USA, point out that the although the study has a number of limitations – including an open-label, single-centre design – the study has the advantage of closely resembling actual clinical practice, and including many patients who would have been excluded from earlier trials comparing the two drugs. They write that, "Even if heparin alone had produced statistically similar outcomes to bivalirudin, it would have been a win for heparin. A drug that costs less than a 1/400th of another that has similar efficacy and safety ought to be used preferentially."

The design of the HEAT-PPCI trial has attracted some criticism within the medical community because of its use of delayed consent: patients provided their consent to participate only after they had been given either heparin or bivalirudin, leading some doctors to raise concerns that the trial design did not conform to medical ethics standards.

However, in a second linked Comment, David Shaw, of the Institute for Biomedical Ethics in Basel, Switzerland, disputes these criticisms, writing that, "In this context, the strategy was preferable to attempting to obtain consent from potentially incompetent patients needing extremely urgent cardiac treatment… In routine clinical care, it would be perfectly normal for a doctor to choose either heparin or bivalirudin without involvement of the patient in the decision."

"Informed consent for percutaneous coronary intervention is frequently not sought at all; why patients should be asked to consent in advance to formal randomisation of a drug used in the intervention is thus unclear. It would have been unethical to have done the study differently. Attempting to get consent from patients would have increased the risk of harming them by delaying treatment, and could also have affected recruitment."