http://www.eurekalert.org/pub_releases/2013-05/uom-lef051613.php

Leading explanations for whooping cough's resurgence don't stand up to scrutiny

Whooping cough has exploded in the United States and some other developed countries in recent decades, and many experts suspect ineffective childhood vaccines for the alarming resurgence.

ANN ARBOR - Some say the vaccine wears off quicker than public health officials had previously believed. Others suggest that the vaccine protects against illness but does not prevent transmission of the bacterial disease, which is also known as pertussis.

But a University of Michigan-led research team has concluded that neither of these proposed mechanisms for the resurgence of pertussis is supported by the best available evidence. In a study that reviewed 30 years of data from Thailand, they found that vaccines provided long-lived - possibly lifelong - protection against the disease and substantially reduced transmission, as well.

"What we found goes against much of what is currently suspected about pertussis resurgence," said U-M population ecologist and epidemiologist Pejman Rohani. "It's not difficult for us epidemiologists to propose some possible mechanism behind the resurgence, but what's been missing so far is an effort to challenge each of these hypotheses to explain the data. That's exactly what we did."

A paper summarizing the team's findings is scheduled for online publication in the journal Proceedings of the National Academy of Sciences on May 20. The lead author is Julie Blackwood, a postdoctoral research associate in Rohani's lab at the U-M Department of Ecology and Evolutionary Biology.

Thailand was selected as the study site largely because a unique high-resolution dataset of pertussis incidence - including monthly case notifications from 72 provinces between 1981 and 2000 - was obtained from that country's Ministry of Public Health. Equally detailed U.S. incidence data are not available from the federal Centers for Disease Control and Prevention, Rohani said.

The researchers expressed several of the leading hypotheses for the resurgence of pertussis in mathematical terms, then used statistical methods to test how well each of these transmission models explained the Thai data. The best fit came from a model that assumed lifelong immunity following either vaccination or naturally acquired infection.

The researchers found no evidence for a pertussis resurgence in Thailand. In fact, their findings highlighted the success of the country's childhood immunization program, pointing to a vaccine-induced increase in "herd immunity," a reduction in the probability of infection that occurs in a population as the number of immune individuals increases.

"We found very few cases overall, and especially in infants," Blackwood said. "So the big underlying finding is that the vaccine is adequately protecting infants from contracting the infection."

The situation with pertussis in Thailand cannot be directly compared with trends in the U.S. for many reasons, including the fact that the two countries use different types of whooping cough vaccine. Thailand mainly uses what's called a whole-cell vaccine, while an acellular vaccine is used in the U.S. In addition, the vaccination schedule in the two countries differs slightly.

Pertussis is a highly infectious respiratory disease that is responsible for nearly 300,000 deaths worldwide annually, primarily among infants in developing countries. In infants, it causes violent, gasping coughing spells.

The U-M-led Thailand study was funded in part by a $1.7 million, five-year National Institutes of Health grant awarded to Rohani and U-M's Aaron King last year. The grant funds efforts to explain the changing patterns of whooping cough outbreaks by using long-term incidence reports from several countries, along with mathematical models of pertussis transmission and statistical methods for extracting information from data.

Funding for the Thailand project was also provided by the U.S. Department of Homeland Security and the Bill and Melinda Gates Vaccine Modeling Initiative. Co-authors of the PNAS paper are Derek A.T. Cummings of Johns Hopkins University, Helene Broutin of the Centre National de la Recherche Scientifique in France and Sopon Iamsirithaworn of Thailand's Ministry of Public Health.

http://www.eurekalert.org/pub_releases/2013-05/osu-tci052013.php

The compound in the Mediterranean diet that makes cancer cells 'mortal'

Scientists design 'fishing' technique to show how foods improve health

COLUMBUS, Ohio – New research suggests that a compound abundant in the Mediterranean diet takes away cancer cells' "superpower" to escape death. By altering a very specific step in gene regulation, this compound essentially re-educates cancer cells into normal cells that die as scheduled.

One way that cancer cells thrive is by inhibiting a process that would cause them to die on a regular cycle that is subject to strict programming. This study in cells, led by Ohio State University researchers, found that a compound in certain plant-based foods, called apigenin, could stop breast cancer cells from inhibiting their own death.

Much of what is known about the health benefits of nutrients is based on epidemiological studies that show strong positive relationships between eating specific foods and better health outcomes, especially reduced heart disease. But how the actual molecules within these healthful foods work in the body is still a mystery in many cases, and particularly with foods linked to lower risk for cancer.
Parsley, celery and chamomile tea are the most common sources of apigenin, but it is found in many fruits and vegetables.
The researchers also showed in this work that apigenin binds with an estimated 160 proteins in the human body, suggesting that other nutrients linked to health benefits – called "nutraceuticals" – might have similar far-reaching effects. In contrast, most pharmaceutical drugs target a single molecule.
"We know we need to eat healthfully, but in most cases we don't know the actual mechanistic reasons for why we need to do that," said Andrea Doseff, associate professor of internal medicine and molecular genetics at Ohio State and a co-lead author of the study. "We see here that the beneficial effect on health is attributed to this dietary nutrient affecting many proteins. In its relationship with a set of specific proteins, apigenin re-establishes the normal profile in cancer cells. We think this can have great value clinically as a potential cancer-prevention strategy."
Doseff oversaw this work with co-lead author Erich Grotewold, professor of molecular genetics and director of Ohio State's Center for Applied Plant Sciences (CAPS). The two collaborate on studying the genomics of apigenin and other flavonoids, a family of plant compounds that are believed to prevent disease.
The research appears this week in the online early edition of the journal Proceedings of the National Academy of Sciences.
Though finding that apigenin can influence cancer cell behavior was an important outcome of the work, Grotewold and Doseff point to their new biomedical research technique as a transformative contribution to nutraceutical research.
They likened the technique to "fishing" for the human proteins in cells that interact with small molecules available in the diet.
"You can imagine all the potentially affected proteins as tiny fishes in a big bowl. We introduce this molecule to the bowl and effectively lure only the truly affected proteins based on structural characteristics that form an attraction," Doseff said. "We know this is a real partnership because we can see that the proteins and apigenin bind to each other."
Through additional experimentation, the team established that apigenin had relationships with proteins that have three specific functions. Among the most important was a protein called hnRNPA2.
This protein influences the activity of messenger RNA, or mRNA, which contains the instructions needed to produce a specific protein. The production of mRNA results from the splicing, or modification, of RNA that occurs as part of gene activation. The nature of the splice ultimately influences which protein instructions the mRNA contains.
Doseff noted that abnormal splicing is the culprit in an estimated 80 percent of all cancers. In cancer cells, two types of splicing occur when only one would take place in a normal cell – a trick on the cancer cells' part to keep them alive and reproducing.
In this study, the researchers observed that apigenin's connection to the hnRNPA2 protein restored this single-splice characteristic to breast cancer cells, suggesting that when splicing is normal, cells die in a programmed way, or become more sensitive to chemotherapeutic drugs.
"So by applying this nutrient, we can activate that killing machinery. The nutrient eliminated the splicing form that inhibited cell death," said Doseff, also an investigator in Ohio State's Davis Heart and Lung Research Institute. "Thus, this suggests that when we eat healthfully, we are actually promoting more normal splice forms inside the cells in our bodies."
The beneficial effects of nutraceuticals are not limited to cancer, as the investigators previously showed that apigenin has anti-inflammatory activities.
The scientists noted that with its multiple cellular targets, apigenin potentially offers a variety of additional benefits that may even occur over time. "The nutrient is targeting many players, and by doing that, you get an overall synergy of the effect," Grotewold explained.
Doseff is leading a study in mice, testing whether food modified to contain proper doses of this nutrient can change splicing forms in the animals' cells and produce an anti-cancer effect.
Additional co-authors are first author Daniel Arango, a Ph.D. student in the Molecular, Cellular and Developmental Biology graduate program; and Kengo Morohashi, Alper Yilmaz, Arti Parihar and undergraduate Bledi Brahimaj of the Department of Molecular Genetics, all at Ohio State; and Kouji Kuramochi of Kyoto Prefectural University in Japan. Doseff, Arango and Parihar are affiliated with Ohio State's Division of Pulmonary, Allergy, Critical Care and Sleep Medicine.

http://www.eurekalert.org/pub_releases/2013-05/afps-ssh052013.php

Study shows how bilinguals switch between languages

Individuals who learn two languages at an early age seem to switch back and forth between separate "sound systems" for each language, according to new research conducted at the University of Arizona.

The research, to be published in a forthcoming issue of Psychological Science, a journal of the Association for Psychological Science, addresses enduring questions in bilingual studies about how bilingual speakers hear and process sound in two different languages.

"A lot of research has shown that bilinguals are pretty good at accommodating speech variation across languages, but there's been a debate as to how," said lead author Kalim Gonzales, a psychology doctoral student at the University of Arizona. "There are two views: One is that bilinguals have different processing modes for their two languages - they have a mode for processing speech in one language and then a mode for processing speech in the other language. Another view is that bilinguals just adjust to speech variation by recalibrating to the unique acoustic properties of each language."

Gonzales's research supports the first view - that bilinguals who learn two languages early in life learn two separate processing modes, or "sound systems."

The study looked at 32 Spanish-English early bilinguals, who had learned their second language before age 8. Participants were presented with a series of pseudo-words beginning with a 'pa' or a 'ba' sound and asked to identify which of the two sounds they heard.

While 'pa' and 'ba' sounds exist in both English and Spanish, how those sounds are produced and perceived in the two languages varies subtly. In the case of 'ba,' for example, English speakers typically begin to vibrate their vocal chords the moment they open their lips, while Spanish speakers begin vocal chord vibration slightly before they open their lips and produce 'pa' in a manner similar to English 'ba.' As a result of those subtle differences, English-only speakers might, in some cases, confuse the 'ba' and 'pa' sounds they hear in Spanish, explains co-author Andrew Lotto, associate professor of speech, language and hearing sciences at the University of Arizona.

"When most people think about differences between languages, they think they use different words and they have different grammars, but at their base languages use different sounds," Lotto said.

"One of the reasons it sounds different when you hear someone speaking a different language is because the actual sounds they use are different; they have a sound code that's specific to that language," he said. "One of the reasons someone might sound like they have an accent if they learn Spanish first is because their 'pa' is like an English 'ba,' so when they say a word with 'pa,' it will sound like a 'ba' to an English monolingual."

For the study, the bilingual participants were divided into two groups. One group was told they would be hearing rare words in Spanish, while the other was told they would be hearing rare words in English. Both groups heard audio recordings of variations of the same two words - bafri and pafri - which are not real words in either language.

Participants were then asked to identify whether the words they heard began with a 'ba' or a 'pa' sound.

Each group heard the same series of words, but for the group told they were hearing Spanish, the ends of the words were pronounced slightly differently, with the 'r' getting a Spanish pronunciation.

The findings: Participants perceived 'ba' and 'pa' sounds differently depending on whether they were told they were hearing Spanish words, with the Spanish pronunciation of 'r,' or whether they were told they were hearing English words, with the English pronunciation of 'r.'

"What this showed is that when you put people in English mode, they actually would act like English speakers, and then if you put them in Spanish mode, they would switch to acting like Spanish speakers," Lotto said. "These bilinguals, hearing the exact same 'ba's and 'pa's would label them differently depending on the context."

When the study was repeated with 32 English monolinguals, participants did not show the same shift in perception; they labeled 'ba' and 'pa' sounds the same way regardless of which language they were told they were hearing. It was that lack of an effect for monolinguals that provided the strongest evidence for two sound systems in bilinguals.

"Up until this point we haven't had a good answer to whether bilinguals actually learn two different codes - so a 'ba-pa' English code and a 'ba-pa' Spanish code - or whether they learn something that's sort of in the middle," Lotto said. "This is one of the first clear demonstrations that bilinguals really do have two different sounds systems and that they can switch between one language and the other and then use that sound system."

This is true primarily for those who learn two languages very young, Lotto said.

"If you learn a second language later in life, you usually have a dominant language and then you try to use that sounds system for the other language, which is why you end up having an accent," he said.

Research on bilingualism has increased in recent years as the global climate has become more intermixed, Lotto noted. These new findings challenge the idea that bilinguals always have one dominant language.
"This raises the possibility that bilinguals can perceive speech like a native speaker in both languages," said Gonzales, whose own son is growing up learning English and Chinese simultaneously.
"The predominant view of late has been that bilinguals will never be able to perceive a second language beyond what a late learner is capable of, or someone who learns a second language late in life. So even if you learn two languages simultaneously from birth, you're always going to perceive one of them like a late learner," Gonzales said. "Our findings cast doubt on that prominent view in the bilingual literature."

http://www.eurekalert.org/pub_releases/2013-05/uoc-mtf052013.php

Molecular trigger for Alzheimer's disease identified

Researchers have pinpointed a catalytic trigger for the onset of Alzheimer's disease – when the fundamental structure of a protein molecule changes to cause a chain reaction that leads to the death of neurons in the brain.

For the first time, scientists at Cambridge's Department of Chemistry have been able to map in detail the pathway that generates "aberrant" forms of proteins which are at the root of neurodegenerative conditions such as Alzheimer's.
They believe the breakthrough is a vital step closer to increased capabilities for earlier diagnosis of neurological disorders such as Alzheimer's and Parkinson's, and opens up possibilities for a new generation of targeted drugs, as scientists say they have uncovered the earliest stages of the development of Alzheimer's that drugs could possibly target.
The study, published today in the journal PNAS, is a milestone in the long-term research established in Cambridge by Professor Christopher Dobson and his colleagues, following the realisation by Dobson of the underlying nature of protein 'misfolding' and its connection with disease over 15 years ago.
The research is likely to have a central role to play in diagnostic and drug development for dementia-related diseases, which are increasingly prevalent and damaging as populations live longer.
"There are no disease modifying therapies for Alzheimer's and dementia at the moment, only limited treatment for symptoms. We have to solve what happens at the molecular level before we can progress and have real impact," said Dr Tuomas Knowles, lead author of the study and long-time collaborator of Professor Dobson.
"We've now established the pathway that shows how the toxic species that cause cell death, the oligomers, are formed. This is the key pathway to detect, target and intervene – the molecular catalyst that underlies the pathology."
In 2010, the Alzheimer's Research Trust showed that dementia costs the UK economy over £23 billion, more than cancer and heart disease combined. Just last week, PM David Cameron urged scientists and clinicians to work together to "improve treatments and find scientific breakthroughs" to address "one of the biggest social and healthcare challenges we face."
The neurodegenerative process giving rise to diseases such as Alzheimer's is triggered when the normal structures of protein molecules within cells become corrupted.
Protein molecules are made in cellular 'assembly lines' that join together chemical building blocks called amino acids in an order encoded in our DNA. New proteins emerge as long, thin chains that normally need to be folded into compact and intricate structures to carry out their biological function.
Under some conditions, however, proteins can 'misfold' and snag surrounding normal proteins, which then tangle and stick together in clumps which build to masses, frequently millions, of malfunctioning molecules that shape themselves into unwieldy protein tendrils.
The abnormal tendril structures, called 'amyloid fibrils', grow outwards around the location where the focal point, or 'nucleation' of these abnormal "species" occurs.
Amyloid fibrils can form the foundations of huge protein deposits – or plaques – long-seen in the brains of Alzheimer's sufferers, and once believed to be the cause of the disease, before the discovery of 'toxic oligomers' by Dobson and others a decade or so ago.
A plaque's size and density renders it insoluble, and consequently unable to move. Whereas the oligomers, which give rise to Alzheimer's disease, are small enough to spread easily around the brain - killing neurons and interacting harmfully with other molecules - but how they were formed was until now a mystery.
The new work, in large part carried out by researcher Samuel Cohen, shows that once a small but critical level of malfunctioning protein 'clumps' have formed, a runaway chain reaction is triggered that multiplies exponentially the number of these protein composites, activating new focal points through 'nucleation'.

It is this secondary nucleation process that forges juvenile tendrils, initially consisting of clusters that contain just a few protein molecules. Small and highly diffusible, these are the 'toxic oligomers' that careen dangerously around the brain cells, killing neurons and ultimately causing loss of memory and other symptoms of dementia. The researchers brought together kinetic experiments with a theoretical framework based on master equations, tools commonly used in other areas of chemistry and physics but had not been exploited to their full potential in the study of protein malfunction before.

The latest research follows hard on the heels of another ground breaking study, published in April of this year again in PNAS, in which the Cambridge group, in Collaboration with Colleagues in London and at MIT, worked out the first atomic structure of one of the damaging amyloid fibril protein tendrils. They say the years spent developing research techniques are really paying off now, and they are starting to solve "some of the key mysteries" of these neurodegenerative diseases. "We are essentially using a physical and chemical methods to address a biomolecular problem, mapping out the networks of processes and dominant mechanisms to 'recreate the crime scene' at the molecular root of Alzheimer's disease," explained Knowles.

"Increasingly, using quantitative experimental tools and rigorous theoretical analysis to understand complex biological processes are leading to exciting and game-changing results. With a disease like Alzheimer's, you have to intervene in a highly specific manner to prevent the formation of the toxic agents. Now we've found how the oligomers are created, we know what process we need to turn off."

http://bit.ly/18o2USr

Why Feeling Anxious about a Vaccine Makes It More Effective (and Other Benefits of Short-Term Stress)

Subjecting mice to minor stress before they are vaccinated boosts the immune system and makes the vaccines more effective

By Ferris Jabr | May 20, 2013

SAN FRANCISCO - Standing at a podium in front of an audience of psychiatrists, clinicians and scientists, Firdaus Dhabhar brings up a video of his infant son on a large projector screen and presses play. Smiling and wriggling, Dhabhar's son rests on his back in a doctor's office - perfectly content. "Watch for the immediate reaction," Dhabhar tells the audience. A nurse expertly injects his son's thigh with a vaccine. For half a second, nothing changes. Then the child stops moving; his eyes widen; his face twists into misery as he begins to cry. Meanwhile, the nurse has not missed a beat, injecting several more vaccines. As she leaves she turns to the camera and says, "Sorry I couldn't make him cry more."

Dhabhar likes to film babies crying when they get their shots; he knows that the wailing is a good sign - so do the nurses in the hospitals he frequents. A Stanford University researcher who studies how stress changes the body, Dhabhar and his colleagues have discovered that subjecting mice to minor stress before they are vaccinated boosts the immune system and makes the vaccines more effective. Mice that were stressed out prior to their inoculations had an easier time overcoming a subsequent infection than mice that the researchers left in peace before their shots. Something similar seems to happen to people. In a study of knee surgery patients, for example, Dhabhar and his teammates found that anticipating surgery increases the number of immune cells circulating in the bloodstream in the days preceding the operation. Studies like these have convinced Dhabhar that stress does not entirely deserve its bad reputation, which was one of the main messages of his recent presentation at the annual meeting of the American Psychiatric Association in San Francisco. Some kinds of short-term stress - as opposed to chronic stress - can improve health.

From an evolutionary perspective, the fact that short-term stress revs up the immune system makes sense. Consider a gazelle fleeing a lioness. Once the gazelle's eyes and ears alert its brain to the threat, certain brain regions immediately activate the famous fight-or-flight response, sending electrical signals along the nervous system to the muscles and many other organs, including the endocrine glands - the body's hormone factories. Levels of cortisol, epinephrine, adrenaline and noradrenaline rapidly increase; the heart beats faster; and enzymes race to convert glucose and fatty acids into energy for cells. All these swift biological changes give the gazelle the best chance of escape. At the same time, Dhabhar and others' research suggests, the brain's recognition of a threat prompts the immune system to prepare for potential injury. The spleen and other organs release immune cells specialized for identifying and destroying invaders and healing damaged tissues. After all, even if the gazelle escapes with its life, it may need to heal wounds sustained during its flight and prevent them from becoming infected.

Somewhat paradoxically, cortisol - one of the hormones released during the fight-or-flight response - has long been known to suppress the immune system. Likewise, many people who are continually stressed over long periods of time have unusually low levels of immune activity. But then again, chronic stress can exacerbate

allergies, asthma and autoimmune disorders in which the immune system is already overactive. So does stress excite or repress the immune system? Here's where things get even more complicated, as they so often do in biology. The condensed answer is that it all depends on the situation and on the individual. Often, short-term stress activates certain parts of the immune system, but not all its components; in general, chronic stress stifles the immune system, but it may also make it more likely to attack benign tissues. In the study with knee surgery patients, people's immune systems did not all respond to anticipation of the operation in the same way. Some people showed an adaptive response: the number of immune cells in their bloodstream increased in the days before the operation, then decreased as those immune cells migrated to the skin, lymph nodes, mucus membranes and other important sites of battle and repair. Other patients had a maladaptive response: their levels of circulating immune cells hardly increased or even dipped below their baseline level. As you might expect, people with an adaptive immune response recovered from surgery more quickly and more fully than people with a maladaptive response.

In recent decades, it has become increasingly clear that stress changes people's health in subtle and obvious, temporary and enduring ways. In fact, depression and related illnesses may be - at least in part - disorders of handling stress. We all come into the world having inherited genes that partially determine how well we deal with stress. As we grow, our experiences bolster or weaken our innate resilience. For some people, a series of mildly stressful events may be enough to trigger depression or another illness; others will remain resilient through years of chronic stress. It will likely take decades of new research to understand such differences in detail. For now, though, we can at least be sure that it's okay to feel stressed when you get a shot - in fact, it's a good thing.

http://www.sciencedaily.com/releases/2013/05/130520095049.htm

Discovery of a Novel Medicine for the Treatment of Chronic Wounds

Every 20 seconds, a limb is lost as a consequence of diabetic foot ulcer that does not heal.

To date, medical solutions that can change this situation are very limited. In his doctoral thesis Yue Shen from the Industrial Doctoral School and the Department of Medical Biochemistry and Biophysics at Umeå University presented a novel medicine for chronic wound treatment that may completely change the lives of millions of patients.

Diabetic wounds are the most severe type of chronic wounds that largely impair the quality of life in patients and inflict an enormous burden on the healthcare system. World-wide, there are more than 350 million diabetic patients and about 20% of them develop diabetic foot ulcers that often do not heal, which eventually lead to amputation. Chronic eardrum perforations are another type of chronic wounds. Today the only existing treatment of chronic eardrum perforations is through surgery.

In his thesis, Yue Shen demonstrates that plasminogen, a well-know plasma protein, acts as a key regulatory molecule of inflammation that can be used to treat different types of chronic wounds including diabetic wounds and chronic eardrum perforations. Yue Shen demonstrates that the level of plasminogen dramatically increases in and around wounds, which leads to an enhanced inflammation that is required for healing. In diabetic wounds that do not heal, the level of plasminogen does not increase and the inflammatory response is suppressed. When plasminogen is injected around diabetic wounds, the healing process starts and the wounds eventually heal fully. In chronic eardrum perforations, local injection and topical application of plasminogen also stimulates the healing and leads to complete healing. Based on these studies, a controlled clinical study using human plasminogen to treat chronic wounds in humans is now planned. The ultimate goal is to develop plasminogen to a medicine for the treatment of various chronic wounds.

The findings in Yue Shen's thesis not only reshape our molecular understanding of the role of plasminogen during wound healing process, but also bring the hope to millions of desperate patients who suffered from chronic wounds. *Further information: http://umu.diva-portal.org/smash/record.jsf?pid=diva2:617977&rvn=1*

http://bit.ly/124hqzQ

Stem-cell treatment restores sight to blind man

An experimental stem-cell treatment has restored the sight of a man blinded by the degeneration of his retinal cells.

16:37 20 May 2013 by Andy Coghlan

The man, who is taking part in a trial examining the safety of using human embryonic stem cells (hESCs) to reverse two common causes of blindness, can now see well enough to be allowed to drive. People undergoing treatment had reported modest improvements in vision earlier in the trial, which began in 2011, but this individual has made especially dramatic progress. The vision in his affected eye went from 20/400 – essentially blind – to 20/40, which is considered sighted.

"There's a guy walking around who was blind, but now can see," says Gary Rabin, chief executive officer of Advanced Cell Technology, the company in Marlborough, Massachusetts that devised the treatment. "With that sort of vision, you can have a driver's licence."
In all, the company has so far treated 22 patients who either have dry age-related macular degeneration, a common condition that leaves people with a black hole in the centre of their vision, or Stargardt's macular dystrophy, an inherited disease that leads to premature blindness. The company wouldn't tell New Scientist which of the two diseases the participant with the dramatic improvement has.
In both diseases, people gradually lose retinal pigment epithelial (RPE) cells. These are essential for vision as they recycle protein and lipid debris that accumulates on the retina, and supply nutrients and energy to photoreceptors – the cells that capture light and transmit signals to the brain.
The company is testing treatments for both conditions by turning hESCs into fresh RPE cells, then giving each trial participant a transplant of the cells beneath the retina in one eye.
Although the aim of the trial is primarily to check that the stem cells are safe, participants have reported improvements in their sight. The company intends to publish the outcomes in full when all the results are in.

http://bit.ly/18q3zD0

B vitamins may slow the advance of Alzheimer's

Those at risk of developing Alzheimer's may be able to slow its onset through daily B vitamins.

20:00 20 May 2013 by Caroline Williams

We already know that a high level of the amino acid homocysteine in the blood is a risk factor for Alzheimer's, and that B vitamin supplements help reduce homocysteine levels. But it was unclear whether or not these supplements would slow the progression of mild cognitive impairment (MCI) to Alzheimer's.
David Smith and Gwenaëlle Douaud at the University of Oxford led a research effort to find out. They used MRI to track changes in the brains of 200 elderly volunteers with MCI over two years. During this time, half were given high doses of vitamin B12, B6 and folic acid – 300, 20 and 4 times the UK guideline daily amounts, respectively. The rest took a placebo.
In 2010, Smith and his colleagues showed that high doses of B vitamins slowed whole-brain shrinkage by up to 53 per cent in patients with above average homocysteine levels. Now Smith and Douaud's team have looked deeper to work out which brain regions are best protected.

Better function

They found that it was the areas of the brain most seriously affected by Alzheimer's, including the hippocampus and cerebellum, that were protected in volunteers given the vitamins. For instance, in those with high homocysteine, the atrophy rate in these brain regions was 5.2 per cent in the placebo group but just 0.6 per cent in the vitamin group. The reduction of atrophy seemed to translate into better brain function too: those given B vitamins performed better on cognitive tests. "It demonstrates for the very first time that it is possible to modify the disease process in Alzheimer's," says Smith.
Simon Ridley at Alzheimer's Research UK cautions that more work is needed to explore the link. "It's important to note the effects in this trial were only seen in a subgroup of people with MCI," he says. "We must also remember that only a proportion of people with MCI will go on to develop Alzheimer's, and it's not yet clear why this is the case."

Bite the bullet

But Smith points out that performing that additional work will take time. He says that since vitamin supplements are safe for most people they could perhaps be offered to high-risk people as a precaution.
"I think we need to bite the bullet and say, is there any reason that elderly people with memory problems shouldn't be offered them in the meantime?" he says.
In fact, he adds, some doctors are already providing B vitamins. "I raised the same question at a conference last year and a psychiatrist in the audience put his hand up and said 'We already do since your first paper came out'. So there's nothing to stop clinicians doing this." *Journal reference: PNAS, DOI: 10.1073/pnas.1301816110*

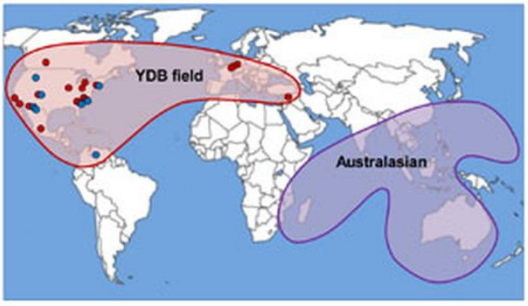
http://phys.org/news/2013-05-mammoth-lament-cosmic-impact-devastating.html

The mammoth's lament: Study shows how cosmic impact sparked devastating climate change

The mammoth's lament: UC research shows how cosmic impact sparked devastating climate change

Phys.org - Herds of wooly mammoths once shook the earth beneath their feet, sending humans scurrying across the landscape of prehistoric Ohio. But then something much larger shook the Earth itself, and at that point these mega mammals' days were numbered.

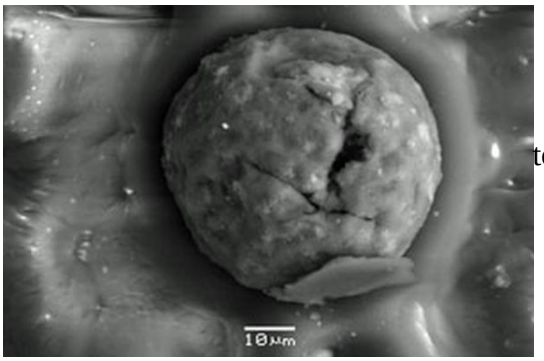
Something – global-scale combustion caused by a comet scraping our planet's atmosphere or a meteorite slamming into its surface – scorched the air, melted bedrock and altered the course of Earth's history. Exactly what it was is unclear, but this event jump-started what Kenneth Tankersley, an assistant professor of anthropology and geology at the University of Cincinnati, calls the last gasp of the last ice age.
"Imagine living in a time when you look outside and there are elephants walking around in Cincinnati," Tankersley says. "But by the time you're at the end of your years, there are no more elephants. It happens within your lifetime."
Tankersley explains what he and a team of international researchers found may have caused this catastrophic event in Earth's history in their research, "Evidence for Deposition of 10 Million Tonnes of Impact Spherules Across Four Continents 12,800 Years Ago," which was published in the Proceedings of the National Academy of Sciences. The prestigious journal was established in 1914 and publishes innovative research reports from a broad range of scientific disciplines. Tankersley's research also was included in the History Channel series "The Universe: When Space Changed History" and will be featured in an upcoming film for The Weather Channel.
This research might indicate that it wasn't the cosmic collision that extinguished the mammoths and other species, Tankersley says, but the drastic change to their environment.
"The climate changed rapidly and profoundly. And coinciding with this very rapid global climate change was mass extinctions."



The Younger Dryas Boundary strewnfield is shown (red) with YDB sites as red dots and those by eight independent groups as blue dots. Also shown is the largest known impact strewnfield, the Australasian (purple). **Credit: Ken Tankersley, University of Cincinnati**

Putting a finger on the end of the ice age

Tankersley is an archaeological geologist. He uses geological techniques, in the field and laboratory, to solve archaeological questions. He's found a treasure trove of answers to some of those questions in Sheriden Cave in Wyandot County, Ohio. It's in that spot, 100 feet below the surface, where Tankersley has been studying geological layers that date to the Younger Dryas time period, about 13,000 years ago.
About 12,000 years before the Younger Dryas, the Earth was at the Last Glacial Maximum – the peak of the Ice Age. Millennia passed, and the climate began to warm. Then something happened that caused temperatures to suddenly reverse course, bringing about a century's worth of near-glacial climate that marked the start of the geologically brief Younger Dryas.
There are only about 20 archaeological sites in the world that date to this time period and only 12 in the United States – including Sheriden Cave. "There aren't many places on the planet where you can actually put your finger on the end of the last ice age, and Sheriden Cave is one of those rare places where you can do that," Tankersley says.



This is an environmental scanning electron microscope image of a carbon spherule from Sheriden Cave. **Credit: Ken Tankersley, University of Cincinnati**

Rock-solid evidence of cosmic calamity

In studying this layer, Tankersley found ample evidence to support the theory that something came close enough to Earth to melt rock and produce other interesting geological phenomena. Foremost among the findings were carbon spherules. These tiny bits of carbon are formed when substances are burned at very high temperatures. The spherules exhibit characteristics that indicate their origin, whether that's from burning coal, lightning strikes, forest fires or something more extreme. Tankersley says the ones in his study could only have been formed from the combustion of rock.
The spherules also were found at 17 other sites across four continents – an estimated 10 million metric tons' worth – further supporting the idea that whatever changed Earth did so on a massive scale. It's unlikely that a wildfire or thunderstorm would leave a geological calling card that immense – covering about 50 million square kilometers.
"We know something came close enough to Earth and it was hot enough that it melted rock – that's what these carbon spherules are. In order to create this type of evidence that we see around the world, it was big," Tankersley says, contrasting the effects of an event so massive with the 1883 volcanic explosion on Krakatoa in

Indonesia. "When Krakatoa blew its stack, Cincinnati had no summer. Imagine winter all year-round. That's just one little volcano blowing its top."
Other important findings include:

Micrometeorites: smaller pieces of meteorites or particles of cosmic dust that have made contact with the Earth's surface.

Nanodiamonds: microscopic diamonds formed when a carbon source is subjected to an extreme impact, often found in meteorite craters.

Lonsdaleite: a rare type of diamond, also called a hexagonal diamond, only found in non-terrestrial areas such as meteorite craters.

Three choices at the crossroads of oblivion

Tankersley says while the cosmic strike had an immediate and deadly effect, the long-term side effects were far more devastating – similar to Krakatoa's aftermath but many times worse – making it unique in modern human history.
In the cataclysm's wake, toxic gas poisoned the air and clouded the sky, causing temperatures to plummet. The roiling climate challenged the existence of plant and animal populations, and it produced what Tankersley has classified as "winners" and "losers" of the Younger Dryas. He says inhabitants of this time period had three choices: relocate to another environment where they could make a similar living; downsize or adjust their way of living to fit the current surroundings; or swiftly go extinct. "Winners" chose one of the first two options while "losers," such as the wooly mammoth, took the last.
"Whatever this was, it did not cause the extinctions," Tankersley says. "Rather, this likely caused climate change. And climate change forced this scenario: You can move, downsize or you can go extinct."
Humans at the time were just as resourceful and intelligent as we are today. If you transported a teenager from 13,000 years ago into the 21st century and gave her jeans, a T-shirt and a Facebook account, she'd blend right in on any college campus. Back in the Younger Dryas, with mammoth off the dinner table, humans were forced to adapt – which they did to great success.

Weather report: cloudy with a chance of extinction

That lesson in survivability is one that Tankersley applies to humankind today.
"Whether we want to admit it or not, we're living right now in a period of very rapid and profound global climate change. We're also living in a time of mass extinction," Tankersley says. "So I would argue that a lot of the lessons for surviving climate change are actually in the past."
He says it's important to consider a sustainable livelihood. Humans of the Younger Dryas were hunter-gatherers. When catastrophe struck, these humans found news ways and new places to hunt game and gather wild plants. Evidence found in Sheriden Cave shows that most of the plants and animals living there also endured. Of the 70 species known to have lived there before the Younger Dryas, 68 were found there afterward. The two that didn't make it were the giant beaver and the flat-headed peccary, a sharp-toothed pig the size of a black bear.
Tankersley also cautions that the possibility of another massive cosmic event should not be ignored. Like earthquakes, tsunamis and volcanoes, these types of natural disasters do happen, and as history has shown, it can be to devastating effect.
"One additional catastrophic change that we often fail to think about – and it's beyond our control – is something from outer space," Tankersley says. "It's a reminder of how fragile we are. Imagine an explosion that happened today that went across four continents. The human species would go on. But it would be different. It would be a game changer."

Breaking barriers and working together toward real change

Tankersley is a member of UC's Quaternary and Anthropocene Research Group (QARG), an interdisciplinary conglomeration of researchers dedicated to undergraduate, graduate and professional education, experience-based learning and research in Quaternary science and study of the Anthropocene. He's proud to be working with his students on projects that, when he was in their shoes, were considered science fiction.
Collaborative efforts such as QARG help break down long-held barriers between disciplines and further position UC as one of the nation's top public research universities.
"What's exciting about UC and why our university is producing so much, is we have scientists who are working together and it's this area of overlap that is so interesting," Tankersley says. "There's a real synergy about innovative, transformative, transdisciplinary science and education here. These are the things that really make people take notice. It causes real change in our world."

Evidence for deposition of 10 million tonnes of impact spherules across four continents 12,800 y ago, www.pnas.org/cgi/doi/10.1073/pnas.1301760110

http://www.eurekalert.org/pub_releases/2013-05/wt-erl052113.php

Estimates reveal low population immunity to new bird flu virus H7N9 in humans

Immunity to the recently circulating H7N9 influenza virus in a population in Vietnam is very low

The level of immunity to the recently circulating H7N9 influenza virus in an urban and rural population in Vietnam is very low, according to the first population level study to examine human immunity to the virus, which was previously only found in birds. The findings have implications for planning the public health response to this pandemic threat.

The study used a new, high throughput method that allows blood samples to be analysed for antibodies to multiple human and animal influenza viruses at the same time and is easier to standardise than previous techniques. However, the assay is yet to be validated clinically for the H7N9 virus, and the researchers caution that the results must be interpreted with care.

Since the first case of H7N9 infection in humans was reported in February 2013, there have been 131 confirmed cases and 36 deaths, all in China apart from one case in Taiwan. All of the infections seem to have come from infected poultry and there is no evidence of sustained transmission between people. One of the first key pieces of information that officials need when considering how best to respond to the threat of a pandemic is how much, if any, immunity the human population has to this virus. This helps to predict where the virus is likely to affect first and how likely it is that the virus will spread further. Having this knowledge also helps to understand the risks of severe infection, as well as helping to target protective measures such as where to direct antiviral medication.

Researchers at the Wellcome Trust Oxford University Clinical Research Unit (OUCRU) in Vietnam tested 1723 blood samples collected in southern Vietnam for the presence of antibodies to five different bird flu viruses, including one from the H7 sub type. The presence of antibodies would be an indication of past exposure to these particular strains of flu. They used a new technique that was developed by their research collaborators at the National Institute of Public Health of The Netherlands that is faster and easier to use than previous methods.

The results reveal that although the level of antibodies to the H7 sub-type of flu virus are higher than any of the H5 sub-types tested, levels of antibodies to all five bird flu viruses are much lower than to human flu viruses. This suggests that people living in this particular area of Vietnam have had very little or no exposure to the H7 sub-type of virus, similar to other bird flu viruses. As this population of people would be expected to be among the first to be affected in the event of a pandemic, these findings have important implications for pandemic preparedness plans in this area.

Dr Maciej Boni, a Sir Henry Dale Fellow at the OUCRU and first author of the study, explains: "H7N9 is a virus that until now has only infected birds so it's not surprising that we don't find much evidence of humans having been exposed to it. It is reassuring that in Vietnam we don't see any evidence that the current outbreaks represent a tip-of-the iceberg observation of widespread H7N9 infection in people. On the other hand, the low antibody levels indicate that there is likely to be very little immunity to this virus."

Around half of the samples were taken from an urban environment, Ho Chi Minh City, and half from a rural area, the nearby Khanh Hoa province. The team found no difference in the level of immunity to bird flu viruses between these two populations, even though people living in rural areas are more likely to live in close proximity to poultry.

"It has been suggested that people who live in closer proximity to chickens and other birds will have higher levels of immunity to bird flu viruses simply because their exposure is likely to be greater. However we find no evidence for this. Our findings would suggest that both rural and urban populations should be treated the same when considering how best to respond to the threat of an outbreak," added Dr Boni.

Professor Jeremy Farrar, Director of the Wellcome Trust Major Overseas Programme in Vietnam and the Oxford University Clinical Research Unit Hospital for Tropical Diseases, explains: "This is the first study to give us information about the level of antibodies and potentially human immunity to this new bird flu virus, H7N9 in the region. But we need to interpret the findings cautiously, these assays are relatively new and we need to understand how they correspond to existing assays and how they reflect past infection and true human immunity.

"We know that antibodies are very important for immunity to other flu viruses but at this stage, we still don't know what level of antibody measured using this assay would provide protection against this novel strain. Further studies will be needed to understand the clinical relevance of these new assays, how they compare with classic techniques and what the apparent absence of antibodies to these viruses in the human population means. However these new techniques do allow for much higher throughput of samples, ease of use and once validated

may allow much more rapid assessment of the spread of infection and levels of population immunity than do traditional assays."
The study, which was carried out in collaboration with scientists at the National Institute for Public Health and the Environment (RIVM) in the Netherlands, is published online this week in the Journal of Infectious Diseases.
Professor Marion Koopmans, who is Head of Virology at the RIVM and senior author of the study, said: "We developed this technique exactly to be used in the current situation: we wanted a standardised test that allowed us to rapidly compare antibodies to the new virus with those to influenza viruses that we already know are common in people. The level of immunity to a new virus is one of the important questions during any emerging disease outbreak. We need only one drop of blood, so that tests can also be run when only small sample volumes are available, for instance when testing children. For outbreak investigations, testing of animals may be needed, and we are currently working on that. To do the clinical validation studies, we need blood samples from patients (and animals) with confirmed H7N9, and we hope to be able to do that soon through collaborations with other groups working on H7N9."

http://www.eurekalert.org/pub_releases/2013-05/uosc-dft052113.php

Drugs found to both prevent and treat Alzheimer's disease in mice

Scientists hope the pharmaceuticals could lead to the development of a silver bullet for combatting the neurodegenerative disease

Researchers at USC have found that a class of pharmaceuticals can both prevent and treat Alzheimer's Disease in mice. The drugs, known as "TSPO ligands," are currently used for certain types of neuroimaging.
"We looked at the effects of TSPO ligand in young adult mice when pathology was at an early stage, and in aged mice when pathology was quite severe," said lead researcher Christian Pike of the USC Davis School of Gerontology. "TSPO ligand reduced measures of pathology and improved behavior at both ages."
The team's findings were published online by the Journal of Neuroscience on May 15. Pike's coauthors include USC postdoctoral scientists Anna M. Barron, Anusha Jayaraman and Joo-Won Lee; as well as Donatella Caruso and Roberto C. Melcangi of the University of Milan and Luis M. Garcia-Segura of the Instituto Cajal in Spain.
The most surprising finding for Pike and his team was the effect of TSPO ligand in the aged mice. Four treatments—once per week over four weeks—in older mice resulted in a significant decrease of Alzheimer's-related symptoms and improvements in memory – meaning that TSPO ligands may actually reverse some elements of Alzheimer's disease.
"Our data suggests the possibility of drugs that can prevent and treat Alzheimer's," Pike said. "It's just mouse data, but extremely encouraging mouse data. There is a strong possibility that TSPO ligands similar to the ones used in our study could be evaluated for therapeutic efficacy in Alzheimer's patients within the next few years."
Next, the team will next focus on understanding how TSPO ligands reduce Alzheimer's disease pathology. Building on the established knowledge that TSPO ligands can reduce inflammation—shielding nerve cells from injury and increasing the production of neuroactive hormones in the brain—the team will study which of these actions is the most significant in fighting Alzheimer's disease so they can develop newer TSPO ligands accordingly.
The research was funded by the National Institutes of Health (grant number AG05142), the American-Australian Association, the Japan Society for the Promotion of Science and the Fondazione San Paolo.

http://www.sciencedaily.com/releases/2013/05/130521011230.htm

Resistance to Last-Line Antibiotic Makes Bacteria Resistant to Immune System

Bacteria resistant to the antibiotic colistin are also commonly resistant to antimicrobial substances made by the human body

Bacteria resistant to the antibiotic colistin are also commonly resistant to antimicrobial substances made by the human body, according to a study in mBio®, the online open-access journal of the American Society for Microbiology.
Cross-resistance to colistin and host antimicrobials LL-37 and lysozyme, which help defend the body against bacterial attack, could mean that patients with life-threatening multi-drug resistant infections are also saddled with a crippled immune response. Colistin is a last-line drug for treating several kinds of drug-resistant infections, but colistin resistance and the drug's newfound impacts on bacterial resistance to immune attack underscore the need for newer, better antibiotics.
Corresponding author David Weiss of Emory University says the results show that colistin therapy can fail patients in two ways. "The way that the bacteria become resistant [to colistin] allows them to also become resistant to the antimicrobials made by our immune system. That is definitely not what doctors want to do when they're treating patients with this last line antibiotic," says Weiss.

Although it was developed fifty years ago, colistin remains in use today not so much because it's particularly safe or effective, but because the choices for treating multi-drug resistant Acinetobacter baumannii and other resistant infections are few and dwindling. Colistin is used when all or almost all other drugs have failed, often representing a patient's last hope for survival.
Weiss says he and his colleagues noted that colistin works by disrupting the inner and outer membranes that hold Gram-negative bacterial cells together, much the same way two antimicrobials of the human immune system, LL-37 and lysozyme, do. LL-37 is a protein found at sites of inflammation, whereas lysozyme is found in numerous different immune cells and within secretions like tears, breast milk, and mucus, and both are important defenses against invading bacteria.
Weiss and his collaborators from Emory, the CDC, Walter Reed Army Institute of Research, and Grady Memorial Hospital in Atlanta set out to find whether resistance to colistin could engender resistance to attack by LL-37 or lysozyme.
Looking at A. baumannii isolates from patients around the country, they noted that all the colistin-resistant strains harbored mutations in pmrB, a regulatory gene that leads to the modification of polysaccharides on the outside of the cell in response to antibiotic exposure. Tests showed a tight correlation between the ability of individual isolates to resist high concentrations of colistin and the ability to resist attacks by LL-37 or lysozyme.
This was very convincing, write the authors, that mutations in the pmrB gene were responsible for cross-resistance to LL-37 and lysozyme, but to get closer to a causative link between treatment and cross-resistance, they studied two pairs of A. baumannii isolates taken from two different patients before and after they were treated for three or six weeks with colistin.
The results helped confirm the cross-resistance link: neither strain taken before treatment was resistant to colistin, LL-37, or lysozyme, but the strains taken after treatment showed significant resistance to colistin and lysozyme. (One post-colistin isolate was no more or less resistant to LL-37 than its paired pre-colistin isolate.) Like the resistant strains tested earlier, both post-colistin isolates harbored crucial mutations in the pmrB gene that apparently bestow the ability to resist treatment.
The authors point out that the apparent link between resistance to colistin and cross-resistance to antimicrobial agents of the immune system could well extend to other pathogens that are treated with colistin, including Pseudomonas aeruginosa and Klebsiella pneumoniae. Weiss says he plans to follow up with studies to determine whether this bears out.
For Weiss, the problems with colistin are symptomatic of a much larger trio of problems: increasing levels of drug resistance, cuts in federal funding for antibiotic research, and lack of incentives for pharmaceutical companies to invest in antibiotic R&D. "We don't have enough antibiotics, and it's really important for the research community and the public to support increases in funding for research to develop new antibiotics," says Weiss.
"We got complacent for a while and the bugs are becoming resistant. This is something we can reverse -- or make a lot better -- if we have the resources."

http://www.sciencedaily.com/releases/2013/05/130521105557.htm

Cancer and Birth Defects in Iraq: The Nuclear Legacy

High levels of uranium contamination in soil illustrates increasing rates of childhood cancers and birth defects at local hospitals, highlight the ongoing legacy of modern warfare

Ten years after the Iraq war of 2003 a team of scientists based in Mosul, northern Iraq, have detected high levels of uranium contamination in soil samples at three sites in the province of Nineveh which, coupled with dramatically increasing rates of childhood cancers and birth defects at local hospitals, highlight the ongoing legacy of modern warfare to civilians in conflict zones.
The radioactive element uranium is widely dispersed throughout Earth's crust and is much sought after as a fuel for nuclear power plants and for use in weapons. Depleted uranium (DU), commonly used in modern munitions such as defensive armour plating and armour-piercing projectiles, is 40 per cent less radioactive than natural uranium, but remains a significant and controversial danger to human health.
The World Health Organisation (WHO) sets a maximum uranium exposure of 1 millisievert (mSv) per year for the general public, but environmental scientists at the University of Mosul and the Institute of Forest Ecology, Universitaet für Bodenkultur (BOKU), Vienna, Austria, led by Riyad Abdullah Fathi have measured significant levels of uranium in soil samples from three sites in the province of Nineveh in the north of Iraq.
Writing in the journal Medicine, Conflict and Survival, Fathi and colleagues link their findings with dramatic increases in cancers reported to the Mosul Cancer Registry and the Iraqi national cancer registry (which began collecting data in 1975).

They conclude that: "The Gulf Wars of 1991 and 2003 left a legacy of pollution with DU in many regions of Iraq. The effects of these munitions may be affecting the general health of Iraqi citizens, manifesting in an increase in cancers and birth defects."
They also warn that, even though some of the contamination measured in this study is specifically linked to known sites, it can be easily spread widely in the air, soil and water, particularly as dust in windstorms.
Their report "Environmental pollution by depleted uranium in Iraq with special reference to Mosul and possible effects on cancer and birth defect rates" begins with a literature review that collates health-related data from a range of sources, including a report by the WHO (in 2003), which states that childhood cancers -- particularly leukemia -- are ten times higher in Iraq than in other industrialised countries.
Although there is already significant evidence of cancers and related illnesses in adults (particularly war veterans), the authors emphasise that it is the dramatic rise in the incidence of cancer and birth defects in children under 15 years of age since the second Gulf War that points to the terrible legacy of DU weaponry. Childhood cancers are now some five times higher than before the two Gulf Wars (currently around 22 children per 100,000, compared with approximately 4 children per 100,000 in 1990).
The focal point of their scientific study was three sites near Mosul: Adayah, a landfill for radioactive waste; Rihanyah, a former research centre for nuclear munitions (disused since 1991); and Damerchy, a small village on the Tigris River (about 10km north of Mosel), which was a scene of fighting in the 2003 conflict.
Particularly high levels of uranium were found at Rihanyah where storage ponds of liquid and solid waste from uranium processing are still a source of radioactive pollution. The accumulation of uranium in wild plants (principally the shrub Lagonychium farctum) was noted in Damerchy, where it is thought to have entered the food chain and is linked to the death of numerous head of cattle.
The team acknowledge that there are numerous other factors that impact on the data for cancer rates in the wider Iraqi population, including population increases and possible inaccuracies due to reluctance to register congenital malformations and deaths or poor administration in hospitals (although almost 70 per cent of births took place outside hospitals). Nevertheless, with the WHO predicting that global cancer levels will rise by 50 per cent between 2003 and 2020, the presence of so much carcinogenic material across Iraq suggests that the public health legacy of the two Gulf Wars is only going to get worse.

http://www.sciencedaily.com/releases/2013/05/130521121219.htm

Vitamin C Can Kill Drug-Resistant TB, Researchers Find

Researchers have determined that vitamin C kills drug-resistant tuberculosis bacteria in laboratory culture.

In a striking, unexpected discovery, researchers at Albert Einstein College of Medicine of Yeshiva University have determined that vitamin C kills drug-resistant tuberculosis (TB) bacteria in laboratory culture.
The finding suggests that vitamin C added to existing TB drugs could shorten TB therapy, and it highlights a new area for drug design. The study was published today in the online journal Nature Communications.
TB is caused by infection with the bacterium M. tuberculosis. In 2011, TB sickened some 8.7 million people and took some 1.4 million lives, according to the World Health Organization. Infections that fail to respond to TB drugs are a growing problem: About 650,000 people worldwide now have multi-drug-resistant TB (MDR-TB), 9 percent of whom have extensively drug-resistant TB (XDR-TB).TB is especially acute in low and middle income countries, which account for more than 95 percent of TB-related deaths, according to the World Health Organization.
The Einstein discovery arose during research into how TB bacteria become resistant to isoniazid, a potent first-line TB drug. The lead investigator and senior author of the study was William Jacobs, Jr. Ph.D., professor of microbiology & immunology and of genetics at Einstein. Dr. Jacobs is a Howard Hughes Medical Institute investigator and a recently elected member of the National Academy of Sciences.
Dr. Jacobs and his colleagues observed that isoniazid-resistant TB bacteria were deficient in a molecule called mycothiol. "We hypothesized that TB bacteria that can't make mycothiol might contain more cysteine, an amino acid," said Dr. Jacobs. "So, we predicted that if we added isoniazid and cysteine to isoniazid-sensitive M. tuberculosis in culture, the bacteria would develop resistance. Instead, we ended up killing off the culture -- something totally unexpected."
The Einstein team suspected that cysteine was helping to kill TB bacteria by acting as a "reducing agent" that triggers the production of reactive oxygen species (sometimes called free radicals), which can damage DNA. "To test this hypothesis, we repeated the experiment using isoniazid and a different reducing agent -- vitamin C," said Dr. Jacobs. "The combination of isoniazid and vitamin C sterilized the M. tuberculosis culture. We were then amazed to discover that vitamin C by itself not only sterilized the drug-susceptible TB, but also sterilized MDR-TB and XDR-TB strains."

To justify testing vitamin C in a clinical trial, Dr. Jacobs needed to find the molecular mechanism by which vitamin C exerted its lethal effect. More research produced the answer: Vitamin C induced what is known as a Fenton reaction, causing iron to react with other molecules to create reactive oxygen species that kill the TB bacteria.
"We don't know whether vitamin C will work in humans, but we now have a rational basis for doing a clinical trial," said Dr. Jacobs. "It also helps that we know vitamin C is inexpensive, widely available and very safe to use. At the very least, this work shows us a new mechanism that we can exploit to attack TB."
The study was supported by a grant (AI26170) from National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health.
Catherine Vilchèze, Travis Hartman, Brian Weinrick, William R. Jacobs. Mycobacterium tuberculosis is extraordinarily sensitive to killing by a vitamin C-induced Fenton reaction. Nature Communications, 2013; 4 DOI: 10.1038/ncomms2898

http://www.sciencedaily.com/releases/2013/05/130521132116.htm

Aggressive Behavior Linked Specifically to Secondhand Smoke Exposure in Childhood

Children exposed to secondhand smoke in early childhood are more likely to grow up to (be) physically aggressive and antisocial

Children who are exposed to secondhand smoke in early childhood are more likely to grow up to (be) physically aggressive and antisocial, regardless of whether they were exposed during pregnancy or their parents have a history of being antisocial, according to Linda Pagani and Caroline Fitzpatrick of the University of Montreal and its affiliated CHU Sainte-Justine hospital. No study to date has controlled for these factors.
"Secondhand smoke is in fact more dangerous that inhaled smoke, and 40% of children worldwide are exposed to it. Moreover, exposure to this smoke at early childhood is particularly dangerous, as the child's brain is still developing," Pagani said. "I looked at data that was collected about 2,055 kids from their birth until ten years of age, including parent reports about secondhand smoke exposure and from teachers and children themselves about classroom behaviour. Those having been exposed to secondhand smoke, even temporarily, were much more likely to report themselves as being more aggressive by time they finished fourth grade."
The study was published in the Journal of Epidemiology and Community Health on May 21, 2013.
Given that it would be unethical to exposure children to secondhand smoke, Pagani relied on longitudinal data collected by Quebec health authorities from birth onward on an annual basis. Because parents went about raising their children while participating in the study, the data provided a natural experiment of variations in the child population of household smoke exposure throughout early childhood. Although no direct causal link can be determined, the statistical correlation suggests that secondhand smoke exposure does forecast deviant behavior in later childhood.
The very detailed information collated for the Quebec Longitudinal Study of Child Development enabled her to do something no other researcher has done to date: distinguish the unique contribution of secondhand smoke exposure on children's later deviant behavior.
"Previous studies looking at groups of children have generally asked mothers whether they smoked or not, and how much at each follow-up, rather than asking whether someone smoked in the home where young children live and play," Dr. Pagani said. "Furthermore, few studies have looked at antisocial behaviour in the parents and even fewer have investigated the subsequent influence of prolonged exposure to secondhand smoke over the long term. None have taken into account the fact that disadvantaged families are less likely to participate in a long study like this one, which of course skews the statistics."
The statistics are backed by other biological studies into the effects of smoke on the brain. Secondhand smoke comprises 85% sidestream smoke emanated from a burning cigarette and 15% inhaled and then exhaled mainstream smoke. Sidestream smoke is considered more toxic than mainstream smoke because it contains a higher concentration of many dispersed respirable pollutants over a longer exposure period.
"We know that the starvation of oxygen caused by smoke exposure in the developing central nervous system can cause low birth weight and slowed fetal brain growth," Dr. Pagani said.
"Environmental sources of tobacco smoke represent the most passive and preventable cause of disease and disability. This study suggests that the postnatal period is important for the prevention of impaired neurobehavioral development and makes the case for the promotion of an unpolluted domestic environment for children."
Linda S Pagani, Caroline Fitzpatrick. Prospective associations between early long-term household tobacco smoke exposure and antisocial behaviour in later childhood. J Epidemiol Community Health, 2013 DOI: 10.1136/jech-2012-202191

http://news.discovery.com/animals/pets/prehistoric-dog-lovers-profiled-130521.htm#mkcpgn=rssnws1

Prehistoric Dog Lovers Liked Seafood, Jewelry, Spirituality

An analysis of ancient dog burials finds that the typical prehistoric dog owner ate a lot of seafood, had spiritual beliefs, and wore jewelry that sometimes wound up on the dog.

May 22, 2013 06:00 AM ET // by Jennifer Viegas

The study, published in PLoS ONE, is one of the first to directly test if there was a clear relationship between the practice of dog burial and human behaviors.

The answer is yes.

"Dog burials appear to be more common in areas where diets were rich in aquatic foods because these same areas also appear to have had the densest human populations and the most cemeteries," lead author Robert Losey, a University of Alberta anthropologist, told Discovery News.

The discovery negates speculation that dogs back in the day were just work animals brought along on hunting trips. "If the practice of burying dogs was solely related to their importance in procuring terrestrial game, we would expect to see them in the Early Holocene (around 9,000 years ago), when human subsistence practices were focused on these animals," Losey continued. "Further, we would expect to see them in later periods in areas where fish were never really major components of the diet and deer were the primary focus, but they are rare or absent in these regions."

For the study, Losey and his team researched dog burials worldwide, but focused particularly on ones located in Eastern Siberia. Siberia appears to have been an ancient hotbed of dog lovers, with the earliest known domesticated dog found there and dating to 33,000 years ago. Dog burials in this region, however, span across a more recent 10,000-year period.

The researchers found that most of the dog burials in this area occurred during the Early Neolithic 7,000-8,000 years ago. Dogs were only buried when human hunter-gatherers were also being buried. When pastoralists later came through, they did not bury dogs, although they did sacrifice them from time to time.

"I think the hunter-gatherers here saw some of their dogs as being nearly the same as themselves, even at a spiritual level," Losey said. "At this time, dogs were the only animals living closely with humans, and they were likely known at an individual level, far more so than any other animal people encountered. People came to know them as unique, special individuals."

The burials reflect that association. One dog, for example, was laid to rest "much like it is sleeping." A man was buried with two dogs, one carefully placed to the left of his body, and the other to the right. A dog was buried with a round pebble, possibly a toy or meaningful symbol, placed in its mouth. Still other dogs were buried with ornaments and implements, such as spoons and stone knives.

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One of the most interesting burials contains a dog wearing a necklace made out of four red deer tooth pendants. Such necklaces appear to have been a fashion and/or symbolic trend at the time, since people wore them too.

"The dog buried wearing the necklace was buried in a region where human diets were relatively rich in riverine fish," Losey said. "The dog, however, was consuming relatively little fish, having a protein diet with more emphasis on terrestrial game. This suggests the dog was likely a recent arrival in the region, and its body chemistry had not yet adjusted to the local fish diet."

All of the hunter-gatherer dogs were similar in appearance to large varieties of huskies, similar to today's Siberian huskies.

Erik Axelsson, a researcher at Uppsala University's Science for Life Laboratory, has also studied prehistoric dogs. He too found that human and dog diets, burial practices and more often paralleled each other, revealing how close the dog-human bond has been for thousands of years.

Axelsson said, "Dogs and humans share the same environment, we eat similar food and we get similar diseases."

Based on the number of burials, we also often spend eternity together too.

http://www.sciencenews.org/view/generic/id/350585/description/Dog_sniffs_out_grammar

Dog sniffs out grammar

A border collie takes command of sentence rules

By Bruce Bower

Chaser isn't just a 9-year-old border collie with her breed's boundless energy, intense focus and love of herding virtually anything. She's a grammar hound. In experiments directed by her owner, psychologist John Pilley of Wofford College in Spartanburg, S.C., Chaser demonstrated her grasp of the basic elements of grammar by responding correctly to commands such as "to ball take Frisbee" and its reverse, "to Frisbee take ball." The dog had previous, extensive training to recognize classes of words including nouns, verbs and prepositions.

"Chaser intuitively discovered how to comprehend sentences based on lots of background learning about different types of words," Pilley says. He reports the results May 13 in Learning and Motivation.

Throughout the first three years of Chaser's life, Pilley and a colleague trained the dog to recognize and fetch more than 1,000 objects by name. Using praise and play as reinforcements, the researchers also taught Chaser the meaning of different types of words, such as verbs and prepositions. As a result, Chaser learned that phrases such as "to Frisbee" meant that she should take whatever was in her mouth to the named object.

Exactly how the dog gained her command of grammar is unclear, however. Pilley suspects that Chaser first mentally linked each of two nouns she heard in a sentence to objects in her memory. Then the canine held that information in mind while deciding which of two objects to bring to which of two other objects.

Pilley's work follows controversial studies of grammar understanding in dolphins and a pygmy chimp.

It's hard to know what a dog or other nonhuman animal is actually thinking about when responding to commands, comments dog researcher and psychology graduate student Krista Macpherson of the University of Western Ontario in London, Canada. Debate about whether these animals understand that the meaning of commands rests on abstract rules will continue with Chaser's behavior, in her view.

COMMAND PERFORMANCE

A border collie named Chaser participates in an experiment testing her ability to understand commands given before she can see any of the objects named in those directives. After hearing a four-word command, Chaser consistently turned around and carried the correct item from the head of the bed to the living room, where she placed it next the appropriate object.

Courtesy of J. Pilley

Chaser started sentence training at age 7. She stood facing a pair of objects she knew by name. An experimenter would say, for instance, "to ball take Frisbee." In initial trials, the experimenter pointed at each item while saying its name.

After several weeks of training, two experiments conducted in Pilley's living room tested Chaser's grammar knowledge. A college student sat with the dog facing two pairs of objects. Chaser had to choose an object from one pair to carry to an object from the other pair. The student read commands that included words for those objects. Only some of those words had been used during sentence training, including "to sugar take decoy." To see whether Chaser grasped that grammar could be used flexibly, Pilley had the student also read sentences in the reversed form of "take sugar to decoy." In 28 of 40 attempts, Chaser grabbed the correct item in her mouth and dropped it next to the correct target.

Another experiment tested Chaser's ability to understand commands when she couldn't see the objects at first. Pilley stood at the end of a bed where Chaser sat facing him, with two objects behind her at the other end of the bed. After hearing a command, Chaser turned around and nabbed one of the objects. She then ran to the living room and delivered the item to one of another pair of objects. She succeeded on all 12 trials. Border collies achieve similar grammatical insights when working with farmers to learn sheep-herding commands, Pilley speculates. With enough training, other dog breeds could also get a paw-hold on grammar, he predicts.

J. Pilley. Border collie comprehends sentences containing a prepositional object, verb and direct object. Learning and Motivation. Published online May 13, 2013. doi:10.1016/j.lmot.2013.02.003. Abstract available: [Go to]

http://arstechnica.com/science/2013/05/linking-simple-chemistry-to-something-like-life/

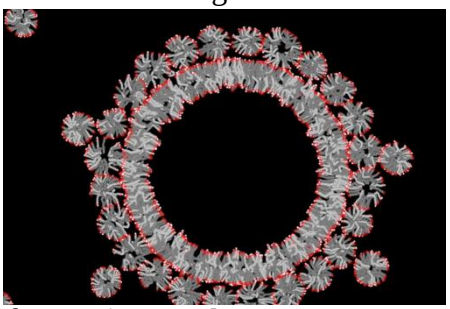
Linking simple chemistry to something like life

How do you go from an RNA to a cell with membranes and proteins?

by John Timmer - May 22 2013, 4:20am TST

Origin of life researchers have made impressive progress in recent years, showing that simple chemicals can combine to make nucleotides, the building blocks of DNA and RNA. Given the right conditions, these nucleotides can combine into ever-longer stretches of RNA. A lot of work has demonstrated that RNAs can perform all sorts of interesting chemistry, specifically binding other molecules and catalyzing reactions.

So the case for life getting its start in an RNA world has gotten very strong in the past decade, but the difference between a collection of interesting RNAs and anything like a primitive cell—surrounded by membranes, filled with both RNA and proteins, and running a simple metabolism—remains a very wide chasm. Or so it seems. A set of papers that came out in the past several days suggest that the chasm might not be as large as we'd tend to think.



A computer model of a growing membrane. **Szostak Lab**

Ironing out metabolism

A lot of the basic chemistry that drives the cell is based on electron transport, typically involving proteins that contain an iron atom. These reactions not only create some of the basic chemicals that are necessary for life, they're also essential to powering the cell. Both photosynthesis and the breakdown of sugars involve the transfer of electrons to and from proteins that contain an iron atom.

DNA and RNA tend to have nothing to do with iron, interacting with magnesium instead. But some researchers at Georgia Tech have considered that fact a historical accident. Since photosynthesis put so much oxygen into the atmosphere, most of the iron has been oxidized into a state where it's not soluble in water. If you go back to before photosynthesis was around, the oceans were filled with dissolved iron. Previously, the group had shown that, in oxygen-free and iron rich conditions, RNAs would happily work with iron instead and that its presence could speed up their catalytic activity.

Now the group is back with a new paper showing that if you put a bunch of random RNAs into the same conditions, some of them can catalyze electron transfer reactions. By "random," I mean RNAs that are currently used by cells to do completely unrelated things (specifically, ribosomal and transfer RNAs). The reactions they catalyze are very simple, but remember: these RNAs don't normally function as a catalyst at all. It wouldn't surprise me if, after a number of rounds of evolutionary selection, an iron-RNA combination could be found that catalyzes a reaction that's a lot closer to modern metabolism.

All of which suggests that the basics of a metabolism could have gotten started without proteins around.

Proteins build membranes

Clearly, proteins showed up at some point. They certainly didn't look much like the proteins we see today, which may have hundreds or thousands of amino acids linked together. In fact, they may not have looked much like proteins at all, if a paper from Jack Szostak's group is any indication. Szostak's found that just two amino acids linked together may have catalytic activity. Some of that activity can help them engage in competition over another key element of the first cells: membrane material.

The work starts with a two amino acid long chemical called a peptide. If that peptide happens to be serine linked to histidine (two amino acids in use by life today), it has an interesting chemical activity: very slowly and poorly, it links other amino acids together to form more peptides. This weak activity is especially true if the amino acids are phenylalanine and leucine, two water-hating chemicals. Once they're linked, they will precipitate out of a water solution.

The authors added a fatty acid membrane, figuring that it would soak up the reaction product. That definitely worked, with the catalytic efficiency of serine-histidine going up as a result. But something else happened as well: membranes that incorporated the reaction product started growing. It turns out that its presence in the membrane made it an efficient scrounger of other membrane material. As they grew, these membranes extended as long filaments that would break up into smaller parts with a gentle agitation and then start growing all over again.

In fact, the authors could set up a bit of a Darwinian competition between membranes based on how much starting catalyst each had. All of which suggests that proteins might have found their way into the cell as very simple chemicals that, at least initially, weren't in any way connected to genetic and biochemical functions performed by RNA. But any cell-like things that evolved an RNA that made short proteins could have a big advantage over its competition.

Proteins go big

How do you go from short peptides to long, complex proteins that rely on a specific sequence of amino acids in order to function? It turns out that you need a fairly specific sequence in order to perform an equally specific function (although even that can be very flexible). However, you may not need to be very specific at all if you just care about having any function at all. In other words, it may have been useful for a cell to just randomly link amino acids together.

This work grew out of a previous study in which someone specified enough of the amino acid sequence to allow a protein to fold up into a small spherical structure. Anything beyond that was made random. The

surprising thing was that these partly random sequences ended up doing all sorts of different things, binding some chemicals, catalyzing reactions, and so forth. But it's hard to make and test a huge complement of random sequences, so the authors turned to computational modeling, trying out a comprehensive set of potential proteins.

It turns out that a lot of them would potentially stick to interesting chemicals and form various binding pockets. In fact, a number of proteins that appear to be entirely unrelated on the sequence level happily formed very similarly shaped binding pockets. All of which suggests that making just any protein, with little regard for its actual sequence, could have a positive impact on the cell's fitness. Once in place, it could be adapted to be a bit more sequence-specific.

Although all of these results are exciting, it's important to place them in context. We're never going to know precisely how life first arose, since the actual evidence for the events no longer exists. But we can come up with plausible pathways from basic chemistry to simple biochemistry, something these studies seem to provide. That's not to say that another study won't come up with something that's even more plausible in the future.

The other thing to note is that these studies may start filling in what seems to be a big chasm between life and non-life, and they have a habit of taking a single gap and dividing it in two. They may identify landmarks on the journey towards life, but they open up new questions about exactly what route was taken between them.

- *Nature Chemistry, 2013. DOI: 10.1038/NCHEM.1649*
- *Nature Chemistry, 2013. DOI: 10.1038/NCHEM.1650*
- *PNAS, 2013. DOI: 10.1073/pnas.1300011110*

http://nyti.ms/12W4hFV

Folk Remedy Extracted From Captive Bears Stirs Furor in China

A Fight Against 'Milking' Bears for Bile: The use of bear bile for traditional Chinese medicine cures is a growing industry in China, but it is also increasingly controversial thanks to an escalating animal rights movement.

By ANDREW JACOBS

CHENGDU, China - It was, at first glance, a rather modest initial public offering by a small Chinese company seeking to expand production of the key ingredient used in traditional remedies said to shrink gallstones, reduce fevers and sooth the aftereffects of excessive drinking. But Guizhentang Pharmaceutical, the country's largest producer of bear bile extract, apparently overlooked one important factor before submitting its application to the Shenzhen Stock Exchange: China's increasingly audacious animal rights movement.

Guizhentang's proposal to triple the company's stock of captive bears, to 1,200 from 400, provoked a firestorm from those opposed to bear bile farming, a process that involves inserting tubes into the abdomens of bears and "milking" them, sometimes for years.

Protesters in bear suits picketed drugstores, hackers briefly brought down Guizhentang's Web site and more than 70 Chinese celebrities, including the basketball star Yao Ming and the pop diva Han Hong, circulated a petition calling on the stock exchange to reject the I.P.O. After some of China's biggest news media outlets posted harrowing undercover footage revealing cages so tight the bears could barely move, Guizhentang last month withdrew its application, saying it needed more time to put together its filing.

For China's animal welfare advocates, the victory signaled the growing clout of a movement that is frequently derided as bourgeois, frivolous or worse. Its most vociferous opponents paint animal advocates as foreign-financed traitors who would do away with such hallowed Chinese traditions as dog meat hot pot, ivory carving and dried deer penis, consumed to increase virility.

Deborah Cao, a lawyer who frequently writes about animal rights in China, said campaigns like the one that defeated Guizhentang showed how social media brought together the generation of educated Chinese urbanites who grew up with household pets and anthropomorphic Disney characters. "It's a bottom-up, grass-roots movement, one that is contributing to an emerging civil society increasingly aware of individual rights and obligations, be it to humans or animals," she said. Such activism is even more notable given the constraints the Communist Party typically imposes on public lobbying, street protests or any unsanctioned organizing.

Advocates have not yet persuaded the government to enact animal welfare legislation. But optimists say they have started to chip away at the long-held notion that animals exist to satisfy the medicinal and gastronomical needs of humans. Activists point to the growing visibility of public awareness campaigns targeting the consumption of shark fins as well as a recent spate of vigilante rescue efforts that have blocked trucks laden with cats and dogs from reaching the slaughterhouse. In December, the state-run broadcaster CCTV ran a series of exposés highlighting the illegal consumption of monitor lizards, rhesus monkeys, barking deer and other wildlife, and the police crackdown on black market dealers that followed.

"Animal rights activists are walking an incredibly sensitive tightrope, but I think they're reaching a tipping point right now," said Jill Robinson, the director of Animals Asia, an organization based in Hong Kong that has been campaigning for two decades to end bear bile farming.
Still, despite what appears to be growing public opposition to the practice, the Chinese government is not prepared to end the lucrative trade in ursodeoxycholic acid, the active ingredient found in bear gallbladders. Although scientists have engineered a synthetic alternative, traditionalists claim it lacks the therapeutic punch of raw bile, which can sell for as much as $24,000 a kilogram, roughly half the price of gold.
Scientists have scrutinized the health effects of bear bile but have come to no definitive conclusions. But sold in powdered form as capsules, or as a tonic, bile is considered by many to be an elixir of sorts. Bile marketers say it fortifies the liver, reduces flu symptoms and improves eyesight.
Yang Tingying, a vendor at the wholesale Chinese medicine market here in Chengdu, the provincial capital of Sichuan, insisted that bear bile cures all manner of liver ailments, including hepatitis. "It's the best because it's from nature," she said, pulling out a pair of desiccated gall bladders, which are illegal to sell.
To the distress of its opponents, the industry has grown significantly in the 13 years since Chinese officials first pledged to gradually reduce the number of captive bears to 1,500 from 7,000. These days, there are an estimated 20,000 bears on nearly 100 domestic bear farms, an expansion fueled in part by marketing efforts promoting novel uses for bear bile, like a hangover cure for well-to-do businessmen who engage in nightly carousing. Besides China, there are bear bile farms in Vietnam, Laos, Myanmar and North Korea.
For animal welfare advocates, the challenge is to convince Chinese consumers that the barbarity of bile farming outweighs the supposed medicinal benefits of natural bile — or that the risks of consuming bile from sick bears pumped with antibiotics are high. In addition to circulating videos of harvesting practices, organizations like Animals Asia wield a number of secret weapons, including Sun Li, Caesar and Buddha. They are among the 158 rescued bears that roam the group's sanctuary outside Chengdu. The center receives school groups, celebrities and Chinese reporters, all of whom are invariably smitten with the bears.
Most of the animals came from farms closed by the authorities because they had fewer than 50 bears, a violation of industry rules. The bulk of the animals are Asiatic black bears, a threatened species better known as the moon bear for the distinctive white crescent that arcs across its chest.
Nicola Field, the sanctuary's chief veterinarian, said bears often arrived emaciated, their abdomens riddled with the infections, hernias and tumors that are hallmarks of a extraction process requiring open wounds for thrice-daily milkings. The bears' teeth are invariably worn down from gnawing on the bars of their cages and their feet are often in pitiful shape because few of the animals have ever walked on the ground. "The catalog of abuse they've endured is appalling," Ms. Field said. The years of pain and confinement are so traumatizing that some of the rescued bears spend endless hours butting their heads against walls or gnawing on their limbs.
Industry supporters have mounted their own pro-bile public relations campaign, stressing China's history of traditional medicine and suggesting that animal rights advocates are doing the bidding of foreign drug companies out to promote Western medicine at the expense of homegrown remedies.
During a news conference last year called to counter critics, Fang Shuting, chairman of the China Association of Traditional Chinese Medicine, suggested that bears enjoy the process, which he likened to turning on a tap. "Natural, easy and without pain," he said. "After they're done, the bears can even play happily outside."
His remarks backfired, producing a torrent of ridicule on social media and refutations from experts who said bear farmers could not possibly let the animals leave their cages. "Bears are smart like dogs and remember pain," said Zhang Xiaohai, who has visited a number of bear farms as an undercover investigator for Animals Asia. "They would never willingly come back to be milked again."
But Mr. Zhang and others find hope in the attitudes of young Chinese like Guan Zhiling, who was visiting the sanctuary recently with her high school classmates. "It's brutal and disrespectful to the bears, and a disgrace to the human race," she said.

http://www.scientificamerican.com/article.cfm?id=a-real-life-tricorder-is-now-available-Scanadu-2013-05

A Real-Life Tricorder Is Now Available for You to Buy and Scan Yourself

The Scanadu Scout, which you can use to measure your vital signs by just holding it to your temple for 10 seconds, is now available for $150 on Indiegogo

By Ariel Schwartz

Get excited, Star Trek fans and self-tracking enthusiasts: your real-life tricorder is now available for pre-order. Scanadu, a startup based at the NASA Ames Research Center, has been working on a non-invasive tricorder for over two years. By the end of 2012, the company had a prototype ready--a handheld Yves Behar-designed device that tracks pulse transit time (to measure blood pressure), temperature, ECG, oximetry, heart rate, and breathing rate. A 10 second scan of a person's temple yields data that has a 99% accuracy rate. That information

is automatically sent via Bluetooth to the user's smartphone. Today, the Scanadu Scout tricorder is available for pre-order on Indiegogo. It's a chance for early adopters to check out Scanadu's technology, and an opportunity for Scanadu to gather some of the data it needs for FDA approval.

The Scout.

The first 1,000 devices ordered on Indiegogo will cost $149, but the price goes up to $199 after that. Originally, Scanadu hoped to price the Scout at $150 across the board, but had to shift because the newest version of the Scout has expanded horsepower (from 8 to 32 bits) and now runs on Micrium, the operation system that NASA uses for Mars sample analysis on the Curiosity rover. Scanadu co-founder Walter De Brouwer, an entrepreneur who first created a backpack-sized tricorder in the 1990s, decided to add in a big horsepower-hogging extra feature to the new Scout: the ability to remotely trigger new algorithms and plug in new sensors (like a spectrometer).

A Real-Life Tricorder Is Now Available for You to Buy and Scan Yourself

"If we find new algorithms to find relationships between several readings, we can use more of the sensors than we would first activate," says De Brouwer. "If you know a couple of the variables, you could statistically predict that something is going to happen. The more data we have, the more we can also predict, because we're using data mining at the same time as statistics."

One of the Scout's cornerstone algorithms, for example, allows it to read blood pressure without the cuff that we're all so used to seeing in doctor's offices. In the future, Scanadu could discover an algorithm that connects, age, weight, blood pressure, and heart rate with some other variable--and then remotely trigger that relationship.

The Scout doesn't yet have FDA approval, which is part of the reason for running an Indiegogo campaign. Everyone who pre-orders a Scout has their data sent to a cloud service, where Scanadu will collect it in a big file for the FDA.

"It's going to be a consumer product in the future, but right now we are positioning it as a research tool so that it can be used to finalize the design and collect data to eventually gain regulatory approval," says De Brouwer. "In the end, you have to prove how people are going to use the device, how many times a day, and how they are going to react to the information."

Anyone who opts-in will also gain access to the data of other users who have also elected to share their vitals. People will be able to tweak search parameters (i.e. body temperatures in California) to see only what's relevant for them.

In the future, De Brouwer imagines this could be used for population scanning, kind of like Google Flu Trends with data from real individuals.

If your child has flu symptoms, you could one day search the Scout's stats to see if other kids at her school are also sick.

"I think very soon we will be used to numbers and readings and how to change our behavior almost in real time," says De Brouwer. He believes that separating people from self-tracking devices will be "like taking your email away."

There are no algorithms in place yet to warn users if their vitals are abnormal, but that's on De Brouwer's to-do list. And based on feedback from Indiegogo supporters, Scanadu may add in new features before releasing the Scout to consumers.

ScanaFlo.

Scanadu also has another product, the ScanaFlo, that will be submitted for FDA approval in July. That urine testing kit uses a smartphone app to check for an array of issues with the liver, kidney, metabolism, and urinary tract. Peeing on a ScanaFlo paddle allows the device to measure protein, glucose, leukocytes, nitrates, bilirubin, blood, urobilinogen, specific gravity, urine pH--and it checks for pregnancy. Everyone who pre-orders a Scout will get two ScanaFlo paddles.

"We're all very proud of the design and how it performs. With the the smartphone app that we have, it will perform better than the $10,000 machines you can now buy," says De Brouwer. Data from both the Scout and the ScanaFlo will be available on the app.

No word on when the ScanaFlo will go on sale, but Indiegogo backers can expect to receive their Scouts in the first quarter of 2014.

http://phys.org/news/2013-05-the-new-retirement-no.html

The new retirement: No retirement?

For growing numbers of Americans, the new retirement may really mean no retirement.

That's the conclusion of an article in the current issue of the ISR Sampler, the annual magazine of the University of Michigan Institute for Social Research.

"For most of the 20th century we saw retirement ages fall while life expectancy rose," said David Weir, an ISR research professor and director of the ISR Health and Retirement Study. "About 20 years ago, the trend in retirement age reversed and it has been inching up slowly ever since."

People are retiring later for a lot of reasons, but a key one is economic. Employer health insurance benefits for retirees are eroding, spurring many employees to hold out until they qualify for Medicare at age 65. Changes to Social Security, such as the increase in the age at which people can receive full benefits from 65 to 67, also may be playing a role. And people are living longer, requiring additional savings to support those extra years.

Some 40 percent of older Americans delayed retirement in the years after the Great Recession, according to an analysis of data from ISR's Health and Retirement Study and its Cognitive Economics Study.

"The typical household lost about 5 percent of its total wealth between the summers of 2008 and 2009," said ISR economist Brooke Helppie McFall.

People don't intend to work long enough to recoup all the money they lost, but on average, those who postponed retirement expect to work about 1.6 years longer than planned, she said. And even as the economy has begun to turn around, many households still find themselves facing a more precarious future.

"While the stock market has recovered most of its pre-recession value, housing prices have not, and for most people their house is their biggest asset," Weir said.

Economics are just part of the reason why many Americans are working longer, he said. Many married men are likely to stay on the job longer now because their wives are working. Couples typically want to coordinate their retirements, and if a wife is working until age 62 or 65, that's an incentive for her often slightly older husband to keep working, too.

And some people aren't retiring for a simpler reason: they love their jobs. Not surprisingly, working beyond normal retirement age by choice is particularly common among the wealthier and more highly educated, those who are likely to have better health and jobs they can still do effectively at an advanced age, Weir said. Overall, many more jobs than before rely on cognitive skills, rather than physical abilities, studies show, and the number of retirement-age employees who are physically able to do work into later years has increased, as well.

Although people are working longer, most still decide to retire at some point. But even that process has changed. According to an analysis of Health and Retirement Study participants born between 1942 and 1947, nearly two-thirds of those who retired from full-time work passed through some sort of bridge job—either part time or of short duration—before leaving the work force entirely.

Going part time may seem an obvious bridge step. More surprising is the move to different full-time work after retirement, according to Nicole Maestas, a RAND economist and researcher with ISR's Michigan Retirement Research Council.

She said the number of people who retire, take a break for a couple of years and then return to work has been increasing since the early 1990s. Some 40 percent of workers between the ages of 51 and 61 who stop work will return in some full-time capacity, according to her analysis of data from the Health and Retirement Study. Maestas coined the term "unretirement" for this phenomenon.

"The New Retirement: No Retirement?" by Susan Rosegrant, appears in the Spring 2013 issue of the ISR Sampler. Read the full article, including stories of those who've chosen different retirement, or unretirement, paths, at http://home.isr.umich.edu/sampler/the-new-retirement

http://bit.ly/13VtwWv

Earth's tides are shoving the moon away faster

EARTH is shoving the moon away faster now than it has done for most of the past 50 million years, says a new model for the way tides influence the lunar orbit.

The result helps solve a mystery concerning the moon's age that has long vexed astronomers. The moon's gravity creates a daily cycle of low and high tides. This dissipates energy between the two bodies, slowing Earth's spin on its axis and causing the moon's orbit to expand at a rate of about 3.8 centimetres per year. If that rate has always been the same, the moon should be 1.5 billion years old, yet some lunar rocks are 4.5 billion years old.

Enter Matthew Huber of Purdue University in West Lafayette, Indiana. His team gathered data on ocean depths and continental contours that existed 50 million years ago, and fed that into a model to simulate ancient tides.

Energy dissipation back then was only half what it is today, so the moon was pushed away at a slower rate (Geophysical Research Letters, doi.org/mjz).
The key is the North Atlantic Ocean, which is now wide enough for water to slosh across once per 12-hour cycle, says Huber. Like a child sliding in a bathtub, that creates larger waves and very high tides, shoving the moon faster.

http://www.bbc.co.uk/news/magazine-22530625

Coffee addiction: Do people consume too much caffeine?

US officials are investigating the safety of caffeine in snacks and energy drinks, worried about the "cumulative impact" of the stimulant - which is added to a growing number of products. Is our tea and coffee-fuelled society too dependent on the world's favourite drug?

By Jon Kelly BBC News Magazine, Washington DC

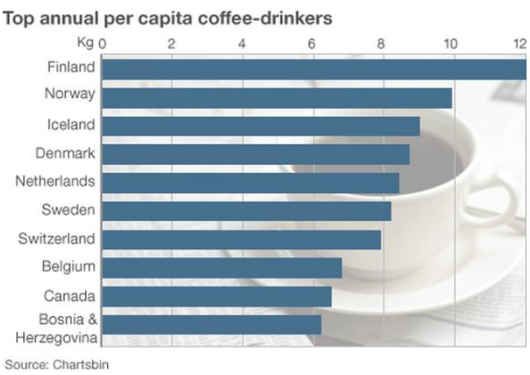
The bubbling kettle, the aroma from the mug, the first bitter mouthful of the morning.
It's a ritual without which the working day would be, for millions of people, frankly horrifying.
Caffeine is, according to New Scientist, the planet's most popular "psychoactive drug." In the United States alone, more than 90% of adults are estimated to use it every day. But now even the US - home of Coca-Cola, Starbucks and the 5-Hour Energy shot - is questioning the wisdom of adding it to everyday foodstuffs like waffles, sunflower seeds, trail mix and jelly beans.
In a statement, the Food and Drug Administration (FDA) highlighted the "unfortunate example" of Wrigley chewing gum producing packs of eight sticks which each contained as much caffeine as half a cup of coffee. Subsequently, Wrigley said it would "pause" production of the product.
The agency is also looking at highly-caffeinated energy drinks, and said it was concerned about the "cumulative impact" of adding stimulants to products.
According to the US Substance Abuse and Mental Health Services Administration, the number of people seeking emergency treatment after ingesting energy drinks doubled to more than 20,000 in 2011. However, the energy drink industry says its products are safe and insists there is no proof of a link with any harmful reactions.
There have been documented cases of fatal overdoses caused by "caffeine toxicity", though these are very rare.
Scientists at Johns Hopkins University, studying its addictive properties, found that withdrawal symptoms included tiredness, headaches, difficulty concentrating, muscle pain and nausea.
But there is far from any kind of scientific consensus that caffeine use is harmful. A recent study by the Harvard School of Public Health suggested that "coffee drinking doesn't have any serious detrimental health effects" and that drinking up to six cups a day was "not associated with increased risk of death from any cause".
In moderation, caffeine may have some positive effects. Research suggests it could be associated with a reduced risk of prostate cancer and breast cancer. A recent study linked drinking coffee and tea with a lower risk of type two diabetes. As a result, the FDA has pledged to "determine what is a safe level" of caffeine use.
The agency's move has been welcomed by those who fear caffeine is already encroaching too much into our daily lives - often in products where it may not be expected.
"Many people just aren't aware of how much caffeine they are taking," says Lynn Goldman, dean of the George Washington University School of Public Health and Health Services.
As a result, she says, they could unwittingly create problems for themselves with insomnia, indigestion, or their blood pressure.
It's especially worrying for parents, who can find it hard to regulate their children's intake.
But challenging the hegemony of caffeine may be a difficult task on a planet that consumes 120,000 tonnes of the substance per annum.
In Finland, the world's most caffeinated country, the average adult consumes 400mg of the drug every day - equivalent to four or five cups of coffee a day, and equal to the maximum daily limit recommended by the UK Food Standards Agency.

Beverage	Caffeine (mg)	Quantity
Coffee	77-150	6oz/170g
Tea	40-80	5oz/142g
Coca-Cola	34.5	12oz/340g
Pepsi	38	12oz/340g
Red Bull	80	8.3oz/235g

SOURCE: ARIZONA STATE UNIVERSITY

"We think that, when used in moderation, caffeine doesn't pose a risk," says Sanna Kiuru, a senior officer at Evira, the Finnish food safety authority. "It's mainly adults who drink coffee, not children. For us the levels are quite moderate."
Even buzz-loving Finns have been troubled by the rise of stealth stimulants, however.
"We have been concerned about the rise in caffeine in different foods," says Kiuru. Highly-caffeinated energy drinks in Finland are obliged to carry warning labels - a practice that will be extended across the EU from 2014.
For most caffeine consumers, its chief benefit is that, by stimulating alertness, it helps you get more done.
This is a trait that makes it unusual among recreational substances, says Stephen Braun, author of Buzz: The Science and Lore of Alcohol and Caffeine. "Its appeal is that it helps us earn more money," he adds. "What

makes it different from other drugs is that it's used as a productivity tool - not for pleasure, like cannabis, or as a relaxant, like alcohol."
Perhaps the closest analogy is with coca leaves, chewed by labourers to give them extra energy in countries like Peru and Bolivia.
It's no coincidence, Braun believes, that caffeine's popularity boomed in Europe at the dawn of the industrial revolution, when the race for ever-increased productivity accelerated. Many of history's creative minds have also been associated with some truly epic feats of caffeine consumption. According to one biographer, the French novelist and playwright Balzac drank as many as 50 cups of coffee a day. "Were it not for coffee one could not write, which is to say one could not live," he once insisted.



For seven years, the film-maker David Lynch ate at the same Los Angeles diner every day, drinking up to seven sweetened cups of coffee "with lots of sugar" in one sitting, which he said would guarantee that "lots of ideas" arrived. Ludwig van Beethoven was said to have painstakingly counted out exactly 60 coffee beans per cup when he brewed coffee.
Perhaps the most well-publicised recent tales of caffeine excess featured the somewhat less critically revered singer Robbie Williams, who reportedly consumed 36 double espressos and 20 cans of Red Bull a day.
It is the routine task itself, as much as the stimulant properties of caffeine, that makes the process so significant, Mason Currey, author of Daily Rituals: How Artists Work.
"A lot of artists use the process of making the coffee as a gateway to the creative process," he adds.
"You need to get into the right mindset to do that sort of work, and the preparation ritual provides a focus."
Cup of tea Does the very ritual of preparing caffeinated drinks help minds focus?
But attempts to clamp down on the spread of the substance have historically proved futile.
In 1911, the US government sued the Coca-Cola Company, on the basis that the caffeine in its drink was "injurious to health", but Coca-Cola prevailed in the courts.
One problem with attempting to regulate the substance, says Braun, is that it affects everyone in differently - people's varying physiologies and metabolisms making it impossible to prescribe a "safe" limit that works for everyone. "Ultimately, you have to become your own scientist - there isn't an alternative to careful self-experimentation," he says.
Most people are likely to have ascertained by adulthood how much, or little, tea or coffee they can tolerate at a time. But critics say this doesn't apply to energy drinks and caffeinated foodstuffs, whose effects are arguably more difficult to judge.
However profitable these products may prove for their manufacturers though, Currey suspects they well never acquire the mystique of coffee and tea. "There's something that's not quite as special and evocative about them," he says. "Buying an 5-Hour Energy drink from the 7-Eleven [convenience store] doesn't have the ambience of brewing a cup of coffee. I can't imagine future biographers of great artists and writers describing this stuff in the same way." *Additional reporting by Mark Bosworth in Helsinki*

http://www.eurekalert.org/pub_releases/2013-05/ncsu-bbc051713.php

Bittersweet: Bait-averse cockroaches shudder at sugar

Sugar isn't always sweet to German cockroaches, especially to the ones that avoid roach baits.

In a study published May 24 in the journal Science, North Carolina State University entomologists show the neural mechanism behind the aversion to glucose, the simple sugar that is a popular ingredient in roach-bait poison. Glucose sets off bitter receptors in roach taste buds, causing roaches to avoid foods that bring on this taste-bud reaction. This aversion has a genetic basis and it eventually spreads to offspring, resulting in increasingly large groups of cockroaches that reject glucose and any baits made with it.
In normal German cockroaches, glucose elicits activity in sugar gustatory receptor neurons, which react when exposed to sugars like glucose and fructose – components of corn syrup, a common roach-bait ingredient. Generally, roaches have a sweet tooth for these sugars.
"We don't know if glucose actually tastes bitter to glucose-averse roaches, but we do know that glucose triggers the bitter receptor neurons that would be triggered by caffeine or other bitter compounds," says Dr. Coby Schal, the Blanton J. Whitmire Distinguished Professor of Entomology at NC State and the corresponding author of the paper. "That causes the glucose-averse roach to close its mouth and run away from glucose in tests."
In the study, the researchers conducted tests on the roach tongue, the paired mouth appendages called paraglossae. The tests showed the unexpected electrophysiological reactions that glucose stimulates both sugar

and bitter receptor neurons, confirming behavioral tests that showed roaches quickly fleeing from glucose when presented with it.
But it's not just a sugar aversion. Roaches exposed to fructose were happy to partake of its sweetness. Glucose-averse roaches that were forced to taste glucose refused to ingest the sugar, akin to a child who spits out her bitter-tasting food. Normal cockroaches, meanwhile, were happy to eat glucose. Researchers learned this by combining the glucose with food coloring and watching it get ingested or rejected by the normal or glucose-averse roaches, respectively.
Study co-author Dr. Jules Silverman, the Charles G. Wright Distinguished Professor of Entomology at NC State, discovered glucose aversion and described its inheritance pattern more than 20 years ago. "It is extremely gratifying that we now understand the neural mechanism that underlies this unusual, yet adaptive, behavior," he said.
There is a cost, however, to cockroaches with glucose aversion. In the absence of glucose-toxicant mixtures, glucose-averse cockroaches grow more slowly than normal roaches in laboratory settings where there are no nutritional stresses. "Now we want to understand how this trait persists in nature, where the food supply is probably limited," Silverman said. "Cockroaches have to adapt to a varied and unreliable food supply, and glucose-aversion places an additional restriction on obtaining adequate nutrition."
Schal says that the pest-control arms race has mostly been about pests gaining resistance to the insecticides themselves. This paper, however, shows an arms race that includes behavioral resistance to certain types of food – in this case, glucose.
"Most times, genetic changes, or mutations, cause the loss of function," Schal says. "In this case, the mutation resulted in the gain of a new function – triggering bitter receptors when glucose is introduced. This gives the cockroach a new behavior which is incredibly adaptive. These roaches just got ahead of us in the arms race."
Ayako Wada-Katsumata, an NC State senior research scholar, performed most of the experiments and is the first author of the paper. She is now investigating whether roaches can learn to associate glucose with specific odors and thus use their memory to ignore baits that contain glucose. The research was supported by the National Science Foundation, the U.S. Department of Housing and Urban Development, and the Blanton J. Whitmire Endowment at NC State.
"Changes in taste neurons support the emergence of an adaptive behavior in cockroaches"
Authors: Ayako Wada-Katsumata, Jules Silverman and Coby Schal, North Carolina State University
Published: May 24, 2013, in Science
Abstract: *In response to the anthropogenic assault of toxic baits, populations of the German cockroach have rapidly evolved an adaptive behavioral aversion to glucose (a phagostimulant component of baits). We hypothesized that changes in the peripheral gustatory system are responsible for glucose aversion. In both wild-type and glucose-averse (GA) cockroaches, D-fructose and D-glucose stimulated sugar–gustatory receptor neurons (GRNs), whereas the deterrent caffeine stimulated bitter-GRNs. In contrast, in GA cockroaches, D-glucose also stimulated bitter-GRNs and suppressed the responses of sugar-GRNs. Thus, D-glucose is processed as both a phagostimulant and deterrent in GA cockroaches, and this newly acquired peripheral taste sensitivity underlies glucose aversion in multiple GA populations. The rapid emergence of this highly adaptive behavior underscores the plasticity of the sensory system to adapt to rapid environmental change.*

http://www.eurekalert.org/pub_releases/2013-05/uoc--usb052313.php

UC Santa Barbara scientists discover cinnamon compounds' potential ability to prevent Alzheimer's

Cinnamon: Can the red-brown spice with the unmistakable fragrance and variety of uses offer an important benefit? The common baking spice might hold the key to delaying the onset of – or warding off – the effects of Alzheimer's disease.

That is, according to Roshni George and Donald Graves, scientists at UC Santa Barbara. The results of their study, "Interaction of Cinnamaldehyde and Epicatechin with Tau: Implications of Beneficial Effects in Modulating Alzheimer's Disease Pathogenesis," appears in the online early edition of the Journal of Alzheimer's Disease, and in the upcoming Volume 36, issue 1 print edition.
Alzheimer's disease is the most common form of dementia, a neurodegenerative disease that progressively worsens over time as it kills brain cells. No cure has yet been found, nor has the major cause of Alzheimer's been identified.
However, two compounds found in cinnamon – cinnamaldehyde and epicatechin – are showing some promise in the effort to fight the disease. According to George and Graves, the compounds have been shown to prevent the development of the filamentous "tangles" found in the brain cells that characterize Alzheimer's.

Responsible for the assembly of microtubules in a cell, a protein called tau plays a large role in the structure of the neurons, as well as their function.
"The problem with tau in Alzheimer's is that it starts aggregating," said George, a graduate student researcher. When for the protein does not bind properly to the microtubules that form the cell's structure, it has a tendency to clump together, she explained, forming insoluble fibers in the neuron. The older we get the more susceptible we are to these twists and tangles, Alzheimer's patients develop them more often and in larger amounts.
The use of cinnamaldehyde, the compound responsible for the bright, sweet smell of cinnamon, has proven effective in preventing the tau knots. By protecting tau from oxidative stress, the compound, an oil, could inhibit the protein's aggregation. To do this, cinnamaldehyde binds to two residues of an amino acid called cysteine on the tau protein. The cysteine residues are vulnerable to modifications, a factor that contributes to the development of Alzheimer's.
"Take, for example, sunburn, a form of oxidative damage," said Graves, adjunct professor in UCSB's Department of Molecular, Cellular, and Developmental Biology. "If you wore a hat, you could protect your face and head from the oxidation. In a sense this cinnamaldehyde is like a cap." While it can protect the tau protein by binding to its vulnerable cysteine residues, it can also come off, Graves added, which can ensure the proper functioning of the protein.
Oxidative stress is a major factor to consider in the health of cells in general. Through normal cellular processes, free radical-generating substances like peroxides are formed, but antioxidants in the cell work to neutralize them and prevent oxidation. Under some conditions however, the scales are tipped, with increased production of peroxides and free radicals, and decreased amounts of antioxidants, leading to oxidative stress.
Epicatechin, which is also present in other foods, such as blueberries, chocolate, and red wine, has proven to be a powerful antioxidant. Not only does it quench the burn of oxidation, it is actually activated by oxidation so the compound can interact with the cysteines on the tau protein in a way similar to the protective action of cinnamaldehyde. "Cell membranes that are oxidized also produce reactive derivatives, such as Acrolein, that can damage the cysteines," said George. "Epicatechin also sequesters those byproducts."
Studies indicate that there is a high correlation between Type 2 diabetes and the incidence of Alzheimer's disease. The elevated glucose levels typical of diabetes lead to the overproduction of reactive oxygen species, resulting in oxidative stress, which is a common factor in both diabetes and Alzheimer's disease. Other research has shown cinnamon's beneficial effects in managing blood glucose and other problems associated with diabetes.
"Since tau is vulnerable to oxidative stress, this study then asks whether Alzheimer's disease could benefit from cinnamon, especially looking at the potential of small compounds," said George.
Although this research shows promise, Graves said, they are "still a long way from knowing whether this will work in human beings." The researchers caution against ingesting more than the typical amounts of cinnamon already used in cooking.
If cinnamon and its compounds do live up to their promise, it could be a significant step in the ongoing battle against Alzheimer's. A major risk factor for the disease – age – is uncontrollable. In the United States, Alzheimer's presents a particular problem as the population lives longer and the Baby Boom generation turns gray, leading to a steep rise in the prevalance of the disease. It is a phenomenon that threatens to overwhelm the U.S. health care system. According to the Alzheimer's Association, in 2013, Alzheimer's disease will cost the nation $203 billion.
"Wouldn't it be interesting if a small molecule from a spice could help?" commented Graves, "perhaps prevent it, or slow down the progression."
John Lew, associate professor in the Department of Molecular, Cellular & Developmental Biology, also participated in this study, as well as previous research that has demonstrated cinnamon extract's inhibitory effect on tau aggregation.

http://www.eurekalert.org/pub_releases/2013-05/rb-fst052313.php

First successful treatment of pediatric cerebral palsy with autologous cord blood

Awoken from a persistent vegetative state

Bochum's medics have succeeded in treating cerebral palsy with autologous cord blood. Following a cardiac arrest with severe brain damage, a 2.5 year old boy had been in a persistent vegetative state – with minimal chances of survival. Just two months after treatment with the cord blood containing stem cells, the symptoms improved significantly; over the following months, the child learned to speak simple sentences and to move.
"Our findings, along with those from a Korean study, dispel the long-held doubts about the effectiveness of the new therapy", says Dr. Arne Jensen of the Campus Clinic Gynaecology. Together with his colleague Prof. Dr. Eckard Hamelmann of the Department of Paediatrics at the Catholic Hospital Bochum (University Clinic of the RUB), he reports in the journal "*Case Reports in Transplantation*".

The parents searched the literature for treatment options

At the end of November 2008, the child suffered from cardiac arrest with severe brain damage and was subsequently in a persistent vegetative state with his body paralysed. Up to now, there has been no treatment for the cause of what is known as infantile cerebral palsy. "In their desperate situation, the parents searched the literature for alternative therapies", Arne Jensen explains. "They contacted us and asked about the possibilities of using their son's cord blood, frozen at his birth."

"Threatening, if not hopeless prognosis"

Nine weeks after the brain damage, on 27 January 2009, the doctors administered the prepared blood intravenously. They studied the progress of recovery at 2, 5, 12, 24, 30, and 40 months after the insult. Usually, the chances of survival after such a severe brain damage and more than 25 minutes duration of resuscitation are six per cent. Months after the severe brain damage, the surviving children usually only exhibit minimal signs of consciousness. "The prognosis for the little patient was threatening if not hopeless", the Bochum medics say.

Rapid recovery after cord blood therapy

After the cord blood therapy, the patient, however, recovered relatively quickly. Within two months, the spasticity decreased significantly. He was able to see, sit, smile, and to speak simple words again. Forty months after treatment, the child was able to eat independently, walk with assistance, and form four-word sentences. "Of course, on the basis of these results, we cannot clearly say what the cause of the recovery is", Jensen says. "It is, however, very difficult to explain these remarkable effects by purely symptomatic treatment during active rehabilitation."

In animal studies, stem cells migrate to damaged brain tissue

In animal studies, scientists have been researching the therapeutic potential of cord blood for some time. In a previous study with rats, RUB researchers revealed that cord blood cells migrate to the damaged area of the brain in large numbers within 24 hours of administration. In March 2013, in a controlled study of one hundred children, Korean doctors reported for the first time that they had successfully treated cerebral palsy with allogeneic cord blood.

Bibliographic record *A. Jensen, E. Hamelmann (2013): First autologous cell therapy of cerebral palsy caused by hypoxic-ischemic brain damage in a child after cardiac arrest—individual treatment with cord blood, Case Reports in Transplantation, DOI: 10.1155/2013/951827*

http://www.eurekalert.org/pub_releases/2013-05/mu-bfc052313.php

Bacterium from Canadian High Arctic offers clues to possible life on Mars

Recent discovery of a bacterium that is able to thrive at the coldest temperature ever reported for bacterial growth

Permafrost microbe discovered growing at –15°C, the coldest temperature ever reported for bacterial growth

The temperature in the permafrost on Ellesmere Island in the Canadian high Arctic is nearly as cold as that of the surface of Mars. So the recent discovery by a McGill University led team of scientists of a bacterium that is able to thrive at –15ºC, the coldest temperature ever reported for bacterial growth, is exciting. The bacterium offers clues about some of the necessary preconditions for microbial life on both the Saturn moon Enceladus and Mars, where similar briny subzero conditions are thought to exist.

The team of researchers, led by Prof. Lyle Whyte and postdoctoral fellow Nadia Mykytczuk, both from the Dept. of Natural Resource Sciences at McGill University, discovered Planococcus halocryophilus OR1 after screening about 200 separate High Arctic microbes looking for the microorganism best adapted to the harsh conditions of the Arctic permafrost.

"We believe that this bacterium lives in very thin veins of very salty water found within the frozen permafrost on Ellesmere Island," explains Whyte. "The salt in the permafrost brine veins keeps the water from freezing at the ambient permafrost temperature (~-16ºC), creating a habitable but very harsh environment. It's not the easiest place to survive but this organism is capable of remaining active (i.e. breathing) to at least -25ºC in permafrost."

In order to understand what it takes to be able to do so, Mykytczuk, Whyte and their colleagues studied the genomic sequence and other molecular traits of P. halocryophilus OR1. The researchers found that the bacterium adapts to the extremely cold, salty conditions in which it is found thanks to significant modifications in its cell structure and function and increased amounts of cold-adapted proteins. These include changes to the membranes that envelop the bacterium and protect it from the hostile environment in which it lives.

The genome sequence also revealed that this permafrost microbe is unusual in other ways. It appears to maintain high levels of compounds inside the bacterial cell that act as a sort of molecular antifreeze, keeping the microbe from freezing solid, while at the same time protecting the cell from the very salty exterior environment.

The researchers believe however, that such microbes may potentially play a harmful role in extremely cold environments such as the High Arctic by increasing carbon dioxide emissions from the melting permafrost, one of the results of global warming.
Whyte is delighted with the discovery and says with a laugh, "I'm kind of proud of this bug. It comes from the Canadian High Arctic and is our cold temperature champion, but what we can learn from this microbe may tell us a lot about how similar microbial life may exist elsewhere in the solar system."

http://www.sciencedaily.com/releases/2013/05/130523180316.htm

Technique to Detect Breast Cancer in Urine Developed

New screening method that uses urinalysis to diagnose breast cancer

A Missouri University of Science and Technology researcher has developed a new screening method that uses urinalysis to diagnose breast cancer -- and determine its severity -- before it could be detected with a mammogram. A study to confirm this technique's effectiveness is under way at Mercy Breast Center in Springfield, Mo.
Dr. Yinfa Ma, Curators' Teaching Professor of chemistry at Missouri S&T, uses a device called a P-scan, to detect the concentration of certain metabolites called pteredines in urine samples. These biomarkers are present in the urine of all human beings, but abnormally high concentrations can signal the presence of cancer. Ma believes the levels continue to rise as the cancer advances.
Ma has had good results in limited testing and is now expanding testing in a larger study to prove that the technique works. This blind study is part of the validation process required by the FDA to eventually make the P-Scan available in clinics across the country as an inexpensive, non-invasive test that could be used during routine physical examinations.
In April, Ma began a clinical trial with Mercy Breast Center and commercialization partner Emergence BioScreening of St. Louis. The study focuses on 300 breast cancer patients and a control group of 100 individuals who have been clinically tested and found to be free of cancer. He hopes to conclude the study within a year. Nearly one in eight women will develop invasive breast cancer during her lifetime. Around 85 percent of women diagnosed with breast cancer have no family history of the disease.
"When we heard about this study, we were excited to be a partner," said Dr. Roger Holden, Mercy hematologist and oncologist. "We know early detection is the key to beating cancer, and if we can detect it in the very earliest stages, before we can see it, there is such a potential for successful treatment and even new treatments."
This is a blind study, which means that Ma doesn't know which samples he tests are those of cancer patients and which are from healthy individuals. All patients are assigned a number and their diagnosis and personal information are kept confidential.
"We are hoping more and more cancer patients will assist us with this project," Ma says. "It might not help current patients, but it will help millions of people in the future. Using this technology for early cancer screenings in the future could save many lives." Using the P-scan, Ma will be able to detect the presence of cancer and its level of advancement -- often before it could be detected on a mammogram.
"Mammogram technology is not sensitive," Ma says. "Some early cancer cannot be detected by a mammogram. If this P-Scan technology works, it will be much easier to incorporate into regular physical screening.
"A patient donates urine and 10 minutes later I have a result. If this works, it will be an amazing diagnostic tool."
The P-scan works by using a capillary to pass a small sample of urine into the device, separate different pteredine molecules and then pass the sample through a light source. The researchers then use a spectrophotometer to identify and measure the pteredines in the sample. Pteredines are normal metabolites that are present in the urine of all human beings. But when cancer is present, the levels rise.
"Cancer cells grow much faster than normal cells," Ma explains. "So they release more waste into the urine and we begin to see a rise in the metabolite levels."
Ma believes these markers are indicators of specific types of cancer and he hopes to prove that in future trials. Once he and his fellow researcher prove the technology works for breast cancer, they can begin to determine if studying pteredine levels in urine samples is an accurate way to detect and diagnose other types of cancers as well. "We will go cancer by cancer until we know," Ma says.
Currently all testing is done manually. But once the validation study is complete, Ma will work with Emergence BioScreening in St. Louis on the next step in the process -- building an automated, FDA-approved instrument that can be manufactured for clinical use. Ma and his students plan to build the prototype P-scan instrument with funding from the University of Missouri System Intellectual Property Fast Track Funding Program.

"I want people to realize that their help is so important for the development of technology that can save more lives in the future," Ma says. "I hope they will consider participating in this study to help many others in the future.
"I am very excited about this project," Ma says. "If it works, it will save lives. That's my motivation."
For more information about participation in the study, contact Adrianna Moore or Pearlena Hamlet at the Mercy Breast Center.

http://phys.org/news/2013-05-scientists-breast-cancer-advance-previous.html

Scientists make breast cancer advance that turns previous thinking on its head

Some enzymes released by cancerous cells could have a protective function

UEA scientists make breast cancer advance that turns previous thinking on its head Scientists at the University of East Anglia have made an advance in breast cancer research which shows how some enzymes released by cancerous cells could have a protective function.
New research published today in the Journal of Biological Chemistry reveals that an enzyme called MMP-8 (matrix metalloproteinase-8) could be acting as a locator to the immune system, which then becomes activated to attack tumours. It was originally thought that the production of MMPs by breast cancer cells worked to promote cancer growth.
Lead researcher Prof Dylan Edwards from UEA's School of Biological Sciences said: "MMPs are a family of enzymes that are released from cancer cells. They were once thought to act like 'molecular scissors' to snip away at the scaffolding structures outside cells and clear a path for the cancer cells to invade and spread to other organs.
"Drugs that target this broad family of enzymes were trialled to treat cancer in the 1990s but largely failed. This led us to think that not all of these enzymes were bad guys that promoted tumour growth and spread."
Scientists from UEA worked with clinicians at the Norfolk and Norwich University Hospital to look in detail at the patterns of MMPs in breast tumours from patients. Previous research published in 2008 revealed that one of these enzymes, known as MMP-8, has a protective role which holds tumours in check. And patients whose breast tumours have more of this particular enzyme seemed to have better outcomes.
The latest research was funded by cancer charity the Big C and carried out by PhD student Sally Thirkettle.
Prof Edwards said: "She has shown that if she makes breast cancer cells produce MMP-8, it causes them to produce two other inflammatory factors (IL-6 and IL-8) that have previously been shown to promote cancer. However, breast tumour cells that over-produce MMP-8 don't survive long-term - the enzyme stops them growing."
"We now think that in tumours, MMP-8 acts as a sort of 'find me' signal to the immune system, which then becomes activated to attack the tumour, which may help to explain its protective function.
"The fact that a protective enzyme such as MMP-8 was also blocked by the first generation anti-MMP drugs used in the 1990s also partly explains why these drugs failed in the clinic," he added.
It is still unknown exactly how MMP-8 causes IL-6 and IL-8 to be activated - but the findings are an important step forward which will help direct further research.
More information: *'Matrix metalloproteinase-8 (collagenase-2) induces the expression of interleukins-6 and -8 in breast cancer cells' by Sally Thirkettle, Julie Decock, Hugh Arnold, Caroline J Pennington and Dylan R Edwards (all UEA, UK) and Diane M Jaworski (University of Vermont College of Medicine, US) is published in the Journal of Biological Chemistry on May 24, 2013.*

http://www.eurekalert.org/pub_releases/2013-05/uoy-tao052313.php

The ascent of man: Why our early ancestors took to 2 feet

Upright gait may have its origins in the rugged landscape of East and South Africa

A new study by archaeologists at the University of York challenges evolutionary theories behind the development of our earliest ancestors from tree dwelling quadrupeds to upright bipeds capable of walking and scrambling.
The researchers say our upright gait may have its origins in the rugged landscape of East and South Africa which was shaped during the Pliocene epoch by volcanoes and shifting tectonic plates.
Hominins, our early forebears, would have been attracted to the terrain of rocky outcrops and gorges because it offered shelter and opportunities to trap prey. But it also required more upright scrambling and climbing gaits, prompting the emergence of bipedalism.
The York research challenges traditional hypotheses which suggest our early forebears were forced out of the trees and onto two feet when climate change reduced tree cover.
The study, 'Complex Topography and Human Evolution: the Missing Link', was developed in conjunction with researchers from the Institut de Physique du Globe in Paris. It is published in the journal Antiquity.

Dr Isabelle Winder, from the Department of Archaeology at York and one of the paper's authors, said: "Our research shows that bipedalism may have developed as a response to the terrain, rather than a response to climatically-driven vegetation changes.
"The broken, disrupted terrain offered benefits for hominins in terms of security and food, but it also proved a motivation to improve their locomotor skills by climbing, balancing, scrambling and moving swiftly over broken ground - types of movement encouraging a more upright gait."
The research suggests that the hands and arms of upright hominins were then left free to develop increased manual dexterity and tool use, supporting a further key stage in the evolutionary story.
The development of running adaptations to the skeleton and foot may have resulted from later excursions onto the surrounding flat plains in search of prey and new home ranges.
Dr Winder said: "The varied terrain may also have contributed to improved cognitive skills such as navigation and communication abilities, accounting for the continued evolution of our brains and social functions such as co-operation and team work.
"Our hypothesis offers a new, viable alternative to traditional vegetation or climate change hypotheses. It explains all the key processes in hominin evolution and offers a more convincing scenario than traditional hypotheses."

http://www.eurekalert.org/pub_releases/2013-05/esoc-dhi052213.php

Death highest in heart failure patients admitted in January, on Friday, and overnight

Data from nearly 1 million patients over 14 years

Lisbon - Mortality and length of stay are highest in heart failure patients admitted in January, on Friday, and overnight, according to research presented today at the Heart Failure Congress 2013. The analysis of nearly 1 million heart failure admissions over 14 years was presented by Dr David P. Kao (Denver, Colorado).
The Heart Failure Congress 2013 is taking place during 25-28 May in Lisbon, Portugal. The Congress is the main annual meeting of the Heart Failure Association of the European Society of Cardiology (1).
Identifying peaks in admissions and mortality should assist targeted resource allocation at higher risk times. Seasonal, weekly and hourly variations have been observed in heart failure admissions but the reasons are unclear. Until now, the relationship of these variations with mortality and length of stay has not been investigated in a single study.
The current study (2) examined the impact of day, month and hour of admission on in-hospital mortality and length of stay in 949,907 hospitalisations for congestive heart failure. Data was analysed from all hospitals in the state of New York from 1994 to 2007. A greater number of factors were included in the analysis than ever before so that the researchers could confirm or refute previous theories on the reasons behind variations in heart failure morbidity and mortality (for example substance use).
The researchers found that daily heart failure admissions increased significantly over time (+1.1 admissions/day/year) while in-hospital mortality and length of stay decreased (-0.3%/year and -0.3 days/year, $p<0.0001$ for all). Dr Kao said: "These findings confirm the huge decline in mortality in hospitals for heart failure over the past 14-15 years following major advances in therapy."
Daily heart failure admissions peaked in February ($p<0.0001$), while in-hospital mortality ($p<0.0001$) and length of stay ($p=0.01$) peaked in January. Mortality and length of stay were lowest for admissions between 06h00-12h00 and highest overnight (18h00-24h00) by a small margin (adjusted OR of death 1.22, $p<0.0001$). Mortality and length of stay were lowest in patients admitted on Monday (adjusted OR of death 1.09, $p<0.001$) and highest on Friday ($p<0.0001$).
Numerous theories have been mooted for the cause of seasonal variations in heart failure morbidity and mortality, for example that the holiday spike is caused by alcohol and drug use. Dr Kao said: "For the first time we've shown that there wasn't a higher rate of alcohol and drug use reported in heart failure patients during December and January, when heart failure mortality was the highest."
Seasonal variations affected rate of heart failure hospitalization and mortality in patients over the age of 30, and the effect was greater with advancing age. An increase in concurrent pneumonia in the winter could impact on heart failure mortality, but there was less seasonal variation in other respiratory diseases like chronic obstructive pulmonary disease (COPD).
The findings suggest that staffing may have an impact on seasonal variations in mortality and length of stay. Dr Kao said: "The fact that patients admitted right before the weekend and in the middle of the night do worse and are in hospital longer suggests that staffing levels may contribute to the findings."
He added: "The seasonal effect on in-hospital death from heart failure remained even after controlling for time and weekday of admission, 17 other medical conditions including substance use, kidney disease, and

pneumonia, and demographic factors including gender, ethnicity, and medical coverage status. Seasonal variations in morbidity and mortality occur in many diseases, particularly heart disease, and the cold weather itself may have a part to play."
Dr Kao concluded: "Doctors and hospitals need to be more vigilant during these higher risk times and ensure that adequate resources are in place to cope with demand. Patients should be aware that their disease is not the same over the course of the year and they may be at higher risk during the winter. People often avoid coming into hospital during the holidays because of family pressures and a personal desire to stay at home but they may be putting themselves in danger."

http://www.eurekalert.org/pub_releases/2013-05/esoc-fdt052213.php

First drug to improve heart failure mortality in over a decade

Coenzyme Q10 decreases all cause mortality by half in randomized double blind trial

Lisbon - Coenzyme Q10 decreases all cause mortality by half, according to the results of a multicentre randomised double blind trial presented today at Heart Failure 2013 congress. It is the first drug to improve heart failure mortality in over a decade and should be added to standard treatment, according to lead author Professor Svend Aage Mortensen (Copenhagen, Denmark).
Heart Failure 2013 is being held from 25-28 May in Lisbon, Portugal. It is the main annual meeting of the Heart Failure Association of the European Society of Cardiology (1).
Coenzyme Q10 (CoQ10) occurs naturally in the body and is essential to survival. CoQ10 works as an electron carrier in the mitochondria, the powerhouse of the cells, to produce energy and is also a powerful antioxidant. It is the only antioxidant that humans synthesise in the body.
CoQ10 levels are decreased in the heart muscle of patients with heart failure, with the deficiency becoming more pronounced as heart failure severity worsens. Statins are used to treat many patients with heart failure because they block the synthesis of cholesterol, but these drugs also block the synthesis of CoQ10, which further decreases levels in the body.
Double blind controlled trials have shown that CoQ10 improves symptoms, functional capacity and quality of life in patients with heart failure with no side effects. But until now, no trials have been statistically powered to address effects on survival.
The Q-SYMBIO study (2) randomised 420 patients with severe heart failure (New York Heart Association (NYHA) Class III or IV) to CoQ10 or placebo and followed them for 2 years. The primary endpoint was time to first major adverse cardiovascular event (MACE) which included unplanned hospitalisation due to worsening of heart failure, cardiovascular death, urgent cardiac transplantation and mechanical circulatory support. Participating centres were in Denmark, Sweden, Austria, Slovakia, Poland, Hungary, India, Malaysia and Australia.
CoQ10 halved the risk of MACE, with 29 (14%) patients in the CoQ10 group reaching the primary endpoint compared to 55 (25%) patients in the placebo group (hazard ratio=2; p=0.003). CoQ10 also halved the risk of dying from all causes, which occurred in 18 (9%) patients in the CoQ10 group compared to 36 (17%) patients in the placebo group (hazard ratio=2.1; p=0.01).
CoQ10 treated patients had significantly lower cardiovascular mortality (p=0,02) and lower occurrence of hospitalisations for heart failure (p=0.05). There were fewer adverse events in the CoQ10 group compared to the placebo group (p=0.073).
Professor Mortensen said: "CoQ10 is the first medication to improve survival in chronic heart failure since ACE inhibitors and beta blockers more than a decade ago and should be added to standard heart failure therapy."
He added: "Other heart failure medications block rather than enhance cellular processes and may have side effects. Supplementation with CoQ10, which is a natural and safe substance, corrects a deficiency in the body and blocks the vicious metabolic cycle in chronic heart failure called the energy starved heart."
CoQ10 is present in food, including red meat, plants and fish, but levels are insufficient to impact on heart failure. CoQ10 is also sold over the counter as a food supplement but Professor Mortensen said: "Food supplements can influence the effect of other medications including anticoagulants and patients should seek advice from their doctor before taking them."
Patients with ischaemic heart disease who use statins could also benefit from CoQ10 supplementation. Professor Mortensen said: "We have no controlled trials demonstrating that statin therapy plus CoQ10 improves mortality more than statins alone. But statins reduce CoQ10, and circulating CoQ10 prevents the oxidation of LDL effectively, so I think ischaemic patients should supplement statin therapy with CoQ10."

http://bit.ly/Z8qE0V

Saudis say Dutch patent on MERS virus hampers research

The normally civil world of international health diplomacy was shattered yesterday, when Saudi Arabia complained that a patent taken out by Dutch scientists who isolated the Middle Eastern Respiratory Syndrome (MERS) virus was impeding Saudi efforts to track the virus within its own borders.

Updated 16:14 24 May 2013 by Debora MacKenzie

"Deals between scientists because they want to take intellectual property… are issues we need to address," said World Health Organization director-general Margaret Chan in response. "No IP will stand in the way of public health."

The Dutch researchers, based at Erasmus Medical Center in Rotterdam, the Netherlands, say the patent does nothing to stop the Saudis developing their own tests for the coronavirus that causes MERS. The Dutch have themselves developed and published tests for both the virus and antibodies to it, essential for tracking its spread. And they say they have sent the virus to 40 labs, some of which are developing their own tests, and that they are willing to send the virus to any laboratories who can handle it safely.

There have so far been 44 known cases of MERS worldwide, with more than 20 deaths. The Dutch team says it has repeatedly offered tests for MERS to the Saudis. Ab Osterhaus, head of the virology department at Erasmus, says the Saudis have not replied.

There has been criticism that the Saudis have been slow to investigate the epidemic. Speaking at the World Health Assembly, the annual meeting of the World Health Organization's 194 member countries, Ziad Memish, the deputy Saudi health minister, said that the country has been struggling to develop diagnostics because the virus has been patented.

Reuters quoted him as saying: "The virus was sent out of the country and it was patented, contracts were signed with vaccine companies and antiviral drug companies, and that's why they have a Material Transfer Agreement… and that should not happen." A Material Transfer Agreement specifies what providers and recipients of biological material can and cannot do with it.

Routine patenting

Patenting sounds like profiteering. But all labs that discover viruses routinely patent the sequences they work to uncover, and their prospective applications. Osterhaus says this is needed for the discovery to be used for public health. "If we don't patent it, no company will develop vaccines or diagnostic tests with it, because they won't be able to acquire clear ownership," he says. Commercial companies are the major source of tests and vaccines in most countries.

Alternatively, one company might acquire a patent on a viral discovery, then demand royalties to work on the virus, even if the company itself is not. Osterhaus says that is not what they are doing at Erasmus. "If any lab asks us for a sample, we send it to them free, if they have the containment to use it safely," he says.

If the Saudis develop their own tests, says Ron Fouchier, who identified MERS, they would not have to pay royalties to Rotterdam "unless they start selling it for lots of money to the rest of the world".

Even then the Saudis may still be able to claim some rights over the virus, as the 1993 Biodiversity Convention gives countries ownership of their genetic resources. It is not clear, however, to what extent that applies to pathogens. The Saudis' problems seem to stem from how the virus was identified. "There was a lag of three months where we were not aware of the discovery of the virus," Memish said in Geneva.

The virus was identified in June 2012, and announced in September, when technical details of the research had been double-checked as normal, says Osterhaus. With only one known infection, there seemed little need for more urgency. Osterhaus has offered to meet with Memish to resolve the dispute.

http://www.sciencedaily.com/releases/2013/05/130524104634.htm

Cause of Infantile Amnesia Revealed

New Neuron Formation Could Increase Capacity for New Learning, at Expense of Old Memories

New research presented today shows that formation of new neurons in the hippocampus -- a brain region known for its importance in learning and remembering -- could cause forgetting of old memories by causing a reorganization of existing brain circuits. Drs. Paul Frankland and Sheena Josselyn, both from the Hospital for Sick Children in Toronto, argue this reorganization could have the positive effect of clearing old memories, reducing interference and thereby increasing capacity for new learning.

These results were presented at the 2013 Canadian Neuroscience Meeting, the annual meeting of the Canadian Association for Neuroscience -- Association Canadienne des Neurosciences (CAN-ACN).

Researchers have long known of the phenomenon of infantile amnesia: This refers to the absence of long-term memory of events occurring within the first 2-3 years of life, and little long-term memories for events occurring

until about 7 years of age. Studies have shown that though young children can remember events in the short term, these memories do not persist. This new study by Frankland and Josselyn shows that this amnesia is associated with high levels of new neuron production -- a process called neurogenesis -- in the hippocampus, and that more permanent memory formation is associated with a reduction in neurogenesis.
Dr. Frankland and Dr. Josselyn's approach was to look at retention of memories in young mice in which they suppressed the usual high levels of neurogenesis in the hippocampus (thereby replicating the circuit stability normally observed in adult mice), but also in older mice in which they stimulated increased neurogenesis (thereby replicating the conditions normally seen in younger mice). Dr. Frankland was able to show a causal relationship between a reduction in neurogenesis and increased remembering, and the converse, decreased remembering when neurogenesis increased.
Dr. Frankland concludes: " Why infantile amnesia exists has long been a mystery. We think our new studies begin to explain why we have no memories from our earliest years."
This research was supported by funds from the Canadian Institutes of Health Research and the "Chase an Idea in Paediatric Neuroscience" grant from The Centre for Brain & Behaviour at the Hospital for Sick Children.

http://www.sciencedaily.com/releases/2013/05/130525143733.htm

Newly Understood Circuits Add Finesse to Nerve Signals

An unusual kind of circuit fine-tunes the brain's control over movement and incoming sensory information, and without relying on conventional nerve pathways, according to a study published this week in the journal Neuron.

Brain circuits signal beyond the neat pathways shown in this nerve connectivity map. (Credit: Meredith Reid)

Researchers at the University of Alabama at Birmingham (UAB) discovered new details of a mechanism operating in the cerebellum, the brain region that processes nerve signals coming in from the spinal cord and cortex.
"Our results explain a second layer of nerve signal transmission that depends, not on whether a nerve cell is wired into a defined signaling pathway, but instead on how close it is to the pathway," said Jacques Wadiche, Ph.D., assistant professor in the Department of Neurobiology within the UAB School of Medicine, investigator in the Evelyn McKnight Brain Institute at UAB and senior study author. "It has become clear that this kind of nerve circuit is intimately linked with autism and movement disorders like ataxia, and we hope the mechanisms detailed here contribute to the design of new treatments."
Beyond nerve pathways Nerve cells are known to occur in defined pathways that transmit messages in one direction. This pathway-specific view of nerve signaling has been reinforced by high-tech imaging studies yielding detailed connectivity maps. Along these lines, the Obama Administration will soon ask Congress for $100 million in research funding to further improve such maps.
Within nerve pathways, each nerve cell sends an electric pulse down an extension of itself called an axon until it reaches a synapse, a gap between itself and the next cell in line. When it reaches an axon's end, the pulse triggers the release of chemicals called neurotransmitters that float across the gap, where they either cause the downstream nerve cell to "fire" and pass on the message, or stop the message. In this way, each synapse between nerve cells in a pathway "decides" whether or not a message continues on.
In recent years, studies have found that neurotransmitters also spill into tissue surrounding axons in a type signaling not restricted to synaptic connections. With the term itself implying a mess, "spillover" was thought to degrade the capacity of nerve cells to precisely pass on signals.
The current study adds to recent evidence arguing that spillover may instead enhance message transmission, with the results revolving around three nerve cell types in the cerebellum: climbing fibers, Purkinje cells and interneurons.
Climbing fibers, which carry information from the brainstem into the cerebellum, play key roles in motor timing and sensory processing. Within these fibers, nerve cells release the excitatory neurotransmitter glutamate into synapses that then strive to pass messages deeper into the cerebellum. Purkinje cells are paired with climbing fibers and intent on inhibiting their signals.
When excited by glutamate from climbing fibers at one end, Purkinje cells release another neurotransmitter called GABA at their downstream synapse to stop the message. An excitatory signal triggers an inhibitory one as a counter-balance, a form of feedback critical to the function of the central nervous system. Lack of

inhibition, for instance, causes circuits to seize, seizures and the death of Purkinje cells, the latter of which has been linked by post mortem studies to a higher incidence of autism spectrum disorders.
Previously, researchers thought that incoming signals from climbing fibers caused a single, strong response in the cerebellum: the activation of Purkinje cells that released GABA. The current study argues that such signals also trigger the firing of interneurons, nearby inhibitory middlemen that connect sets of nerve cells.
Interneurons within, and outside of, the glutamate spill zone around climbing fibers may have different effects on the other interneurons and Purkinje cells they connect to, according to the current finding. The interactions either inhibit or excite many Purkinje cells surrounding an active climbing fiber and refine its messages in a feedback system more sophisticated than once thought.
Glutamate has its effect by fitting into AMPA and NMDA receptor proteins, like a key into a lock, on the surfaces of nerve cells it signals to. The consensus has been that glutamate receptors occur only within synapses. Finding them on nerve cells outside of synapse-defined pathways represents "a fundamental shift in understanding," said Wadiche, and may result in longer-lasting inhibition within key signaling pathways.
"A 2007 study published in Nature Neuroscience found that many climbing fibers signal to interneurons in the outer layer of the cerebellum outside nerve pathways and exclusively through glutamate spillover," said Luke Coddington, a graduate student in Wadiche's lab and study author. "Our team built on that observation to show how spillover affects the function of interneurons, Purkinje cells, and ultimately, the entire cerebellum. Spillover-mediated signaling recruits local microcircuits to extend the reach and finesse of climbing fiber signaling."
Linda Overstreet-Wadiche, Ph.D., was also senior co-author of the study, with important contributions also coming from Stephanie Rudolph and Patrick Vande Lune, all within the Department of Neurobiology.
Luke T. Coddington, Stephanie Rudolph, Patrick Vande Lune, Linda Overstreet-Wadiche, Jacques I. Wadiche. Spillover-Mediated Feedforward Inhibition Functionally Segregates Interneuron Activity. Neuron, 2013; DOI: 10.1016/j.neuron.2013.04.019

http://www.businessinsider.com/lariam-worse-than-malaria-report-2013-5

'Horror Movie In A Pill': Side-Effects Of Lariam Worse Than Malaria

AN RTÉ INVESTIGATION into the use of Lariam as an anti-malarial by the Irish Defence Forces found a "plausible link" between the drug and a number of suicides of soldiers.

Sinead O'Carroll, TheJournal.ie | May 26, 2013, 7:30 AM | 425 |

Two of the world's leading authorities on the medication said the results of the probe require urgent investigation. The Prime Time programme revealed new research showing a higher risk of suicide among members of the army who had taken Larium during their deployments overseas than those who didn't.
"These figures are consistent with Lariam causing symptoms of mental illness including anxiety and depression, and are also consistent with the known association of these conditions with a strongly increased risk of suicide. These figures also indicate evidence of more serious events, such as psychosis, potentially leading to more sudden and impulsive suicides," said Dr Remington Nevin, an epidemiologist and former US Army major.
Overall, these figures are the strongest evidence yet of a powerful causal association between Lariam exposure and suicide. RTÉ's reporter Rita O'Reilly examined 28 suicides within the Defence Forces, 11 of whom had taken Lariam. Four of those had taken their lives within a year of returning home from overseas duty.
Dr Nevin describes Lariam as a "horror movie in a pill". The US military no longer uses Lariam as the drug of choice and the FDA in America has launched a full neurological review of the medicine. The Irish Medicines Board first highlighted the risk of neuropsychiatric side effects in its drug safety newsletter in May 1996. Information leaflets were also updated in 2003 with details of reported suicide and suicide ideation related to the use of the medication. However, the Defence Forces and the Minister for Justice says there are no plans as yet to discontinue its use.
Alternatives have been ruled out because of other side-effects, including sensitivity to the sun, and not being viable for long-term stints. Until recently, Malerone was only authorised for periods of 28 days. There are also prohibitive costs involved (Malerone is €4 per day).
The Defence Forces say they screen personnel to ensure they will be able to tolerate Lariam before being sent on duty. Not being suitable for Lariam because of a history of mental health issues can rule a member of the Defence Forces out of any overseas trips, putting them well behind their counterparts in terms of promotion and other prospects – something that is of major concern for career soldiers and a group campaigning for the cessation of Lariam as the anti-malaria drug of choice.
Dr Elspeth Ritchie, formerly of the US Army, said the side-effects of Lariam are actually worse than contracting malaria. "Aviators are barred from taking Lariam," she told RTÉ. "If aviators are barred, someone who drives a tank and shoots a gun should be precluded too."

Dave O'Shea from Action Lariam for Irish Soldiers believes that serving soldiers still find it difficult to speak out about the issue. Since the programme aired on Thursday, the support group has been contacted by more than 50 people about Lariam use.
He also believes the revelations have changed people's attitudes towards him.
O'Shea first took Lariam while in Liberia with the Defence Forces in 2003. Just two weeks later he started getting side effects, which included memory loss, insomnia, lumps on his skin and mood swings.
He recalls a number of incidences where he "wasn't himself". There was that one time he jumped through a pane of glass and blacked out. The suicidal thoughts followed soon after and he describes his life since then as being on a "descending scale".
Since he first spoke to TheJournal.ie last June, the solider has received "severe therapy" which is helping keep his life on a positive track.
He is among a number of former army personnel taking claims to the courts but says the litigation process is still in its infancy. There are a total of 22 compensation cases, seven of which are at the High Court.

http://bit.ly/1aq8NxJ

Alien Debris Found in Lunar Craters

Strange minerals detected at the centers of impact craters on the moon may be the shattered remains of the space rocks that made the craters and not exhumed bits of the moon's interior, as had been previously thought.

May 26, 2013 01:00 PM ET // by Larry O'Hanlon

Lunar Orbiter image of the 93-mile-wide Copernicus Crater with this bright central peaks.

The foreign matter in the craters is probably asteroid debris and some could even be from Earth, which has thrown off its share of material as it's been battered by asteroids and comets over the eons.
The discovery comes not from finding anything new in the craters themselves, but by planetary scientists who were looking at models of how meteorite impacts affect the moon. Specifically, the researchers simulated some high-angle, exceptionally slow impacts -- at least slow compared to possible impact speeds -- and they were surprised at what they found.
"Nobody has done it at such high resolution," said planetary scientist Jay Melosh of Purdue University. Melosh and his colleagues published a paper on the discovery in the May 26 online issue of the journal Nature Geoscience.
They found that when a slow enough impact happened, at speeds of less than 27,000 miles per hour (43,000 kph), the rock that struck doesn't necessarily vaporize. Instead, it gets shattered into a rain of debris that is then swept back down the crater sides and piles up in the crater's central peak.
In the case of craters like Copernicus (pictured top), the foreign material stands out because it contains minerals called spinels. These only form under great pressure -- in the Earth's mantle, for instance, and perhaps in the mantle of the moon. But spinels are also common in some asteroids, said Melosh, which are fragments of broken or failed planets from earlier days in the formation of our solar system.
The team has concluded, therefore, that the unusual minerals observed in the central peaks of many lunar impact craters are not lunar natives, but imports.
That conclusion could also explain why the same minerals, if they were instead from the interior of the moon, are not found in the largest impact basins -- as would be expected if the impact event was larger and penetrated deeper into the moon.
"An origin from within the Moon does not readily explain why the observed spinel deposits are associated with craters like Tycho and Copernicus instead of the largest impact basins," writes Arizona State University researcher Erik Asphaug in a commentary on the paper. "Excavation of deep-seated materials should favor the largest cratering events."
The new impact modeling also implies that pockets of early Earth material might be in cold storage on the moon, says Asphaug. The young Earth was bombarded with asteroids that sent terrestrial debris into space at speeds that were pretty slow and within the range of this model.
"Even more provocative," explains Asphaug, "is the suggestion that we might someday find Earth's protobiological materials, no longer available on our geologically active and repeatedly recycled planet, in dry storage up in the lunar 'attic'."

http://www.eurekalert.org/pub_releases/2013-05/uosc-hhd052213.php

Healthy habits die hard: In times of stress, people lean on established routines -- even healthy ones

Developing good habits is more important than self-control in meeting goals

Stress and exhaustion may turn us into zombies, but a novel study shows that mindless behavior doesn't just lead to overeating and shopping sprees — it can also cause us to stick with behaviors that are good for us.

Across five experiments appearing in the June issue of the Journal of Personality and Social Psychology, published by the American Psychological Association, the researchers provide an important new twist to the established idea that we have finite resources for self-regulation, meaning it's harder to take control of our actions when we're already stressed or tired.

Turns out we're just as likely to default to positive habits, such as eating a healthy breakfast or going to the gym, as we are to self-sabotage. Led by Wendy Wood and David Neal of USC, this research shows that lack of control doesn't automatically mean indulgence or hedonism – it's the underlying routine that matters, for better or worse.

"When we try to change our behavior, we strategize about our motivation and self-control. But what we should be thinking about instead is how to set up new habits. Habits persist even when we're tired and don't have the energy to exert self-control," says Wood, Provost Professor of Psychology and Business at USC, who holds joint appointments in the USC Dornsife College of Letters, Arts and Sciences and the USC Marshall School of Business.

Wood, who serves as vice dean for social sciences at USC Dornsife, is one of the world's leading experts on habit, the automatic behaviors that make it possible for us to function everyday (imagine if we had to relearn every morning how to brush our teeth or what route to take to work).

Learned habits also play a big role in our health; research has shown that exercise, overeating and smoking are significant risk factors for major diseases. Indeed, obesity and smoking are the two primary reasons Americans die before people in other high-income countries, according to a recent National Academy of Sciences report led by Eileen Crimmins of the USC Davis School of Gerontology.

But while most disease prevention efforts focus on self-control, the latest research from Wood shows that the best way to prevent disease might be knowing how to let go: "Everybody gets stressed. The whole focus on controlling your behavior may not actually be the best way to get people to meet goals," she said. "If you are somebody who doesn't have a lot of willpower, our study showed that habits are even more important."

For example, in one experiment Wood and her co-investigators followed students for a semester, including during exams. They found that during testing periods, when students were stressed and sleep-deprived, they were even more likely to stick to old habits. It was as if they didn't have the energy to do something new, Wood explains.

Students who ate unhealthy breakfasts during the semester – such as pastries or doughnuts – ate even more of the junk food during exams. But the same was true of oatmeal eaters: those in the habit of eating a healthy breakfast were also more likely to stick to routine and ate especially well in the morning when under pressure. Similarly, students who had a habit of reading the editorial pages in the newspaper everyday during the semester were more likely to perform this habit during exams – even when they were limited in time. And regular gym-goers were even more likely to go to the gym when stressed.

"You might expect that, when students were stressed and had little time, they wouldn't read the paper at all, but instead they fell back on their reading habits," Wood says. "Habits don't require much willpower and thought and deliberation." Wood continues: "So, the central question for behavior change efforts should be, how can you form healthy, productive habits? What we know about habit formation is that you want to make the behavior easy to perform, so that people repeat it often and it becomes part of their daily routine."

Aimee Drolet of UCLA was a co-author of the study.

http://www.eurekalert.org/pub_releases/2013-05/sovp-ssp052213.php

Small, speedy plant-eater extends knowledge of dinosaur ecosystems

Dinosaurs are often thought of as large, fierce animals, but new research highlights a previously overlooked diversity of small dinosaurs.

In the Journal of Vertebrate Paleontology, a team of paleontologists from the University of Toronto, Royal Ontario Museum, Cleveland Museum of Natural History and University of Calgary have described a new dinosaur, the smallest plant-eating dinosaur species known from Canada. Albertadromeus syntarsus was identified from a partial hind leg, and other skeletal elements, that indicate it was a speedy runner. Approximately 1.6 m (5 ft) long, it weighed about 16 kg (30 lbs), comparable to a large turkey.

Albertadromeus lived in what is now southern Alberta in the Late Cretaceous, about 77 million years ago. Albertadromeus syntarsus means "Alberta runner with fused foot bones". Unlike its much larger ornithopod cousins, the duckbilled dinosaurs, its two fused lower leg bones would have made it a fast, agile two-legged runner. This animal is the smallest known plant-eating dinosaur in its ecosystem, and researchers hypothesize that it used its speed to avoid predation by the many species of meat-eating dinosaurs that lived at the same time.

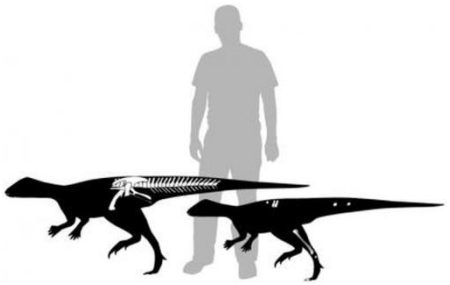
This is a life reconstruction of the new small-bodied, plant-eating dinosaur Albertadromeus syntarsus. **Julius T. Csotonyi.**

Albertadromeus was discovered in 2009 by study co-author David Evans of the Royal Ontario Museum as part an on-going collaboration with Michael Ryan of the Cleveland Museum of Natural History to investigate the evolution of dinosaurs in the Late Cretaceous of North America. The known dinosaur diversity of this time period is dominated by large bodied plant-eating dinosaurs.

Why are so few small-bodied dinosaurs known from North America some 77 million years ago? Smaller animals are less likely to be preserved than larger ones, because their bones are more delicate and are often destroyed before being fossilized. "We know from our previous research that there are preservational biases against the bones of these small dinosaurs," said Caleb Brown of the University of Toronto, lead author of the study. "We are now starting to uncover this hidden diversity, and although skeletons of these small ornithopods are both rare and fragmentary, our study shows that these dinosaurs were more abundant in their ecosystems than previously thought."

The reason for our relatively poor understanding of these small dinosaurs is a combination of the taphonomic processes (those related to decay and preservation) described above, and biases in the way that material has been collected. Small skeletons are more prone to destruction by carnivores, scavengers and weathering processes, so fewer small animals are available to become fossils and smaller animals are often more difficult to find and identify than those of larger animals.

"Albertadromeus may have been close to the bottom of the dinosaur food chain but without dinosaurs like it you'd not have giants like T. rex," said Michael Ryan. "Our understanding of the structure of dinosaur ecosystems is dependent on the fossils that have been preserved. Fragmentary, but important, specimens like that of Albertadromeus suggest that we are only beginning to understand the shape of dinosaur diversity and the structure of their communities."



Skeletal outlines illustrate both the relative size and completeness of two of the small ornithopod specimens described in the paper. Bones indicated in white are present. Human (in gray) for scale. **Illustration by C. Brown**

"You can imagine such small dinosaurs filling the niche of animals such as rabbits and being major, but relatively inconspicuous, members of their ecological community" said Anthony Russell of the University of Calgary.

http://www.bbc.co.uk/news/health-22646103

Stroke patients see signs of recovery in stem-cell trial

Five seriously disabled stroke patients have shown small signs of recovery following the injection of stem cells into their brain.

Pallab Ghosh By Pallab Ghosh Science correspondent, BBC News

Prof Keith Muir, of Glasgow University, who is treating them, says he is "surprised" by the mild to moderate improvements in the five patients. He stresses it is too soon to tell whether the effect is due to the treatment they are receiving. The results will be presented at the European Stroke Conference in London.

Complete paralysis

BBC News has had the first exclusive interview with one of the patients involved.

They are taking part in a small clinical trial involving nine patients in their 60s, 70s and 80s at Glasgow's Southern General Hospital to assess the safety of the procedure which involves injecting stem cells into the damaged brain part. It is one of the first trials in the world to test the use of stem cells in patients.

Results to be presented on Tuesday show that there have been no adverse effects on the patients so far and there have been improvements to more than half participating in the trial.

However, at this stage it is not possible to say whether the improvements are due to the close medical attention the patients are receiving. It is well documented that the feeling of wellbeing resulting from such attention, known as the placebo effect, can have a positive effect on people's health.
But it is thought that stroke patients do not recover after the first six months of their stroke. All the patients involved in the trial had their strokes between six months and five years before they received the treatment. The recovery of any one of them - let alone five - was not expected, according to Prof Muir, who is in charge of the trial.
"It seems odd that it should all just be chance and a placebo effect," he told BBC News. "We are seeing things that are interesting and somewhat surprising. "We've seen people who now have the ability to move their fingers where they have had several years of complete paralysis," Prof Muir said.
"We have seen some people that have been able to walk around their house whereas previously they had been dependent on assistance and we have had improvements that have enabled people to recognise what is happening around them."

'Temporary change'

These improvements have made it easier for the patients to do day-to-day tasks such as dressing themselves, walking and being more independent. "My expectation had been that we would see very little change and if we did see change it would be a relatively short-lived temporary change. (But) we have seen changes that have been maintained over time," Prof Muir said.
Among the patients to have shown improvements is 80-year-old Frank Marsh, who had a stroke five years ago. Prior to his attack Mr Marsh, a former teacher, was fit and active: a member of the Glasgow Phoenix Choir and a keen piano player. The stroke left him with poor strength and co-ordination in his left hand and poor balance. He needs a walking stick to help him move around the house and he can no longer play the piano.
After the injection of stem cells into the damaged area of his brain, his balance and mobility improved as did his hand strength. He can now also tie up his shoe laces.
Mr Marsh said he believed the operation had gradually led to improvements.
"I can now grip things that I couldn't grip before, like the hand rails at the swimming baths," he said.

Phase two trial

His wife, Clare, also a teacher, said that the small improvements had made him more independent. "He had reached a plateau and wasn't really improving (after his stroke). But following the operation he is able to do things he couldn't do before, such as make coffee, dressing and holding on to things."
Mr Marsh added that he hoped the improvements would continue: "I'd like to get back to my piano. I'd like to walk a bit steadier and further."
However, Mrs Marsh felt that there would be no further progress for her husband, but hoped that others might benefit from the clinical trial that he is participating in.
"The great potential is what it is going to do for the future," she said. "I told Frank at the beginning that this may not help you, but it might help your grandson."
Mrs Marsh is right in that even if it is proved that the stem-cell treatment really works it will be a long time before any treatment might be widely available.
The results so far pave the way for a so-called phase two trial later this year which will be desirable to determine whether any improvement is due to the treatment.
If the phase two trial does show that the stem-cell treatment is the cause of the improvements, it could still take many years before it becomes widely available. Larger phase three trials will be needed to assess who the treatment is most suitable for and at what stage it might be most effective.

Ethical approval

Commenting on the research, Dr Clare Walton of the Stroke Association said: "The use of stem cells is a promising technique which could help to reverse some of the disabling effects of stroke. We are very excited about this trial; however, we are currently at the beginning of a very long road and significant further development is needed before stem cell therapy can be regarded as a possible treatment."
The stem cells were created 10 years ago from one sample of nerve tissue taken from a foetus. The company that produces the stem cells, Reneuron, is able to manufacture as many stem cells as it needs from that original sample.
It is because a foetal tissue sample was involved in the development of the treatment that it has its critics. Among them is anti-abortion campaigner Lord Alton. "The bottom line is surely that the true donor (the foetus) could not possibly have given consent and that, of course, raises significant ethical considerations," he said.
Reneuron says the trial - which it funded - has ethical approval from the medicine's regulator. It added that one tissue sample was used in development 10 years ago and that foetal material has not been used since.