

Alcohol in moderation is good for sick hearts too

A study by the Catholic University of Campobasso, Italy, shows that a regular and moderate alcohol consumption is beneficial for people who had a previous heart attack or other ischemic vascular events

It was still an open question in medicine. Whereas scientific research has shown beneficial effects of moderate alcohol consumption in healthy people, it was not clear whether this could be valid also for patients who already had heart attack, stroke or another ischemic vascular event. A positive answer comes now from a study performed by the Research Laboratories at the Catholic University of Campobasso, Italy: moderate consumption, defined as one or two glasses of wine a day or the equivalent amounts of beer or other alcoholic beverages, significantly reduces the risk of death from any cause in those who already suffered from ischemic vascular disease.

The research, published in the Journal of the American College of Cardiology (JACC), was performed using the statistic procedure of meta-analysis which allows to combine different studies conducted worldwide to achieve more precise results. Researchers analyzed the most important scientific studies performed during the last years. Eight in total in four Countries: United States, Sweden, Japan and Great Britain. Each study took into account patients already affected by an ischemic vascular event. During the years following the disease onset, patients were followed by researchers to know which were the lifestyle habits, including alcohol consumption, able to avoid a new clinical event. The meta-analysis allowed to pool all those studies for a total of 16,351 people examined.

"We observed – says Simona Costanzo, epidemiologist and first author of the study – that regular and moderate consumption has beneficial effects even for people already affected by heart attack, or stroke. Not only they are less likely to be affected by similar diseases again, but all-cause mortality too resulted to be lower than in those who did not consume any alcoholic beverage".

The effect is very similar to that observed in healthy people. "Risk reduction - Costanzo argues - is about 20%. This means that one event out of five can be spared. It is a huge advantage, comparable to the one already recorded for healthy individuals".

"Studied by our research group for a long time – says Augusto Di Castelnuovo, Head of the Statistic Unit at the Research Laboratories of the Catholic University in Campobasso and co-author of the study - the beneficial effects of moderate alcohol consumption in healthy people are well established. Now we have reason to believe that alcoholic beverages work by the same protective mechanisms also for people already affected by ischemic vascular diseases".

But, as all researches state, the key word is moderation. "When we talk about moderate alcohol consumption, we mean something quite far from what we use to see in TV fictions – says Licia Iacoviello, Head of the Laboratory of Environmental and Genetic Epidemiology and responsible of the Moli-sani Project – We refer to moderation as drinking regularly, at low doses, within a healthy lifestyle, such as the Mediterranean diet. A glass of wine or beer during meals has always been an integral part of the Mediterranean way of eating. Our research highlights another crucial issue: drinking has not only to be moderate, but also regular. A moderate consumption spread along the week is positive. The same amount of weekly alcohol, concentrated in a couple of days is definitely harmful".

"Despite these new positive results- argues Giovanni de Gaetano, Director of the Research Laboratories - we do believe that teetotallers, either healthy or ill, should not start drinking with the aim to earn more health. Our study, as those conducted by our group in the past, is not a kind of invitation to start drinking, but the recognition of a particular lifestyle. This time we need to be cautious since we deal with sick people. We recommend to them to discuss with their own doctor the best choice in terms of alcoholic beverage consumption".

The study was supported in part by a grant from the European Research Advisory Board (ERAB).

Brown University-Led Team Explains How Dinosaurs Rose to Prominence

A scientific team led by Brown University has learned how dinosaurs became rulers of Earth more than 200 million years ago. Widespread volcanism and a spike in atmospheric carbon dioxide wiped out half of all plant species, and extinguished early crocodile relatives that had competed with the earliest dinosaurs. Results appear in the Proceedings of the National Academy of Sciences.

PROVIDENCE, R.I. [Brown University] — A shade more than 200 million years ago, the Earth looked far different than it does today. Most land on the planet was consolidated into one continent called Pangea. There was no Atlantic Ocean, and the rulers of the animal world were crurotarsans – creatures closely related to modern crocodiles.

Yet the Earth stood on the cusp of an epic shift in climate, and the reign of the dinosaurs was about to begin. Now, an international scientific team led by Brown University paleobiologist Jessica Whiteside has explained what led to the dinosaurs' rise as the Triassic Period ended. In a paper published in the Proceedings of the National Academy of Sciences, the scientists constructed a climate record marking the Triassic-Jurassic boundary by combining fossil evidence of plant and animal extinctions with the carbon signature found in the wax of ancient leaves and wood found in lake sediments intermixed with basalts, marking the volcanic activity.

With those evidentiary threads, the researchers found strong support that massive, widespread volcanic eruptions led to a spike in atmospheric carbon dioxide and other greenhouse gases that wiped out half of plant species and marked the end of the Triassic, one of the five great mass extinctions of Earth history.

The team also established through the fossil record that the abrupt rise in atmospheric gases decimated crurotarsans, which had competed vigorously with the earliest dinosaurs during the Triassic. Thanks to the climatic catastrophe, those early, small dinosaurs were freed from their main competitors to become the dominant force in the animal world.

"The big thing is many people have heard why dinosaurs went extinct," said Whiteside, assistant professor of geological sciences, "but the question why they came to be is much more exciting."

What scientists know is that more than 200 million years ago, the supercontinent Pangea broke up when the North American and the African plates began to drift apart. As the two plates parted, creating the basin that would become the Atlantic Ocean, fissures cleaved the area, triggering massive outflows of lava covering more than 9 million square kilometers (3.5 million square miles), an area roughly equal to the continental United States. Scientists call this area the Central Atlantic Magmatic Province (CAMP). The volcanic eruptions lasted about 600,000 years, a length of time that Whiteside estimated in a 2007 paper in *Palaeogeography, Palaeoclimatology, Palaeoecology*.

The researchers zeroed in on rift basins preserving the CAMP to figure out precisely what happened to the climate and to plants and animals. The team, including researchers from Academia Sinica in Taiwan, Columbia University, and the Woods Hole Oceanographic Institution, analyzed fossils and carbon signatures from two ancient basins in the northeast United States — the Newark and Hartford basins — as well as a basin in England. At these sites, the researchers found evidence where fossilized sediments from lakes that dotted Pangea before the plates' separation were preserved between lava flows. The team dated the oldest flows to 201.4 million years ago, providing an upper limit to when volcanism began.

Those fossils told a clear tale: For plants, pollen counts combined with the carbon record (the ratio of C12 and C13, two carbon isotopes) showed half the flora species in the Triassic perished in the volcanism that marked the end of the period. It also showed a spike in fern spores around the time of the first lava flows, which makes sense as ferns are among the first plant species to return in an environment scarred by volcanism.

For animals, the scientists linked footprints previously found in rocks in the Hartford and Newark basins to establish that crurotarsans perished in the mass volcanism that marked the end of the Triassic. After the lava flows, the "fossil record for crurotarsans is nearly completely gone," Whiteside said. Freed from their main competitor, early theropods — a category including all meat-eating dinosaurs from velociraptors to *Tyrannosaurus rex* — became dominant. Evidence for the rise was documented in a paper published in 2002 by Paul Olsen (corresponding author on the PNAS paper) that shows theropod footprints after the mass extinction at the end of the Triassic had become much larger, corresponding to larger body sizes.

Why did the early dinosaurs survive the volcanism that extinguished the Triassic crurotarsans? "They had the blind luck of being unwittingly adapted to get through that climate catastrophe," Whiteside said. "How they did is quite difficult to explain."

While previous research on end-Triassic mass extinctions has been done in other regions, such as Greenland, this paper marked the first time that scientists had gathered and calibrated evidence from the CAMP, said Olsen, a paleontologist who has studied mass extinction events for three decades at Columbia.

"There are dozens of papers claiming to show the connection between carbon isotopes excursions in the CAMP," Olsen said, "but this is the only study that has ever shown isotope excursions from the same place that the lava flows were present."

"It's not that we're the first people to say there's a link" (between volcanism and end-Triassic mass extinction), Whiteside added, "but we're the first people to document it."

Other authors on the paper are Timothy Eglinton from the Department of Marine Geology and Geophysics at the Woods Hole Oceanographic Institute, Michael Brookfield at the Institute of Earth Sciences Academia Sinica in Taiwan, and Raymond Sambrotto from the Lamont-Doherty Earth Observatory at Columbia.

The National Science Foundation funded the research.

Growing by Biblical portions: Last Supper paintings over Millennium depict growing appetites

ITHACA, N.Y. - The sizes of the portions and plates in more than four dozen depictions of the Last Supper – painted over the past 1,000 years – have gradually grown bigger and bigger, according to a Cornell University study published in *The International Journal of Obesity* (April 2010), a peer-reviewed publication.

The finding suggests that the phenomenon of serving bigger portions on bigger plates – which pushes people to overeat – has occurred gradually over the millennium, says Brian Wansink, the John S. Dyson Professor of Marketing and of Applied Economics and director of the Cornell Food and Brand Lab.

"We took the 52 most famous paintings of the Last Supper (from the book 'Last Supper,' 2000) and analyzed the size of the entrees, bread and plates, relative to the average size of the average head in the painting," said Wansink.

The study found that the size of the entrées in paintings of the Last Supper, which according to the New Testament occurred during a Passover evening, has progressively grown 69 percent; plate size has increased 66 percent and bread size by about 23 percent, over the past 1,000 years.

The research, conducted with Wansink's brother, Craig Wansink, professor of religious studies at Virginia Wesleyan College, Norfolk, Va., and an ordained Presbyterian minister.

The analysis was aided by computer-aided design technology that allowed items in the paintings to be scanned, rotated and calculated regardless of their orientation in the painting.

The researchers started with the assumption that the average width of the bread is twice the width of the average disciple's head.

"The last thousand years have witnessed dramatic increases in the production, availability, safety, abundance and affordability of food," said Cornell's Wansink, author of "Mindless Eating: Why We Eat More Than We Think." "We think that as art imitates life, these changes have been reflected in paintings of history's most famous dinner."

Helium rain on Jupiter

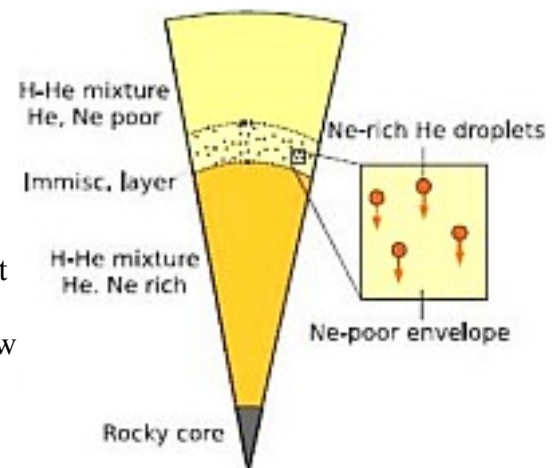
New research suggests that helium rain could be washing neon out of Jupiter's upper atmosphere

When NASA's Galileo probe reached Jupiter in 1995 and began sending back data about the gas giant, astronomers were in for a surprise: Jupiter was unusually poor in helium and neon, the two lightest noble gases. New simulations of the physics inside the planet reveal why. The results, which provide a glimpse into Jupiter's turbulent innards, are reported in the current issue of *Physical Review Letters* and highlighted with a Viewpoint by Jonathan Fortney (University of California, Santa Cruz) in the March 22 issue of *Physics* (<http://physics.aps.org>.)

This schematic depiction of the interior of a gas giant (e.g. Jupiter or Saturn) shows Helium-rich droplets forming within the immiscibility layer and raining downwards, leading to a slow increase in the helium concentration in the deep interior. Neon is absorbed in the droplets and carried out of the upper atmosphere. Hugh F. Wilson and Burkhard Militzer, University of California, Berkeley

To understand how a planet might have formed and what the inside of it might be like, astronomers compare the abundances of its constituent elements with the amounts of those elements found in the sun and meteorites. Jupiter, like the sun, is mostly hydrogen and helium. But the Galileo probe showed that, while it was richer than the sun in six elements, the planet seemed to be missing a small amount of helium and a substantial amount of neon - although neon makes up 1/600 of the mass of the solar system, it made up only 1/6000 of the mass of Jupiter's upper atmosphere, where Galileo made its observations. Astronomers had assumed that Jupiter was a homogenous mix of hydrogen and helium, but this couldn't explain the observed lack of neon. Some physicists suggested that the neon was somehow sinking out of the upper atmosphere, but no one knew how this could happen.

A pair of astronomers from the University of California Berkeley has solved the mystery. Using computer simulations of the hot gases deep within the giant planet, the researchers have shown that there must be an atmospheric layer where helium condenses into droplets rather than mixing smoothly with hydrogen. Neon dissolves into these droplets, which gradually fall toward the planet's interior as helium rain. Not only do the simulations explain a long-standing mystery, but they also hint at what might be happening inside other planets. For instance, because Saturn is smaller and colder than Jupiter, physicists expect that helium rain will be even more prevalent inside this as-yet-unprobed planet.



Exposed: green consumers' dirty little secrets

* 13:23 22 March 2010 by Peter Aldhous

Green consumers sometimes take the moral high ground – but it's all too easy to slide back down. New research suggests that those who make "green" purchases are subsequently more likely to behave selfishly, cheat and steal. "Another way to think about it is that you're off the hook – you've done your good deed," explains Benoît Monin, a psychologist at Stanford University in California who studies the phenomenon, called "moral self-licensing".

Moral self-licensing has been shown elsewhere, too. In the run-up to the 2008 US presidential election, for instance, Monin found that people who expressed their support for Barack Obama, thereby winning credit as non-racists, were more likely to later declare that whites would be better suited than blacks for a hypothetical job vacancy in a police department (*Journal of Experimental Social Psychology*, vol 45, p 590).

To find out if green consumerism gives people a similar licence to behave badly, Nina Mazar and Chen-Bo Zhong of the University of Toronto in Canada set up experiments in which students were presented with simulated online stores.

Good shop, bad shop

Students were asked to fill their online shopping baskets with up to \$25-worth of items, and half were presented with a store stocked mostly with "green" products – compact fluorescent instead of incandescent light bulbs, for instance – to make it more likely that they would shop green. The other half were given a store stocked with a majority of conventional products.

After their online shopping spree, the students were asked to carry out one of two tasks.

One group was told to allocate \$6 between themselves and another participant. Mazar and Zhong found that green shoppers in this group kept more for themselves than the others did.

The most striking results, however, came from the group that carried out the second task. Students were shown a pattern of dots and asked to say whether more fell to the left or the right of a diagonal line. They were told they would get half a cent each time they said more dots were on the left, but 5¢ each time they said more were on the right – providing a clear incentive to lie about the results to earn more money.

Those who played the game both accurately and truthfully would make \$2.07. The winnings of those who had shopped in the conventional store did not differ significantly from this sum. The green shoppers, however, earned on average 36¢ more, showing that they had lied to boost their income.

Light green fingers

Finally, the volunteers in the second group were shown on screen how much they had won and told to take the right amount of cash from an envelope. Both groups took more than their due, but the green shoppers on average stole 48¢ more than those who had shopped in the conventional store. "It's a very impressive paper," says Monin.

It remains unclear how far the moral glow of green consumerism makes people feel they have licence to cheat and steal in the real world. Douglas Medin, a psychologist at Northwestern University in Evanston, Illinois, says that more work must be done to see whether the same thing happens in different situations and cultures.

But moral self-licensing could explain the counterproductive results of some attempts to reduce environmental footprints, such as the recent finding that people in the UK who have made their homes more energy-efficient are more likely to turn up their heating or keep it on for longer.

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When Your Looks Take Over Your Life

By JANE E. BRODY

Is there a part of you that you hate to look at and perhaps try to hide from others? Do you glance at your image in distress whenever you pass a reflective surface?

Many of us are embarrassed by or dissatisfied with some body part or other. I recall that from about age 11 through my early teens I sat in class with my hand over what I thought was an ugly bump on my nose. And I know a young woman of normal weight who refuses to sit down in a subway car because she thinks it makes her thighs look huge.

But what if such self-consciousness about a perceived facial or body defect becomes all consuming, an obsession or paranoia that keeps the person from focusing on school or work, pursuing normal social activities, even leaving the house to shop or see a doctor? What if it leads to attempted suicide?

Such are the challenges facing tens of thousands of Americans who suffer from body dysmorphic disorder, or B.D.D., a syndrome known for more than a century but recognized only recently by the official psychiatric diagnostic manual. Even more recently, effective treatments have been developed for the disorder, and its emotional and neurological underpinnings have begun to yield to research.

New Findings

A pioneering researcher, Dr. Jamie D. Feusner, and his colleagues at the David Geffen School of Medicine at the University of California, Los Angeles, recently found patterns of brain activity in people with B.D.D. that appeared to differ from those of others. The differences showed up in areas involved in visual processing. The more severe the symptoms, the more the person's brain activity on imaging scans differed, on average, from normal levels, the researchers reported in the February issue of *The Archives of General Psychiatry*.

These brain changes may help explain how people can become overly focused on a perceived defect of their face, hair, skin or facial or body shape that others may not notice — indeed, that may not even exist. Some turn to alcohol and drugs to try to cope with the extreme distress. Others seek cosmetic surgery — which fails to relieve anxiety and can even make the problem worse, leaving scars where nothing was apparent before.

Some men have a form of B.D.D. called muscular dysmorphic disorder, thinking they look puny and weak when in fact their muscles are highly developed through compulsive weight training.

Dr. Katharine A. Phillips, a professor of psychiatry at Brown Medical School, is perhaps the best known authority on B.D.D. and the author, most recently, of “Understanding Body Dysmorphic Disorder: An Essential Guide” (Oxford University Press, 2009).

In an interview, Dr. Phillips described how crippling the disorder can become for those who spend hours in front of a mirror trying to “fix” their “ugly hair” or disguise a facial blemish only they can see. Some pick at an unnoticeable mark on their skin until they do indeed have a visible lesion. Some won't leave the house unless they can totally cover their face and hair. Those who do go out without masking the area of concern sometimes suddenly flee and hide when they think someone has noticed it or is staring at them.

Many trace their problem to a childhood emotional trauma, like being teased about their looks, parental neglect, distress over parents' divorce, or emotional, sexual or physical abuse. But Dr. Phillips says most people survive such traumas without developing B.D.D., especially if other factors in their lives lift their self-esteem.

Rather, she explained, the disorder seems to have a combination of genetic, emotional and neurobiological underpinnings. “It's likely that the genes a person is born with provide an essential foundation for B.D.D. to develop,” Dr. Phillips wrote. She noted that in about 20 percent of cases, a parent, a sibling or a child also had the disorder. Imaging studies done by Dr. Feusner, Dr. Phillips and others suggest that some brain circuits may be overactive in people with the disorder.

One presumed factor - societal emphasis on looks - is far less important than you might think. Dr. Phillips said the incidence of B.D.D. was nearly the same all over the world, regardless of cultural influences. Also, unlike eating disorders, which mainly affect women seeking supermodel thinness, nearly as many men as women have body dysmorphic disorder.

Which Treatments Work?

The good news is that even though research into the causes of the disorder is in its relative infancy, treatments have been found to help a large percentage of those affected, as long as their problem is recognized and they manage to overcome their embarrassment long enough to get to a qualified therapist.

The two most effective approaches are cognitive behavioral therapy and treatment with serotonin-enhancing drugs, either alone or in combination. In cognitive therapy, patients gradually learn to reorder their thinking, expose their “defect” to others and view themselves more realistically as whole individuals rather than seeing only the presumed defect. In studies using serotonin-enhancing drugs, half to three-quarters of people with B.D.D. have improved, although Dr. Phillips warned that it can take as long as three months to see the benefit of a proper dose. (Moreover, there is still controversy about how many people achieve long-lasting benefits from the serotonin drugs.)

What does not work is plastic surgery and other cosmetic treatments. Even if the treatments modify one presumed defect, the person is likely to come up with another, and another, and another, leading to a vicious cycle of costly and often deforming as well as ineffective remedies.

Most important, Dr. Phillips said, is not to give up. Effective treatment is out there and it can make a tremendous difference - even a lifesaving difference. Her new book lists centers around the country that specialize in treating B.D.D.

New Superbug Surpasses MRSA Infection Rates in Community Hospitals **By Duke Medicine News and Communications**

While prevention methods appear to be helping to lower hospital infection rates from MRSA, a deadly antibiotic-resistant bacterium, a new superbug is on the rise, according to research from the Duke Infection Control Outreach Network.

New data shows infections from *Clostridium difficile* are surpassing methicillin-resistant *Staphylococcus aureus* (MRSA) infections in community hospitals.

“We found that MRSA infections have declined steadily since 2005, but *C. difficile* infections have increased since 2007,” said Becky Miller, MD, an infectious diseases fellow at Duke University Medical Center.

C. difficile is a multi-drug resistant bacterium that causes diarrhea and in some cases life-threatening inflammation of the colon. The infections are currently treated with one of two antibiotics. But relapses are common and occur in one-quarter of patients despite treatment, according to Miller.

“This is not a nuisance disease,” said Daniel Sexton, MD, director of the Duke Infection Control Outreach Network (DICON). “A small percentage of patients with *C. difficile* may die, despite treatment. Also, it is likely that the routine use of alcohol-containing hand cleansers to prevent infections from MRSA does not simultaneously prevent infections due to *C. difficile*.”

Miller and her team evaluated data from 28 hospitals in DICON, a collaboration between Duke and 39 community hospitals located in Georgia, North Carolina, South Carolina, and Virginia. The group tries to improve infection control programs by compiling data on infections occurring at member hospitals, identifying trends and areas for improvement, and providing ongoing education and leadership to community providers.

During a 24-month period, there were 847 cases of *C. difficile* infections in the 28 hospitals and the rate of *C. difficile* infection was 25 percent higher than the rate of infection due to MRSA.

Miller presented her findings at the Fifth Decennial International Conference on Healthcare-Associated Infections on March 20 in Atlanta, Georgia. “*C. difficile* is very common and deserves more attention,” she said. “Most people continue to think of MRSA as the big, bad superbug. Based on our data, we can see that this thinking, along with prevention methods, will need to change.”

In the past, hospitals were focused on MRSA and developed their prevention methods on MRSA as the issue, Sexton said. “I have always thought that we need to be looking more globally at all the problems and this new information about *C. difficile* provides more data to support that,” he said.

C. difficile has been a low priority for hospitals, but now it is a relatively important priority, Sexton said. “The key is to develop prevention methods aimed at *C. difficile* while still maintaining the success we have had with MRSA,” Miller said.

Dotty sensor sees in glorious technicolour

* 16:36 22 March 2010 by Paul Marks

Want to catch the colours of a rainbow? Then cameras need to ditch their colander-like image sensors. That's the basic idea behind a new sensor which claims to capture unparalleled amounts of light and colour.

Nanoengineer Ted Sargent of the University of Toronto, Canada, realised that the image sensors currently used in digital cameras and cellphones waste most of the light that hits them. The sensors, or complementary metal-oxide semiconductor (CMOS) photodiodes, are built in such a way that metal tracks have to criss-cross their surface. These tracks, which carry signals from the photodiode, block much of the light, so just a fraction hits the pixels. That means the resulting picture is nowhere near as sharp and colourful as it could be.

"CMOS isn't a logical platform for light sensing," Sargent says. "It doesn't treat every photon as precious." It would be better to have the sensing area above the connectors, he says.

Quantum film

This week, InVisage of Menlo Park, California, where Sargent is chief technology officer, revealed a prototype 2-megapixel "quantum film" sensor, whose entire surface senses light – with the troublesome tracks hidden safely away beneath it.

The sensing layer is a film of quantum dots – crystals of a semiconductor material just 2 nanometres wide. It was created by dispersing the crystals in a solution, then layering them onto the surface of a chip using a technique called spin coating. "We get a quantum film many hundreds of quantum dots deep, with millions of dots per pixel," says Sargent.

A quantum dot nanocrystal confines electrons to a region so small that they no longer behave like electrons in a regular semiconductor. Usually, only an incoming photon of a certain wavelength can excite an electron to jump energy level, allowing light to be sensed at that wavelength. But confinement in a quantum dot artificially limits the energy levels an electron can jump between, allowing the crystal to sense photons of particular wavelengths.

Tuned nanocrystals

The nanocrystal's light-sensing properties can be tuned simply by changing its dimensions. "We have tuned ours to absorb the entire visible spectrum and we generate an electron for every photon absorbed," says Sargent.

The electron then flows into a conventional CMOS image-sensing circuit beneath it. The result is a chip that, for an equivalent size, has a megapixel resolution four times as great.

But InVisage faces "significant but surmountable" challenges competing with existing silicon technology on sensing speeds and cost, says Seth Coe-Sullivan of QD Vision in Watertown, Massachusetts, which makes quantum dot displays. The biggest challenge, however, is probably going to be demonstrating long-term reliability against CMOS, he predicts.

Although quantum film's colour sensitivity has "great potential", it will not be economically viable unless its developers can show the system works seamlessly with the other standard components used in imaging, says Edoardo Charbon, an imaging expert at the Technical University of Delft in the Netherlands.

Bone-hard biomaterial

Football players, skiers, tennis players – they all fear a crucial ligament rupture. If the knee ligaments are damaged the patient usually has to undergo a surgery to restore the stability of the joint. In the surgical procedure the torn ligament is replaced by a piece of tendon from the leg, which is fixed to the bone by means of an interferential screw. The problem is that the screws are made of titanium. After a certain time the patient has to undergo a further surgery so that the material can be removed.



Researchers at the Fraunhofer Institute for Manufacturing Engineering and Applied Materials Research (IFAM) in Bremen want to spare cruciate ligament victims and other bone patients this additional procedure. They have therefore developed a screw which is biocompatible and also biodegradable over time. »We have modified biomaterials in such a way that they can be formed into robust bioactive and resorbable screws by means of a special injection molding process,« explains Dr. Philipp Imgrund, head of the biomaterial technology department at IFAM. »Depending on the composition they biodegrade in 24 months.« Biodegradable screws made of polylactic acid are already used in the medical field, but they have the disadvantage that when they degrade they can leave holes in the bone. The IFAM researchers have therefore improved the material and developed a moldable composite made of polylactic acid and hydroxylapatite, a ceramic which is the main constituent of the bone mineral. »This composite possesses a higher proportion of hydroxylapatite and promotes the growth of bone into the implant,« says Imgrund.

The engineers at IFAM have developed a granulate from the biomaterials which can be precision-processed using conventional injection molding methods, obviating the need for any post-processing such as milling. The complex geometry is achieved in a net-shape process, producing a robust screw. The properties of this prototype come very close to those of real bone. Its compressive strength is more than 130 newtons per square millimeter, whereas real bone can withstand between 130 and 180. What's more, the injection molding process has a positive side effect. Normally, the powder injection molded part has to be compressed at very high temperatures of up to 1400° Celsius. »We only need 140 degrees for our composite materials,« says Imgrund. In future the engineers intend to develop other bioimplants using their energy-saving process.

Iceland waits for volcanic shoe to drop

* Updated 15:53 23 March 2010 by **Nic Fleming**

Icelandic communications links and even transatlantic flights could be disrupted by a second, more destructive volcano following this weekend's eruption. Some 500 people were evacuated from their homes after the Eyjafjallajökull volcano 120 kilometres south-east of Reykjavik shot ash and molten lava into the air on Saturday night.

Initial fears that the eruption had occurred directly beneath the Eyjafjallajökull glacier – which could have caused glacial melt, flooding and mudslides – proved unfounded.

But volcanologists have warned that previous Eyjafjallajökull eruptions have triggered eruptions of neighbouring Katla, one of the largest volcanoes in Iceland. Katla erupted every 40 to 80 years in the thousand years before the last eruption in 1918.

"The eruption is long overdue at Katla and there is quite a bit of anxiety in Iceland about the potential size of eruption," says Dave McGarvie of the Open University in Milton Keynes, UK.



You ain't seen nothing yet (Image: Araldo Di Crollanza/Rex Features)

Coast changer

The larger volcano, beneath the larger Mýrdalsjökull glacier, has a reputation for triggering huge jökulhlaup – the Icelandic term for the sudden release of meltwater from glaciers and ice sheets. Its last eruption generated a peak discharge of 1.6 million cubic metres per second within 4 to 5 hours and moved so much debris that Iceland's coastline was extended by 4 kilometres.

A new Katla eruption would be unlikely to kill anyone, because the area is sparsely populated and eruptions are usually preceded by earthquakes that would give plenty of time to evacuate. It would cut the main road link in the south of the island, however.

Because the lower atmosphere is thinner closer to the poles, the giant cloud of fine particles released would more easily reach the stratosphere – where aircraft cruise – than would dust from volcanoes in most other countries. Depending on the wind, this could disrupt air travel in the north Atlantic, forcing aircraft travelling between the UK and Scandinavian countries and North America to take slower, more expensive routes further south than normal.

History repeats

The three eruptions of Eyjafjallajökull in the last 1100 years – in 920, 1612 and 1821 – have all triggered larger Katla eruptions.

"With the current methods we have of resolving the plumbing systems of these volcanoes we can't explain why one triggers the other, but we know there is a symbiotic relationship," says McGarvie.

Iceland is well prepared for volcanoes, with sophisticated monitoring systems combining GPS, seismometers and satellite data as well as established civil defence plans.

A quarter of the island's population died from the famine that resulted from the 1783 eruption of the Laki volcano, the worst in modern times in high latitudes. It sent a huge cloud of haze across Europe and parts of North America, triggering dramatic climatic changes, from the largest recorded snowfall in New Jersey to one of the longest droughts seen in Egypt.

Baby Fat May Not Be So Cute After All

By RONI CARYN RABIN

Schools have banned cupcakes, issued obesity report cards and cleared space in cafeterias for salad bars. Just last month, Michelle Obama's campaign to end childhood obesity promised to get young people moving more and revamp school lunch, and beverage makers said they had cut the sheer number of liquid calories shipped to schools by almost 90 percent in the past five years.

But new research suggests that interventions aimed at school-aged children may be, if not too little, too late. More and more evidence points to pivotal events very early in life - during the toddler years, infancy and even before birth, in the womb - that can set young children on an obesity trajectory that is hard to alter by the time they're in kindergarten. The evidence is not ironclad, but it suggests that prevention efforts should start very early.

Among the findings are these:

- * The chubby cherub-like baby who is growing so nicely may be growing too much for his or her own good, research suggests.
- * Babies whose mothers smoked during pregnancy are at risk of becoming obese, even though the babies are usually small at birth.
- * Babies who sleep less than 12 hours are at increased risk for obesity later. If they don't sleep enough and also watch two hours or more of TV a day, they are at even greater risk.

Some early interventions are already widely practiced. Doctors recommend that overweight women lose weight before pregnancy rather than after, to cut the risk of obesity and diabetes in their children; breast-feeding is also recommended to lower the obesity risk.

But weight or diet restrictions on young children have been avoided. "It used to be kind of taboo to label a child under 5 as overweight or obese, even if the child was - the thinking was that it was too stigmatizing," said Dr. Elsie M. Taveras of Harvard Medical School, lead author of a recent paper on racial disparities in early risk factors.

The new evidence "raises the question whether our policies during the last 10 years have been enough," Dr. Taveras said. "That's not to say they've been wrong — obviously it's important to improve access to healthy food in schools and increase opportunities for exercise. But it might not be enough." Much of the evidence comes from an unusual long-term Harvard study led by Dr. Matthew Gillman that has been following more than 2,000 women and babies since early in pregnancy.

Like children and teenagers, babies and toddlers have been getting fatter. One in 10 children under age 2 is overweight. The percentage of children ages 2 to 5 who are obese increased to 12.4 percent in 2006 from 5 percent in 1980. Yet most prevention programs have shied away from intervening at very young ages, partly because the school system offers an efficient way to reach large numbers of children, and partly because the rate of obese teenagers is even higher than that of younger children — 18 percent.

The Robert Wood Johnson Foundation, which helped finance Dr. Taveras's study, is spending \$500 million over 8 years to fight childhood obesity, but only in children 3 and up. And a multimillion-dollar National

Institutes of Health childhood obesity project that is giving out \$8 million over eight years explicitly excludes pregnant women and infants under 1.

Things are starting to change: late last year an Institute of Medicine study committee was charged for the first time with developing obesity prevention recommendations specifically for the 0-to-5 set. The report, due in about 18 months, will look at the role of sleep and early feeding patterns, as well as physical activity.

"Everybody's been pointing to this early period and saying that it looks like something is going on and it has long-lasting effects," said Dr. Leann L. Birch, director of Penn State's Center for Childhood Obesity Research, who is leading the committee.

Scientists like Dr. Birch worry about what are called epigenetic changes. The genes inherited from mother and father may be turned on and off and the strength of their effects changed by environmental conditions in early development. Many doctors are concerned about women being obese and unhealthy before pregnancy because, as they point out, the womb is the baby's first environment.

One of the most convincing studies on the link between gestational diabetes in the mother and diabetes in her children was done almost 10 years ago among Pima Indians. Siblings born after the mother developed Type 2 diabetes had a higher body mass index throughout childhood and were almost four times as likely to develop diabetes as siblings born before the diagnosis.

"The intrauterine environment of a woman with diabetes overnourishes the fetus," said the study's author, Dana Dabelea, an epidemiologist at the Colorado School of Public Health. And that, she added, may "reset the offspring's satiety set point, and make them predisposed to eat more."

Experts say change may require abandoning some cherished cultural attitudes. "The idea that a big baby is a healthy baby, and a crying baby is probably a hungry baby who should be fed, are things we really need to rethink," Dr. Birch said.

Correction: An earlier version of this story incorrectly stated that the RWJ foundation will be spending \$500 million over 14 years, when in fact they are spending the money over 8 years.

'Muscular' UK Space Agency set up

By Jonathan Amos Science correspondent, BBC News

The new UK Space Agency (UKSA) will take over responsibility for government policy and the key budgets for space, according to ministers.

The agency, which comes into being on 1 April, will also represent Britain on space matters in all negotiations with international partners. The UKSA's name, logo and remit were announced at a conference in London.

Its establishment should bring more coherence to space policy - something critics say has been missing for years. In particular, it is hoped an executive agency that can champion British interests abroad will help an already successful space industry to grow still further.

"People in the UK are not aware of just how good Britain is both at space research and in terms of our space industry; [a space agency] is going to make people more aware of that," Lord Drayson, the minister for science and innovation, told BBC News.

"But in practical terms, it's going to make the decision-making by government in all aspects of space policy much more joined up, better co-ordinated - a single point within government which has responsibility for making sure that we get everything in alignment such that the space research we do, the space industry that we're building, fulfils its true potential."

British space policy and budgets have until now been devolved to a partnership of government departments and science funding councils. The UKSA will, step by step, assume control of these partners' monies (about £230m per year) and their management functions.

It will start in the areas related to Britain's membership of the European Space Agency (Esa), where most of the civil space budget is spent. It will then extend to areas that engage with the EU, which has begun in recent years to develop major space projects of its own, such as the Galileo satellite-navigation system.

In addition to the UKSA announcement, the government says £24m will be put into an International Space Innovation Centre (ISIC) at Harwell in Oxfordshire, the site of a new Esa technical facility. This is in addition to £16m from industry.

Ministers say the ISIC will help establish hubs of excellence in the UK to:

- * exploit the data generated by Earth Observation satellites,
- * use space data to understand and counter climate change and
- * advise on the security and resilience of space systems and services.

The announcements are part of the government's response to a major report produced last month by industry and academia on the future prospects for Britain in space.



The Space Innovation and Growth Strategy (Space-IGS) laid out a path it believed could take the UK from a position where it currently claims 6% of the global market in space products and services to 10%, by 2030, creating 100,000 new hi-tech jobs in the process.

The government says it agrees with most of the Space-IGS recommendations, including developing a National Space Technology Strategy.

One key area of dissent however is the call to double UK spending on Esa programmes over the next decade. The Space-IGS wanted Britain to try to initiate and lead at least three missions between now and 2030.

Ministers say they cannot make such commitments in the current economic climate.

"We will require a compelling business case for each proposal or mission," said Lord Drayson.

The government says it also wants more information from industry on how satellite broadband services could be expanded, and on the feasibility of establishing a UK-based Earth observation (EO) programme.

At the moment, the UK buys Earth imagery acquired by foreign spacecraft. The Space-IGS said there was a case for the UK to have its own EO fleet.

Space-IGS chairman and LogicaCMG CEO Andy Green welcomed the government response to the report.

He conceded ministers would find the Esa funding issue difficult but hoped that as economic conditions improved, the question could be raised again.

"They've been swift, I think they've been serious; they've put a lot of effort into it," he told BBC News.

"But as I've said today, we really have to concentrate on making a reality of this - [it's a] big ambition to go from 6% to 10%, create 100,000 jobs. That will need investment from industry, investment from government; and we'll see how that goes as we go up to the next spending round."

The creation of a space agency is just the latest in a series of initiatives affecting British space interests.

In July last year, Esa finally opened a technical centre in the UK - the only one of the agency's senior members not to have such a showcase facility. It also appointed a British national, Major Tim Peake, to its astronaut corps in May.

Our eye position betrays the numbers we have in mind, new study

It will be harder to lie about your age or your poker hand after new research by the University of Melbourne, Australia has revealed that our eye position betrays the numbers we are thinking about.

In the study, participants were asked to state a series of random numbers. By measuring their vertical and horizontal eye position, researchers were able to predict with reliable confidence the next chosen number - before it was spoken.

Specifically, a leftward and downward change in eye position announced that the next number would be smaller than the last. Correspondingly, if the eyes changed position to the right and upward, it forecast that the next number would be larger. The degree of eye movement reflected the size of the numerical shift.

The paper was published today online in the prestigious journal Current Biology.

First author, Dr Tobias Loetscher of the University of Melbourne's School of Behavioural Sciences and previously of the Department of Neurology, University Hospital Zurich, Switzerland says the research demonstrates how the eyes and their position give insight into the nature of the systematic choices made by the brain's random number generator. "When we think of numbers we automatically code them in space, with smaller number falling to the left and larger numbers to the right. That is, we think of them along a left-to-right oriented mental number line - often without even noticing this number-space association ourselves."

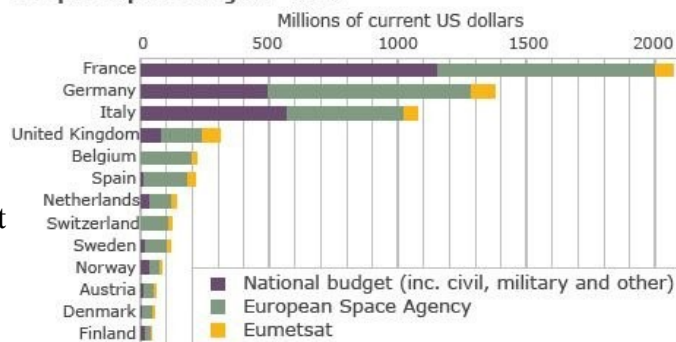
"This study shows that shifts along the mental number line are accompanied by systematic eye movements. We suggest that when we navigate through mental representations - as for example numbers - we re-use brain processes that primarily evolved for interacting and navigating in the outside world."

Dr Michael Nicholls also of the School of Behavioural Sciences adds, "Clearly, the eyes not only allow us to see the world around us, but they also present a window to the working of our mind, as this study shows."

"This study will hopefully provide a template to investigate how the human mind works via a connection with the space and world around us," he says.

The study involved asking twelve right-handed men to select from a set of random numbers. Paced by an electronic metronome they named 40 numbers between 1 and 30 in a sequence as random as possible. For each number, the researchers measured the average eye position during the 500 millisecond interval before the numbers were stated.

European space budgets* 2005



*Only those countries with budget > \$25million

Source: European Space Technology Platform

Ingredient in tequila plant may fight osteoporosis and other diseases

SAN FRANCISCO - The plant that gave the world tequila contains a substance that seems ideal for use in a new genre of processed foods -- so-called "functional foods" - with health benefits over and above serving as a source of nutrients, scientists reported here today at the 239th National Meeting of the American Chemical Society (ACS). Foods spiked with "fructans" from the agave plant may help protect against osteoporosis by boosting the body's absorption of calcium and could have other health benefits, they said.



The agave plant, the source of tequila, also may supply a healthful food additive. Erika Mellado, National Polytechnic Institute, Guanajuato, Mexico

"Fructans are considered functional food ingredients because they affect body processes in ways that result in better health and reduction in the risk of many diseases," said Mercedes López, Ph.D., who delivered the report. She is with the National Polytechnic Institute, Guanajuato, Mexico. "Experimental studies suggest that fructans may be beneficial in diabetes, obesity, stimulating the immune system of the body, decreasing levels of disease-causing bacteria in the intestine, relieving constipation, and reducing the risk of colon cancer."

Fructans are non-digestible carbohydrates. They consist of molecules of fructose -- the sugar found in honey, grapes, and ripe fruits -- linked together into chains. Rich natural sources include artichokes, Jerusalem artichokes, garlic and onions, and chicory. Fructans do not occur in tequila, however, because they change into alcohol when agave is used to make tequila, López said.

So-called "inulin-type" fructans from chicory find wide use in the United States and other countries in ice cream, breakfast cereals, baked goods, sauces, beverages, and other foods. Small fructans have a sweet taste, while those formed from longer chains of fructose have a neutral taste and give foods a smooth, pleasant texture. Scientific studies have suggested that fructans stimulate the growth of healthful bacteria in the large intestine in a way that increases the body's absorption of minerals, including the calcium and magnesium important for bone growth.

In the new study, López and colleagues set out to determine what effects agave fructans actually have on bone growth. They tested the effects of agave fructans on laboratory mice, used as stand-ins for humans in such research. Mice fed agave fructans absorbed more calcium from food, excreted less calcium in their feces, and showed a 50 percent increase in levels of a protein associated with the build-up of new bone tissue.

"These results suggest that the supplementation of the standard diet with agave fructans prevented bone loss and improved bone formation, indicating the important role of agave fructans on the maintenance of healthy bone," López said. "They can be used in many products for children and infants to help prevent various diseases, and can even be used in ice cream as a sugar substitute."

López said her findings suggest that agave fructans could be used in all of the same foods as chicory fructans. One advantage: Agave grows abundantly in Mexico and other countries with climates that do not favor growth of chicory. In addition, the scientists cited hints from past research that agave fructans may have greater health benefits. Agave fructans, for instance, seem to stimulate production of greater amounts of incretins than the inulin-type fructans from chicory. Incretins are a group of gastrointestinal hormones that increase in the amount of insulin released by the pancreas. That could be beneficial for individuals with diabetes or high blood sugar levels who are at risk of diabetes, López said. One incretin stimulated by agave fructans is a good satiety enhancer, which would make people feel full on less food.

"We still have a long way to go to determine for which health benefits agave fructans perform better than chicory fructans," López said. "However, the early results are encouraging, and we working on it."

Hard plastics decompose in oceans, releasing endocrine disruptor BPA

SAN FRANCISCO - Scientists today reported widespread global contamination of sea sand and sea water with the endocrine disruptor bisphenol A (BPA) and said that the BPA probably originated from a surprising source: Hard plastic trash discarded in the oceans and the epoxy plastic paint used to seal the hulls of ships.

"We were quite surprised to find that polycarbonate plastic biodegrades in the environment," said Katsuhiko Saido, Ph.D. He reported on the discovery today at the 239th National Meeting of the American Chemical Society, being held here.

Saido and Hideto Sato, Ph.D., and colleagues are with Nihon University, Chiba, Japan. "Polycarbonates are very hard plastics, so hard they are used to make screwdriver handles, shatter-proof eyeglass lenses, and other very durable products. This finding challenges the wide public belief that hard plastics remain unchanged in the environment for decades or centuries. Biodegradation, of course, releases BPA to the environment."

The team analyzed sand and seawater from more than 200 sites in 20 countries, mainly in Southeast Asia and North America. All contained what Saido described as a "significant" amount of BPA, ranging from 0.01 parts

per million (ppm) to 50 ppm. They concluded that polycarbonates and epoxy resin coatings and paints were the main source.

In research reported at the ACS's August 2009 National Meeting, Saido and colleagues first busted the myth of the everlasting quality of plastics. They revealed that light, white-foamed plastic decomposed rapidly at temperatures commonly found in the oceans. In decomposing, that plastic releases potentially toxic substances. In the new report, Saido's group now has added hard plastics and hard epoxy resins — to the plastics that decompose under conditions commonly found in the oceans. Millions of gallons of epoxy resins are used each year to seal the hulls of ships, protecting them from rust and fouling with barnacles and other deposits.

"When epoxy resin breaks down, it releases BPA, a typical endocrine disruptor," Saido explained. "This new finding clearly demonstrates the instability of epoxy, and shows that BPA emissions from epoxy do reach the ocean. Recent studies have shown that molluscs, crustaceans and amphibians could be affected by BPA, even in low concentrations."

He said that waste plastics are finding their way into the environment through littering, and also may be carried by water into the oceans, spreading this pollution widely. Each year as much as 150,000 tons of plastic debris wash up on the shores of Japan alone, Saido said. Vast expanses of waste, consisting mainly of plastic, float elsewhere in the oceans. The so-called Great Pacific Garbage Patch between California and Hawaii was twice the size of Texas and mainly plastic waste. Plastics are, in fact, the main source of garbage in marine debris, according to Saido. "This process is expedited by the low temperatures at which plastic degradation can occur, temperatures present in oceans," he added.

"Marine debris plastic in the ocean will certainly constitute a new global ocean contamination for long into the future," Saido predicted

New form of insulin can be inhaled rather than injected

SAN FRANCISCO - Scientists today described a new ultra-rapid acting mealtime insulin (AFREZZA™) that is orally inhaled for absorption via the lung. Because the insulin is absorbed so rapidly, AFREZZA's profile closely mimics the normal early insulin response seen in healthy individuals. AFREZZA is awaiting approval by the U. S. Food and Drug Administration (FDA). This presentation took place at the 239th American Chemical Society National Meeting, being held here this week.

Andrea Leone-Bay, Ph.D. and colleagues at MannKind Corporation said that the new insulin product, uses the Technosphere® technology, a delivery technology that is applicable to a wide variety of other drugs that are currently injected. Like insulin, these medications are proteins that would be digested and destroyed in the stomach if taken by mouth.

One such product, MKC-180, is a Technosphere® formulation of a natural hormone that controls appetite and is under investigation as a therapy for obesity using pulmonary delivery. "In nonclinical studies remarkable reductions in food intake have been observed," Leone-Bay said. MannKind is also evaluating Technosphere® technology with drugs that treat pain and osteoporosis.

"Our proprietary Technosphere® Technology platform is based on particles formed by the self-assembly of a small molecule," Leone-Bay explained. "Drugs can be loaded onto these particles, which are then dried to form a dry powder. Using a thumb-sized device, patients inhale a small amount of the powder, roughly equivalent to a pinch of salt. This powder dissolves immediately after inhalation and the drug is absorbed into the patient's bloodstream. Most importantly, the drug is absorbed ultra-rapidly so it becomes effective much more quickly than an injection of the same drug. For some drugs, ultra-rapid systemic delivery provides distinct clinical advantages over injection, including profiles that match the body's natural responses in processes like hormone secretion."

AFREZZA™ (insulin human rDNA origin) Inhalation Powder is an ultra-rapid acting insulin intended for use at mealtime to control the rapid rise in blood sugar levels that occurs in people with diabetes immediately after a meal. At other times, people with diabetes would take injections of other kinds of insulin.

Leone-Bay said AFREZZA™ controls glucose as well as current state-of-the-art treatments, poses a lower risk of hypoglycemia than that typically associated with mealtime insulin therapy, and leads to less weight gain compared to other insulin treatments," according to Leone-Bay. "Additionally, and importantly, AFREZZA™ provides the unique benefit of a small, discreet, and easier-to-use inhalation device."

New method could revolutionize dating of ancient treasures

SAN FRANCISCO - Scientists today described development of a new method to determine the age of ancient mummies, old artwork, and other relics without causing damage to these treasures of global cultural heritage. Reporting at the 239th National Meeting of the American Chemical Society (ACS), they said it could allow scientific analysis of hundreds of artifacts that until now were off limits because museums and private collectors did not want the objects damaged.

"This technique stands to revolutionize radiocarbon dating," said Marvin Rowe, Ph.D., who led the research team. "It expands the possibility for analyzing extensive museum collections that have previously been off limits because of their rarity or intrinsic value and the destructive nature of the current method of radiocarbon dating. In theory, it could even be used to date the Shroud of Turin."

Rowe explained that the new method is a form of radiocarbon dating, the archaeologist's standard tool to estimate the age of an object by measuring its content of naturally-occurring radioactive carbon. A professor emeritus at Texas A&M University College Station, Rowe teaches at a branch of the university in Qatar. Traditional carbon dating involves removing and burning small samples of the object. Although it sometimes requires taking minute samples of an object, even that damage may be unacceptable for some artifacts. The new method does not involve removing a sample of the object.

Conventional carbon dating estimates the age of an artifact based on its content of carbon-14 (C-14), a naturally occurring, radioactive form of carbon. Comparing the C-14 levels in the object to levels of C-14 expected in the atmosphere for a particular historic period allows scientists to estimate the age of an artifact. Both the conventional and new carbon dating methods can determine the age of objects as far back as 45,000 to 50,000 years, Rowe said.

In conventional dating methods, scientists remove a small sample from an object, such as a cloth or bone fragment. Then they treat the sample with a strong acid and a strong base and finally burn the sample in a small glass chamber to produce carbon dioxide gas to analyze its C-14 content.

Rowe's new method, called "non-destructive carbon dating," eliminates sampling, the destructive acid-base washes, and burning. In the new method, scientists place an entire artifact in a special chamber with a plasma, an electrically charged gas similar to gases used in big-screen plasma television displays. The gas slowly and gently oxidizes the surface of the object to produce carbon dioxide for C-14 analysis without damaging the surface, he said.

Rowe and his colleagues used the technique to analyze the ages of about 20 different organic substances, including wood, charcoal, leather, rabbit hair, a bone with mummified flesh attached, and a 1,350-year-old Egyptian weaving. The results match those of conventional carbon dating techniques, they say.

The chamber could be sized to accommodate large objects, such as works of art and even the Shroud of Turin, which some believe to be the burial cloth of Jesus Christ, Rowe said. He acknowledged, however, that it would take a significant amount of data to convince museum directors, art conservators, and others that the new method causes no damage to such priceless objects.

The scientists are currently refining the technique. Rowe hopes to use it, for instance, to analyze objects such as a small ivory figurine called the "Venus of Brassempouy," thought to be about 25,000 years old and one of the earliest known depictions of a human face. The figurine is small enough to fit into the chamber used for analysis.

Funding for this project is provided by the National Science Foundation, the National Center for Preservation Technology and Training, and Texas A&M University.

Another perk of painkillers? Decreased hormone levels may reduce cancer risk

Philadelphia – Postmenopausal women who regularly use aspirin and other analgesics (known as painkillers) have lower estrogen levels, which could contribute to a decreased risk of breast or ovarian cancer.

"We observed some significant inverse associations between concentrations of several estrogens and the use of aspirin, aspirin plus non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs), and all analgesics combined," said Margaret A. Gates, Sc.D., research fellow at the Channing Laboratory at Brigham and Women's Hospital and Harvard Medical School. "Our results suggest that among postmenopausal women, regular users of aspirin and other analgesics may have lower estrogen levels than non-users," Gates added.

These study results are published in *Cancer Epidemiology, Biomarkers & Prevention*, a journal of the American Association for Cancer Research.

Gates and colleagues examined the association between use of aspirin, NSAIDs and acetaminophen and concentrations of estrogens and androgens among 740 postmenopausal women who participated in the Nurses' Health Study. Frequency of all analgesic use was inversely associated with estradiol, free estradiol, estrone sulfate and the ratio of estradiol to testosterone.

Average estradiol levels were 10.5 percent lower among women who regularly used aspirin or non-aspirin NSAIDs. Similarly, free estradiol levels were 10.6 percent lower and estrone sulfate levels were 11.1 percent lower among regular users of aspirin or other NSAIDs. Among regular users of any analgesic (aspirin, NSAIDs or acetaminophen), levels of these hormones were 15.2 percent, 12.9 percent and 12.6 percent lower, respectively, according to Gates.

Michael J. Thun, M.D., M.S., vice president emeritus of epidemiology and surveillance research at the American Cancer Society, said the question of whether regular use of aspirin and other NSAIDs is causally related to reduced breast cancer risk is important, but still unresolved.

Thun believes these study results do not confirm whether aspirin-like drugs caused the reduction in circulating estradiol. However, the results do provide evidence that aspirin and other NSAIDs might reduce circulating levels of estradiol by about 10 percent, according to Thun, who is an editorial board member of *Cancer Epidemiology, Biomarkers & Prevention*, and was not associated with this study.

"Hopefully these findings will motivate a trial to determine whether the association between aspirin use and hormone levels is causal," he said. "Until then, we have a possible mechanism for a potentially important, but as yet unproven chemopreventive benefit."

Gates agreed and said that additional research, like a randomized trial of NSAID use and hormone levels, is needed to confirm these results and to determine whether the decrease in hormone levels translates to a reduced risk of breast or ovarian cancer. If an inverse association between analgesic use and risk of breast or ovarian cancer is confirmed, then this research may have important public health implications.

"Although the overall risks and benefits would need to be weighed, analgesics could be implemented as a chemopreventive and may decrease the risk of several cancers," she said.

Patients at risk for complications after coronary artery fistula closure

Study highlights:

* After surgery to repair abnormally connected heart arteries called coronary artery fistula (CAF) some patients fare worse than others.

* This study suggests that CAF that drain into the coronary sinus (at the back of the heart) are more likely to have complications after corrective surgery.

DALLAS - Long-term complications after procedures to close coronary artery fistulas are particularly prevalent among those whose abnormal connections to the heart result in drainage into the coronary sinus, according to a study published in *Circulation: Cardiovascular Interventions*, a journal of the American Heart Association.

A coronary artery fistula is an abnormal connection between a coronary artery and a chamber of the heart or vessel. The coronary sinus is the end portion of a large vein at the back of the heart that receives blood from the heart's veins and empties into the right atrium.

The study found that procedures to close a CAF were associated with increased long-term risks of angina, coronary thrombosis (a clot in one of the heart's blood vessels), heart failure and heart attack.

To determine which patients are most at risk for these complications after closure, researchers reviewed the medical records of 76 patients diagnosed with congenital coronary artery fistula. Sixty-four patients underwent transcatheter closure or surgical repair of the fistula. The researchers found that 15 percent of patients had major complications following closure, including heart attack, angina with coronary thrombosis, or symptomatic cardiomyopathy (heart failure). The only angiographic finding associated with major complications was drainage of the coronary artery fistula into the coronary sinus.

Other predictors associated with adverse outcomes included older age at diagnosis, tobacco use, diabetes, hypertension and hyperlipidemia (or high cholesterol).

Physicians should consider reducing atherosclerotic risk factors and long-term use of blood thinning medications after coronary artery fistula closure, especially for patients with fistula that drain into the coronary sinus, the researchers said.

Stopping clinical trials early often exaggerates treatment effects

ROCHESTER, Minn. -- An international study of nearly 100 clinical trials that were stopped early due to positive treatment effects has found that many of those effects were exaggerated. The authors of the study -- published in the current issue of the *Journal of the American Medical Association* -- recommend that researchers resist pressures to end clinical trials early and continue trials for longer periods before even considering premature termination.

"Our research shows that in most cases early stopping of clinical trials resulted in misleading estimates of treatment effects. These misleading estimates are likely to result in misguided decisions about the trade-off between risks and benefits of a therapy," says Victor Montori, M.D., Mayo Clinic endocrinologist and corresponding author of the study. "On average, treatments with no effect would show a reduction in relative risk of almost 30 percent in stopped early trials. Treatments with a true relative risk reduction of 20 percent would show a reduction of over 40 percent."

The clinical trials that Dr. Montori and colleagues studied were ended early because of a convincing -- and usually large -- apparent difference between an experimental treatment and an existing standard therapy. The studies were ended so participants taking a placebo or less effective medications could also take the studied

drug. It usually also allows physicians to prescribe the therapy sooner because it will reach the market earlier. Dr. Montori says almost everyone involved benefits from a trial ending early -- doctors, researchers, funding sources, pharmaceutical firms, scientific journals, even reporters -- everyone except the patient, who may end up receiving a therapy on the basis of misleading information about its benefits.

The researchers examined 63 medical questions regarding 91 truncated trials and compared them to 424 comparable trials that were not stopped early. Results showed that the studies that were stopped -- especially smaller trials of a few hundred participants -- had exaggerated or misleading treatment effects. Those misleading findings are often compounded downstream because researchers are less likely to return to the topic after what is perceived as a significant successful finding.

The authors recommend that researchers use restraint and truncate clinical trials only near the end of a study and then only with "a very good reason." Otherwise, says Dr. Montori, patients and physicians will be making treatment choices based on inaccurate information, or worse, opting for one treatment when another may be more appropriate.

The study was supported by the Medical Research Council of the U.K. Other authors include Dirk Bassler, M.D.; Matthias Briel, M.D.; Qi Zhou, Ph.D.; Stephen Walter, Ph.D.; Gordon Guyatt, M.D.; and Diane Heels-Ansdell, all of McMaster University, Ontario; Melanie Lane, Mayo Clinic; and Paul Glasziou, M.B.B.S., Ph.D., University of Oxford, England.

Farming's rise cultivated fair deals

Market economies may owe more to cultural evolution than to Stone Age instincts

By Bruce Bower

Blanche DuBois, Tennessee Williams' wide-eyed protagonist who relied on "the kindness of strangers," had nothing on ancient farmers.

In rapidly expanding settlements, early cultivators had no choice but to bargain for daily goods with lots of folks they didn't know. A fundamental redefinition of a fair deal soon followed, according to a new cross-cultural study.

Around 10,000 years ago, residents of large farming communities had to learn to make fair exchanges with strangers and to retaliate against selfish exploiters, researchers propose in the March 19 Science.

Before the rise of modern agriculture and resulting trade, the researchers contend, people rarely had to behave this way with strangers. During Stone Age days, members of small hunter-gatherer groups exchanged favors only with those they knew.

"Cultural and institutional evolution harnessed and extended our evolved psychology so that we could cooperate and exchange goods in vast communities," says anthropologist and study director Joseph Henrich of the University of British Columbia in Vancouver.

To arrive at this conclusion, the team set up money-swapping games played by people from small societies around the world — farmers, hunter-gatherers, seaside foragers, livestock herders, and wage laborers — and looked at how each group divvied up resources. Participants who regularly have to deal with outsiders treated strangers more fairly, sharing a pool of money or valuables more equally, the team found.

Game players' willingness to split up resources fairly with an unknown partner rose sharply with their "market integration," or the extent that they lived in communities with market economies. The researchers measured market integration by calculating the degree to which families purchased food, rather than hunting or growing it.

Fair play also rose substantially among volunteers who subscribed to Christianity or Islam, as opposed to local religions. Large-scale religions with strict moral codes galvanize a "golden rule" approach to social exchanges, the researchers propose. Supernatural threats, such as the prospect of spending eternity in hell, and community-building rituals jointly promote fairness toward strangers, in their view.

In addition, participants from the largest communities were most likely to punish players whom they regarded as offering unfair deals. That meant canceling the deal and getting nothing or paying part of one's own pool of money to cause an even bigger loss for the unfair player.

That's not good news for traditional economic theories that regard self-interest as the engine of commerce. If those theories are right, players should take whatever someone else gives them, because that's better than nothing.

Neither do the new results bode well for evolutionary psychologists who argue that people in small Stone Age groups evolved brain circuits for kin favoritism, tit-for-tat exchanges and protecting one's own reputation. In their view, these biologically ingrained social tactics now often lead people astray, Blanche Dubois-style, by inducing excessive trust in strangers.

“This new study powerfully challenges the view in evolutionary psychology that cultural inventions during the last 10,000 years are irrelevant to human cooperation,” remarks economist Ernst Fehr of the University of Zurich.

Market economies didn't exist during the Stone Age, Fehr notes. But Henrich's study indicates that the relatively recent expansion of market economies inspired a growing concern for dealing fairly with strangers, he says. People living in communities most like those of Stone Age hunter-gatherers - small in numbers and lacking a “moralizing god” - made the most unfair offers to strangers and were least likely to punish stingy partners. Reputation concerns and a focus on give-and-take exchanges can't explain such behaviors, Fehr asserts.

Henrich's data suggest that modern economic development has prompted people to find new ways to be selfish within vast markets, comments economist Karla Hoff of the World Bank in Washington, D.C.

Henrich's new data build on a previous study of fair play in 15 small-scale societies (SN: 2/16/02, p. 104). In each group, a person given a chunk of money or other valuable stuff tended to offer a substantial, but highly variable, share to an anonymous partner. Partners often rejected offers deemed to be too low, resulting in both parties getting nothing.

In the new study, three economic games were played by 2,148 volunteers from 15 small-scale populations, including five communities from the earlier project. Community sizes ranged from 20 to 4,600 people.

One game allotted an amount of money, set at one day's local wage, to a pair of players who could not see each other. One player decided how much to keep and how much to give to the other player. This provided a basic measure of fair play toward strangers.

A second game worked in much the same way. But the receiving player first decided the amount that he or she considered a minimum acceptable offer. If that minimum was met, the deal went through. If not, both players got nothing.

A third game was similarly framed, but also provided one-half day's local wage to a third person who observed the action. The observer first determined the amount of a minimum acceptable offer between the other players. If the offer fell short, the observer forked over 20 percent of his or her pot and the offending player lost triple that amount.

Going from a fully subsistence-based society with a local religion to a fully market-based society grounded in Christianity or Islam led to increases in amounts offered by players of about 23 percent in the first game, 20 percent in the second game and 11 percent in the third game.

Pulling power points the way to the world's strongest insect

Following months of gruelling tests and trials, scientists now reveal the World's strongest insect to be a species of dung beetle called *Onthophagus taurus*.

In an experiment to find out why animals vary so much in strength and endurance, Dr Rob Knell from Queen Mary, University of London and Professor Leigh Simmons from the University of Western Australia found the strongest beetle could pull an astonishing 1,141 times its own body weight - the equivalent of a 70kg person lifting 80 tonnes (the same as six full double-decker buses).



Writing in the journal *Proceedings of the Royal Society B*, the scientists also found these insect athletes need to pay just as much attention to their diet as human athletes. Even the strongest beetles were reduced to feeble weaklings when put on a poor diet for a few days.

"Insects are well known for being able to perform amazing feats of strength," explained Dr Knell from Queen Mary's School of Biological and Chemical Sciences, "and it's all on account of their curious sex lives. Female beetles of this species dig tunnels under a dung pat, where males mate with them. If a male enters a tunnel that is already occupied by a rival, they fight by locking horns and try to push each other out." Knell and Simmons tested the beetles' ability to resist a rival by measuring how much weight was needed to pull him out of his hole.

"Interestingly, some male dung beetles don't fight over females," said Dr Knell. "They are smaller, weaker and don't have horns like the larger males. Even when we fed them up they didn't grow stronger, so we know it's not because they have a poorer diet.

"They did, however, develop substantially bigger testicles for their body size. This suggests they sneak behind the back of the other male, waiting until he's looking the other way for a chance to mate with the female. Instead of growing super strength to fight for a female, they grow lots more sperm to increase their chances of fertilising her eggs and fathering the next generation."

New scale for measuring addiction to work

Researchers from the Jaume I University have proven the usefulness of DUWAS, a new scale for measuring addiction to work, a disorder that affects around 12% of all working people in Spain. The experts say that 8% of the working population in Spain devotes more than 12 hours per day to their job.

"Addiction to work is a kind of psychosocial problem that is characterised by two primary features – working excessively and working compulsively", Mario Del Líbano, lead author of the paper and a researcher at the Faculty of Human and Social Sciences of the Jaume I University in Castellón de la Plana, tells SINC.

The results, published in the Spanish journal *Psicothema*, not only confirm the bifactorial structure of workaholism, in other words its two dimensions, but also relate the results with psychosocial wellbeing (perceived health and happiness), in order to highlight the negative features of addiction to work in Spain.

"People are only workaholics if, on top of working excessively, they work compulsively in order to reduce anxiety and the feelings of guilt that they get when they're not working", Del Líbano explains.

"This study helps to evaluate addiction along with other phenomena that affect the psychosocial health of workers, without the time taken to fill in the questionnaire having any impact on their motivation", he adds.

The new scale, called DUWAS (Dutch Work Addiction Scale), has been validated as a result of the criticisms about its validity and reliability made by two evaluation tools that have been most used to date – the WorkBAT (Workaholism Battery) and the WART (Work Addiction Risk Test).

The cut-off point – 50 hours per week

Data on the worldwide prevalence of addiction to work vary from one study to another. It is placed at around 20% in countries such as Japan, while in Spain the figures are between 11.3% and 12%, according to research carried out in 2004 by Sánchez Pardo, Navarro Botella and Valderrama Zurián, and Del Líbano's group in 2006, respectively.

The International Labour Organisation (ILO) says that 8% of the working population devotes more than 12 hours per day to their profession in order to escape from personal problems. According to the experts, spending more than 50 hours per week working could be a determining factor in addiction.

Addiction to work is characterised by extreme activity in and devotion to work (with people even working outside working hours, at weekends and on holidays), compulsion to work (inability to delegate), disproportionate involvement with work (people relating their self esteem to their work), and focusing on work to the detriment of their daily lives (poor interpersonal communication).

Some risk factors that can lead to such addiction include financial, family and social pressures; fear of losing one's job; competition in the labour market; the need to achieve a desired level of success; fear of overbearing, demanding or threatening bosses; high levels of personal work efficiency; and lack of personal affection, with the person trying to make up for this with their work.

In addition, workaholic people can also end up taking illegal substances to help them work harder, enabling them to increase their workplace performance and overcome tiredness and the need for sleep.

References: Del Libano, Mario; Llorens, Susana; Salanova, Marisa; Schaufeli, Wilmar. "Validity of a brief workaholism scale". Psicothema 22(1): 143-150, febrero de 2010.

Machiavellian insects evolve bigger, social brains

* 15:46 23 March 2010 by Rowan Hooper

It is easy to think of insects, with their pinhead-sized brains, as automatons robotically carrying out their tasks. But a discovery about the brain of the humble sweat bee not only highlights the complexities of insect brains, it also helps answer one of the big questions of human evolution: why have we got such big brains?

The bees' unusual social structure has allowed biologists to collect some of the best evidence yet that living in a society can boost brain size.

Queen sweat bees have more up top (Image: Christian Ziegler)

In the pantheon of social insects, sweat bees (*Megalopta genalis*) have a lowly position. Their micro-societies are made up of just two individuals: a queen and a single worker. They can also live on their own, and this ability to switch between a social and a solitary lifestyle makes them valuable models for studying brain evolution.

That's because many evolutionary biologists believe the increase in the size of the brain relative to body size in animals such as primates was driven by the demands of living in societies. This is known as the social – or Machiavellian – intelligence hypothesis.



Mushrooming brain

William Wcislo of the Smithsonian Tropical Research Institute in Balboa, Panama, and his colleagues dissected the brains of sweat bee queens, workers and asocial individuals and measured the size of an area called the mushroom bodies. Work on honeybees has shown that this region integrates information from the rest of the brain and is associated with learning and other memory functions.

The researchers found that the mushroom bodies were larger in queen sweat bees than they were in either worker bees or asocial bees. This shows that the parts of the brain that are involved in higher functions of cognition, like learning and memory, are more developed in queen bees than in their subordinates. It also suggests dominance drives differences in brain size in sweat bees.

Wcislo and his colleagues conclude that the pressures of a social life, and particularly of having to maintain dominance over a subordinate, is what is driving the increase in brain size in these insects. "Even in the simplest social group possible, cognitive demands help shape brain evolution," Wcislo says.

The experiments are the first to test the social intelligence hypothesis by comparing the brain size of animals belonging to the same species. Previous comparisons of different birds and primates have shown that more social animals tend to have larger brains. However, many other differences between species could also influence brain size.

Augmented development

Sean O'Donnell of the University of Washington, Seattle, who works on brain development in social insects, including sweat bees, says this is the first time that it has been shown that participation in a social group is associated with augmented brain development. "Social interactions seem to impose important cognitive challenges that must be met by enhanced investment in certain brain regions," he says.

It's exciting, O'Donnell adds, that common patterns relating brain development and structure to sociality are found across wide gulfs of evolutionary time. "The similarities in brain-behaviour relationship do suggest some profound commonalities that may have been achieved by distinct mechanisms," he says.

Journal reference: Proceedings of the Royal Society B, DOI: 10.1098/rspb.2010.0269

Virtual Biopsy Probe System is 'Almost Perfect' in Detecting Precancerous Polyps During Colonoscopy, Mayo Researchers Say

JACKSONVILLE, Fla. - The newest generation of "virtual biopsy" colonoscopy probes being tested at the Mayo Clinic campus in Florida demonstrate that it might soon be possible to use such a device to determine whether a colon polyp is benign and not remove it for biopsy. Currently, all colon polyps are extracted during a colonoscopy and sent to a pathologist for examination, which adds time, expense, and some surgical risk, to the procedure.

In the March issue of *Gastroenterology*, the researchers report that the most advanced of these two devices, the probe-based Confocal Laser Endomicroscopy (pCLE), is much more accurate than virtual chromoendoscopy, also known as narrow-band imaging. The pCLE — an imaging tool only one-sixteenth of an inch in diameter — can magnify a polyp by a factor of 1,000 to detect potentially dangerous changes in even single cells, such as enlargement of the nuclei. Narrow-band imaging uses blue light to enhance an image.

The researchers found that pCLE was 91 percent accurate in detecting precancerous polyps and narrow-band imaging was 77 percent accurate, when compared to biopsy findings..

"We are getting closer to where we want to be, which is 100 percent accurate," says the study's senior author, Michael Wallace, M.D., M.P.H., professor of medicine at the College of Medicine, Mayo Clinic, in Florida. "Some day soon we will be able to use these probes to virtually biopsy a polyp, removing only those that could become cancerous."

Half of all polyps now removed during a colonoscopy are benign, Dr. Wallace says.

Both methods tested by Dr. Wallace and his team are being used in some institutions such as Mayo Clinic to look at the area where a polyp has just been removed to make sure no precancerous cells remain at the surgical edges. That can be determined by looking at changes in cell color and size, how nuclei look, and whether cells are crowded together due to abnormal growth.

In this study, researchers administered a standard colonoscopy to 75 patients, and during the procedure used narrow-band imaging as well as pCLE to determine cancer risk in the polyps. In all, 119 polyps were removed from the patients and sent to pathologists for analysis. Eighty-one polyps were precancerous and 38 were benign. Both methods were equally specific, meaning that they had the same ability to detect benign polyps, but the pCLE system was much more sensitive in detecting precancerous polyps.

Dr. Wallace continues to test the pCLE system in colonoscopy, and is also researching its use in inflammatory bowel disease and Barrett's esophagus. Patients with inflammatory bowel disease require frequent biopsies of their colon to screen for development of colon cancer, and the probe may be able to eliminate many

of these biopsies, he says. "A patient with this condition usually needs 42 biopsies of their colon during a single examination, but only 1 in every 1,000 biopsies ever show precancerous changes," he says. "We have a clinical trial under way using pCLE that suggests we may be able to substantially reduce the need for these biopsies."

Similarly, Dr. Wallace's data shows that the probe system could reduce biopsies in Barrett's esophagus, a potentially precancerous condition in which the tissue lining the esophagus is replaced by tissue that is similar to the lining of the intestine. To rule out cancer development, physicians normally biopsy every four inches of the esophagus in patients who have Barrett's esophagus. "We believe the probe system will perform virtual biopsies that are just as valuable," Dr. Wallace says.

The study was funded by an American Society of Gastrointestinal Endoscopy Research Award. Dr. Wallace receives research grant support from Mauna Kea Technologies.

Telephone Pole-Like Fungus Was Tallest Ever

These towering fungi lived on algae and bacteria and grew over 26 feet high some 420 million years ago.

By Jennifer Viegas Tue Mar 23, 2010 11:29 AM ET

THE GIST:

* *The world's tallest fungus, **Prototaxites**, grew over 26 feet high some 420 million years ago.*

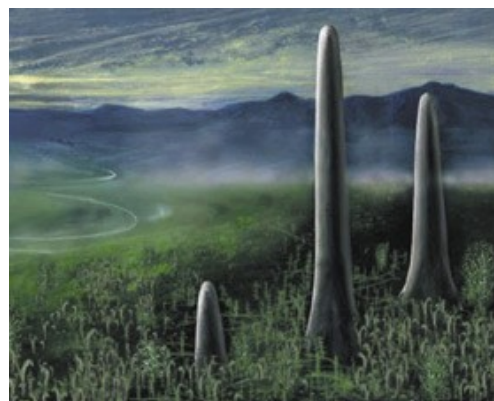
* *Scientists believe the fungus grew tall in order to better distribute its spores via the wind.*

* *Some have not yet ruled out that this species was actually a liverwort and not a fungus.*

The world's tallest fungus, according to a new paper, was the giant *Prototaxites*, which towered over the Silurian and Devonian landscapes from around 350 to 420 million years ago.

*An illustration of the fungus, **Prototaxites**, that grew over 26 feet high and lived 350 to 420 million years ago.*

Mary Parrish



Fossils for the over 26-foot-tall giant have led to scientific debate over the years, with some experts believing it was a huge plant, algae or lichen. The new study, however, published in the latest Proceedings of the Royal Society B, presents evidence that it was a fungus that likely derived at least some of its hefty nutrition load from bacteria, algae and moss.

The ancient fungus didn't closely resemble any modern species, but it looked surprisingly like a familiar man-made structure. Each of the ancient enormous fungi "formed large trunks with little evidence of branching, so they would have looked like telephone poles of various sizes," co-author Kevin Boyce told Discovery News.

Like modern fungi, most of the organism would have consisted of an underground network of thread-like structures called hyphae that handle feeding, explained Boyce, an associate professor in the Department of Geophysical Sciences at the University of Chicago. "The above-ground structure - what actually gets preserved as a fossil - would have been involved in spore dispersal, like a mushroom," he added. "For that purpose, the higher off the ground you can get, the farther spores will travel on the wind."

He and his colleagues first began to suspect *Prototaxites* was a fungus and not a plant after they analyzed carbon isotopes in its fossils. These remaining carbon atoms can suggest what existing, and once-living, organisms ate. Boyce explained that since plants derive their energy from the sun and its carbon from carbon dioxide in the air, the carbon isotope signatures for plants tend to look the same.

"But if you're an animal," he said, "you will look like whatever you eat."

While *Prototaxites* was definitely not an animal, its carbon isotopic composition displays much wider variation than what is seen in plants. For the new study, to investigate this conundrum, Boyce and co-author Erik Hobbie of the University of New Hampshire traveled to Lyman Glacier in the Cascade Mountains of Washington state to study a modern fungus called *Arrhenia obscurata*.

Hobbie explained to Discovery News that "recently deglaciated modern landscapes," such as this part of Washington, "share characteristics with the ancient Silurian/Devonian landscape that was being slowly colonized by land plants for the first time." These shared characteristics include sparse vegetation, a high abundance of fine-grained sediments, and abundant shallow floodplains and pools.

As suspected, the fungus *Arrhenia*, like *Prototaxites*, displayed wide isotopic variability. Hobbie said that's because "both would have been feeding on dead organic matter in the sediment."

Patricia Gensel, a professor in the Department of Biology at the University of North Carolina at Chapel Hill, told Discovery News that the new "findings need to be taken seriously." But she believes the case hasn't been closed yet on another hypothesis, proposed by researcher Linda Graham, that the mysterious fossils actually were rolled liverwort mats.

Carol Hotton, a research associate in the Department of Paleobiology at the National Museum of Natural History, told Discovery News that she "whole-heartedly seconds the results" of the new study, but that "it still leaves us with the problem of trying to figure out how Prototaxites actually functioned as a fungus."

Less controversial is the belief that Prototaxites went extinct at a time when the first forests and terrestrial animal life were spreading and diversifying.

"A Prototaxites trunk would have presumably taken a long time to grow and the ecological stability that would require would have become less available as ecosystems and ecological succession became more complex," Boyce said, adding that burrows in the last known specimens indicate "that something had also figured out how to eat it."

Emotions key to judging others

Study offers a new piece to the puzzle of how the human brain constructs morality

A new study from MIT neuroscientists suggests that our ability to respond appropriately to intended harms - that is, with outrage toward the perpetrator - is seated in a brain region associated with regulating emotions.

Patients with damage to this brain area, known as the ventromedial prefrontal cortex (VMPC), are unable to conjure a normal emotional response to hypothetical situations in which a person tries, but fails, to kill another person. Therefore, they judge the situation based only on the outcome, and do not hold the attempted murderer morally responsible.

The finding offers a new piece to the puzzle of how the human brain constructs morality, says Liane Young, a postdoctoral associate in MIT's Department of Brain and Cognitive Sciences and lead author of a paper describing the findings in the March 25 issue of the journal *Neuron*.

"We're slowly chipping away at the structure of morality," says Young. "We're not the first to show that emotions matter for morality, but this is a more precise look at how emotions matter."

How they did it: Working with researchers at the University of Southern California, led by Antonio Damasio, Young studied a group of nine patients with damage (caused by aneurysms or tumors) to the VMPC, a plum-sized area located behind and above the eyes.

Such patients have difficulty processing social emotions such as empathy or embarrassment, but "they have a perfectly intact capacity for reasoning and other cognitive functions," says Young.

The researchers gave the subjects a series of 24 hypothetical scenarios and asked for their reactions. The scenarios of most interest to the researchers were ones featuring a mismatch between the person's intention and the outcome — either failed attempts to harm or accidental harms.

When confronted with failed attempts to harm, the patients had no problems understanding the perpetrator's intentions, but they failed to hold them morally responsible. The patients even judged attempted harms as more permissible than accidental harms (such as accidentally poisoning someone) — a reversal of the pattern seen in normal adults.

"They can process what people are thinking and their intentions, but they just don't respond emotionally to that information," says Young. "They can read about a murder attempt and judge it as morally permissible because no harm was done." This supports the idea that making moral judgments requires at least two processes — a logical assessment of the intention, and an emotional reaction to it. The study also supports the theory that the emotional component is seated in the VMPC.

Next steps: Young hopes to study patients who incurred damage to the VMPC when they were younger, to see if they have the same impaired judgment. She also plans to study patient reactions to situations where the harmful attempts may be directed at the patient and therefore are more personal.

Source: "Damage to ventromedial prefrontal cortex impairs judgment of harmful intent," Liane Young (MIT), Antoine Bechara (USC), Daniel Tranel (University of Iowa), Hanna Damasio (USC), Marc Hauser (Harvard), and Antonio Damasio (USC). Neuron, March 25, 2010.

Great apes know they could be wrong

Study suggests nonhuman animals also have metacognitive abilities - they know about what they have seen

Great apes – orangutans, chimpanzees, bonobos and gorillas – realize that they can be wrong when making choices, according to Dr. Josep Call from the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. Dr. Call's study was just published online in Springer's journal, *Animal Cognition*.

In a series of three experiments, seven gorillas, eight chimpanzees, four bonobos and seven orangutans, from the Wolfgang Köhler Research Center at the Leipzig Zoo in Germany, were presented with two hollow tubes, one baited with a food reward, the other not. The apes were then observed as they tried to find the reward.

In the first experiment, the apes were prevented from watching the baiting but the tubes were shaken to give them auditory information about the reward's location instead. Dr. Call wanted to see if when the apes were

prevented from acquiring visual information, but offered auditory cues instead, they would be able to use the auditory information to reduce their reliance on visual searching.

In the second experiment, the apes were shown the location where the food was hidden and then at variable time delays encouraged to retrieve it. The purpose of this experiment was to see if forgetting the location would lead to the apes looking harder for it.

In the last experiment, the researcher compared the apes' response between visible and hidden baiting conditions, when the quality of the food reward varied. The author hypothesized that the apes would check more often when a high quality reward was at stake, irrespective of whether or not they had seen where it was placed.

Although the apes retrieved the reward very accurately when they had watched the baiting, Dr. Call found that they were more likely to check inside the tube before choosing when high stakes were involved, or after a longer period of time had elapsed between the baiting and the retrieval of the reward. In contrast, when the apes were provided with auditory information about the food's location, they reduced the amount of checking before choosing. According to Dr. Call, taken together, these findings show that the apes were aware that they could be wrong when choosing.

Dr. Call concludes: "The current results indicate that the looking response appears to be a function of at least three factors: the cost of looking inside the tube, the value of the reward and the state of the information. The combination of these three factors creates an information processing system that possesses complexity, flexibility and control, three of the features of metacognition*. These findings suggest that nonhuman animals may possess some metacognitive abilities, too."

***Metacognition: cognition about cognition, or knowing about knowing.**

Reference 1. Call J (2010). Do apes know that they could be wrong? *Animal Cognition* DOI 10.1007/s10071-010-0317-x

Universe Has Billions More Stars Than Thought

Counting all of those twinkling lights in the night sky just got a lot harder.

THE GIST:

*** Astronomers could have miscounted the number of galaxies in the universe.**

*** Old, distant galaxies are often missed because their light may be obstructed.**

*** The discovery could add powerfully to knowledge about the timeline by which stars and then galaxies formed.**

Astronomers may have underestimated the tally of galaxies in some parts of the universe by as much as 90 percent, according to a study reported on Wednesday in *Nature*, the weekly British science journal.

Surveys of the cosmos are based on a signature of ultraviolet light that turns out to be a poor indicator of what's out there, its authors say. In the case of very distant, old galaxies, the telltale light may not reach Earth as it is blocked by interstellar clouds of dust and gas -- and, as a result, these galaxies are missed by the map-makers.

"Astronomers always knew they were missing some fraction of the galaxies... but for the first time we now have a measurement. The number of missed galaxies is substantial," said Matthew Hayes of the University of Geneva's observatory, who led the investigation.

Hayes' team used the world's most advanced optical instrument -- Europe's Very Large Telescope (VLT) in Chile, which has four 8.2-meter (26.65-foot) behemoths -- to carry out the experiment.

They turned two of the giants towards a well-studied area of deep space called the GOODS-South field.

The astronomers carried out two sets of observations in the same region, hunting for light emitted by galaxies born 10 billion years ago.

The first looked for so-called Lyman-alpha light, the classic telltale used to compile cosmic maps, named after its U.S. discoverer, Theodore Lyman. Lyman-alpha is energy released by excited hydrogen atoms.

The second observation used a special camera called HAWK-1 to look for a signature emitted at a different wavelength, also by glowing hydrogen, which is known as the hydrogen-alpha (or H-alpha) line.

The second sweep yielded a whole bagful of light sources that had not been spotted using the Lyman-alpha technique.

They include some of the faintest galaxies ever found, forged at a time when the universe was just a child.

The astronomers conclude that Lyman-alpha surveys may only spot just a tiny number of the total light emitted from far galaxies. Astonishingly, as many as 90 percent of such distant galaxies may go unseen in these exercises. "If there are 10 galaxies seen, there could be a hundred there," said Hayes.

The discovery could add powerfully to knowledge about the timeline by which stars and then galaxies formed.

"Now that we know how much light we've been missing, we can start to create far more accurate representations of the cosmos, understanding better how quickly stars have formed at different times in the life

of the universe," co-author Miguel Mas-Hesse said in a press release issued by the European Southern Observatory (ESO).

Only a small part of the light spectrum is visible to the human eye, which is why astronomers use ultraviolet, gamma and other radiation sources as additional sources for observation.

Does 'man flu' really exist?

Men may have a weaker immune system and could be more vulnerable to so-called 'man flu', scientists propose. Evolutionary factors and hormonal differences may make males more susceptible to infection than females, says a Cambridge University team.

Their theory, outlined in a scientific journal, suggests there is a trade-off between a strong immune system and reproductive success. But a leading flu expert says there is no difference in men's immunity.

Previous experiments have found differences in the ability of females and males to deal with infection.

Across a range of animal species, males tend to be the 'weaker sex' in terms of immune defences, says the Cambridge team. This is usually explained by the difference in hormones.

High testosterone levels, they say, lead to more coughs and colds.

Let's mate

The study, published in Proceedings of the Royal Society B journal, investigated the reason for these differences. Dr Olivier Restif, one of the authors, said: "If you assume that males are more exposed to infection, then can natural selection influence that process?"

To find out, scientists developed a mathematical model that highlighted the role of other factors, like ecology and epidemiology, in shaping the immune systems of men and women.

"If males are more exposed to infection than females (for behavioural reasons for example), it is possible to see them evolve lower immuno-competence than females," the authors wrote.

Risk taking

In particular, they found that men with a predilection to risky, dangerous behaviour who have to compete for access to females would be more open to infections.

But John Oxford, Professor of virology at the University of London, disagrees. He says his team at the University of London deliberately infected men and women with the flu virus. He says there was no noticeable difference between their recovery times or their immunity. "But the women did complain more," he added.

Children with food allergies should carry 2 doses of emergency medicine

Recommendation is one of several in review of emergency departments' approaches to food-related anaphylaxis

Boston, Mass. – In a large six-year review of emergency department (ED) data, researchers at Children's Hospital Boston, in collaboration with Massachusetts General Hospital, found that many children with severe food-related allergic reactions need a second dose of epinephrine, suggesting that patients carrying EpiPens should carry two doses instead of one.

Since 1997, the number of school-aged children with food allergies has increased nearly 20 percent, according to the Centers for Disease Control and Prevention. The study, publishing in the April issue of Pediatrics, is the largest to date to investigate emergency treatment of food-related anaphylaxis in children, according to the authors.

"Food allergies are an increasingly important topic in pediatrics," says Susan Rudders, MD, of Children's Division of Allergy and Immunology and first author of the paper. "There's not a lot of data about the epidemiology of food allergies because it's a hard thing to study." Difficulties imposed on previous studies included insensitive clinical tests for food allergies – such as through a skin test or blood test – and lack of a universally accepted definition of anaphylaxis.

In reviewing the charts of children under 18 seen in two Boston EDs from 2001 to 2006, the researchers identified 1,255 children who made visits for food-related allergic reactions. Of these, more than half had anaphylaxis, the most severe allergic reaction involving at least two organ systems or low blood pressure (as defined by the National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network in 2006). Common symptoms included trouble breathing, skin rashes, swelling and gastrointestinal problems.

Of those children with anaphylaxis who were treated with epinephrine, 12 percent needed more than one dose because of a resurgence of symptoms, either before or after being taken to the ED. This finding is consistent with those of smaller previous studies.

"Until we're able to clearly define the risk factors for the most severe reactions, the safest thing may be to have all children at risk for food-related anaphylaxis carry two doses of epinephrine," Rudders says. To offset

the added cost, Rudders suggests that school nurse offices carry un-assigned extra doses of injectable epinephrine for the children who need them.

The study also characterized the state of anaphylaxis treatment in the two EDs. The study, spanning 2001-2006, suggests that EDs may not always follow current practice guidelines, which have not changed much since 1998. Current practice guidelines recommend a protocol for food-related anaphylaxis: doctors use epinephrine as the first line of treatment, refer patients to allergists, instruct patients to avoid suspected foods and prescribe self-injectable epinephrine.

However, consistent with trends seen nationwide, emergency physicians were more likely to treat children in the emergency department with corticosteroids and antihistamines. Upon discharge from the ED, less than half of patients were prescribed epinephrine, and even fewer were referred to an allergist or received instructions on avoiding suspected foods. These last recommendations are important in light of the fact that 44 percent of the children studied had a known history of food allergies, but still ate these foods accidentally. These findings may be due to lack of a universal understanding of anaphylaxis in the ED before 2006, Rudders says. That gap in knowledge has been closing since, and Rudders hopes her study will move things forward.

"As food allergies are becoming more prominent in the media, some of these [shortcomings] will catch up," Rudders says. "Recognizing anaphylaxis, promptly treating with epinephrine and sending children home with self-injectable epinephrine are going to become increasingly important."

Rudders was supported by the National Institutes of Health. Carlos Camargo, Jr., MD, DrPH of Massachusetts General Hospital is the senior author.

Citation: Susan A. Rudders, Aleena Banerji, Blanka Corel, Sunday Clark, Carlos A. Camargo, Jr. "Multicenter Study of Repeat Epinephrine Treatments for Food-Related Anaphylaxis." Pediatrics March 22, 2010 (online).

DNA identifies new ancient human

By Paul Rincon Science reporter, BBC News

Scientists have identified a previously unknown type of ancient human through analysis of DNA from a finger bone unearthed in a Siberian cave. The extinct "hominin" (human-like creature) lived in Central Asia between 48,000 and 30,000 years ago.

An international team has sequenced genetic material from the fossil showing that it is distinct from that of Neanderthals and modern humans. Details of the find, dubbed "X-woman", have been published in Nature journal.

Ornaments were found in the same ground layer as the finger bone, including a bracelet.

Professor Chris Stringer, human origins researcher at London's Natural History Museum, called the discovery "a very exciting development".

"This new DNA work provides an entirely new way of looking at the still poorly-understood evolution of humans in central and eastern Asia."

The discovery raises the intriguing possibility that three forms of human - Homo sapiens, Neanderthals and the species represented by X-woman - could have met each other and interacted in southern Siberia.

The tiny fragment of bone from a fifth finger was uncovered by archaeologists working at Denisova Cave in Siberia's Altai Mountains in 2008. An international team of researchers extracted mitochondrial DNA from the bone and compared the genetic sequence with those from modern humans and Neanderthals.

Origin unknown

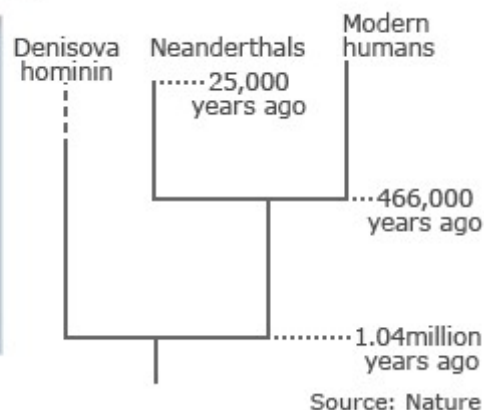
Mitochondrial DNA comes from the cell's powerhouses and is passed down the maternal line only.

The analysis carried out by Johannes Krause from the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, and colleagues revealed the human from Denisova last shared a common ancestor with modern humans and Neanderthals about one million years ago.

This is known as the divergence date; essentially, when this human's ancestors split away from the line that eventually led to Neanderthals and ourselves.

The Neanderthal and modern human evolutionary lines diverged much later, around 500,000 years ago. This shows that the individual from Denisova is the representative of a previously unknown human lineage that derives from a hitherto unrecognised migration out of Africa.

Evolutionary chain: "New hominin"



"Whoever carried this mitochondrial genome out of Africa about a million years ago is some new creature that has not been on our radar screens so far," said co-author Professor Svante Pääbo, also from the Max Planck Institute for Evolutionary Anthropology.

The divergence date of one million years is too young for the Denisova hominin to have been a descendent of *Homo erectus*, which moved out of Africa into Asia some two million years ago.

And it is too old to be a descendent of *Homo heidelbergensis*, another ancient human thought to have originated around 650,000 years ago. However, for now, the researchers have steered away from describing the specimen as a new species.

Dr Krause said the ground layer in which the Denisova hominin fragment was found contain tools which are similar to those made by modern humans in Europe.

Slice of time

"We have ornaments, there is a bracelet, so there are several elements in the layers that are usually associated with modern human archaeology," he told BBC News.

"That's quite interesting, but of course, it is hard to prove that the bone is strongly associated to this archaeology, because it is possible that bones could have moved within the site. "We are also not sure how exactly the excavation was done. It could have come from a deeper layer, so that's hard to say."

Professor Clive Finlayson, director of the Gibraltar Museum, said the find presented a number of questions, such as to what extent culture could continue to be used as a proxy for different prehistoric human groups.

Referring to his research on Neanderthals and modern humans in southern Iberia, he told BBC News: "The assumption is that when one group - the moderns - arrives the other group disappears. Here you have a very clear example of co-existence for long periods.

"Where is the rule that says you can have only one species in an area? Especially if they're at low density... the implications are big."

The research contributes to a more complex picture that has been emerging of humankind during the Late Pleistocene, the period when modern humans left Africa and started to colonise the rest of the world.

Professor Finlayson has previously argued: "A time slice at a point in the late Pleistocene would reveal a range of human populations spread across parts of Africa, Eurasia and Oceania.

"Some would have been genetically linked to each other, behaving as sub-species, while the more extreme populations may well have behaved as good species with minimal or no interbreeding."

It was long known that modern humans overlapped with Neanderthals in Europe, apparently for more than 10,000 years.

But in 2004, researchers discovered that a dwarf species of human, dubbed "The Hobbit", was living on the Indonesian island of Flores until 12,000 years ago - long after modern humans had colonised the region.

Difficult classification

Neanderthals appear to have been living at Okladnikov Cave in the Altai Mountains some 40,000 years ago. And a team led by Professor Anatoli Derevianko, from the Russian Academy of Sciences, has also found evidence of a modern human presence in the region at around the same time.

Professor Stringer commented: "Another intriguing question is whether there might have been overlap and interaction between not only Neanderthals and early moderns in Asia, but also, now, between either of those lineages and this newly-recognised one.

"The distinctiveness of the mitochondrial DNA patterns so far suggests that there was little or no interbreeding, but more extensive data will be needed from other parts of the genome, or from the fossils, for definitive conclusions to be reached."

Experts have been wondering whether X-woman might have links with known fossil humans from Asia, which have controversial classifications.

"Certain enigmatic Asian fossils dated between 250,000-650,000 years ago such as Narmada (in India), and Yunxian, Dali and Jinniushan (in China) have been considered as possible Asian derivatives of *Homo heidelbergensis*, so they are also potential candidates for this mystery non-erectus lineage," said Prof Stringer.

"However, there are other and younger fragmentary fossils such as the Denisova ones themselves, and partial skulls from Salkhit in Mongolia and Maba in China, which have been difficult to classify, and perhaps they do signal a greater complexity than we have appreciated up to now."

Other experts agreed that while the Siberian specimen may be a new species, this has yet to be shown.

"We really don't know," Ian Tattersall of the American Museum of Natural History in New York, told the Associated Press news agency.

Dr Tattersall, who wasn't involved in the new research, added: "The human family tree has got a lot of branchings. It's entirely plausible there are a lot of branches out there we don't know about."

New Tulane University study says diabetes at epidemic proportions in China

A large population-based study of diabetes in China conducted by investigators from Tulane University and their colleagues in China has concluded that the disease has reached epidemic proportions in the adult population of China. The study estimates that 92.4 million adults age 20 or older (9.7 percent of the population) have diabetes and 148.2 million adults (15.5 percent) have prediabetes, a key risk factor for the development of overt diabetes and cardiovascular disease. The results are published in the March 25 edition of *The New England Journal of Medicine*.

The study builds on several recent large studies in China that have documented a rapid increase in diabetes in the population. The current study administered an oral glucose tolerance test to 46,239 adults aged 20 or older from 14 provinces and municipalities throughout China in order to identify cases of previously undiagnosed diabetes. Subjects of the study who had been previously diagnosed with diabetes were identified through questioning by the study's data collectors.

Following recent rapid economic development in China, cardiovascular disease has become the leading cause of death in the country. Diabetes is a major risk factor for cardiovascular disease, and the prevalence of diabetes in China, as this study indicates, is high and increasing. Diabetes increases the risk of cardiovascular complications and premature death, and results in a massive economic burden for society.

The researchers noted a higher prevalence of diabetes among urban residents in China than among rural ones, a result consistent with observations that have been made in developing countries throughout the world. "Urbanization is associated with changes in lifestyle that lead to physical inactivity, an unhealthful diet and obesity, all of which have been implicated as contributing factors in the development of diabetes," says Dr. Jiang He, Joseph S. Copes, M.D. Chair and Professor, Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine and the senior author of the study.

With its very large population, China may bear a higher diabetes-related burden than any other country, assert the researchers. Especially alarming is the finding that the majority of cases of diabetes (60.7 percent) are undiagnosed and untreated. The researchers conclude that diabetes and its consequences have become a major public health crisis in China, and recommend that the country quickly develop and institute national strategies for preventing, detecting and treating diabetes in the general population.

Researchers Puzzled by Role of Osteoporosis Drug in Rare Thighbone Fractures

By GINA KOLATA

The case reports first surfaced about two years ago and they were frightening. A few orthopedists reported that women taking osteoporosis drugs to prevent broken bones were showing up with rare and serious fractures of their thighbones. The bone was snapping like a twig, sometimes splintering. Often there was no trauma, like a serious fall, to bring it on. And some of the women were younger, in their 50s, with pre-osteoporosis but without the extremely fragile bones of people with the full-blown degenerative condition.

But case reports can be hard to interpret — they may or may not indicate a real cause and effect. And the Food and Drug Administration says it has not been able to find evidence of an increased risk of the unusual fractures in its analyses, including one of data from makers of bisphosphonates, the osteoporosis drugs.

Now, a paper published online Wednesday in *The New England Journal of Medicine*, also fails to find clear evidence that bisphosphonates are causing the fractures.

The researchers, led by Dennis M. Black, a professor of epidemiology and biostatistics at the University of California, San Francisco, report that the thighbone fractures are so rare, even in women taking bisphosphonates for up to 10 years, that it is not clear whether the drugs make them more likely. And, they report, if there is a risk, it is far outweighed by the drugs' clear benefit in preventing fractures of the hip and spine in people with osteoporosis.

Thighbone fractures "are much much less common than typical hip fractures," said Dr. Elizabeth Shane, a professor of medicine at the College of Physicians and Surgeons at Columbia University, who wrote an editorial accompanying Dr. Black's paper. "While these fractures are devastating, so are the more common types of hip fractures that are prevented by bisphosphonates."

The risk-benefit analysis applies only to women with osteoporosis. Those with the pre-osteoporosis condition, osteopenia, have a much lower risk of broken bones. It is not clear whether most women with osteopenia benefit from the drugs, Dr. Shane said.

The idea with osteopenia was that the drugs might prevent osteoporosis and protect patients from fractures. That has not been demonstrated, Dr. Shane said. Current guidelines, she added, discourage treating most osteopenia patients.

Dr. Black began his study when case reports of thighbone fractures emerged, realizing that he and his colleagues were in a perfect position to investigate. They had organized three large studies of bisphosphonates

for companies that make the drug, Novartis and Merck, involving a total of 14,195 women with osteoporosis or osteopenia who took either a bisphosphonate or a placebo for up to 10 years.

"We had access to all the data," Dr. Black said. "So when this issue came up we decided to go through all the hip and thigh fractures." They found hip fractures in 284 of the women and the unusual thighbone fractures in 10 women, who had a total of 12 such fractures. The number of fractures was so low it was impossible to say if there really was an increased risk with the drugs.

"The point is, these fractures are so rare you can't say very much about them," Dr. Black said.

They occur in the long bone of the thigh, before it makes a turn into the pelvis. And they are unusual because most fractures of the thighbone occur in the part that fits into the hip socket. They also are hard to heal, notes Dr. Clifford J. Rosen, a professor of medicine at Tufts University School of Medicine, because the long thighbone does not have much of a blood supply. When the bone breaks it can even splinter, unlike a typical fracture at the hip, Dr. Rosen says. And surgeons may have to insert a long rod in the bone to set it.

In order to get more information on the thighbone fractures, the American Society of Bone and Mineral Research has convened a task force, with Dr. Shane as a co-chairwoman, to analyze all the published and unpublished data it can find on the unusual fractures. The food and drug agency says it is working with members of the task force.

Dr. Black says he suspects there might be other factors that make some people susceptible to the unusual fractures - taking other drugs that also affect bone growth, for example. And, he says, patients have to be aware that drugs, including bisphosphonates, have risks. "There are risks we know about and risks we don't know about with all drugs," Dr. Black said. "I think people would be naïve to assume there is no risk."

Finding a potential new target for treating rheumatoid arthritis ***Study reveals a novel pathway in autoimmune disease***

By enhancing the activity of immune cells that protect against runaway inflammation, researchers at NYU Langone Medical Center may have found a novel therapy for rheumatoid arthritis and other autoimmune diseases. In a new study published in the March 25, 2010 online edition of *Science*, the researchers reveal how treating these immune cells with an investigational drug wards off inflammation by holding a particular enzyme at bay.

"This is an unusual mechanism that could provide a potential therapeutic approach for the treatment of autoimmune diseases like rheumatoid arthritis or inflammatory diseases like Crohn's disease," says Michael Dustin, PhD, the Irene Diamond Professor of Immunology and professor of pathology at NYU Langone Medical Center.

The new study was spearheaded by Alexandra Zanin-Zhorov, PhD, a post-doctoral fellow in Dr. Dustin's lab, in collaboration with Juan Lafaille, PhD, associate professor of pathology and medicine, and Steven Abramson, MD, professor of medicine and pathology and director of the Division of Rheumatology. The research was supported in large part by a five-year grant from the National Institutes of Health Roadmap for Medical Research funding initiative, under its Nanomedicine Development Center Program.

Joint-destroying rheumatoid arthritis is generally considered an autoimmune disorder spurred on by the hyperactivity of conventional T cells that fight off infections, cancer, and other diseases. Within the past few years, researchers at NYU and other institutions have learned that other immune system components known as regulatory T cells counterbalance the tendency of conventional T cells to become overactive, thus holding inflammation in check.

These regulatory T cells exert their influence by communicating with other parts of the immune system. Through molecular detective work and powerful microscopy, the new study's collaborators found that an enzyme known as protein kinase C theta is only partly activated in regulatory T cells. When the regulatory cells are most active, in fact, most of the interfering enzyme is physically kept far away from the area important for cell-cell communication.

"It's a very unique distribution," Dr. Dustin says. "In conventional T cells this enzyme is normally moved to the area where the cells are making contact. But in regulatory T cells, the enzyme is as far away as it can get from where the cells are communicating."

Based on that observation, the researchers began testing inhibitors of this kinase enzyme, including a molecule known as Compound 20 that had been in development by pharmaceutical company Boehringer Ingelheim. Surprisingly, the compound boosted the normal activity of regulatory T cells by about five-fold. The researchers found that specifically blocking the activity of the kinase enzyme augmented the natural tendency of the regulatory T cell to keep it out of the communication channels. Thus, the compound enhanced the regulatory cells' anti-inflammation activity.

The Yin and Yang of T cells in Rheumatoid Arthritis

In rheumatoid arthritis, either an abnormal surge by infection-fighting T cells or a dip in the activity of inflammatory-fighting T cells - or perhaps both - could cause the immune system to attack our own joints instead. "Therefore, if you have an abnormal and suppressed regulatory T cell function, you have enhanced potential for autoimmunity," says Dr. Abramson.

The researchers bolstered previous evidence for such a link by examining the blood of 25 patients with varying degrees of rheumatoid arthritis. "In essence, what we were able to show is that if you look at this regulatory T cell population in rheumatoid arthritis patients, it is abnormally low in function, and the sicker the patients are, the more depressed that cell function is," says Dr. Abramson.

The defective regulatory cells from these patients were revived in tissue cultures with this enzyme inhibitor, the study showed. "We could get them back to almost a normal level of activity, like what you'd see in a healthy individual," says Dr. Dustin.

The researchers also tested the Compound 20 inhibitor in a mouse version of Crohn's disease, which is characterized by intestinal inflammation. When the researchers treated the regulatory T cells with the enzyme inhibitor and then injected them into the mice, their anti-inflammation activity rose so much that they essentially protected the mice from the disease, even though the cells were outnumbered four to one by their pro-inflammatory counterparts.

"The theory is that if you could restore normal regulatory T cell function, then you could restore their ability to suppress the inflammation process, and prevent this abnormal destruction of your joints," Dr. Abramson says.

The study's other co-authors include Yi Ding, Sudha Kumari, and Mukundan Attur from NYU Langone Medical Center, Keli L. Hippen and Bruce R. Blazar from the University of Minnesota, and Maryanne Brown from Boehringer Ingelheim.

Other sources of support for the study include a Leukemia and Lymphoma Translational Research grant, and the Osaka University Immunology Frontier Research Center. Dr. Dustin and Dr. Zanin-Zhorov have applied for patents for the use of Compound 20 and RNAi against protein kinase.

Studies reveal associations between pregnancy, breastfeeding, breast cancer and survival

Barcelona, Spain: Women who are diagnosed with breast cancer in the 12 months after they have completed a pregnancy are 48% more likely to die than other young women with breast cancer according to new research to be presented at the seventh European Breast Cancer Conference (EBCC7) in Barcelona today (Friday). [1]

However, the study of 2,752 breast cancer patients by Australian researchers found that if the breast cancer was diagnosed while the women were pregnant, their risk of dying was nearly the same as other, non-pregnant women diagnosed with breast cancer – only three percent higher.

Assistant Professor Angela Ives, a research fellow at The University of Western Australia, will tell the conference that the findings suggest that the cumulative effect of pregnancy may play a role in breast cancer prognosis and this, along with whether a woman breast feeds, needs further investigation.

However, she said: "It is important to stress that our findings should not discourage women from breast feeding as we know that this is beneficial to both mother and baby in a number of ways. While most breast symptoms or abnormalities identified in young women are benign, it is important that when a woman is pregnant or breast feeding any symptoms or abnormalities are not assumed to be due to the pregnancy or breast feeding, particularly if the symptoms persist. It is important that both health professionals and young women are breast aware, even during pregnancy and breast-feeding, and promptly have symptoms investigated to allow early diagnosis.

"For women who are diagnosed with breast cancer after pregnancy, they and their clinicians may wish to consider different forms of treatment to improve survival."

Prof Ives said that because very little is known about gestational breast cancer (breast cancer that is diagnosed while a woman is pregnant or up to 12 months after completion of a pregnancy, including terminations or miscarriages) she and her colleagues decided to find out more so that women could make informed choices about their breast cancer management and pregnancy outcome.

Using the Western Australia Data Linkage System, they identified a group of 2,752 women, aged less than 45, diagnosed with breast cancer in Western Australia between January 1982 and December 2003. They followed them to December 2007 or to their date of death, if earlier.

"The WA Data Linkage System is one of only five comprehensive record linkage systems in the world. It brings together population-based hospital morbidity data, birth and death records, mental health services data, cancer registrations and midwives' notifications, linked back to 1980. In this case we have been able to identify all cases of gestational breast cancer diagnosed in WA and all other cases of breast cancer in similar aged women to identify what is different about them," she said.

The researchers took account of additional factors such as age at diagnosis, histological tumour grade, stage of disease and whether the cancer had spread to the lymph nodes. From the total number of women, 182 were diagnosed with gestational breast cancer, 55 while they were pregnant and 127 after the end of the pregnancy. Prof Ives found that, as might be expected, histological tumour grade, disease stage and lymph node involvement were all associated with a worse survival for all the women. The finding of the increased risk of death if breast cancer was diagnosed after pregnancy remained after adjusting for lymph node status, disease stage at diagnosis, histological tumour grade and age.

Prof Ives said: "It has been assumed over many years that actually being pregnant at diagnosis led to poor survival, but this study has shown that it might be the amount of time that a woman is pregnant and her body's responses to being pregnant that encourage the growth of a breast cancer. Another explanation might be that the changes in the breast while pregnant and then breast feeding mask a breast cancer, which is, therefore, more advanced when it is diagnosed. It could be a combination of both. In addition, we do know that pregnancy and breast-feeding reduce the long-term risk of a woman developing breast cancer, but we also know that, in the short term, having been pregnant may increase the risk of developing breast cancer. There needs to be further research into these possible explanations for our findings."

Prof Ives and her colleagues are now investigating what might be happening at cell level with the way tumours grow (angiogenesis) and the role played by the body's immune response. They are also carrying out further research on the cumulative effect of pregnancy and breast-feeding and time from conception to date of cancer diagnosis on survival.

In a second study [2], Dr Salma Butt (M.D. and a PhD student at the Department of Surgery, Malmö University Hospital, Sweden) examined the link between the length of time that women breast-fed and the different types of breast cancer they subsequently developed. She found that although the risk of developing breast cancer was the same regardless of the duration of breast-feeding, women who had breast-fed for six months or longer had a statistically significant risk of developing more aggressive types of breast cancer. However, Dr Butt and her colleagues do not know yet whether this means that these women are more likely to die from their cancer.

Dr Butt said: "Several previous studies have investigated the association between breast-feeding and breast cancer risk, but, to our knowledge, no studies have investigated breast-feeding and risk associated with different types of breast cancer. Furthermore, no study has investigated the association between breastfeeding, types of breast cancer and survival yet. "Our findings need be followed by studies on survival to see if these more aggressive breast tumours actually lead to a higher death rate or not, because we do know that breast cancers that do not have aggressive characteristics can also have high rates of mortality if they are diagnosed late. This is something that we intend to study next."

Dr Butt and her colleagues examined data collected prospectively from a group of 17,035 women in The Malmö Diet and Cancer Study. They evaluated 622 cases of breast cancer for a range of factors that indicated how aggressive the tumours were (e.g. invasiveness, tumour size, axillary lymph node status, HER2 status, Ki67, which is an indicator for tumour proliferation, etc). They analysed the duration of breast feeding for each child, total amount of time a woman had breast-fed, and the average time of breast-feeding per child; the average duration of breast feeding was divided into four groups: less than 2.2 months, less than four months, four months or more, and 6.2 months or more.

Dr Butt said: "We found a statistically significant risk of grade III tumours in women with an average time of breast-feeding of 6.2 months or more. The risk of tumours expressing higher levels of Ki67 was also significantly associated with longer duration of breast-feeding. We concluded that long duration of breast-feeding was associated with more unfavourable types of breast cancer."

She stressed that these findings should not discourage women from breast-feeding as there were several strong studies that showed that breast-feeding could reduce a woman's overall risk of breast cancer, and that longer breast-feeding times were good for both mother and baby.

"The most important thing would be to identify women with a higher risk of aggressive types of breast cancer and offer them intensified screening, in order to identify their tumours early."

She said the study was an epidemiological one that could show risk associations but not causes. "The biological mechanisms behind this are still to be identified. What is known is that breast-feeding reduces the number of ovulatory menstrual cycles over a lifetime, thereby reducing the impact of hormone levels present during normal menstrual cycles and, in particular, reducing the progesterone exposure. This may explain the finding in previous studies of a reduced risk of breast cancer in women who had breast-fed. However, breast-feeding stimulates the production of prolactin, a hormone that has been reported to have tumour-promoting effects. But the relation between breastfeeding, prolactin and breast cancer is complex and not fully understood."

Autism susceptibility genes identified

Two genes have been associated with autistic spectrum disorders (ASD) in a new study of 661 families. Researchers writing in BioMed Central's newly launched journal Molecular Autism found that variations in the genes for two brain proteins, LRRN3 and LRRTM3, were significantly associated with susceptibility to ASD.

Anthony Monaco from the Wellcome Trust Centre for Human Genetics, University of Oxford, UK, worked with an international team of researchers to study four candidate genes in families from the UK, the Netherlands, Italy and Germany. He said, "To our knowledge, this is one of the most comprehensive genetic analyses of association between these important genes in brain connections and ASD risk". The proteins encoded by these two genes have been implicated in brain development, which is often impaired in autistic individuals. In particular, LRRN3 is thought to play a role in the development and maintenance of the nervous system, while LRRTM3 is part of a family of proteins thought to organize synaptic connections.

According to Monaco, "A focused candidate gene study was carried out using association approaches to identify common variants in the UK cohort and in additional European populations. This study covered four brain-enriched leucine-rich repeat candidates and taken together, there is converging evidence that common genetic variants in LRRTM3 and LRRN3 confer susceptibility to ASD. Future studies of these genes and their function will provide valuable insights into their role in ASD pathogenesis".

Notes to Editors 1. Polymorphisms in leucine-rich repeat genes are associated with autism spectrum disorder susceptibility in populations of European ancestry Inês Sousa, Taane G Clark, Richard Holt, Alistair T Pagnamenta, Erik J Mulder, Ruud B Minderaa, Anthony J Bailey, Agatino Battaglia, Sabine M Klauck, Fritz Poustka, Anthony P Monaco and International Molecular Genetic Study of Autism Consortium Molecular Autism 2010, 1:7 doi:10.1186/2040-2392-1-7 Article available at journal website <http://www.molecularautism.com/content/1/1/7>

Chymase inhibitors could enhance treatment for damaged hearts

Millions of patients with high blood pressure and heart failure take a class of drugs known as ACE (angiotensin-converting enzyme) inhibitors. These drugs prevent the body from processing angiotensin II, a hormone that constricts blood vessels.

Scientists at Emory University, University of Alabama, Birmingham, and Fukuoka University in Japan have shown that another enzyme present in the heart called chymase is also capable of processing angiotensin II. Adding drugs that interfere with chymase to ACE inhibitors significantly boosted recovery of heart function in animals after heart attack, the researchers found.

The results, to be published in the April 2010 issue of the Journal of Clinical Investigation, could lead to improved treatments for people with high blood pressure, heart failure and other conditions.

"The development of ACE inhibitors was a major advance in the treatment of hypertension and heart failure, and they have become the standard of care," says senior author Ahsan Husain, PhD, professor of medicine (cardiology) at Emory University School of Medicine. "But ACE inhibitors don't work for everyone, and we think we have found a way to make them more effective."

Doctors have reported for years that taking an ACE inhibitor usually reduces a patient's blood pressure, but angiotensin II often returns to high levels over several months, a phenomenon called "ACE inhibitor escape." This is bad news because angiotensin II drives the release of other hormones, leading to fluid retention, and also has direct effects on the heart. For example, after a heart attack, it promotes scarring and enlargement of the heart. In addition, ACE inhibitors have been reported to be less effective for some population groups such as African Americans.

Sometimes an inadequate response to ACE inhibitors leads doctors to add drugs that can block some of angiotensin II's effects (angiotensin II receptor blockers), but the clinical evidence for an additional benefit from these drugs is still up for debate, Husain says.

Much of Husain's laboratory's research over the last 20 years has been aimed at understanding the production of angiotensin II in the heart. In 2008, Husain came to Emory from University of Alabama, Birmingham, where he had been working with the first author of the paper, assistant professor Chih-Chang (Kevin) Wei, PhD, and professor Louis Dell'Italia, MD. Naoki Hase at Teijin Pharma and Yukiko Inoue and Hidenori Urata, MD at Fukuoka University in Japan also contributed to the paper.

Wei, Husain and colleagues showed that chymase in the heart comes from mast cells, inflammatory cells that play a central role in allergies and asthma. Mast cells are missing in mice with mutations in the gene for the blood cell growth factor receptor c-kit. In these mice, angiotensin II almost disappears after treatment with ACE inhibitors. But giving normal mice ACE inhibitors induces mast cells to release chymase, restoring their ability to produce angiotensin II. Previous research by Husain and Urata demonstrated that chymase activity is especially abundant in heart tissue from patients with heart failure. Inflammation arising from atherosclerosis or myocarditis may be attracting mast cells to the heart, Husain says.

To test whether chymase makes a difference in recovery after a heart attack, Wei, Husain and colleagues compared the effects of an experimental chymase inhibitor (provided by Teijin Pharma) to a standard ACE inhibitor on hamsters that had a simulated heart attack.

Combining the ACE inhibitor and the chymase inhibitor improved ejection fraction, a measure of heart function, and reduced the amount of dead tissue and scarring more than either drug by itself. The experiments on recovery after heart attack were performed on hamsters because mouse heart cells do not respond as much to angiotensin II as human or hamster heart cells do.

Chymase inhibitors are not available for clinical use, although pharmaceutical companies have begun investigations of their usefulness for conditions such as inflammatory bowel disease and asthma.

"Now, cardiovascular studies of chymase inhibitors in humans need to be done," Husain says. "Our hope is that pharmaceutical companies will see this as an opportunity to address a significant need."

The research was supported by the National Institutes of Health and the American Heart Association. Husain has received research funding from Teijin Pharma for a separate chymase-related project.

Reference: C.C. Wei et al Mast cell chymase limits the cardiac efficacy of Ang I-converting enzyme therapy in rodents J. Clin. Invest. 120, 1-11 (2010).

For a trimmer figure, add an extra helping of gut bugs

LOSING weight without eating less or exercising more sounds too good to be true. Not if you get bacteria to do the work for you. Gut bacteria play a vital role in digestion. Last year, researchers found that replacing the bacteria in mouse intestines with human gut flora decreased the amount of fat absorbed by the gut.

Now it seems that increasing levels of one type of human gut microbe can help people shed excess weight.

Yukio Kadooka of Snow Brand Milk Products, a dairy company in Saitama, Japan, and colleagues gave 87 overweight volunteers 100 grams of fermented milk - which is used to make yoghurt - twice a day, while they continued with their normal diets. The milk drunk by half of the group was enriched with *Lactobacillus gasseri*. After 12 weeks, these volunteers had lost an average of 1 kilogram, while their counterparts showed no change in weight.

Scans revealed that they had lost 4.6 per cent of their "bad", visceral fat, which surrounds internal organs and is implicated in metabolic syndrome, and 3.3 per cent of their subcutaneous fat. Hip and waist circumference also went down by an average of 1.7 and 1.5 centimetres respectively (European Journal of Clinical Nutrition, DOI: 10.1038/ejcn.2010.19).

"For doing absolutely nothing, that's a lot," says Matthew Digby, who researches dietary milk proteins at the University of Melbourne in Australia and was not involved in the study.

The bacteria may cause weight loss by inhibiting fat absorption in the intestine, says Kadooka.

New test takes guesswork out of diagnosing early stage Alzheimer's disease

New research in the FASEB Journal reports that a novel enzyme-linked immunosorbent assay could be a critical diagnostic tool for the detection of A-Beta oligomers, proteins which cause Alzheimer's disease

A new test developed by Japanese scientists may revolutionize how and when physicians diagnose Alzheimer's disease. According to a research report published online in The FASEB Journal (<http://www.fasebj.org>), the new test measures proteins in the spinal fluid known to be one of the main causes of brain degeneration and memory impairment in Alzheimer's patients: high molecular weight A-Beta oligomers. This tool, once fully implemented, would allow physicians to diagnose and treat Alzheimer's disease in its early stages, a time when diagnosing the disease is very difficult.

"Alzheimer's disease is a growing problem, due to aging of the population in all developed countries," said Takahiko Tokuda, M.D., Ph.D., a researcher from the Department of Neurology at the Kyoto Prefectural University of Medicine Graduate School of Medical Science in Japan who was involved in the work. "We hope that our new diagnostic test will, in the future, significantly improve the lives of people with Alzheimer's disease, and lead to much better ways of treating this devastating disorder."

Scientists developed a tool (enzyme-linked immunosorbent assay) that specifically measures A-Beta oligomers. They then compared the levels of these protein aggregates in human cerebrospinal fluid samples among three groups of people: 1) patients with diagnosed Alzheimer's disease; 2) patients with mild cognitive impairment who went on to develop Alzheimer's disease; and 3) a control group with no symptoms of Alzheimer's disease. Results showed that the levels of the fragments being measured directly correlated to the extent of memory impairment, with the highest levels found in those with confirmed Alzheimer's and intermediate levels in those with mild cognitive impairment. This shows that by measuring the levels of A-Beta oligomers in cerebrospinal fluid, physicians may be able to identify Alzheimer's disease before it can be clinically diagnosed using current methods.

"Baby boomers are getting older and Alzheimer's disease will have a tremendous impact on the memory of a generation and the lives of its children," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "This test is not only useful for the early detection of Alzheimer's disease, but promises to be a marker for the efficacy of newer treatments that are already on the drawing board."

Move over predators: Plants can control the food chain too -- from the bottom up

ITHACA, N.Y. - Forget top-to-bottom only. New Cornell University evolutionary biology research shows how plants at the bottom of the food chain have evolved mechanisms that influence ecosystem dynamics as well. (Science, March 26, 2010.)

"The ecology and interactions of most organisms is dictated by their evolutionary history," said Anurag Agrawal, associate professor of ecology and evolutionary biology (EEB), the study's senior author.

In food webs, predators help suppress populations of prey by eating them; that frees species lower in the food chain, such as plants, to flourish, a dynamic called a "trophic cascade." Most trophic cascade studies have focused on the ability of predators to increase plant biomass by eating herbivores. Such studies typically find strong trophic cascades in aquatic environments, where big fish eat minnows, which eat the tiny algae-eating crustaceans called daphnia.

Agrawal, first author Kailen Mooney, who is a former Cornell postdoctoral researcher and now assistant professor at the University of California-Irvine, and colleagues studied trophic cascades in 16 milkweed species, famed for their interactions with monarch butterflies, and also fed upon by aphids.

Plants have evolved three main strategies for increasing their biomass as much as they can against the forces that limit their growth, said the researchers: They grow as quickly as possible; develop direct defenses, such as toxins or prickly leaves, against herbivores; and attract such predators as ladybugs that eat their pests.

But plants do not have the resources to develop all three defenses. Since Darwin, evolutionary biologists have hypothesized that over millions of years of evolution, plant species are subject to trade-offs, developing some defense strategies in lieu of others; a key finding of the new study is that these evolutionary trade-offs drive how modern ecosystems are structured. In the case of milkweed, some favored fast growth and the ability to attract predators while putting less energy into resisting herbivores.

The study found that one of the major factors leading to greater milkweed biomass (or growth) is the production of volatile compounds called sesquiterpenes, which attract such predators as aphid-eating ladybugs. But surprisingly, the plants' biomass increases regardless of whether ladybugs or other aphid predators are present.

The reason, the researchers suggest, is because the trait to produce sesquiterpenes appears genetically linked to faster growth; the strategy here is to replace leaves faster than they can be eaten. At the same time, milkweed species that put more energy into growing faster put less energy into resisting such pests as aphids.

"Because no species can do everything, milkweeds that grow fast necessarily have lower resistance to aphids," said Agrawal. "Thus species that grow fast benefit the most from predators" of aphids.

The findings have implications for agriculture, as conventional strategies for controlling pests often involve spraying insecticides, said Agrawal. "By including the evolutionary history in our understanding of natural pest management, we gain insight into plant strategies that have stood the test of time, and this may provide hints for breeding crops with traits that ensure robust lines of defense," he added.

Co-authors include Andre Kessler, assistant professor, and postdoctoral researcher Rayko Halitschke, both in EEB at Cornell. The study was funded by the National Science Foundation, Cornell Center for a Sustainable Future and University of California-Irvine's School of Biological Sciences.

Microbes thrive in harsh, Mars-like lakes

* 21:09 26 March 2010 by David Shiga

Life not only survives but thrives in Australian lakes where conditions may be as harsh as those on ancient Mars, a new DNA analysis suggests.

Minerals on Mars studied by the NASA rovers suggest water once flowed on the planet's surface, but was very salty and acidic, raising doubts about whether it could have supported life.

But in 2007, Melanie Mormile of Missouri University of Science and Technology in Rolla and colleagues cultured a bacterium from water sampled from one of several salty, acidic lakes in Western Australia.

The lakes are very shallow and periodically fill with rainwater before partially evaporating, which concentrates the salts within them. They may be the closest equivalents on Earth of the shallow pools thought to have once dotted Mars.



Shallow lakes that lie between dunes in Australia can be extremely acidic and salty (Orbital image: Image Science and Analysis Laboratory/NASA-JSC)

Minerals in the lakes also contain strange, microscopic structures dubbed "hairy blobs" that researchers have suggested are fossilised microbes.

A team led by Mormile has now turned up dozens more species by analysing DNA extracted from water and sediment in 11 of the lakes.

Vinegar pool

The most acidic lake has a pH like that of vinegar, yet it contains DNA evidence for 23 microbial species, most of which appear to be new to science. "There's actually quite a diversity of life in these lakes," Mormile told *New Scientist*.

The microbes probably did not simply fall into the lakes but lived and thrived there – some appear to be relatives of *Salinibacter ruber*, which is known to grow in other extremely salty environments (see *The most extreme life-forms in the universe*).

The results bolster the possibility that life could have lived in the salty, acidic lakes present on Mars in the ancient past, the researchers say.

But the researchers do not yet know what gives the Australian lake microbes their ability to survive the tough conditions. "It would be really interesting to look at the mechanisms that enable them to do that," Mormile says. *Journal reference: Astrobiology (DOI: 10.1089/ast.2008.0293)*

Junk-fed rats have 'drug addict' brains

* 18:00 28 March 2010 by **Aria Pearson**

Junk food may seem like an addictive drug because it is. In rats, at least, too much fatty food raises the threshold for feelings of satisfaction, sparking a cycle of compulsive overeating.

In people, addictive drugs such as heroin and cocaine desensitise the brain by raising the threshold of "reward" activity that is needed to feel satisfied: more drug is needed to achieve the same effect.

Paul Kenny and colleagues at the Scripps Research Institute in Jupiter, Florida, wondered if a diet rich in high-calorie, fatty food might also cause desensitisation and lead to obesity.

They used electrodes to measure the sensitivity of rats' brains to reward activity. Some ate normal rat food while others had limited or unlimited access to junk foods, tasty to both rats and humans. After 40 days, the brains of those that ate junk freely were less sensitive to reward activity than those in the other groups. They were also obese.

Compulsive eaters

To see if these rats would display compulsive eating in the face of negative consequences - a telltale sign of addiction - all the rats were taught that a flash of light led to a painful electric shock.

Rather than try to avoid the shock when the light came on, as the rats with limited or no access to junk food did, "addicted" rats just kept on eating. "We see the same thing in animals with extended access to cocaine," says Kenny. Like drug-addicted humans, the obese rats also had fewer receptors for the reward chemical dopamine.

The term "food addiction" is slowly becoming accepted in the field of psychiatry, says Jon Davis, an addiction biologist at the University of Cincinnati in Ohio.

"Once we start to consider obesity and pathological overeating as a psychiatric illness we're going to move a lot closer towards understanding how to come up with therapies or treatments," he says.

Pietro Cottone, a neuroscientist at Boston University, is not surprised that an excess of tasty food might "short-circuit" the brain's reward sensing system. "In western societies, we are observing a sudden increase in food availability. We didn't evolve to survive under these conditions," he says.

Paired drugs kill precancerous colon polyps, spare normal tissue

Combination could provide chemoprevention via short-term therapy, long-term effect

HOUSTON - A two-drug combination destroys precancerous colon polyps with no effect on normal tissue, opening a new potential avenue for chemoprevention of colon cancer, a team of scientists at The University of Texas M. D. Anderson Cancer Center reports in the advance online edition of the journal *Nature*.

The regimen, tested so far in mouse models and on human colon cancer tissue in the lab, appears to address a problem with chemopreventive drugs - they must be taken continuously long term to be effective, exposing patients to possible side effects, said senior author Xiangwei Wu, Ph.D., associate professor in M. D. Anderson's Department of Head and Neck Surgery.

"This combination can be given short term and periodically to provide a long-term effect, which would be a new approach to chemoprevention," Wu said.

The team found that a combination of Vitamin A acetate (RAc) and TRAIL, short for tumor necrosis factor-related apoptosis-inducing ligand, kills precancerous polyps and inhibits tumor growth in mice that have deficiencies in a tumor-suppressor gene. That gene, adenomatous polyposis coli (APC) and its downstream signaling molecules, are mutated or deficient in 80 percent of all human colon cancers, Wu said.

Ineffective separately, powerful together

Early experiments with APC-deficient mice showed that the two drugs combined or separately did not harm normal colon epithelial cells. Separately, they showed no effect on premalignant polyps called adenomas.

RAc and TRAIL together killed adenoma cells, causing programmed cell suicide known as apoptosis. RAc, researchers found, sensitizes polyp cells to TRAIL.

The scientists painstakingly tracked the molecular cascade caused by APC deficiencies, and found that insufficient APC sensitizes cells to TRAIL and RAc by suppressing a protein that blocks TRAIL.

Reductions in polyps, improved survival

APC-deficient mice were treated with 15 cycles of the RAc/TRAIL combination over six weeks. Others received either RAc or TRAIL and a control group received nothing. One month later, control mice and those treated with one of the drugs averaged between 35 and 42 polyps, while those receiving the combination averaged 10.

To test the combination's potential as short-term therapy, APC-deficient mice were treated with two cycles of the combination in one week, causing a 69 percent polyp reduction two weeks later. A 10-fold increase in dose left treated mice with only 10 percent of the polyps found in controls.

A longer term test of relative survival using five treatments over four months improved survival from 186 days for controls to beyond 213 days for treated mice, with five of seven treated mice living more than eight months.

Cell death in human colon polyps

Next, the researchers treated biopsy samples of normal tissue and tumor regions from patients with familial adenomatous polyposis - an inherited condition that inevitably leads to colon cancer if the colon is not removed. Treatment of normal tissue caused little cell death, while 57 percent of polyp cells were killed via apoptosis.

Targeted therapies today aim at blocking some aspect of the tumor that drives its growth, Wu said, whereas RAc and TRAIL together kill precancerous polyps outright. Since APC is deficient or mutated in other types of cancer, the combination therapy could become a more general drug.

Before human clinical trials can be considered, Wu said, the team will conduct additional research to understand potential side effects and also will try to develop an injectable version of the combination, which is administered intravenously now.

One of the genes activated by the APC-deficient pathway, β -catenin, is involved with stem cell self-renewal and maintenance in adult tissues. The team conducted a series of experiments and determined that RAc/TRAIL does not affect stem cells in mice.

Today, concerns about cardiovascular side effects limit chemopreventive agents for colon cancer mainly to high-risk patients, Wu said. "We hope this combination, if it proves to lack toxicities, might be available as a chemopreventive agent to a broader, general population."

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